Bangkok Hospital Group

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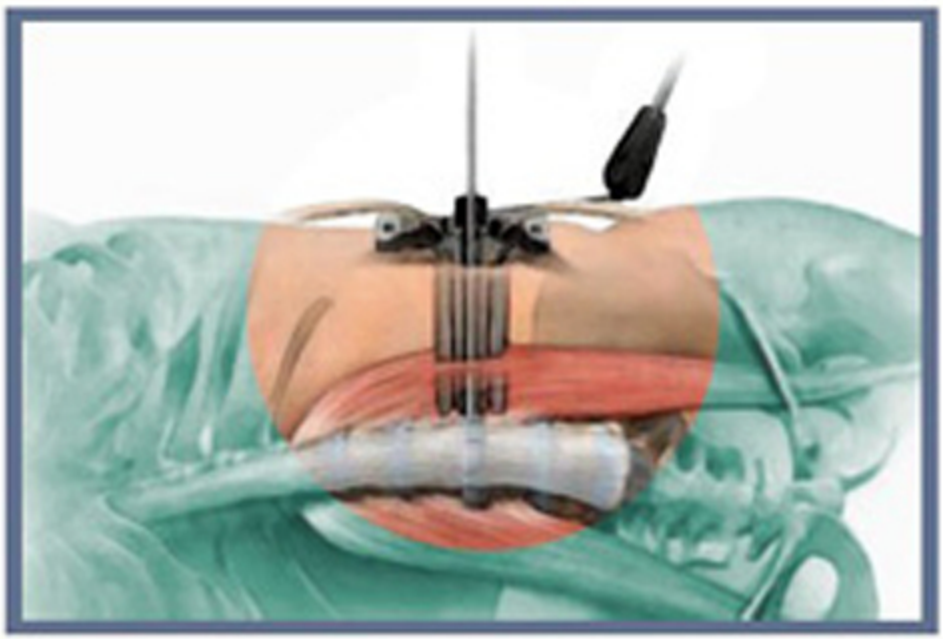
Highlights

The New Lumbar Spinal Fusion Technologies

Direct Lateral Interbody Fusion (DLIF)



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Editorial

The Editors of the 4th Edition of the Bangkok Medical Journal are pleased to offer readers another rich smorgasbord of diverse articles from our own doctor-authors as well as guest authors. Pediatric Syncope is looked at from both a neurological and cardiological perspective. Dr. Montri's respective review of 126 children explores etiologies and considers the usefulness of using EEG in determining fainting caused by epilepsy. Dr. Apichai's CME article reminds us that syncope may sometimes be the first presentation of a serious cardiac pathology, and details the conditions as well as the indications for investigative work ups. Another cardiac offering, a case report by Dr. Kumpanart highlights the importance of exercise and dietary control in secondary CAD prevention.

The Bangkok Spine Academy presents new follow up data. Preliminary reports on 12 patients who underwent Direct Lateral Interbody Fusion this year are encouraging. The study used patient questionnaires and it can be argued that this kind of patient involvement in their own treatment encourages medical compliance as well as facilitating better communication with physicians.

In line with thinking about how we convey information and different modes of communication, prospective contributors who are non-native English speaking (NNES) writers will find help offered by medical discourse expert Dr. Naruemol who in this issue looks at reporting verbs used in international medical journals.

Our current CEO and Group Vice President, Dr. Chatree, records what we have learned during our recent five year quality development program in Patient Safety and Risk Management. This article highlights to us how far we have come from the initial difficult early days of the hospital: a founding member and ex-Chairman of the Board, Professor Sanoe Indrasukhsri gives a poignant reminiscence about the struggles to establish the hospital 41 years ago. Similarly the history of the AO foundation in Thailand shows the dedication of those who worked to facilitate the transfer of knowledge, instrumentation and best practices of orthopedic surgery in Thailand and Asia up to International standards.

In addition we have investigations into enhanced cancer detection in breast imaging, and a history of ceramic on ceramic bearings used in hip replacements. There is also an interesting introduction to Evidence Based Practice, the idea of which first appeared in medicine but which is now extending beyond to public policy.

And so, without further ado, find a comfortable seat, and read on. Bon appetite!

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Bangkok Hospital Medical Center's Five-Year Experience with Patient Safety and Risk Management, 2006-2010

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Keywords:
patient safety, risk management, occurrence report, hospital customer assessment, customer satisfaction, customer complaint, healthcare

OBJECTIVES: Bangkok Hospital Medical Center (BMC) implemented the Patient Safety and Risk Management (PSRM) program in 2006 as an expansion of the Five-Year Quality Culture Development Program that aimed to emphasize the importance of a culture of quality and patient safety in the hospitals. The PSRM program emphasizing the concept of managing risk covers clinical, emotional, proactive, and reactive dimensions of the management process of unexpected adverse events. To highlight the commitment of BMC to patient safety and to measure our progress, the PRSM program during 2006-2010 was evaluated.

MATERIALS AND METHODS: The trend of occurrence reports (filed by staff) and customer complaint reports, in addition to the severity level of quality concerns identified in those reports was analyzed. The impact of the program including customer satisfaction, cost of adverse events, and patient safety culture at BMC were evaluated.

RESULTS: Annual occurrences, customer complaints, and total adverse event report rates from 2006-2010 were consistent, with the average percent rate of 1.08 %, 0.19 % and 1.27% respectively. The proportion of quality concerns in those reports fell to around 40% in the first three years and rose to around 70% in 2009-2010. However serious quality concerns (i.e., severe adverse events, events impacting on reputation and sentinel events) were relatively small and remained constant. The study showed that PSRM program did help to improve customer satisfaction and reduce the costs of dealing with adverse events. In addition, results of the BMC employee survey indicated that BMC's culture was good in learning and communication in patient safety, teamwork, management support for patient safety, and overall perceptions of safety.

CONCLUSION: Implementation of the PSRM program was successful in part due to BMC's quality improvement and patient safety environment. Patient safety must be managed seriously, faithfully, and proactively to prevent and mitigate adverse events. Risk management needs to include not only clinical aspects but also emotional affects.

Bangkok General Hospital was established at Soi Soonvijai, Bangkok, Thailand in 1972 by the Bangkok Dusit Medical Service Public Company (BDMS). Since then, BDMS has grown progressively and today the company operates 28 hospitals located in Thailand and Cambodia. Three of those hospitals, i.e., Bangkok Heart Hospital (BHT), Bangkok International Hospital (BIH), and Wattanosoth Cancer Hospital (WSH), were established in 2005 in addition to the Bangkok General Hospital at Soi Soonvijai; and today they are called collectively the Bangkok Hospital Medical Center (BMC).

A. The Initiative of Safety and Quality Culture

One of the foremost goals of BMC is to provide safe and high-quality medical care. Therefore in 2005, BMC implemented the Five-Year Quality Culture Development Program, which aimed to emphasize the importance of a culture of quality and patient safety in BMC. The concepts of quality improvement and patient safety (QPS) were the most significant components of this initiative. The objectives of the program were as follows:

- Bring BMC up to the international benchmark for a culture of excellence in clinical quality
- Establish a service standard of traditional Thai hospitality and quality in a hospital setting
- Develop a more efficient organization

The yearly program goals were initiated and achieved as follows:

- In 2006, developing basic quality improvement and patient safety (QPS) standards in accordance with Thailand's hospital accreditation standards (HA) and the Joint Commission International hospital standards (JCI)
- In 2007, obtaining successful accreditation from both Thailand's HA and JCI
- In 2008, Benchmarking against Agency for Healthcare Research and Quality (AHRQ) safety culture data, as well as obtaining JCI's Disease and Condition-Specific Care Certification [now Clinical Care Program Certification (CCPC)]
- In 2009, scheduling tracers and using continuous quality improvement (CQI) techniques to ensure the consistency of patient care practices according to the standards, in order to transform the health care staff from *"following standards"* to a *"culture of quality and safety"*. (*"Tracer"* or tracer methodology is an evaluation method in which surveyors selects a patient and uses that individual's record as a roadmap to trace that patient's journey through an organization, in order to assess and evaluate the organization's compliance with selected standards and the organization's systems of providing care and services.)
- In 2010, confirming continuous quality improvement and safety by passing the triennial reaccreditation surveys of Thailand's HA and JCI

Subsequently, to emphasize the concept of managing risk, BMC expanded the program to include Patient Safety and Risk Management (PSRM) program.

B. Patient Safety and Risk Management (PSRM)

The PSRM is a program that covers the management process of unexpected adverse events in four dimensions as follows:

1. Clinical dimension: aims to manage tangible legal aspects of adverse events.
2. Emotional dimension: aims to manage intangible patient or family feelings appropriately in order to obtain their cooperation, their co-decision, and thus their co-responsibility.
3. Proactive dimension: aims to develop BMC readiness for risk reduction and risk avoidance.
4. Reactive dimension: aims to develop rapid reporting, rapid responses, root cause analyses, and recovery or continuous quality improvement for adverse events.

The goal of the PSRM program is to complete each adverse event case while the patient is still in hospital care, and to encourage the patient not to seek care outside of BMC responsibility until the PSRM process is completed.

The response to adverse events is a key aspect of PSRM program. When an unexpected adverse event happens, the risk management team at BMC will categorize those events into the Five Levels of Quality Concerns and sentinel event. The severity levels in the Five Levels of Quality Concerns are comprised of Level 0 (near-miss event), Level 1 (no-harm event), Level 2 (mild adverse event), Level 3 (moderate adverse event), Level 4 (severe adverse event), and Level 5 (reputation event). The most severe adverse event is the sentinel event, which should be reported to JCI.

C. Patient Safety and Risk Management (PSRM) Program Evaluation

The purpose of PSRM program evaluation is to highlight commitment of BMC to patient safety through this program. The program during the period of 2006 – 2010 was evaluated in the following aspects.

- Reported rate of occurrences, customer complaints (direct complaints), and total adverse events (total occurrences) in BMC. The term "occurrence" used in these reports indicate an adverse event incident.
- Quality concerns and their severity level that were identified in the occurrences and customer complaints
- Impact of the program on patient satisfaction (i.e., Customer Satisfaction Index of overall experiences (CSI), HEART[a] and HCAHPS[b] score)
- Cost of adverse event or risk management, and
- Patient safety culture at BMC

Note: [a] HEART is a self-administered questionnaire to evaluate patient perception on five categories of BMC staff performance, i.e., Hearty Greeting (H), Empathy (E), Attention (A), Relation (R), and Trust (T).

[b] The questionnaire is developed by Hospital Customer Assessment of Healthcare Provider and System (HCAHPS) to evaluate patient satisfaction on 10 domains.[1]

Results of the PSRM Program Evaluation

1. Occurrence and Customer Complaint Reports

From 2006 to 2010, the annual total number of outpatient visits and inpatient days at BMC gradually increased despite a period of slight decline of growth rate in 2009, due to the political unrest in Bangkok. The number of outpatient visits grew from 643,903 visits in 2006 to 704,646 in 2010 with a compound annual growth rate (CAGR) of 2.28%. Inpatient days grew from 110,324 days in 2006 to 114,824 in 2010 with CAGR of 1 % (Figure 1).

Meanwhile, across the five years of PSRM program implementation, the annual occurrence and customer complaint report rates of both OPD and IPD at BMC were consistent. The average percent (rate per 100 patient visits) of annual occurrence and customer complaint reports were 1.08 % (with range of 1.02 – 1.12 %) and 0.19 % (with range of 0.14 – 0.23 %) respectively (Figure 2).

The combination of occurrences and customer complaint reports is called *"total adverse events"*. At BMC, the percentage rate of total adverse event reports less than 1% are considered *"under reporting"*, the cause of which should be investigated. However the annual percentage rates of total adverse events reported at BMC from 2006 to 2010, with average of 1.27% and range of 1.25 – 1.31%, were not under reported.

The annual percentage rates of total adverse events reported by outpatient services were very low and remained relatively constant, with a slight increase of the report rates in the last two years. In the meantime, the annual report rates of total adverse events by inpatient services were 7 – 10 times greater than outpatients but also remained relatively constant. The average annual report rate of inpatients was 3.55 % (with range of 3.24 – 3.94%) (Figure 3). Therefore BMC has focused on improving inpatient interventions as opposed to outpatient interventions.

In outpatient services, the annual occurrence report rate was 3 – 7 times higher than the annual report rate of customer complaints. This ratio for inpatient services was higher than for outpatients. In the inpatient, the ratio of occurrence report rate to customer complaint report rate was 6 – 16 times. It declined to around 7 times in 2009 – 2010.

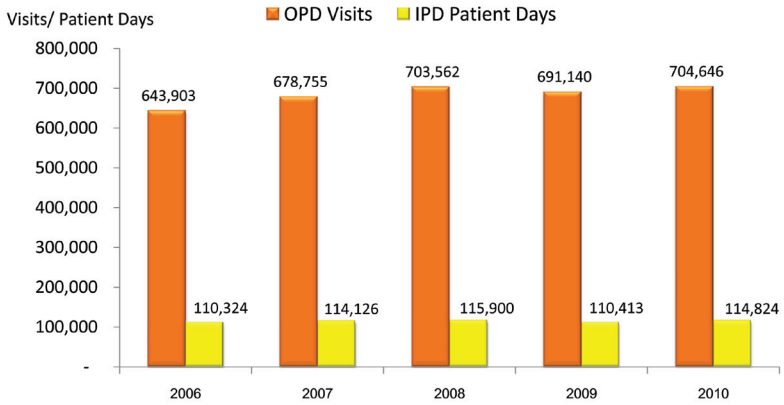

Figure 1: *The total annual outpatient (OPD) visits and inpatient (IPD) days at BMC from 2006 to 2010*

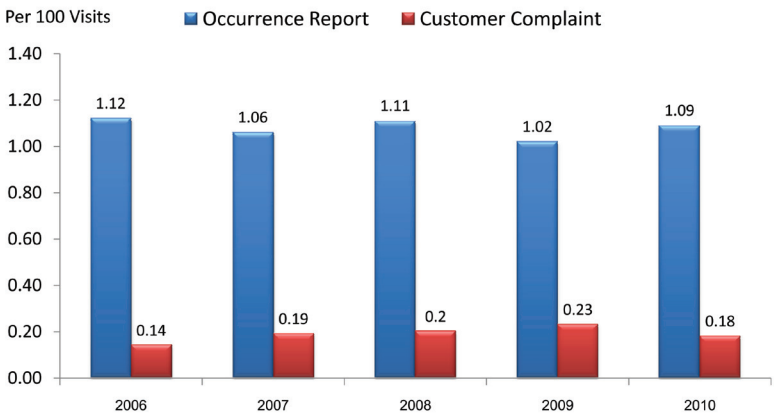

Figure 2: *Rate of annual occurrence and customer complaint reports per 1,000 visits of both OPD and IPD at BMC from 2006 to 2010*

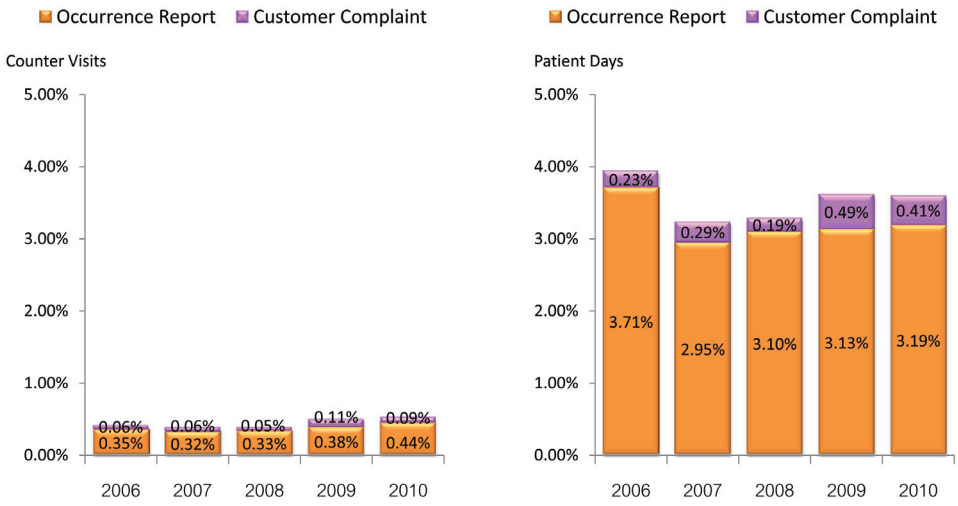

Figure 3: *Percent rate of annual outpatient and inpatient experience of occurrences and customer complaints at BMC from 2006 to 2010*

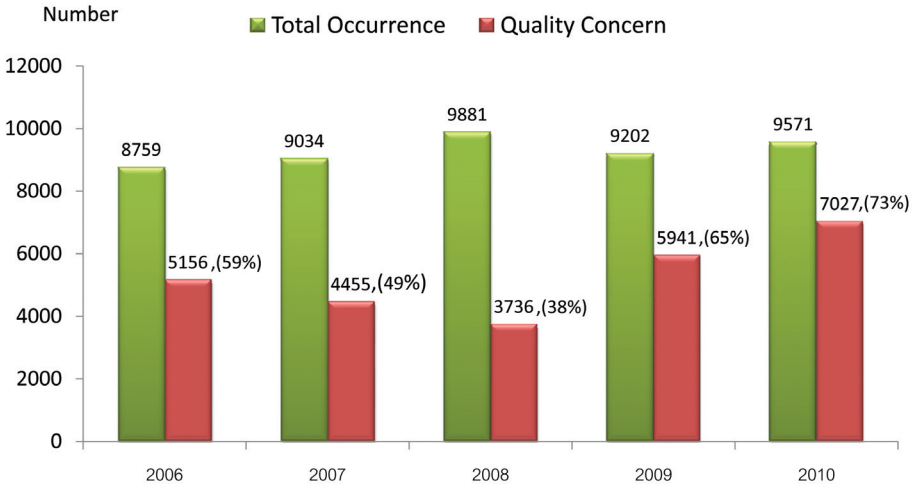

Figure 4: *Annual proportion of quality concerns to annual total occurrences (combination of occurrence and customer complaint reports) at BMC from 2006 to 2010*

2. Levels of Quality Concern in Occurrences and Customer Complaint Reports

There is an increasing trend in quality concerns as a proportion of annual total occurrences (total adverse events). The proportion increased from 59% in 2006, to 65% in 2009 and 73% in 2010 although it gradually declined to 38% in the first three years of PSRM program (Figure 4). The factors affecting this increasing trend are multifarious. Although not all of these factors have been fully identified, BMC hypothesizes that the main features are as follows:

I. Heightened awareness by clinical personnel of real quality problems. For the first three years of the program implementation, the BMC personnel were undergoing a learning process. In the last two years, they started to become more experienced in identifying quality issues and their severity level.

II. Increased patient awareness of the quality standard of patient care in BMC. This would indicate the increasing role of patients and/or their families in ensuring patient safety through providing feedback where gaps or deviation of the quality standard were noticed.

In order to appropriately handle occurrences/customer complaints with quality concern, the severity of adverse concerns has been categorized into levels 0-5 and sentinel events. The levels 4-5 and sentinel events are considered as serious occurrences, which require immediate action to correct the damage and prevent its further extension. Across the five years of PSRM program implementation, the proportion of serious occurrences in both OPD and IPD services at BMC was relatively small and remained constant (Figure 5 and 6).

The most reported levels of quality concerns in customer complaints from both OPD and IPD were level 1

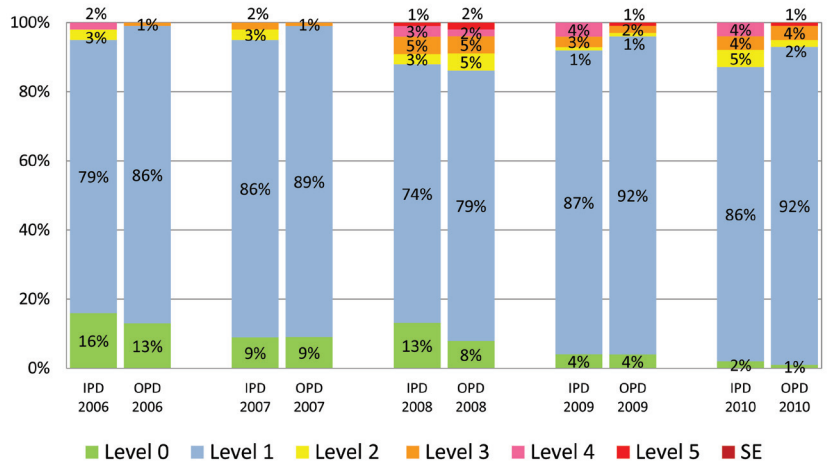

Figure 5: *Proportion of severity levels of quality concerns in outpatient and inpatient complaint reports at BMC from 2006 to 2010 (SE is sentinel event)*

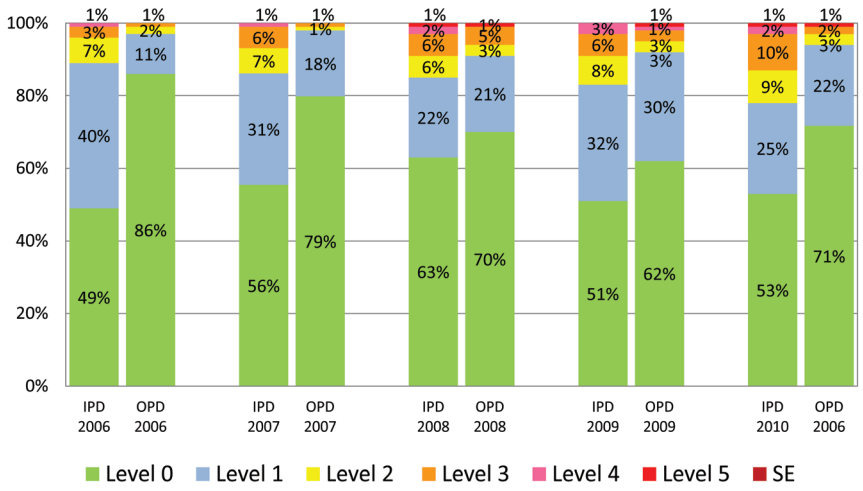

Figure 6: *Proportion of severity levels of quality concerns in outpatient and inpatient occurrence reports at BMC from 2006 to 2010 (SE is sentinel event)*

(no harm event) and level 0 (near miss event). The severity level 1 as reported by OPD was slightly greater in number than IPD although both had approximately the same annual proportion (80-90%) over the course of the program (Figure 5). Meanwhile reports of quality concern level 0 (near miss event) in both OPD and IPD were declining steadily (Figure 5).

For occurrence reports, the main severity levels of quality concerns found were level 0 and level 1 in both OPD and IPD. The severity level 0 was more frequent among outpatients than inpatients. The annual proportion of severity level 0 in OPD and IPD were around 60-90% and 50-60% respectively across the program period. In outpatient reports, the proportion of level 0 declined over time, but in inpatients it remained within the same range. Reports for all other severity levels remained in the same range over the five-year span (Figure 6).

3. Patient Satisfaction Scores

In the BMC, the Customer Satisfaction Index (CSI) score of overall experience in both OPD and IPD improved. The annual average CSI score in OPD and IPD gradually increased from 4.16 out of 5.0 and 4.27 out of 5.0 in 2006 to 4.59 and 4.56 in 2009 respectively (Figure 7). However the scores slightly declined in 2010, which would probably be due to the change in collection method of CSI questionnaires (we outsourced in order to remain as objective as possible).

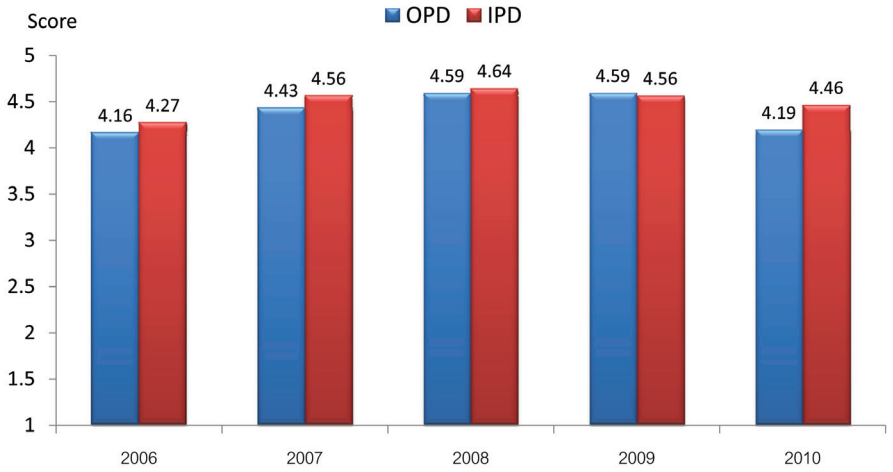

Figure 7: *Annual average of Customer Satisfaction Index (CSI) scores of overall experiences in OPD and IPD at BMC from 2006 -2010.*

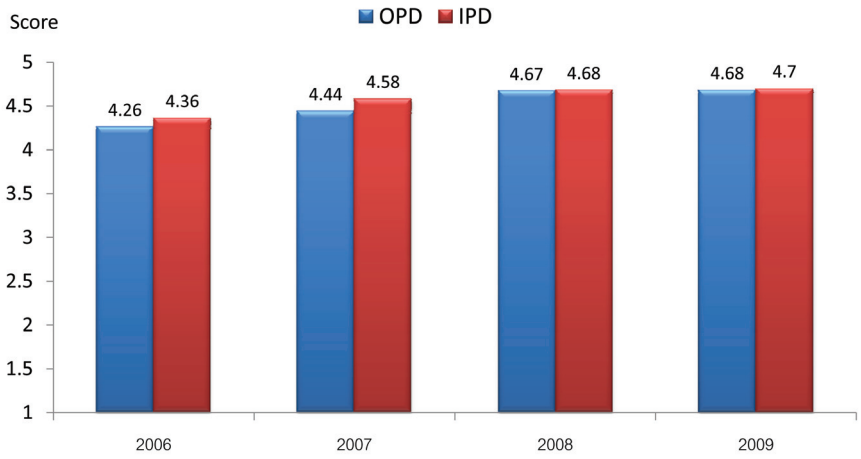

Figure 8: *Annual average HEART scores for OPD and IPD services at BMC from 2006-2010.*

Along with the CSI, BMC collected HEART score, which is the patients' perception rating five categories of BMC staff performance, i.e., Hearty Greeting (H), Empathy (E), Attention (A), Relation (R), and Trust (T). In correlation with the CSI score, the annual average HEART scores at both OPD and IPD also gradually increased (Figure 8).

To compare patient satisfaction in BMC healthcare services with other international healthcare organizations, after careful research BMC concluded that the method by Hospital Customer Assessment of Healthcare Provider and System (HCAHPS)[1] survey is the most acceptable method due to its successful implementation in many parts of the world, including the United States and other western countries. HCAHPS was therefore implemented at BMC, along with a dedicated personnel-training program. With the aforementioned actions, the annual average total top (top box) scores of BMC increased from 47% in 2009 to 52% in 2010 (Figure 9). The top box score is percentage of patient perception rating of highest level (8-10) for hospital performance.

4. Cost of Adverse Events/Risk Management

The total cost of reactive risk management to correct or mitigate damage to BMC's reputation by adverse events is comprised of the cost of discounts, rework, and settlements in arbitration processes. In 2004, before the implementation of the PSRM program, the total cost of risk management was 0.76% of total revenue. In 2005, the year that the PSRM program was started, this cost was reduced significantly to 0.26% of total revenue. After that time, the annual cost increased again but subsequently settled in an annual range of 0.37% to 0.57% of total revenue (Figure 10).

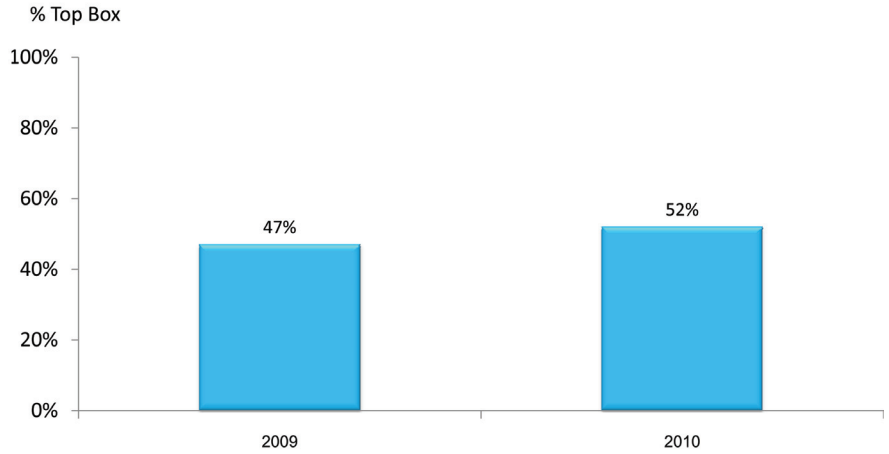

Figure 9: *Annual average HCAHPS total top (top box) scores of BMC in 2009 and 2010.*

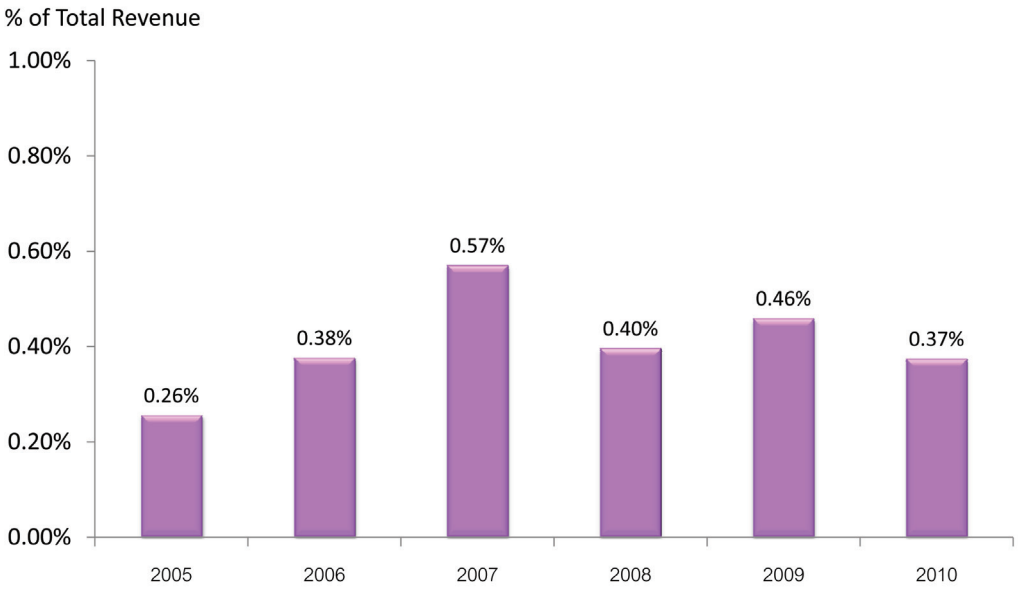

Figure 10: *Annual cost of risk management versus total revenue from 2005 to 2010*

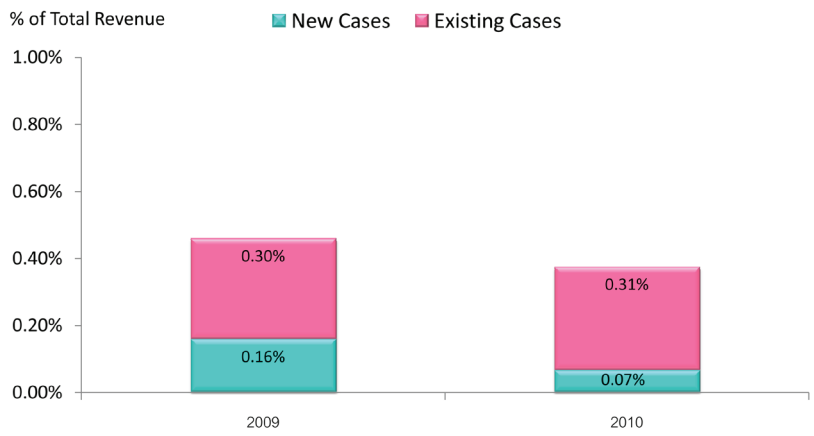

Figure 11: *Cost of risk management by case type versus total revenue in 2009 and 2010*

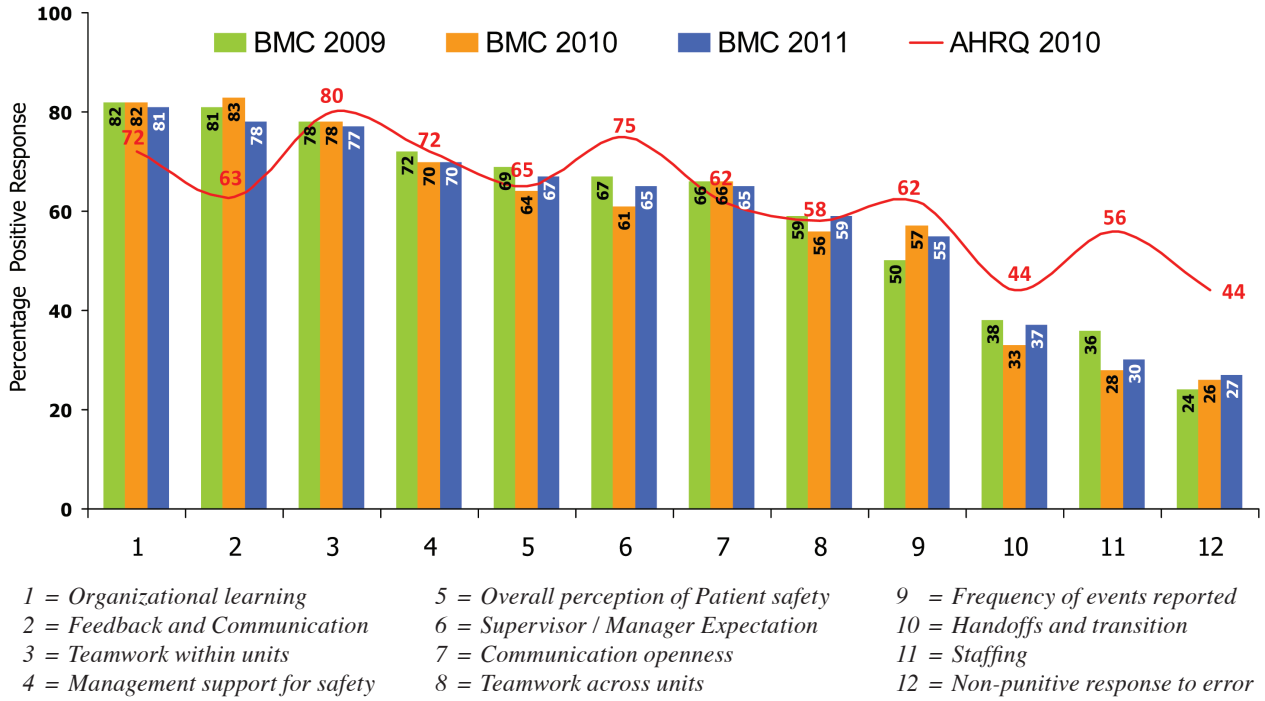

Figure 12: *Employees' Opinions on BMC's Safety Culture versus AHRQ Benchmarks from 2009 to 2011*

An independent factor is found in the Thai legal environment of the Consumer Protection Act[2], which allows consumers to petition for compensation from the consumer court for any adverse event. This factor could have negatively impacted the cost of risk management in PSRM program. To prevent this factor, in 2009, BMC started its Emotional Risk Management program. After implementation of the program, we discovered that the retrospective risk management costs in new cases declined significantly; from 0.16% of total revenue in 2009 to 0.07% in 2010 (Figure 11). Meanwhile the long-term expenses of the existing cases in both years (approximately 0.30% of total revenue) remained relatively constant (Figure 11). This resulted in a declining trend of total cost of risk management at BMC (Figure 10).

5. Patient Safety Culture at BMC

To make sure BMC had created a culture of patient safety, BMC surveyed its employees from 2009 to 2011 on their perception of the BMC's patient safety culture. The findings were compared with the benchmarks from the United States–based Agency for Healthcare Research and Quality (AHRQ). The survey showed that staff believed BMC's culture was conducive to learning and communication in patient safety, teamwork, management support for patient safety, and overall perceptions of safety; however it did not meet AHRQ benchmarks for handoffs, supervisor/manager expectations, and non-punitive responses to errors (Figure 12).

Summary

BMC's five-year experience in PSRM program can be summarized as follows:

- The total adverse event reports consisted of occurrence reports and direct complaint reports. In BMC, the average annual report rate of occurrence reports was 1.08% and direct complaints was 0.19%. Thus the annual total adverse event report rate was 1.27%, which was not under-reported according to the criterion.
- All adverse event reports were investigated upon receipt. In 2006-2010, around 60-70 % of adverse events were found to be actual quality issues. The percentage of quality issues fell from around 60% to 40% in 2006-2008, but rose to around 70% in 2009-2010. BMC's analysis indicates this increasing trend was due to more than one factor, including increased awareness of BMC's emphasis on occurrence/complaint reporting by providers, patients and their families.
- The study showed that the inpatient total occurrence reports occurred around seven times more frequently than the outpatient reports; and that in inpatient services, occurrence reports were made around seven times more frequently than customer complaints in the last two years.
- After a review of the proportions of the severity of quality concern events, the study showed that the most frequently filed occurrences were at

severity level 0 (60%-90%) and the most frequently filed direct complaints were at severity level 1 (80%-90%). Severity level 1 direct complaints declined steadily from 2006 to 2010, most likely as the result of BMC establishing and promoting the concept of rapid reporting and rapid response.

- The study showed an improvement in customer satisfaction, both through its customer satisfaction index and the HCAHPS survey. Furthermore, the study indicated better outcomes when questionnaires were collected by BMC employees as opposed to when questionnaires were collected by outside personnel, which may indicate bias.
- The PSRM program helped to reduce the cost of risk management from 0.76% of total revenue in 2004 to 0.26% of total revenue in 2005. The cost rose to 0.57% of total revenue in 2007 and gradually declined afterwards due to the implementation of Emotional Risk Management in 2009. The study showed that the proportion of cost from new cases declined from 0.16% of total revenue in 2009 to 0.07% of total revenue in 2010, while the cost from old cases stayed at 0.3% of total revenue for both 2009 and 2010.
- Employees' opinions of safety culture indicated that staff believed BMC's culture was good in the areas of learning and communication in patient safety, team work, management support for patient safety, and over all perceptions of safety, but needed improvement in the areas of handoffs, supervisor/manager expectations, and non-punitive responses to errors.

Recommendations for Other Organizations

- As crucial as a patient safety program is for patients and families, a risk management program is critical for the entire health care organization.
- Organizations must manage patient safety seriously, faithfully, and proactively to prevent and mitigate adverse events.
- Organizations must perform risk management not only in clinical terms, according to the proper standards of care, but must also consider risk man agement in emotional terms in order to be able to resolve events with the most favorable outcome.
- Implementation of the PSRM program was successful in part due to BMC's Quality Improvement and Patient Safety environment, achieved by implementation of standards by Hospital Accreditation Thailand and JCI standards.
- The PSRM program may also be supported by regularly scheduled tracers until they become part of the organizational culture. For BMC, this process took approximately 3.5 years. BMC follows the theory that continuous practice leads to expertise, ("deliberate effort to improve performance") as espoused in the theory of 10,000 hours by psychologist K. Anders Ericsson.[3]
- BMC believes that Clinical Risk Management mitigates tangible consequences like direct complaints and legal due process, but the BMC also strives to attend to intangible consequences with Emotional Risk Management.
- BMC is not seeking "win-loss solutions"; instead, it is seeking "peaceful win-win solutions."

Acknowledgements

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References

1. Centers for Medicare & Medicaid Services. Hospital Consumer Assessment of Healthcare Providers and Systems. Accessed 7 Mar 2012. http://www.hcahpsonline.org.
2. Consumer Protection Act (B.E. 2522) (Thailand). Accessed 7 Mar 2012. http://www.thailawforum.com/database1/ConsumerProtecting-law.html.
3. Ericsson KA, Prietula MJ, Cokely ET. The making of an expert. Harv Bus Rev 2007; 85:114-21

Original Article

Fainting in children: Syncope or Seizure

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Keywords:
fainting, syncope, seizure, children, EEG, electroencephalogram, epilepsy consciousness

OBJECTIVES: The purpose of this study was to identify the etiologies and to assess the diagnostic usefulness of electroencephalogram (EEG) study in children with fainting.

MATERIALS AND METHODS: A retrospective review was conducted at the Bangkok Child Health Center, Bangkok Hospital. Fulfilled criteria enrolled pediatric population under 18 years of age with history of fainting or syncope-like attacks who had completed cardiologic and neurologic work up including chest x-ray, electrocardiogram (ECG), echocardiogram, a standard 24 hours Holter monitoring, Tilt-table testing and at least one standard EEG recording.

RESULTS: Fainting in children is predominant in girls. Seizure or epilepsy is the second most common etiology (12.5%) preceded by syncope (77.5%) either reflex syncope, orthostatic syncope or that which is cardiac in origin. Our study demonstrated a greater yield of EEG study in identifying causes of fainting than other previous studies.

CONCLUSION: Obtaining a detailed illness and witness account is of cardinal importance and very helpful in determining the etiology of fainting. Proper investigations should be tailored to individual patients. EEG recording plays a significant role in patients with historical uncertainty or those with a history strongly suggestive of seizures.

Fainting with collapse is a relatively common symptom that challenges the physician to uncover its possible etiology. The most diagnosed cause of fainting in children is syncope: up to 20% of children have experienced syncope between 8 and 18 years of age.[1-4] According to the Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC)[5], syncope is defined as a transient loss of consciousness caused by transient global cerebral hypoperfusion with spontaneous complete recovery. It is classified into three groups by etiology:

1] reflex (neurally mediated) syncope including i) vagovagal, ii) situational, iii) carotid sinus syncope, and iv) atypical forms (without apparent triggers and/or atypical presentation).

2] syncope due to orthostatic hypotension (OH) including i) primary and ii) secondary autonomic failure, iii) drug-induced orthostatic hypotension, and iv) volume depletion.

3] cardiac syncope (cardiovascular) comprising of i) arrhythmia as primary cause e.g. bradycardia, tachycardia, drug induced bradycardia and tachyarrhythmia, and ii) structural disease. (Appendix 1)

However, there are also copious conditions incorrectly diagnosed as syncope. One such condition of great concern to parents and physicians is epilepsy, due to its threatening appearance and implications for treatment and long-term prognosis. Despite taking a very careful history, without neurological work up (especially doing an electroencephalogram or EEG), the diagnosis of epilepsy is often difficult to distinguish from other benign conditions in children with unexplained fainting. It could be misdiagnosed as common syncope resulting in delays investigating etiology of seizure which impede prompt treatment. Therefore the objectives of this study were to identify the etiologies of childhood syncope, and to assess the diagnostic usefulness of EEG study in determining fainting caused by epilepsy in children who were brought to the Bangkok Child Health Center, Bangkok Hospital.

Materials and Methods

A retrospective review was conducted on pediatric patients under 18 years of age who were brought to the Bangkok Child Health Center at the Bangkok Hospital during the period from January 2007 to December 2010 with history of fainting or syncope-like attacks. We enrolled all children who had completed cardiologic and neurologic work up including chest x-ray, electrocardiogram (ECG), echocardiogram, a standard 24 hours Holter monitoring, Tilt-table testing, at least one standard EEG recording using the International 10-20 system of electrode placement for a minimum of 30 minutes or greater, and/or neuroimaging study either CT scan or MRI scan of the brain. Medical records were systematically reviewed to ascertain demographic characteristics in the clinical data such as frequency of symptoms prior to diagnosis, past medical history, and results of cardiologic and neurologic investigations.

Etiology of fainting in this study was divided into 4 groups: syncope, seizure or epilepsy, migraine, and unknown cause. As aforementioned, the classification of syncope by the ESC (2009 version) was used to categorize type of syncope. Regarding seizure and/or epilepsy, the classification of epilepsies and epileptic syndromes (1989) by the International League Association of Epilepsy (ILAE) [6] (Appendix 2)was used.

Statistical analysis

Descriptive data were presented as absolute numbers and percentages. All statistical analyses were performed using SPSS for Windows, version 16.0 (Statistical Package for Social Science).

Results

Demographic background

A total of 126 children with history of fainting were brought to the Bangkok Child Health Center during the period from January 2007 to December 2010. Of these, 40 children fulfilled the inclusion criteria of this study by completion of both cardiac and neurological investigations. The initial blood tests for electrolytes and glucose of all enrolled population were normal. Table 1 shows demographic and characteristics of 40 enrolled children. The majority were girls (60%) with male to female ratio of 0.7:1. The mean age was 117.3 months (range: 7 months to 15 years). Medical history showed no preexisting disease in 82.5%, a history of febrile seizures in 5%, epilepsy in 2.5%, acute lymphoblastic leukemia and allergic rhinitis or asthma in 5% each. Only 7.5% of cases had ever taken regular medication.

Historical features

Fainting during prolonged standing was discovered in 37.5% of cases. The second most common activities associated with attacks (22.5%) were specific triggers which induced fainting such as pain, blood phobia, dehydration, or warm bath. The mean frequency of symptoms before diagnosis was 2.7 attacks (range: 1-15). Time to diagnosis was 132.5 days averagely (range: 1 day - 4 years). Nearly half of cases (47.5%) did not have warning symptoms prior to fainting. Most developed symptoms associated with fainting, including dizziness or light headedness (52.5%), palpitation (10%), headaches 10%), acute transient visual loss (7.5%) and automatism (5%) e.g. lip smacking or involuntary repetitive movement. Clinically post-fainting, 82.5% returned to normal baseline, 15% with confusion, and 2.5% with transient motor deficit.

Etiology of fainting

Table 2 details the etiology of fainting in our enrolled population. Syncope was identified in 77.5% of cases: 55% with reflex syncope, 12.5% with orthostatic (OH) syncope, and 7.5% with cardiac syncope. Epilepsy was diagnosed in 12.5% of cases. Five percent were provided diagnosis of migraine. Unknown etiology remained in 5% of cases. Regarding investigations, all inclusion children had normal chest x-ray results. In those with diagnosis of syncope, the positive results of cardiac work up were small: 2.5% having abnormal ECG or echocardiogram or Holter monitoring, and 10% having abnormal tilt table testing. All children with diagnosis of epilepsy had epileptiform discharges in EEG recording and all cardiac work ups were unremarkable. Figure 1 and 2 demonstrated examples of EEG tracings of chidren with recurrent fainting and eventually discovered diagnosis of epilepsy.

Table 1: Patient's characteristics and causes of syncope (n = 40)

Parameters	No. of cases	Etiology of fainting with collapse			
		Syncope	Epilepsy	Migraine	Unknown
Total (%)	**40 (100.0)**	**31 (77.5)**	**5 (12.5)**	**2 (5.0)**	**2 (5.0)**
Gender (%)					
Male	16 (40.0)	13 (32.5)	1 (2.5)	1 (2.5)	1 (2.5)
Female	24 (60.0)	18 (45.0)	4 (10.0)	1 (2.5)	1 (2.5)
Age (months)					
Mean (range)	117.3 (7-180)	118.6 (1-180)	114.4 (54-141)	137.0 (131-143)	85.5 (7-164)
Median (SD)	126.5 (38.3)	120 (35.0)	129.0 (36.5)	137.0 (8.5)	85.5 (111.0)
Underlying illness (%)					
None	33 (82.5)	24 (60.0)	5 (12.5)	2 (5.0)	2 (5.0)
History of febrile convulsion	2 (5.0)	2 (5.0)	0	0	0
Epilepsy	1 (2.5)		0	0	0
Acute lymphoblastic leukemia	2 (5.0)	1 (2.5)	0	0	0
Allergic rhinitis/Asthma	2 (5.0)	2 (5.0)	0	0	0
History of regular medication use (%)					
Yes	3 (7.5)	3 (7.5)	0	0	0
Activity associated fainting event (%)					
Unpredictable	7 (17.5)	0	5 (12.5)	0	2 (5.0)
During or just after exertion	4 (10.0)	4 (10.0)	0	0	0
Prolonged standing	15 (37.5)	15 (37.5)	0	0	0
Rapid change in posture	6 (15.0)	6 (15.0)	0	0	0
Specific trigger induce fainting e.g. pain, blood phobia, warm bath	9 (22.5)	7 (17.5)	0	2 (5.0)	0
Frequency of attack prior to diagnosis					
Mean (range)	2.7 (1-15)	2.7 (1-15)	3.2 (2-6)	1.5 (1-2)	2.0 (1-3)
Time to diagnosis (days)					
Mean (range)	132.5 (1-1460)	112.2 (1-1095)	359.4 (7-1460)	7.0 (7.7)	6.0 (5-7)
Median (SD)	7.0 (294.9)	7.0 (225.7)	90.0 (618.5)	7.0 (7.7)	6.0 (1.4)
Symptom associated with faint* (%)					
None	19 (47.5)	16 (40.0)	1 (2.5)	1 (2.5)	1 (2.5)
Palpitation and/or sweating	5 (12.5)	5 (12.5)z	0	0	0
Dizziness or lightheadedness	21 (52.5)	15 (37.5)	4 (10.0)	1 (2.5)	1 (2.5)
Headaches	4 (10.0)	1 (2.5)	1 (2.5)	2 (5.0)	0
Acute, transient visual loss	3 (7.5)	2 (5.0)	0	1 (2.5)	0
Automatism e.g. lip smacking, repetitive movement	2 (5.0)	0	2 (5.0)	0	0
Post fainting symptom (%)					
Confusion	6 (15.0)	1 (2.5)	5 (12.5)	0	0
Transient motor deficit	1 (2.5)	0	0	1 (2.5)	0
Investigations (%)**					
Abnormal ECG	1 (2.5)	1 (2.5)	0	0	0
Abnormal echocardiogram	1 (2.5)	1 (2.5)	0	0	0
Abnormal Holter's monitoring	1 (2.5)	1 (2.5)	0	0	0
Abnormal Tilt table test	4 (10.0)	4 (10.0)	0	0	0
Abnormal EEG***	5 (12.5)	0	5 (12.5)	0	0
Performed neuroimaging study	27 (67.5)	17 (42.5)	5 (12.5)	2 (5.0)	2 (5.0)
CT brain (abnormal result)	17 (0)	14 (0)	0	1 (0)	2 (0)
MRI brain (abnormal result)	9 (1)	3 (0)	5 (1)	1 (0)	0

*one subject may have more than one symptom ; **one subject may have more than one abnormal cardiac result;

*** all subjects with abnormal EEG results had normal cardiac work ups

Table 2: Detail of subpopulation of each etiology (n = 40)

Etiology of fainting	No. of cases (%)
Reflex (neurally mediated) syncope	22 (55.0)
Vagovagal e.g. orthostatic stress, pain, blood phobia	20
Situational e.g. post-exercise, warm bath	2
Orthostatic syncope	6 (12.5)
Cardiac syncope	3 (7.5)
Arrhythmia	1
Structural diseases e.g. mitral valve regurgitation /prolapsed, pulmonary hypertension	2
Epilepsy	5 (12.5)
Localization-related epilepsy	5
Migraine	2 (5.0)
Unknown	2 (5.0)

Discussion

It is challenging for physicians to properly determine the diagnosis of children with fainting symptoms. Alertness when interviewing the patient/parents about illness history and complete physical examination are very helpful in distinguishing syncope from seizures and other mimic conditions including breath holding spells, migraine, transient ischemic attack (TIA), and psychogenic pseudosyncope.[4,5,7] More than 70% of patients with syncope could be diagnosed by a detailed history and physical examination.[8] Clinical features that can suggest a diagnosis of syncope on initial evaluation are shown in Appendix 3. Most diagnoses are discovered without laboratory requisition. The remainder of cases, with ambiguous or doubtful history, may require specific consultation. Even during specialists' evaluation, cardiologic and neurologic investigations are not routinely worked up. A standard 24 hours Holter monitoring, tilt-table test and EEG study may not be considered. The limitation in sample size of our study population is due to the above. Moreover, we may have missed some patients who presented with syncope and eventually were found to have specific disease entity; the final diagnosis may have been coded specifically to the disease entity and not reflective of the presenting symptom of syncope. Such patients therefore would not have been enrolled into our study.

With complete cardiac work ups, 77.5% of cases were diagnosed with syncope, a similar figure to that found by Pratt and Fleisher.[1] The most frequent type of syncope found in our study was neurally mediated syncope (55% of all cases); this also concurred with many studies that concluded that the major mechanism responsible for syncope was neurocardiogenic.[9-11] The cardiac syncope including arrhythmia and structural defect was found in 7.5% of cases; similarly Gordon et al.[12] reported up to 9% of syncope in children is caused by cardiac problems such as myocardial disease, atrioventricular node reentrant tachycardia, and sick sinus syndrome.

The differential diagnosis between syncope and epilepsy can be difficult in some cases. An accurate patient history and witness account is cardinal. The yield of EEG recording in patient with syncope is still debatable and controversial. Many studies demonstrated that the EEG has very low diagnostic yield (0.8% - 1.5%) in patients with syncope, and percentage of epileptiform discharges discovered in the EEG tracing was not different from the incidence found in a healthy, asymptomatic population.[13-16] After EEG was performed together with illness history concordance, 12.5% of cases with fainting were diagnosed with epilepsy, again comparable to Pratt and Fleisher's report but also greater than many previous studies.[13-16] We do admit that an EEG should not be routinely performed in patients with fainting. It should be considered in suspicious cases where illness histories are ambiguous. Sheldon and colleagues[17] have proposed a scoring scheme based on symptoms that are very helpful in distinguishing seizures from syncope. If point score is ≥ 1 the likelihood is seizure or if < 1 the likelihood is syncope with 94% sensitivity and specificity. (Appendix 4)

Concerning cost-effectiveness, many studies had looked at cost-effectiveness and diagnostic yield when determining cause of fainting. It is not easy to conclude precisely which medical tests are appropriate for being the initial diagnostic evaluations for a patient with fainting. Under pressure of increased medical-legal issues or the parent's desire to make a more specific diagnosis, it is very hard to determine how many investigations should be considered.

The 12-lead electrocardiography which is absolutely mandatory when a patient presents with loss of consciousness, is useful in providing diagnostic and prognostic information in the evaluation of syncope.[18] The tilt table

test is a useful and reliable diagnostic tool that may help distinguish epilepsy from syncope. The tilt table tests were positive in all children with underlying epilepsy, but whose clinical state was suggestive of syncope.[19] It is not usually needed in subjects with syncope because of the false positive result that could occur even in people without syncope. Therefore this test may not be considered as an initial screening but it is useful in cases of syncope with unclear etiology after careful cardiac and neurological investigation.[20] The main indication for tilt testing in many studies has been to confirm a diagnosis of reflex syncope in patients whom this diagnosis was suspected but not confirmed by initial evaluation.[21-25] According to the guidelines for diagnosis and management of syncope (version 2009), tilt testing is indicated in 1] the case of an unexplained single syncopal episode in high risk settings (e.g. occurrence of, or potential risk of physical injury or with occupational implications), or recurrent episodes in the absence of organic heart disease, or in the presence of organic heart disease, after cardiac causes of syncope have been excluded (Class I, Level B), and 2] when it is of clinical value to demonstrate susceptibility to reflex syncope to the patient (Class I, Level C). The relative indications that tilt testing should or may be considered include to discriminate between reflex and OH syncope (Class IIa, Level C), for differentiating syncope with jerking movements from epilepsy (Class IIb, Level C), for evaluating patients with recurrent unexplained falls (Class IIb, Level C), and for evaluating patients with frequent syncope and psychiatric disease (Class IIb, Level C).[5] The EEG study is crucial for subjects in whom illness histories are strongly suggestive of seizures, or those with unclear illness histories. Despite the low diagnostic yield in helping to determine causes of fainting as mentioned in many previous studies (0.8-1.5%)[13-16], this is not supported by the results of our study: 12.5% of our cases with fainting were found to have diagnosis of epilepsy from a regular EEG recording.

Conclusion

Fainting is a relative common symptom that requires definite etiology for accurate management. Obtaining a detailed personal and family history for all patients is absolutely essential. Syncope, seizure, and other differentials should be considered during taking illness history. Proper investigations should be judged for individual patient. However, the most fundamental investigations including chest-x ray, and ECG are strongly recommended. The EEG recording is significant in patients with history strongly suggestive of seizures.

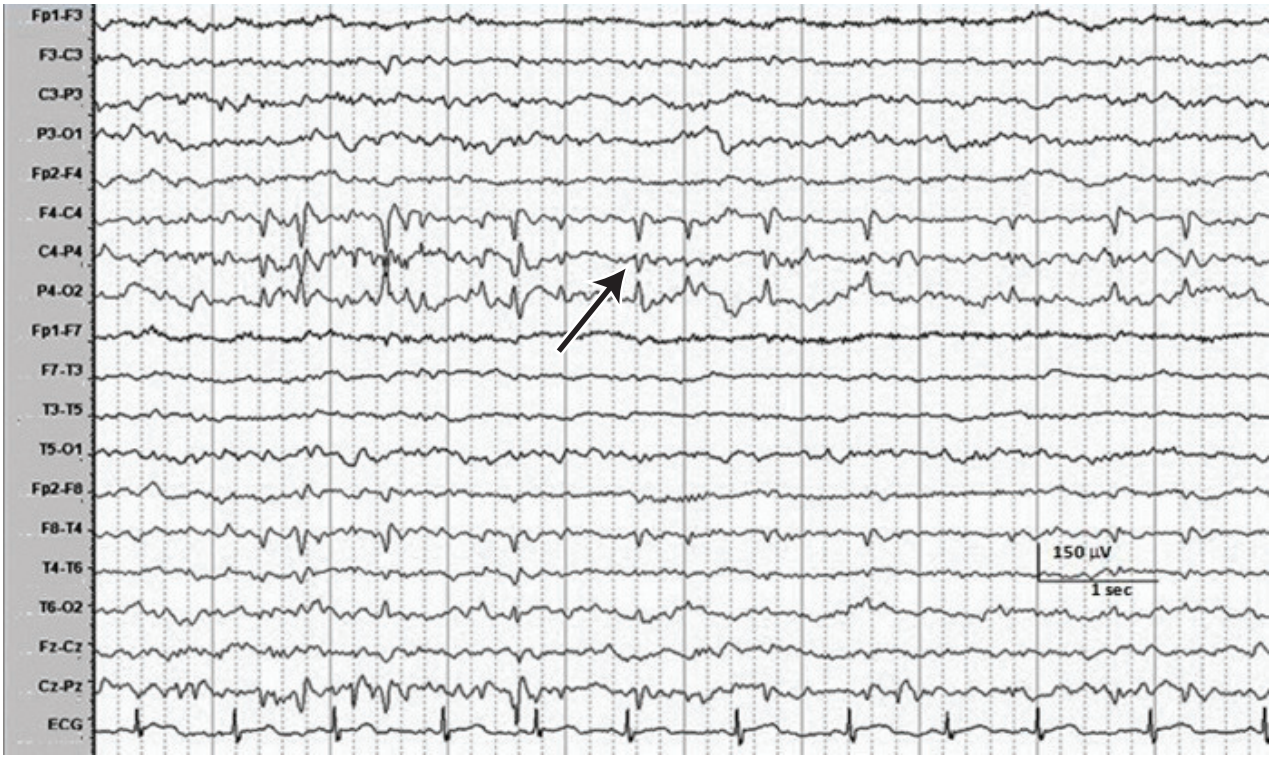

Figure 1: *The EEG of a 10-year-9-month old girl with 4 events of fainting and collapse during 6 months time demonstrates high amplitude sharp waves with phase reversal (arrow) over right centro-parietal region involving C4 and P4 electrodes. EEG setting: bipolar montage with sensitivity of 15 microvolt per millimeter, low frequency filtering of 0.5 Hz, high frequency filtering of 70 Hz, notch filtering of 50 Hz, timebase of 30 mm/sec.*

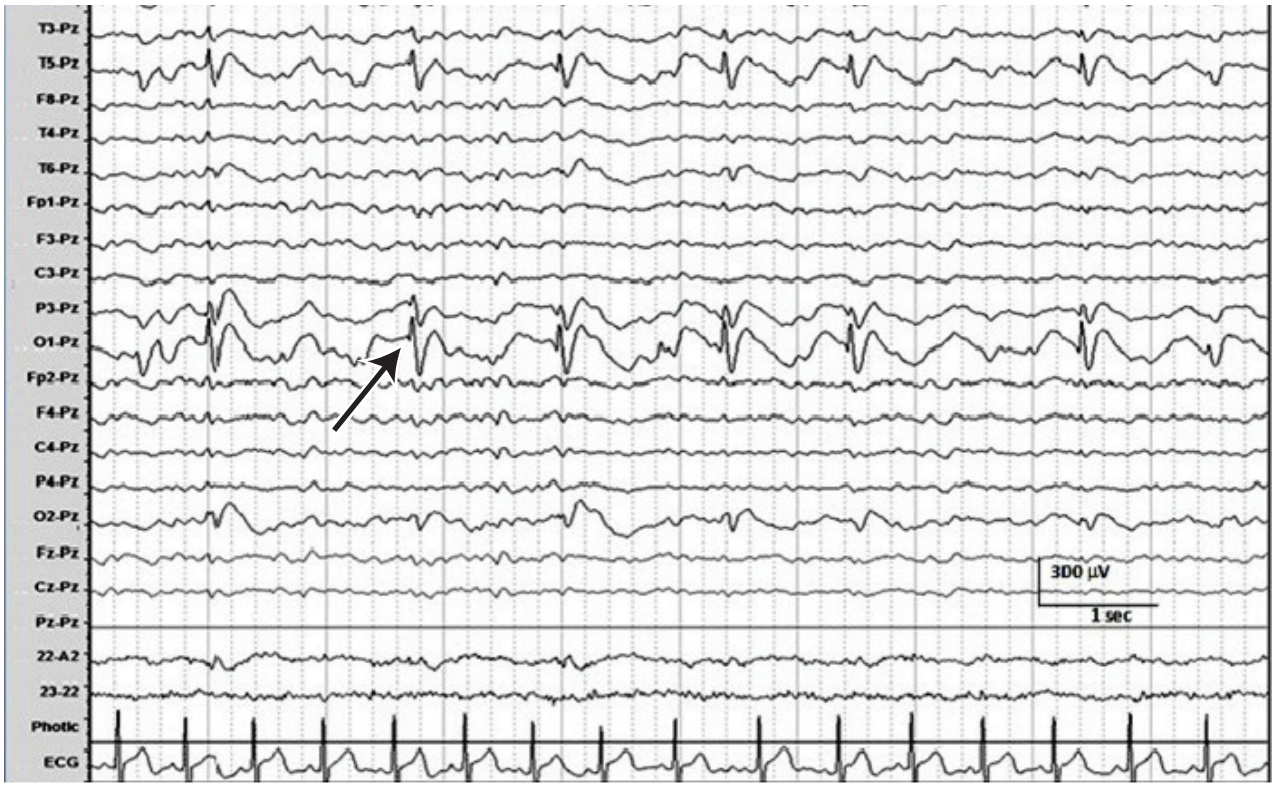

Figure 2: *The EEG of a 4-year-6-month old girl with 2 events of fainting and collapse shows high amplitude spike-and-wave (arrow) at left occipital area (O1 electrode) with electrical field spreading to left parietal and left temporal region involving P3, T3, and T5 electrodes respectively. EEG setting: ref-erential montage using Pz as a reference electrode with sensitivity of 30 microvolt per millimeter, low frequency filtering of 0.5 Hz, high frequency filtering of 70 Hz, notch filtering of 50 Hz, timebase of 30 mm/sec.*

References

1. Pratt J, Fleisher G. Syncope in children and adolescents. *Pediatr Emerg Care* 1989;5:80-2.
2. Ruckman RN. Cardiac causes of syncope. *Pediatr Rev* 1989;9:101-8.
3. McHarg ML, Shinnar S, Rascoff H, et al. Syncope in Childhood. *Pediatric Cardiology* 1997;18:367-71.
4. McLeod KA. Syncope in childhood. *Arch Dis Child* 2003;88:350-3.
5. The Task Force for the Diagnosis and Management of Syncope of the European Society of Cardiology (ESC). Guidelines of the diagnosis and management of syncope (version 2009). *European Heart Journal* 2009;30:2631-71.
6. Commission on Classification and Terminology of the International League Against Epilepsy 1989. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;30:389-99.
7. Ross B, Grubb B. Syncope in the child and adolescent. In: Grubb B, Oshlansky B, eds. Syncope: mechanisms and management. New York: Futura, 1998:305-16.
8. Farwell D, Sulke N. How do we diagnose syncope?. *J Cardiovasc Electrophysiol* 2002;13 : 9-13.
9. Massin MM, Bourguignont A, Coremans C, et al. Syncope in pediatric patients presenting to an emergency department. *J Pediatr* 2004;145:223-8.
10. Massin MM, Malekzadeh-milani S, Benatar A. Cardiac syncope in pediatric patients. *Clin Cardiol* 2007;30:81-5.
11. Bo I, Carano N, Agnetti A, et al. Syncope in children and adolescents: a two-year experience at the Department of Paediatrics in Parma. *Acta Bio* 2009;80:36-41.
12. Gordon T, Moodie D, Passalacqua M, et al. A retrospective analysis of the cost-effective workup of syncope in children. *Cleve Clin J Med* 1987;54:391-4.
13. Abubakr A, Wambacq I. The diagnostic value of EEGs in patients with syncope. *Epilepsy Behav* 2005;6:433-4.
14. Zivin L, Marsan CA. Incidence and prognostic significance of epileptiform activity in the EEG of non-epileptic subjects. *Brain* 1969;91:751-78.
15. Bridgers SL, Ebersole JS. Ambulatory cassette EEG in clinical practice. *Neurology* 1985;35:1767-8.
16. Pires LA, Ganji JR, Jarandila R, et al. Diagnostic pattern and temporal trends in the evaluation of adult patients hospitalized with syncope. *Arch Intern Med* 2001;161: 1889-95.
17. Sheldon R, Rose S, Ricthie D, et al. Historical criteria that distinguish syncope from seizures. *J Am Coll Cardiol* 2002;46:142-8.
18. McKeon A, Vaughan C, Delanty N. Seizure versus syncope. *Lancet Neurol* 2006;5:171-80.
19. Eiris-Punal J, Rodriguez-Nunez A, Fernandez N, et al. Usefulness of head-upright tilt test for distinguishing syncope and epilepsy in children. *Epilepsia* 2001;42: 709-13.

20. Bignole M, Menozzi C, Moya A, et al. Implantable loop-recorder: towards a gold standard for the diagnosis of syncope? *Heart* 2001;85:610-2.
21. Kenny RA, Ingram A, Bayliss J, Sutton R. Head-up tilt: a useful test for investigating unexplained syncope. *Lancet* 1986;1:1352-5.
22. Benditt DG, Ferguson DW, Grubb BP, et al. Tilt table testing for assessing syncope. American College of Cardiology. *J Am Coll Cardiol* 1996;28:263-75.
23. Morillo CA, Klein GJ, Zandri S, et al. Diagnostic accuracy of a low-dose isoproterenol head-up tilt protocol. *Am Heart J* 1995;129:901-6.
24. Bartoletti A, Alboni P, Ammirati F, et al. 'The Italian Protocol': a simplified head-up tilt testing potentiated with oral nitroglycerin to assess patients with unexplained syncope. *Europace* 2000;2:339-42.
25. Parry SW, Gray JC, Baptist M, et al. 'Front-loaded' glyceryl trinitrate-head-up tilt table testing: validation of a rapid first line tilt protocol for the diagnosis of vasovagal syncope. *Age Ageing* 2008;37:411-5.

Appendix 1: Classification of syncope[5]

Reflex (neurally-mediated) syncope

Vasovagal:
- mediated by emotional distress: fear, pain, instrumentation, blood phobia
- mediated by orthostatic stress

Situational:
- cough, sneeze
- gastrointestinal stimulation (swallow, defaecation, visceral pain)
- micturition (post-micturition)
- post-exercise
- post-prandial
- others (e.g., laught, brass instrument playing, weightlifting)

Carotid sinus syncope:
- atypical forms (without apparent triggers and/or atypical presentation)

Syncope due to orthostatic hypotension

Primary autonomic failure:
- pure autonomic failure, multiple system atrophy, Parkinson's disease with autonomic failure, Lewy body dementia

Secondary autonomic failure:
- diabetes, amyloidosis, uraemia, spinal cord injuries

Drug-induced orthostatic hypotension:
- alcohol, vasodilators, diuretics, phenotiazines, antidepressants

Cardiac syncope (Cardiovascular)

Arrhythmia as primary cause:

Bradycardia:
- sinus node dysfunction (including bradycardia/ tachycardia syndrome)
- atrioventriular conduction system disease
- implanted device malfunction

Tachycardia:
- supraventricular
- ventricular (idiopathic, secondary to structural heart disease or to channelopathies)
- implanted device malfunction

Drug induced bradycardia and tachyarrhythmias

Structure disease:

Cardiac:
- cardiac valvular disease, acute myocardial infarction/ ischaemia, hypertrophic cardiomyopathy, cardiac masses (atrial myxoma, tumors, etc), pericardial disease/ tamponade, congenital anomalies of coronary arteries, prosthetic valves dysfunction

Others:
- pulmonary embolus, acute aortic dissection, pulmonary hypertension

Appendix 2: International classification of epilepsies and epileptic syndromes[6]

International Classification of Epilepsies and Epileptic Syndromes (1989)

1. Localization-related (focal, local, focal) epilepsies and syndromes
   - 1.1 Idiopathic
   - 1.2 Symptomatic
   - 1.3 Unknown as to whether the syndrome is idiopathic or symptomatic

2. Generalized epilepsies and syndromes
   - 2.1 Idiopathic (with age-related onset-listed in order of age)
     - Benign neonatal familial convulsions
     - Benign neonatal convulsions
     - Benign myoclonic epilepsy in infancy
     - Childhood absence epilepsy (impulsive petit mal)
     - Juvenile absence epilepsy
     - Juvenile myoclonic epilepsy (impulsive petit mal)
     - Epilepsy with grand mal (GTCS) seizures on awakening
     - Other generalized idiopathic epilepsies, if they do not belong to one of the above syndromes, can still be classified as generalized idiopathic epilepsies
   - 2.2 Cryptogenic or symptomatic (in order of age)
     - West syndrome (infantile spasms, Blitz-Nick-Salaam Krampfe)
     - Lennox-Gastaut syndrome
     - Epilepsy with myoclonic-astatic seizures
     - Epilepsy with myoclonic absences
   - 2.3 Symptomatic
     - 2.3.1 Nonspecific etiology
       - Early myoclonic encephalopathy
     - 2.3.2 Specific syndromes
       - Epieptic seizures may complicate many disease states. Under this heading are included those disease in which seizures are a presenting or predominant feature

3. Epilepsies and symdromes undetermined whether focal of generalized
   - 3.1 With both generalized and focal seizures
     - Neonatal seizures
     - Severe myoclonic epilepsy in infancy
     - Epilepsy with continuous spike-waves during slow wave sleep
     - Acquired epileptic aphasia (Landau-Kleffner syndrome)
   - 3.2 Without unequivocal generalized or focal features

4. Special syndromes
   - 4.1 Situation-related syndromes (Gelegenheitsanfalle)
     - Febrile convulsions
     - Isolated seizures or isolated status epilepticus
     - Seizures occurring only when there is an acute metabolic or toxic event due to, for example, alcohol, drugs, eclampsia, nonketogenic hyperglycemia, uremia

Appendix 3: Clinical features that can suggest a diagnosis of syncope on initial evaluation[5]

Neurally mediated syncope	
- Absence of heart disease	- Nausea, vomiting associated with syncope
- Long history of recurrence syncope	- During a meal or post-prandial
- After sudden unexpected unpleasant sight, sound, smell or pain	- With head rotation or pressure on carotid sinus (as in tumours, shaving, tight collars)
- Prolonged standing or crowded, hot places	
- After exertion	
Syncope due to OH	
- After standing up	- Prolonged standing especially in crowed, hot places
- Temporal relationship with start or changes of dosage of vasodepressive drugs leading to hypotension	- Presence of autonomic neuropathy or Parkinsonism
	- Standing after exertion
Cardiovascular syncope	
- Presence of definite structural heart disease	- During exertion, or supine
- Family history of unexplained sudden death or channelopathy	- Abnormal ECG
- Sudden onset palpitation immediately followed by syncope	
- ECG findings suggesting arrhythmic syncope:	
• Bifascicular block (defined as either LBBB or RBBB combined with left anterior or left posterior fascicular block)	
• Other intraventricular conduction abnormalities (QRS duration > 0.12s)	
• Mobitz I second degree AV block	
• Asymptomatic inappropriate sinus bradycardia (<50 bpm), sinoatrial block or sinus pause > 3s in the absence of negatively chronotropic medications	
• Non-sustained VT	
• Pre-excited QRS complexes	
• Long or short QT intervals	
• Early repolarization	
• RBBB pattern with ST-elevation in leads V1-V3 (Brugada syndrome)	
• Negative T waves in right precordial leads, epsilon waves and ventricular late potentials suggestive of ARVC	
• Q waves suggesting myocardial infarction	

ARVC = arrhythmogenic right ventricular cardiomyopathy
LBBB = left bundle branch block
RBBB = right bundle branch block
AV = atrioventricular
OH = orthostatic hypotension
VT = ventricular tachycardia

Appendix 4: Questionnaire and scoring system for symptoms pertaining to loss of consciousness[17]

Questionnaire	Points
Wake with tonque cutting?	2
Déjà vu or jamais vu?	1
Emotional stress associated with loss of consciousness?	1
Head turning during a spell	1
Unresponsive, unusual posture, limb movement, or amnesia of spells? (any one of these)	1
Confusion after a spell	1
Lightheaded spells	-2
Sweating before spell	-2
Spell associated with prolong sitting or standing	-2
If point score is ≤ 1 the likelihood is seizure or if < 1 the likelihood is syncope	

Endobronchial valves to occlude bronchopleural fistula and recurrent pneumothorax

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Keywords:
Watanabe valves, bronchoscope, pneumothorex

OBJECTIVES. We present our experiences using endobronchial valves to effectively manage patients presenting with pneumothorax and bronchopleural fistula.

MATERIALS AND METHODS. Ten patients underwent the procedure. Seven patients had developed pneumothorax with bronchopleural fistula; two patients were intubated with complicated bronchopleural fistula. One patient had recurrent catamenial right pneumothorax.

RESULTS. The procedure was effective in 9 cases (90 percent). The mortality was low, effectiveness was high and achieved in less than 30 minutes.

CONCLUSION. This technique is an effective intervention for prolonged air leakage.

Patients presenting with pneumothorax and bronchopleural fistula are normally difficult to treat. Surgical options may be limited due to patients being elderly, having emphysema, poor lung functions, underlying heart diseases or poor nutritional status.

We present our experiences using endobronchial valves to effectively manage these problems.

Materials and Methods

From January 2005 till June 2012, ten patients underwent the procedure. Seven patients developed pneumothorax, with bronchopleural fistula; two patients were intubated which was complicated with bronchopleural fistula. One patient had suffered from recurrent pneumothorax almost every month since 20 years whenever she menstruated (catamenial pneumothorax). She underwent surgical pleurodesis several times in the United States ten years ago but pneumothorax still recurred.

Identification of the affected bronchi and technique

A balloon catheter was inserted via the working channel of the flexible bronchoscopy, if there was no leakage or decreased air bubble via the chest drain, the lumen was the target site of occlusion. In one case there was more than one lumen leakage, so up to 3 valves were needed to totally occlude the fistula. In cases of small leakage following the occlusion, we used tetracycline to seal the lumen.

The technique to insert the Watanabe valve

There were 3 sizes of valve (Picture 1). How we selected any valve depended on the diameter of the bronchial lumen detected by the balloon occlusion. Then the selected valve was grasped by the forcep catheter through the working channel. The easiest way is to pass through the large endobronchial tube when the leakage site is the lower lobes. The most difficult position is the upper lobe; to get a proper position, the Watanabe valve may have to be cut in half before inserting into the lumen.

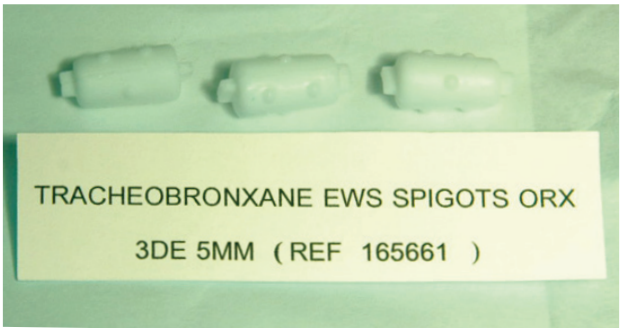

Figure 1: *Shows Watanabe valves*

Results

There were 7 males and 3 females, from 37 to 89 years of age, with a mean age of 71. Eight patients had emphysema with a history of heavy smoking. There were nine cases of pneumothorax with bronchopleural fistula and one case of recurrent catamenial right pneumothorax.

The duration of the leakage before the valve insertion was between 7 - 15 days. The procedure was effective in 9 cases (90 percent). The average operation time was 25 minutes.

One patient on assisted ventilation developed acute respiratory distress syndrome which required high positive end expiratory pressure (PEEP). Despite decreasing the air leak, his pneumothorax could not be completely occluded and the patient expired from underlying sepsis a week later.

Discussion

Patients presenting with pneumothorax and bronchopleural fistula may be poor candidates for surgery due to emphysema, poor lung function with or without respirtory support, heart disease, or poor nutritional status; for such patients, endobronchial valve occlusion may represent an interesting alternative to surgical. In our experience, endobronchial valve occlusion was successfully performed in 9 out of 10 patients. The procedure was performed in a short period of time, and mortality was low, despite the poor underlying health status of the patient population.

The limitations of the technique can be seen when the lesions are located in the upper lobes or when patients are already in respiratory distress. However, newer umbrella valves available nowadays[1, 2] are easier and faster to insert although also more expensive. Anyway, the latest endobronchial valves provide us more options to give better medical care to our patients.

Conclusion

We present our experience in managing patients with pneumothorax and bronchopleural fistula using endobronchial valves which led to subsequent improvement in 9 out of 10 cases. We show the evidence that this technique is an effective intervention for prolonged air leakage.

References

1. Gillespie CT, Sterman DH,Cerfolio RJ, et al. Endobronchial valve treatment for prolonged air leaks of the lung. *Annual Thorac Surg* 2011;91:270-3.
2. Sterman DH. A Multicenter pilot study of a bronchial valve for the treatment of severe emphysema. *Respiration* 2010;79:222-33.

Correlation of the Automated Breast Volume Scanner (ABVS) and Hand-held Breast Ultrasound (HHUS) Findings

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OBJECTIVES: To correlate the findings of Automated Breast Volume Scan (ABVS) and Hand-held Breast Ultrasound (HHUS), and to compare the benefits and drawbacks of each system as an adjunct to mammography.

MATERIALS AND METHODS: A total of 212 adult female patients underwent mammography in the Breast Center of Wattanosoth Hospital in 2010 followed by ABVS and HHUS was interpreted and reported by radiologists immediately. ABVS was interpreted and recorded by one radiologist 3 months later.

RESULTS: There were 504 lesions, interpreted as BIRADS 1 in 37 cases, BIRADS 2 (simple cyst) in 77 cases, BIRADS 3 in 63 cases, BIRADS 4 in 31 cases and BIRADS 5 in 4 cases. Both studies agreed in 306 lesions, there was agreement and ABVS showed additional lesions in 13 cases, the studies were not in agreement about 35 lesions. ABVS showed negative but HHUS showed positive in 24 lesions, HHUS showed negative but ABVS showed positive in 104 lesions although there were pitfalls in ABVS results in 24 lesions.

CONCLUSION: In our study, despite having some drawbacks with nipple artifacts, ABVS showed significant improvement in detection of breast cancer in as compared to HHUS, uncovering 12 additional suspicious lesions, and excluding 3 suspicious lesions. Patients also benefit from a shorter, more comfortable examination without exposure to radiation agents or the need to hold their breath.

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Keywords:
breast cancer, automated breast ultrasound, automated breast volume scanner, ABVS, hand-held breast ultrasound

Breast cancer has become the most common cancer. Statistics from Siriraj Cancer Center in 2008 showed 1,129 new breast cancers, making up 25.79% of all women's cancers.[1] Since there is no effective way to prevent breast cancer, the best that can be done is to treat the disease at its earliest stage. Breast imaging which includes mammography (MM), ultrasound (US), magnetic resonance imaging (MRI) and radionuclide scintigraphy (RNS), has proven to be the most appropriate method to detect lesions.[2-5] Concerning the cost effectiveness and availability, MM and US are the studies of choice in our country.[6-8]

Statistics of breast tissue composition in 191,169 mammograms performed from 1995-2009 in Siriraj Breast Centre show almost entirely fat in 5.64%, scattered density in 20.36%, heterogeneously dense in 63.18% and extremely dense in 10.82%, therefore, 75% of Thai breasts can be classed as difficult breasts, in which lesions may be completely obscured.[9] Mammography has limitations in detection and evaluation of breast lesions in mammographically dense breasts, palpable mass in young women, pregnant and lactating breasts, acute inflammation, post-operation, trauma, male gynecomastia and assessment of augmented breasts. US has no such

limitation. The masses in MM are notified either as round, oval, lobular, which are less significant or as irregular, microlobular and speculated, which are more suspicion. There might be associated findings, such as the presence of microcalcifications and architectural distortion.[10,11]

US is much more informative in evaluation of breast mass, for its shape (round, oval or irregular), orientation (parallel, non-parallel), margin (circumscribed or not, sub grouped into indistinct, angular, microlobulated or speculated), lesion boundary (abrupt interface or echogenic halo), echo pattern (anechoic, hypoechoic, isoechoic, hyperechoic and complex), posterior acoustic features (no posterior acoustic features, enhancement, shadowing and combined pattern), surrounding tissue (in ducts, straightening or thickening of Cooper's ligament, edema, skin thickening, architectural distortion), vasculature and other specific findings. Therefore, apart from seeing the mass, US can define the mass as:

- Cystic lesion, subgrouped into simple, complicated, complex and cluster of microcysts.
- Solid lesion, subgrouped into benign looking, probably benign, low suspicion and high suspicion of malignancy.

The management of each subgroup is different

We compared results between mammography, pathology and US results. The outcome of using both studies together yielded a much more impressive results, namely that when the mass looked benign, it was true benign in 94.9%, probably benign was benign in 88.57%, indeterminate is 50 +/- 3.49% and malignant was true malignant in 95.78% of cases.[12-15]

Of 26,741 MM with US performed during 1999–2004 in Siriraj Breast Centre, US was able to detect 141 cancers in MM negative (182 US BIRADS 4, 32 US BIRADS 5). Concerning detection of breast mass, there were 13,109 cases that in both MM & US were positive, 14,220 cases that were positive in US, negative in MM.[16]

US of axillary adenopathy is superb, giving more internal architecture details, pathology and including more nodes than can be seen by MM. Fine-Needle Aspiration (FNA) of the abnormal node can be performed in one setting, which is far better than to search and do excisional biopsy of sentinel lymph node, performed in the operating room. Normal nodes were also studied.[17]

US has limitation in detection of microcalcifications, especially those with no associated mass. Of 39,830 screenings in Siriraj Breast Centre in 2004, there were 84 breast cancers. We found 19 cases (22.62%) with microcalcifications alone, which were negative in US, and 106 cases (6.02%) of 1761 cancers in 22,442 diagnostic cases had microcalcifications alone.[18] Those are the cases that will be missed if US was performed without MM. However, if the lesion is extensive, US may show where the lesion is and US guided core needle biopsy (CNB) can be performed, with proven specimen radiograph to show the presence of the microcalcifications.

US has technical drawbacks in limitation of field of view (FOV): it is not reproducible, time consuming, requires high skill/experience, operator dependent, not fit for screening. These problems can be overcome by using an automated breast US volume scan, which is a quick study that provides multiplanar images with very high resolution. It is reproducible, thus very beneficial to be used in a comparison study. The automated breast volume scanner (ABVS), like computed tomography (CT) volume scan provide automated acquisition of a large number of thin two-dimensional (2D) slices to produce a three-dimensional (3D) volumetric data set. A reconstruction by post-processing is instantly performed in multiplanar: sagittal, coronal, radial, anti-radial, cranial-caudal (CC), Mediolateral-oblique (MLO), multislices: thin or thick slices, 3D navigation, tomographic display 3D which allows for correlation with mammography or MRI.[19,20]

Materials and Methods

In 2010, we did a study on Correlation of ABVS and HHUS after mammography in 212 female patients at Breast Center of Wattanosoth Hospital. Their average age was 48.06 years. HHUS was interpreted and reported by radiologists immediately. ABVS was interpreted and recorded by one radiologist 3 months later. The results of both studies were recorded, analyzed and correlated.

There were 504 lesions, interpreted as BIRADS 1 in 37 cases, BIRADS 2 (simple cyst) in 77 cases, BIRADS 3 in 63 cases, BIRADS 4 in 31 cases and BIRADS 5 in 4 cases. Both studies agreed in 306 lesions, there was agreement and ABVS showed additional lesions in 13 cases, the studies were not in agreement about 35 lesions, ABVS showed negative but HHUS showed positive in 24 lesions, HHUS showed negative but ABVS showed positive in 104 lesions and there were pitfalls in ABVS results in 24 lesions. (Table 1)

Table 1: Correlation of ABVS and HHUS findings

Correlation ABVS and HHUS findings	Number of lesions
1. Agree	306
2. Agreement and ABVS shows additional lesions	13
3. Not in agreement	35
4. ABVS negative, HHUS positive	24
5. HHUS negative, ABVS positive	104
6. Pitfalls of ABVS	22
Total	504

Table 2: Correlation of 306 agreed findings by ABVS and HHUS.

Findings	Number of lesions
Solid lesions	208
B*1: Negative	58
B2 / B3: Benign solid (looking/ probably)	121
B2 / B3: Benign & cysts	14
B4: Low suspicion	13
B5: High suspicion	2
Cystic lesions	98
Simple cyst	56
Complicated cyst	21
Complex cyst	5
Multiple cysts	16

*B = BIRADS

Details of the findings in each category are as follows:

1. Both studies agreed in 306 lesions, including: 208 solid lesions and 98 cystic lesions. Among solid lesions, there were 58 BIRADS 1, 121 BIRADS 2/3 (benign looking / probably benign), 14 BIRADS 2/3 (benign looking/probably benign and cysts), 13 BIRADS 4: (Low suspicion), 2 BIRADS5 (High suspicion). Among cystic lesions, there are 56 simple cysts, 21 complicated cysts, 5 complex cysts and 16 multiple cysts (Table 2). The MM, HHUS and ABVS are shown in Figure 1.

2. Both studies agreed and ABVS showed additional lesions in 13 cases which included: 8 benign solid lesions, and ABVS found more cysts, 1 BIRADS 5 lesion and ABVS found 1 more nearby similar BIRADS 5 lesion, 2 simple cysts and ABVS found 1 more complicated cyst and 1 more cluster of microcysts, 1 multiple cyst and ABVS found 1 more benign looking solid lesion and 1 more BIRADS 4 (low suspicion) lesion (Table 3 and Figure 2).

3. Both studies disagreed in 35 lesions, which included the following: HHUS found 19 benign solid lesions, while ABVS showed 2 complex cysts, 14 other cystic lesions, 1 benign solid lesion with cyst, 2 BIRADS 4 (low suspicion). There were 6 benign solid with cystic lesions seen by HHUS, but ABVS showed 2 BIRADS 4 (low suspicion) and 4 simple cysts. Apart from that HHUS noted 2 BIRADS 4 (low suspicion), but ABVS showed 2 simple cysts. HHUS revealed 7 simple cysts, but ABVS revealed 3 solid lesions, 3 simple with complicated cysts and 1 complex cyst. One complex cyst was seen by HH US, but ABVS showed only a simple cyst (Table 4 and Figure 3).

Table 3: The ABVS and HHUS agree findings but ABVS shows 13 more lesions.

ABVS and HHUS agree findings but ABVS shows 13 more lesions		Number of lesions
HH US & ABVS agree finding	ABVS additional findings	
Solid lesions	More cysts	8
BIRADS 5	1 more BIRADS 5	1
Simple cyst	1 more complicated cyst	1
Simple cyst	1 more cluster of microcysts	1
Multiple cysts	1 more benign looking solid lesion	1
Multiple cysts	1 more BIRADS 4 (low suspicion) lesion	1

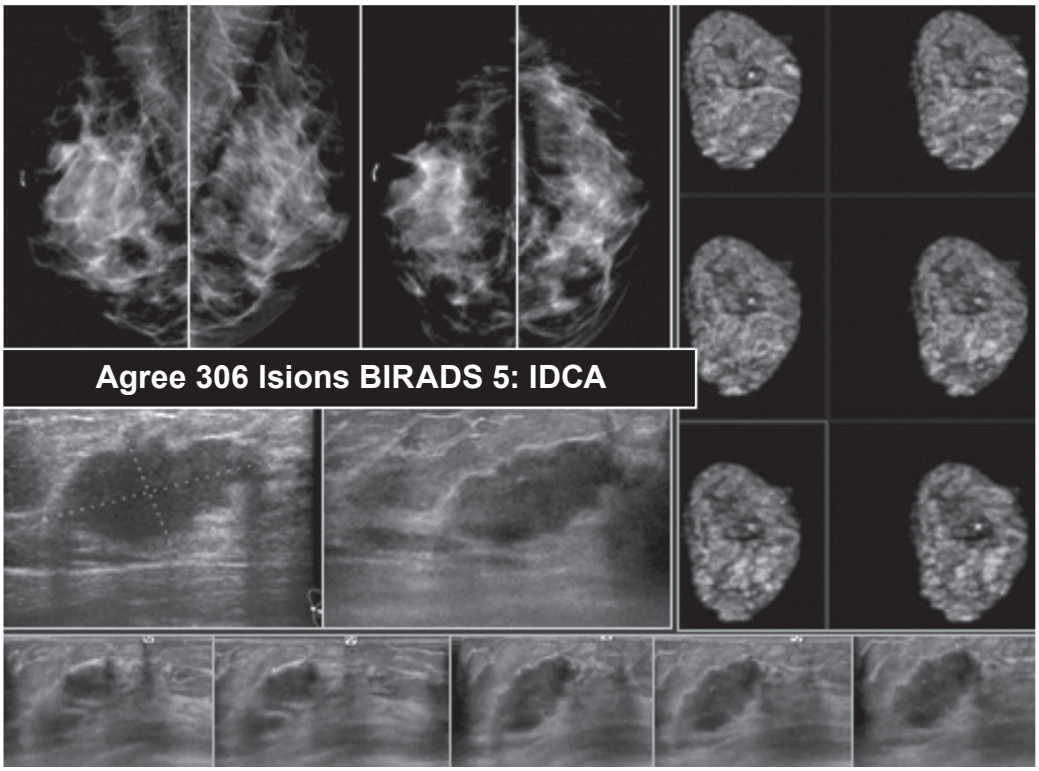

Figure 1: *MM does not show any lesion. HHUS shows a microlobulated solid mass, proven to be invasive ductal carcinoma (IDCA). ABVS shows the same finding in multiple images at 2 mm thickness and multiplanar, including axial, sagittal and coronal planes.*

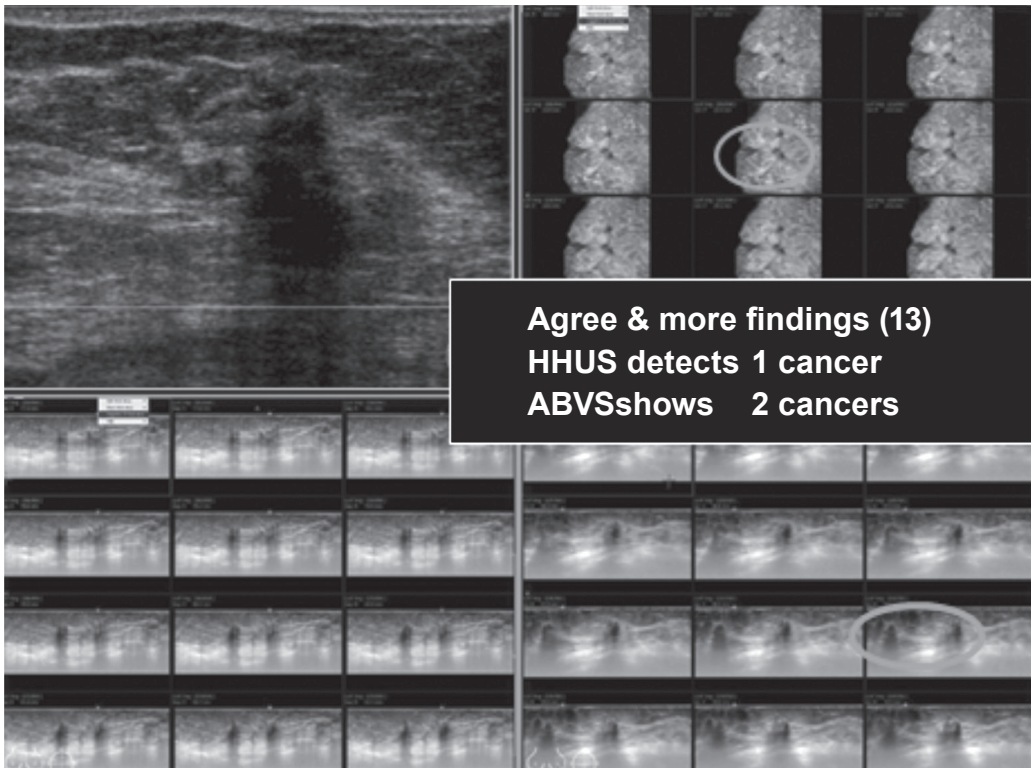

Figure 2: *HHUS shows a small solid mass with increased depth to width ratio and strong acoustic shadowing, proven to be invasive ductal carcinoma. ABVS shows two nearby lesions of the same findings, displayed in multiple images and multiplanar, including sagittal and coronal planes.*

Table 4: The ABVS and HHUS disagreed in 35 lesions.

ABVS and HHUS disagreed in 35 lesions		Number of lesions
HHUS findings	ABVS findings	
Benign solid	Complex cyst	2
Benign solid	Other cystic lesions	14
Benign solid	Benign solid lesions	1
Benign solid	BIRADS 4 (low suspicion)	2
Benign solid & cystic	BIRADS 4 (low suspicion)	2
Benign solid & cystic	Simple cysts	4
BIRADS 4 (low suspicion)	Simple cysts	2
Simple cysts	Benign solid lesions	3
Simple cysts	Simple and complicated cysts	3
Simple cysts	Complex cyst	1
Complex cyst	Simple cysts	1

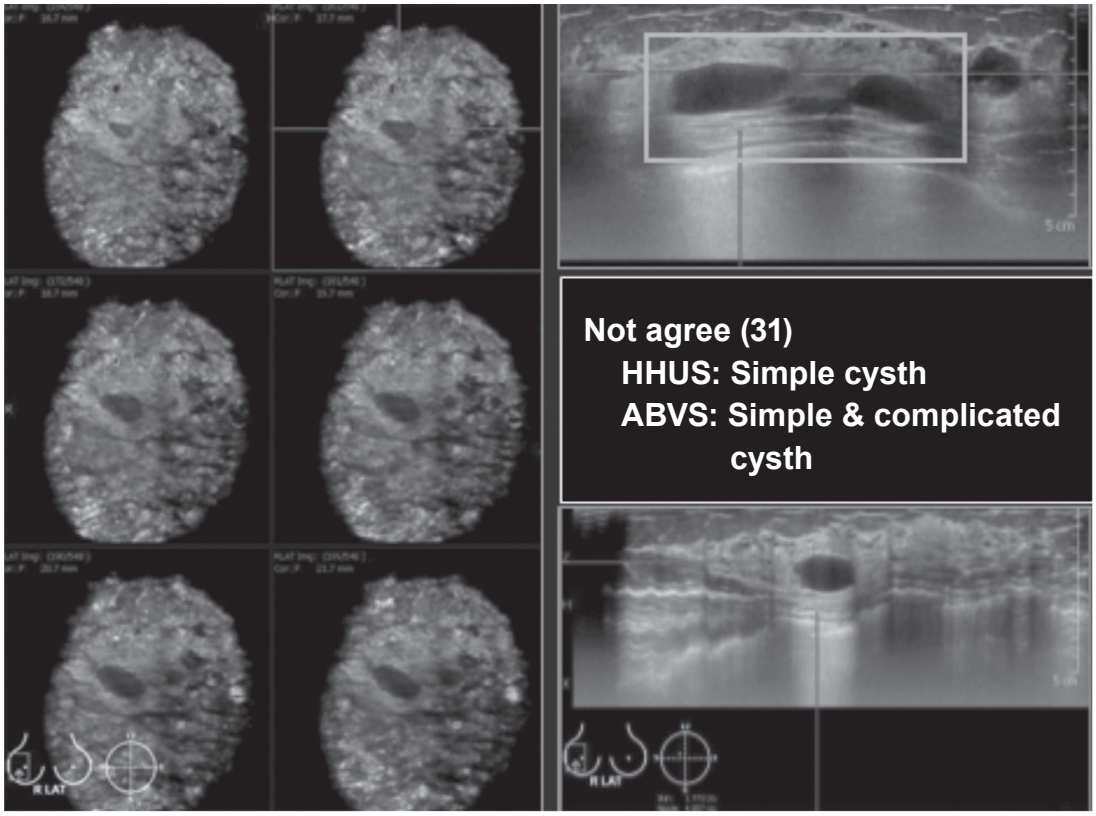

Figure 3: *HHUS shows multiple anechoic simple cysts. ABVS shows some cysts with low echoic contents, compatible with complicated cyst. The large FOV allows good comparison of the lesions in one image, displayed in multiple images and multiplanar, including axial, sagittal and coronal planes.*

Table 5: Negative ABVS but positive HHUS in 24 lesions

ABVS negative and HHUS positive in 24 lesions		Number of lesions
HHUS findings	ABVS findings	
Benign solid	Negative	2
Benign solid & cystic	Negative	14
BIRADS 4 (low suspicion)	Negative	1
Simple cyst	Negative	2
Benign solid & axillary LN*	Negative	2

*LN = Lymph Node

Table 6: Negative HHUS but positive ABVS in 104 lesions.

HHUS negative and ABVSpositive in 104 lesions		Number of lesions
HHUS findings	ABVS findings	
Negative	Benign solid	39
Negative	Benign solid & cystic	2
Negative	BIRADS 4 (low suspicion)	4
Negative	BIRADS 4 (low suspicion)& cyst	2
Negative	BIRADS 5 (high suspicion)	1
Negative	Cystic lesions	56

4. ABVS was negative while HHUS was positive in 24 lesions, including HHUS mistaking fat lobules as benign solids in 12 lesions, as benign solid and cyst in 1 lesion, as BIRADS 4 (low suspicion) in 5, simple cyst in 2 and benign solid with axillary lymph node in 4 lesions (Table 5 and Figure 4).

5. HHUS was negative while ABVS was positive in 104 lesions, including HHUS mistaking lesions for fat lobules or not detecting lesions, while ABVS could identify that there were 39 benign solid lesions, 2 benign solid and cystic lesions, 4 BIRADS 4 (low suspicion), 2 BIRADS 4 (low suspicion) with simple cyst, 1 BIRADS 5 (high suspicion) and 56 cystic lesions (Table 6 and Figure 5).

From our study ABVS showed much more benefit over HHUS. However, ABVS had drawbacks, for example:

- Nipple artifacts, making evaluation markedly limited in 11 cases (Figure 6).
- Motion artifacts in 4 cases (Figure 7).
- Contact artifacts in 3 cases (Figure 8).
- The lesion is out of view in 4 cases (Figure 9).

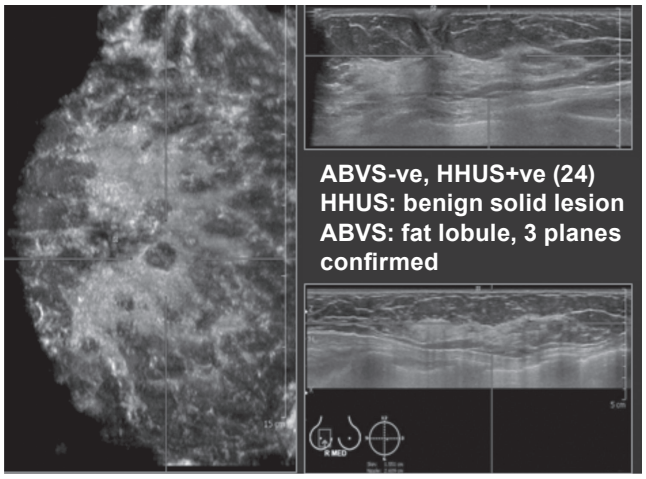

Figure 4: *HHUS shows hypoechoic lesions, while this case, ABVS shows the low echoic lesions continues with subcutaneous fat in another 1 – 2 views, compatible with fat lobule and excluded these false positive lesions seen by HHUS.*

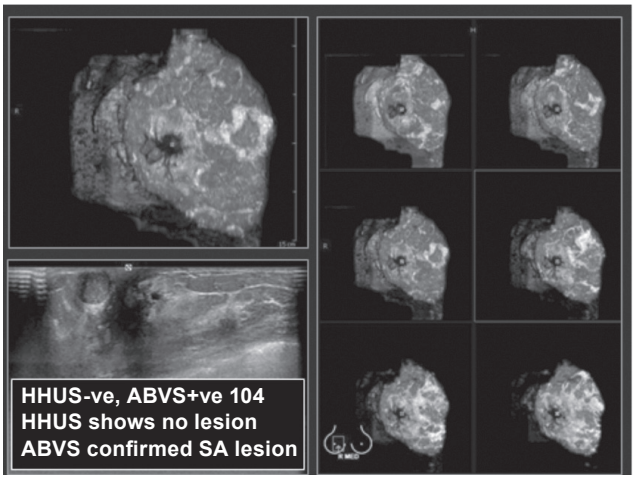

Figure 5: *HHUS detects no lesion. ABVS clearly demonstrates a lobulated hypoechoic solid mass occupied almost entirely inside a cystic lesion, compatible with a complex cystic lesion, confirmed to be a papilloma by core needle biopsy (CNB) and surgical specimen.*

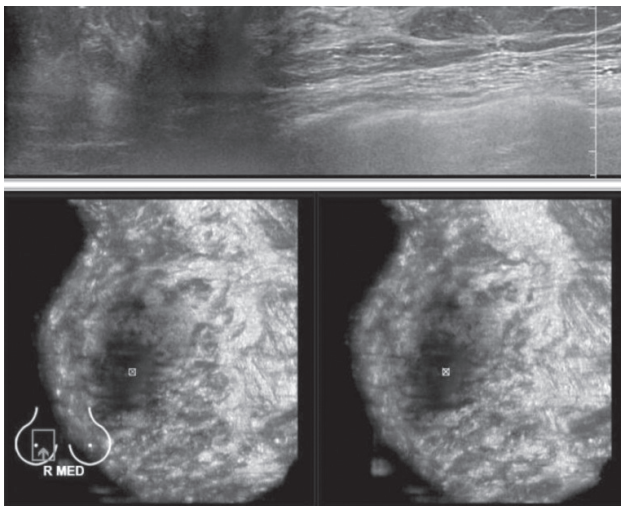

Figure 6: *Shows nipple artifact causing limitation of lesion detected under the nipple.*

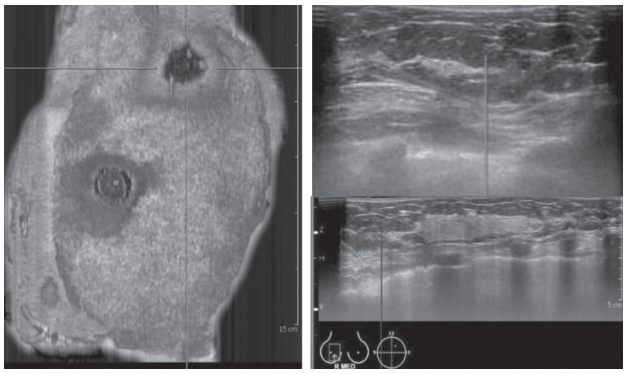

Figure 8: *Shows contact artifact due to air trapped between skin and transducer.*

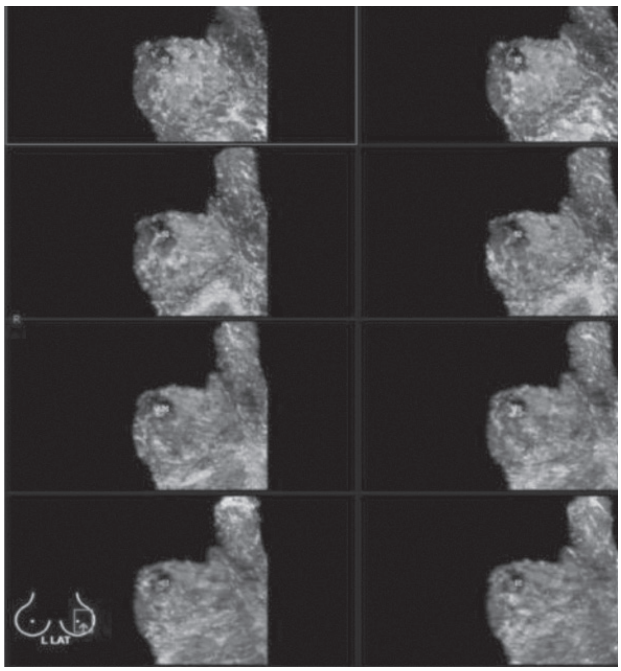

Figure 9: *Shows out of view. The axillary adenopathy seen by mammography and HHUS is not included in the area scanned. Usually axillary lymph node is not totally inside the scanned area.*

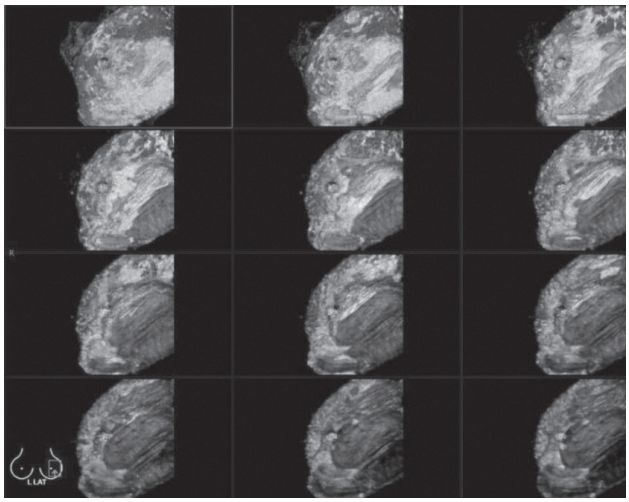

Figure 7: *Shows motion artifact from patient movement during the volume scan.*

Discussion

The result of the correlation of ABVS and HHUS findings were classified into 5 groups: both studies agreed in 306 out of 504 lesions (60.71%), both studies agreed but ABVS showed more lesions in 13 cases (2.58%). Both studies disagreed in 35 cases (6.94%), This was due to ABVS showing more detail and lesions were confirmed with scrolling for the fine details in 3 planes and 2 mm thickness. The echogenicity could be compared, for more confidence of differentiation of simple cysts from solid lesions. ABVS has no operator dependence, unlike HHUS which is known for its operator dependence.

ABVS was negative but HHUS was positive in 24 cases (4.76%), due to ABVS being able to confirm the continuity of fat lobule with subcutaneous fat by scrolling in 3 planes at 2 mm thickness, thus it could exclude the false positive lesions interpretation by HHUS. However, ABVS may not have included lesions in its FOV, due to our trying to limit the scan in order to reduce computer storage space, resulting in ABVS false negative.

HHUS was negative but ABVS was positive in 104 cases (20.63%). This was because HHUS has no multi-slice and multiplanar confirmation and is operator dependent, therefore, the lesions might not have been recognized, while all lesions in area scanned of ABVS were shown in details with confirmation.

From our study ABVS showed benefit over HHUS. Most of the different findings are due to the fact that ABVS has the benefits of a volume scan, whereby the images are readily displayed in multislice and multiplanar. When a lesion is suspected, a cursor is placed at that area and that particular point will be automatically displayed in other views with marker over that point. Scrolling over that point can be applied at 0.5-2.0 mm slice thickness, for

better defining of the area, and confirmation or exclusion of the lesion.

ABVS has a large FOV, covers a large area of the breast, with nipple marking before the automatic volume scan which takes 1 minute for each scan, thus the lesion is standardized, reproducible and take less scanning time. ABVS is actually performed by the experienced technician. ABVS's software adjusts measures and annotates the images on computer screen, and image quality is not different from that of CT volume scan.

However, ABVS had the drawbacks of nipple artifacts thus limiting. Technicians ought to look at the image which comes almost instantly after the scan. If artifacts are noted, technicians should then add a subareolar scan to the already available HHUS. Motion artifacts can be overcome by technicians should stopping, then repeating the scan after requesting the patient's cooperation to remain motionless during the scan.

With contact artifacts, a repeat scan is recommended with more gel filling in the area to avoid air gapping. The technician should note this defect in the work sheet. The lesion may not be included in the scanned area, the out of view. We recommend technicians to check that the FOV includes the breast tissue to the most medial, lateral, superior and inferior parts of the breast, with overlapping scanned area. If mammography shows axillary adenopathy, the technician is urged to add axillary scan.

Conclusion

Overall benefits to patient with ABVS include it being a fast examination; breath holding is not required although the patient must stay completely still during the volume scan. There is no ionizing radiation which is perfect for young or pregnant patients. We did not use contrast agents, thus no related risk to the patient. Apart from that we used minimal compression, so it is more comfortable than mammography.

ABVS has benefits to user as it is a volume scan, with standardized views, and reproducible. ABVS gives a streamlined workflow and the image in coronal plane is more familiar for surgeons and surgical planning, with more diagnostic information captured in less time. It captures volumes with online preview and offline review and manipulation, so it is beneficial in screening (mammography with US), using teleimaging. The technical limitations of HHUS are mostly overcome by ABVS.

References

1. Siriraj Cancer Center, Siriraj Hospital, Mahidol University, Thailand; Statistic Report 2008.
2. Bhothisuwan W, Prabhasawat D, Bhothisuwan K. Lumps in the Breast: Correlation of Ultrasound and Mammography Free Paper in UICC 1986, in K-47: Ultrasound Techniques, Guided Biopsy, article 3728.
3. Bhothisuwan W, Prabhasawat D, Bhothisuwan K. Imaging of Breast Lumps. *Thai Medical Association Annual Meeting 3* 1989:85-7.
4. Bhothisuwan W, Bhothisuwan K. MRI of Breast Lumps. A Correlation with other Breast Imaging, Gross Specimen and Pathology in Educational Lecture in AAR 1994:353.
5. Bhothisuwan W, Bhothisuwan K. Color Displayed MRI of the Breast in Free Paper in SIS in Brazil 1995.
6. Bhothisuwan W. Breast Imaging (in Thai) in Supakorn Rojananin, In Head, Neck and Breast Surgery, Bangkok Ruenkaew Publishing, 1995;1:299-319.
7. Bhothisuwan W, Bhothisuwan K. Breast Imaging and Intervention in Educational Lecture in AOCR 1998 session C07 article 2086.
8. Bhothisuwan W, Bhothisuwan K. Evidence Based Practicing Breast Imaging in Educational lecture: Breast Ultrasound Session, AFSUMB in Thailand 2007.
9. Statistic record and data system from Siriraj Breast Center 1995-2009.
10. Bhothisuwan W: Overview of Breast Imaging, Benefits and Drawbacks in Educational Lecture, WFUMB Center of Excellence Workshop on Breast Ultrasound in Bangladesh 2011.
11. Bhothisuwan W, Bhothisuwan K, Suwanakul P. Correlation of ultrasound with pathology and mammography findings. *J Med Assoc Thai 2004*.
12. McSweeny MB, Murphy CH. Whole breast Sonography, in Symposium on Ultrasound of Small Parts. *Radiol Clin North Am* 1985;23:157-67.
13. Bhothisuwan W. Ultrasound of the Breast in Thailand, from Water Bag Technique to Colour Doppler Ultrasound in Panels and Oral Presentation EP 42 Ultrasound in Breast and Bone Diseases, AFSUMB in China 1995.
14. Bhothisuwan W. Evidence Based Benefits and Drawbacks of Breast Ultrasound in Asian Women, Educational Lecture in 12th World Congress of the World Federation for Ultrasound in Medicine and Biology in Australia 2009.
15. Bhothisuwan W. Correlation of Breast Ultrasound and Mammography in Educational lecture in ABDA with SIS in Indonesia 2010.
16. Bhothisuwan W, Maruekatat N. Early Detection of Breast Cancer Using Breast Ultrasound in Educational Lecture, Fifth Asian Workshop in Ultrasound, AFSUMB Workshop in Philippines 2008.
17. Bhothisuwan W, Bhothisuwan K, Suwanakul P. Axillary Lymph Node Ultrasound with FNA in Breast Cancer in Educational lecture: Indonesia Annual Scientific Meeting in Indonesia 2007.
18. Statistic record and data system from Siriraj Breast Center 2004.
19. Chou Y H, Tiu C M, Chen J, et al. Automated full-field Breast Ultrasonography: The Past and The Present. *J Med Ultrasound* 2007:15:31-44.
20. Bhothisuwan W. Highlight on breast US, new innovation and recent knowledge lesions in Educational Lecture MUST Annual Scientific Meeting in Thailand, 2009.

Discussion

Burn management is seeing dramatic progress at the time being, with burn patients being managed under the co-operation of multispecialists, together with improved dressings, improving outcomes. The fluid electrolyte correction, based on calculation of total body surface area and burn area and expressed as a percentage is an important factor to show the area burn and correlation amount of fluid lost. Factors including age, burn size and, and the presence of inhalation injury to the respiratory system have been used to predict management outcomes. The Baux score is highly correlated with length of stay in hospital and final outcomes. The revised Baux score takes into account the effect of inhalation injury. Patients with inhalation injury would have their score calculated by body area affected + age of patient + 17. The best burn units have revised Baux score of ISO-140. The revised Baux score is more accurate than the original method. Patients with multiple injuries in addition to major burns have the worst prognosis.

Examples of cases with major burn

Severe deep burn

Figure 1: *Deep burn with gangrene of right forearm*

Figure 2: *Deep burn after fasciotomy*

High voltage electrical injury

Figure 3: *A patient with deep electrical burn at chest wall and left forearm.*

Figure 4: *Left leg developed gangrene and was sacrificed*

Figure 5: *Dark myoglobinuria*

Figure 6: *Four days after debridement*

Inhalation Injury

Figure 7: *Severe burn with inhalation injury*

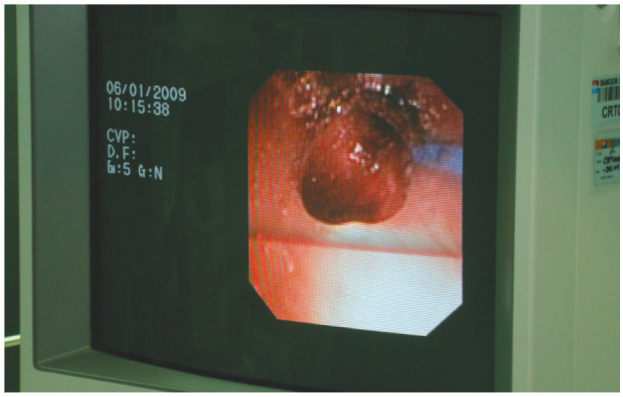

Figure 8: *Inhalation injury, 6 days later still ulcer at bronchus*

Figure 9: *Inhalation injury with dark sputum*

The Application Of The 256-slice Multi-Detector Computed Tomography (MDCT) With Minimally Added Contrast Volumel technique for RVOT Ablation Planning In Brugada Syndrome

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Keywords:
Brugada syndrome, 256-slice MDCT, RVOT, LV-coronary artery, minimally –added contrast volume MDCT technique, conventional MDCT technique, Hounsfield Unit, ROI

OBJECTIVE: To prove that the modified MDCT technique (single scan with minimally added contrast volume technique) can be used effectively in the right ventricular outflow tract (RVOT) and coronary artery structure demonstration and assessment before RVOT ablation with acceptable-readable image quality in cases of Brugada syndrome.

MATERIALS AND METHODS: We retrospectively analyzed image quality of Brugada Syndrome patients who were planned for RVOT ablation and underwent 256-slice MDCT scanning using both conventional and modified techniques, i.e. minimally added contrast volume technique with iodinated contrast injection. The quality of the images obtained from MDCT using the modified technique was assessed in terms of acceptability and readability by the criteria of CT attenuation value of the region of interest (ROI) equal to or more than 250 HU (Hounsfield Unit).

RESULTS: Between 2009 and 2012, a total of 13 Brugada syndrome patients (13 males mean age of 44.2 ± 10.87 years old, mean weight 63.61 ± 9.6 kg) who were planned for RVOT ablation were enrolled. All these patients underwent MDCT to demonstrate RVOT and coronary artery structure for pre-ablation planning. Nine of thirteen patients underwent 256-slice MDCT using the ECG-gated modified, minimally added contrast volume technique. All these nine patients provided the RVOT and coronary artery images that met acceptable-readable criteria, CT attenuation value > 250 HU). Four of thirteen patients underwent 256-slice MDCT scan using conventional technique of CTA for pulmonary artery. RVOT images of two patients and the coronary artery images of another two patients who underwent 250-slice MDCT scan using ECG-gated conventional technique of CTA for pulmonary artery did not meet the acceptable-readable criteria (HU < 250). The analysis showed the optimum contrast volume used in modified technique in our hospital was the value of calculated volume plus 10-15 ml and the total volume was not less than 60 ml for patients weighing 50-75 kilograms, regardless of heart rate, and we would recommend that it should not be less than 60 ml, otherwise image quality is detrimentally affected. Comparing to the MDCT, using the conventional technique in a separate scan to demonstrate RVOT and coronary artery, the exposure dose of radiation of the modified technique was as same as ECG-gated CTA for pulmonary artery scan only and the total contrast dose was also reduced by about one third.

CONCLUSION: Using modified minimally added contrast volume technique with the 256-slice MDCT is very convenient and can be used effectively in demonstrating RVOT and coronary artery for RVOT ablation planning in Brugada's syndrome cases with acceptable and readable image quality

Radiofrequency ablation (RFA) is a new, alternative treatment for Brugada Syndrome.[1] Radiofrequency ablation, using two catheter navigation systems (CARTO and EnSite), offers advanced ablation therapy for complex arrhythmias. In this technique, the Multi-Detector Computed Tomography (MDCT) images are shown as three dimensional (3D) images constructed to localize the target area. In case of Brugada syndrome, the target for ablation is RVOT. In Brugada syndrome patients, coronary artery disease should always be assessed before ablation operation. MDCT scanning with contrast for RVOT and for coronary artery evaluation may be requested. Although a double CT scan (two separate scans) can provide all necessary information, however the large dose of radiation and iodinated contrast exposure and indeed the cost are matters of concern. In this article, we detailed the modified double-purpose technique of CT scan which could reduce the radiation and contrast exposure dose in RVOT and coronary artery imaging whilst maintaining acceptable-readable image quality

Materials and Methods

Between 2009 and 2012, a total of 13 cases of Brugada syndrome were scheduled for RFA and underwent 256-slice MDCT scan for RVOT and coronary artery structure demonstration. Exclusion criteria included patients at risk for severe iodinated contrast agent allergy, severe asthma with bronchodilator dependence or elevated serum creatinine > 1.5 mg/dl. To verify the effectiveness of the modified, minimally added contrast volume technique, we retrospectively assessed the image quality of RVOT and coronary artery in terms of CT attenuation value ≥ 250 HU which is the minimum requirement value for MDCT diagnostic image.[2]

CT angiography (CTA) for RVOT and coronary artery

CT studies were performed on 256-slice MDCT (Brilliance ICT, Philips, Netherlands) scanner with bolus tracking protocol. A bolus volume of iodinated contrast injection was calculated by the formula of scan time (5 -6 sec. for pulmonary artery scanning) plus post threshold delayed time (~5 sec.) and multiplied by flow rate (4.5-6 ml/sec.) as per Philips company protocol. Five to fifteen (5-15) milliliters of contrast agent was added to the calculated volume. A contrast bolus was injected into brachial vein at a flow rate of 4.5-6 ml/sec. , followed by 50 ml. saline solution injection. The tracking position was placed at the pulmonary trunk and scan started automatically at 5 sec. after reaching the threshold (100 HU.). Cardiac scan length covered from the carina angle to 2-3 cm. below the diaphragm using the following parameters: x-ray tube potential 120-140 kV, tube current 471 MA, slice collimation 128x0.625 mm . , table speed of 44 mm/sec., and pitch 0.16. The slice thickness was of 0.625 mm. The mean RVOT- coronary artery scan time was 5 sec. The retrospective electrocardiographic gating was routinely used for cardiac phase selection. The CT attenuation HU value of the ascending aorta was used to represent the HU value of the coronary artery. The CT attenuation HU value was measured at the RVOT itself. The MDCT image data was independently and blindly analyzed by three experienced cardiac CT specialists. The acceptable/readable RVOT and coronary artery image quality for pre-ablation CARTO sound image-merging process and assessment was determined using CT attenuation value ≥ 250 HU as a cutoff criteria. The patient's body weight (kg), calculated and actual contrast use (ml), the total added volume of contrast (ml), the CT attenuation value of RVOT(HU) and of ascending aorta–coronary artery (HU) were reported in range.

Results

In our study, thirteen Brugada syndrome patients were recruited. The average age of the patients was 53.8 years old and the average weight was 63.6 kilograms (range 51-78 kg). The heart rate of all patients ranged from 52-91 beats per minute. All of these patients were planned for RVOT catheter ablation, using CARTO sound navigator. The 256-slice MDCT scan with contrast injection was requested for RVOT and coronary structure demonstration in all patients. Nine patients (9/13) underwent 256-slice CT scan using the modified double purpose technique. All of RVOT structures and coronary artery segments were studied. The MDCT image quality of the right ventricular outflow tract (RVOT) and coronary artery as acceptable/readable use a cutoff criteria of CT attenuation of the region of interest that is equal or more than to 250 HU (Hounsfield unit). CT attenuation value of 250 HU is the minimum requirement value for diagnostic images.[2] Four patients (4/13) underwent the conventional technique for CT angiography for pulmonary artery. The CT attenuation value of the RVOT and ascending aorta-coronary artery of all nine patients (100%) who underwent 256-slice MDCT scan with the modified, minimally added contrast volume technique met the cutoff point criteria (Table 1, Table 2).

Four patients who underwent conventional technique of CTA (CT angiography) for pulmonary artery did not meet the acceptable readable criteria in a single scan as shown in Table 3. The averaged contrast volume used in the conventional technique was as calculated volume. The averaged contrast volume use in modified technique was the calculated volume plus 5-15 ml in any heart rate. By the result of CT attenuation value analysis, the recommended volume of contrast use was calculated volume plus 10-15 ml for the patient's weighs less than 80 kg regardless of the heart rate and the total volume should not be less than 60 ml. For the modified, minimally added contrast volume technique, we used the same protocol as for pulmonary artery scanning and added some contrast agent. The radiation dose exposure of the patients who underwent 256-slice MDCT using the modified technique was the same as the dose needed to perform ECG-gated 256-slice MDCT scan for pulmonary artery.

Table 1: Demonstration of CT attenuation value of RVOT-Coronary artery image evaluation using modified technique (9 cases)

Body weight (kgs)	Calculated contrast volume (ml.)	Actual contrast volume (ml.)	Added contrast volume (ml.)	CT attenuation value of RVOT(HU.)	CT attenuation value of Ascending aorta (HU.)
> 75					
78	50-55	60-65	5-10 (8)	>250	>250
76	50-55	70-75	10-15(15)	>300	>250
> 70					
71	50-55	60-65	10-15 (10)	>300	>250
71	55-60	65-70	10-15 (10)	>400	>250
> 65					
67	55-60	70-75	10-15 (14)	>250	>400
> 60					
61	50-55	60-65	10-15 (12)	>250	>400
> 50					
52	50-55	50-55	15- 20 (15)	>400	>400
51	50-55	60-65	10-15 (10)	>300	>300
51	50-55	60-65	10-15 (10)	>300	>400

Table 2: Demonstration of Average CT attenuation value of RVOT - Coronary artery images using modified technique (9 cases)

Body weight (kgs)	Mean calculated contrast volume (ml.)	Mean actual contrast volume (ml.)	Mean added contrast volume (ml.)	Mean ROI of RVOT (HU.)	Mean ROI of Ascending aorta (HU.)
BW>60 kgs (6 cases)	52.7± 3.5	63.7± 5.9	11.5± 3.5	333.2± 36.6	298.0 ± 77.1
BW<60 kgs (3 cases)	47.6± 2.9	63.3± 5.8	11.7± 2.5	369.9± 40.6	398.9 ± 84.9

Table 3: Demonstration of Average CT attenuation value of RVOT - Coronary artery images using modified technique (9 cases)

Body weight (kgs)	Mean calculated contrast volume (ml.)	Mean actual contrast volume (ml.)	Mean added contrast volume (ml.)	Mean ROI of RVOT (HU.)	Mean ROI of Ascending aorta (HU.)
> 60					
66	50-55	50-55	0	>250	**<250**
66	60-65	60-65	0	**<250**	>300
65	55-60	55-60	0	>400	**<250**
> 50					
51	50-55	50-55	0	**<250**	>250

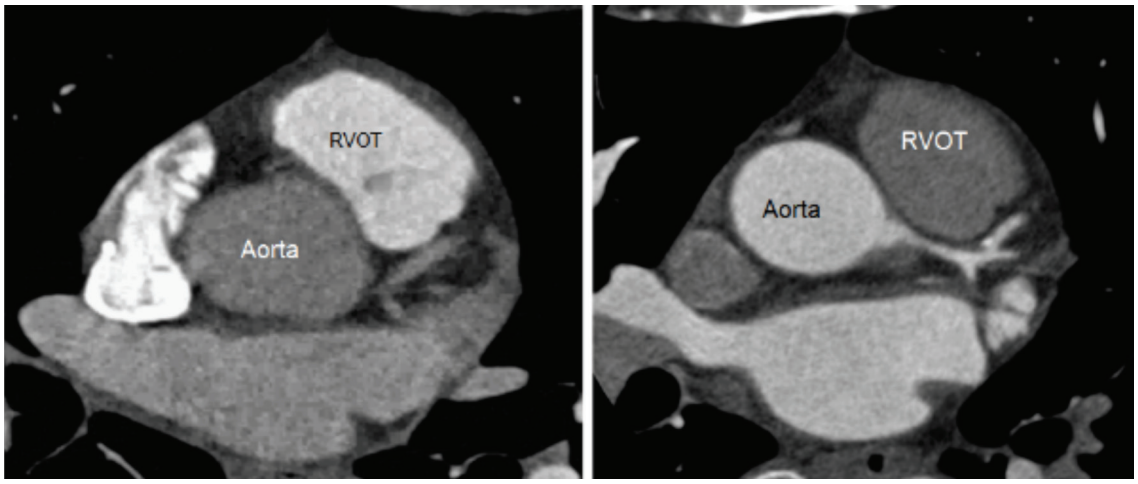

Figure 1: *Demonstration of the RVOT images and ascending aorta-coronary arteries obtained from 256-slice MDCT using conventional technique*

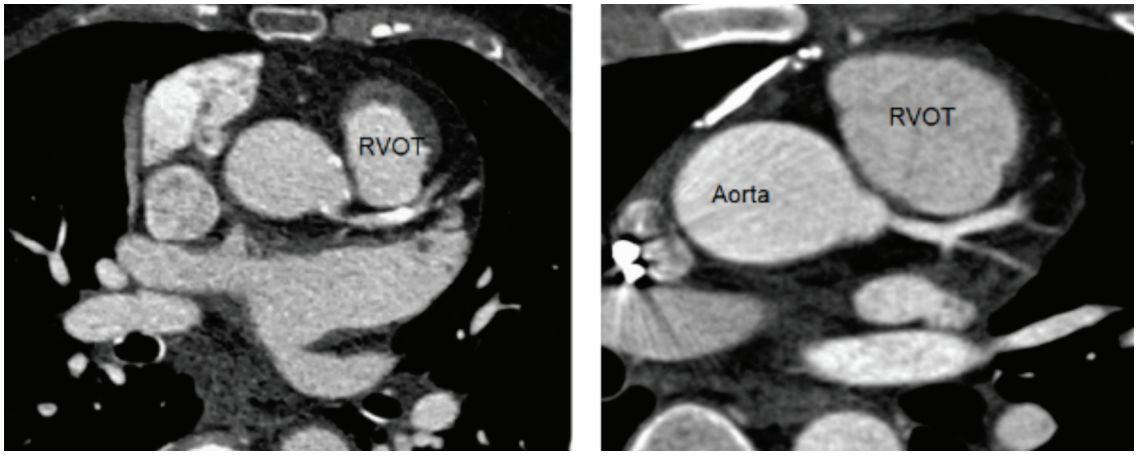

Figure 2: *Demonstration of the RVOT images and ascending aorta-coronary arteries obtained from 256-slice MDCT using modified minimally added contrast volume technique*

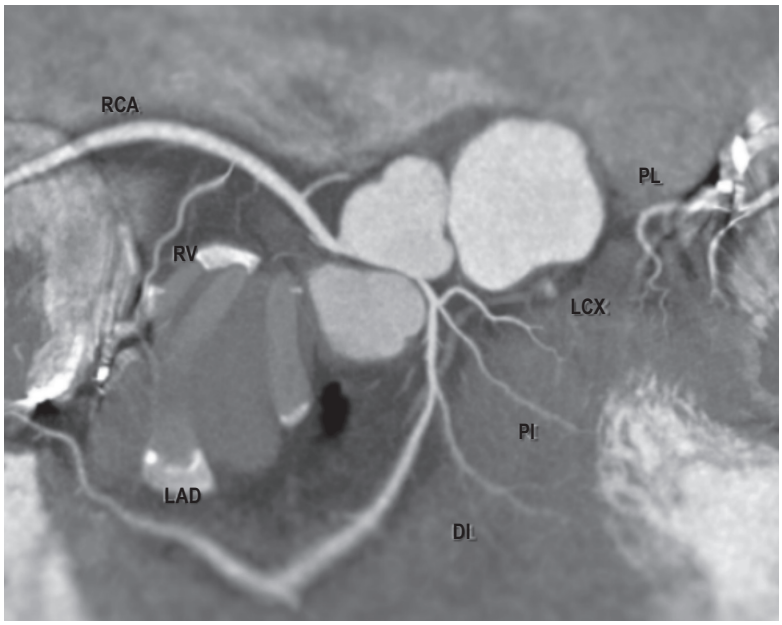

Figure 3: *Multiplanar reconstruction (MPR) image of all coronary arteries obtained from 256-slice MDCT scan with using modified, minimally added contrast volume technique*

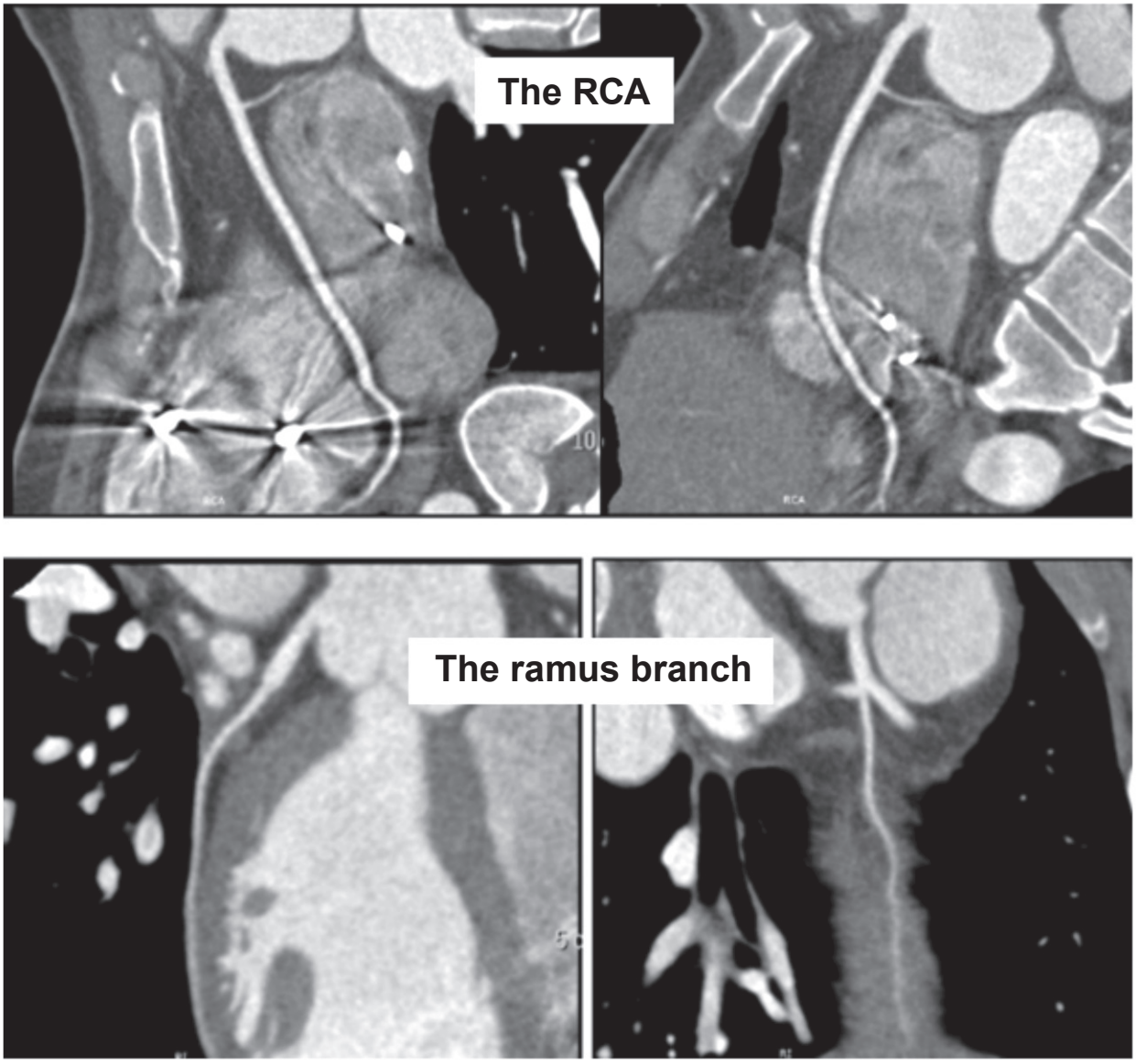

Figure 4: *MPR image of all coronary arteries obtained from 256-slice MDCT scan using modified technique*

Discussion

The modified minimally MDCT technique was proposed with the aim of demonstrating the RVOT and coronary artery in single scan to simultaneously lower the contrast and radiation exposure dose but with no degradation of the image quality. The important factors which impact image quality are heart rate, breath holding and patient weight. For the modified technique, we used the same protocol as for pulmonary artery scanning and added some contrast agent. Comparing to the conventional technique, the averaged volume of contrast use was reduced by about 30% of that used in conventional techniques for coronary artery (at least 45 ml) and pulmonary artery scan (at least 45 ml). In addition, radiation and contrast exposure dose was significantly lower compared to the conventional technique. ECG-gated triple rule-out technique is the model of our study. It has been proposed to be used to rule out diseases of the aorta, coronary and pulmonary arteries. The differences between ECG gated triple rule-out protocol and ours are the location of tracker placement. With regard to our protocol, the tracker location was the pulmonary artery and all protocol parameters were fixed as in CTA for pulmonary artery scan, except the volume of contrast use. Contrast volume that is used as following the triple rule-out technique protocol is higher than our protocol because triple rule-out technique is used for three regions

of study. The total contrast use for 256-slice MDCT using triple-rule-out technique is at least 70 ml (scan time 8 sec. for whole aorta scanning) plus post threshold delayed time (~6 sec.) and multiplied by flow rate (5-6 ml/sec.) as per Philips company protocol. Furthermore, ECG-gated triple protocols remain challenging because of limited ability of subvolume MDCT scanners to rapidly cover a large volume (at least from aortic arch to cardiac inferior wall), the requirement of large volume iodine contrast and high radiation dose.[4] Pre-ablation preparation in Brugada syndrome needs only two regions of study, RVOT and coronary artery. Hence it is not necessary to use triple rule-out protocol for this purpose. The modified, minimally added contrast volume technique protocol has no limitations as triple rule-out protocol and also reduces the contrast and radiation exposure dose by nearly a half compared to two scans with conventional technique (10-12 millisievert (mSv) for ECG-gated pulmonary artery, 16 mSv for ECG -gated coronary artery scan). Compared to triple rule-out protocol, the radiation exposure dose of our modified technique is lower (19 mSv VS 10-12 mSv). By these advantages of our technique, this modified technique could be applied for two regions of study

Conclusion

The 256-slice MDCT scan with modified, minimally added contrast volume technique is a single MDCT scan technique which can be used effectively in demonstrating RVOT and coronary artery for pre-RVOT ablation planning with acceptable and readable image quality in Brugada syndrome patients whose body weight is in the range of about 50-75 kilograms. The proposed calculated formula for contrast volume is scan time (5-6 sec. for pulmonary artery scanning) plus post threshold delayed time (~5 sec.) and multiplied by flow rate (4.5-6 ml/sec.) plus 10-15 ml.

Study limitations

According to the results from our relatively small number of subjects, the proposed calculation for contrast volume use in the modified technique cannot be extended to the patient who has a body weight of more than 75 kilograms without corresponding decrease in image quality. All of our subjects were Thai people, who have on average a lower body weight than Caucasians.

Acknowledgement

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References

1. Nademanee K, Veerakul G, Ghandanamattha P, et al. Prevention of Ventricular Fibrillation Episodes in Brugada Syndrome by Catheter Ablation Over The Anterior Right Ventricular Outflow Tract Epicardium. *Circulation* 2011;123:1270-9.
2. Becker CR, Hong C, Knez A, et al. Optimal contrast application for cardiac 4-detector –row computed tomography. *Invest Radiol* 2003;38: 690-4.
3. Weigold W, Olszewski M, Walker M. Low-dose prospectively gated 256-slice coronary computed tomographic angiography. *Int J Cardiovasc Imaging* 2009;25:217-30.
4. Hsiao EM, Rybicki JF, Steigner M. CT Coronary Angiography: 256-Slice and 320-Detector Row Scanners. *Curr Cardiol Rep* 2010;12:68-75.

How Doctors Report: A Corpus-based Contrastive Analysis of Reporting Verbs in Research Article Introductions Published in International and Thai Medical Journals

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Keywords:
reporting verb, medical research article, corpus, contrastive analysis

OBJECTIVES: This study aims to explore the differences in the use of reporting verbs between medical research article introductions published in the international and Thai medical journals, using a corpus-based approach.

MATERIALS AND METHODS: Two comparable corpora were compiled from 50 medical research article introductions published in English language during 2005-2009: 25 introductions from 5 international journals and 25 introductions from 5 Thai journals. All reporting verbs were identified and categorized into 3 types: experimental, discourse and cognition verbs. The differences in the list of these reporting verbs and their usage were examined.

RESULTS: The frequency of occurrence of reporting verbs in the international corpus was 12.61 per 1,000 words, while that of the Thai corpus was 9.87 per 1,000 words. The international journals used 40 reporting verbs, whereas 24 reporting verbs were identified in the Thai journals. In all three categories, the international journals used more reporting verbs than the Thai medical journals.

CONCLUSION: Reporting verbs were used in the international medical research articles with higher frequencies and a wider variety than the Thai medical research articles. The list and examples from both corpora would assist medical researchers in using reporting verbs to write their research articles appropriately.

The function of the introduction section in a research article is to attract the readers' interest by providing sufficient information that encourages the reader to read the rest of the article.[1] Manske recommends that authors should start their introduction by providing a focused review of that research topic and then state the purpose of the research.[2] For the first part, reviewing related literature is important. After doing extensive research, the author will select relevant studies and refer to them in the manuscript. A reporting verb is normally used in a sentence referring to previous studies. As each reporting verb conveys a different meaning, authors should select the verb appropriate to the object, noun, and tone of the sentence.[3] For example, the reporting verb *"conduct"* is used with an *"experiment"*, not a *'question'*.

According to Thomas and Hawes, reporting verbs can be divided into 3 categories: experimental, discourse, and cognition verbs.[4] The first group, experimental verbs, is used when an author refers to the method or procedures of the cited research. These verbs include **show, find, conduct, observe, demonstrate,** and **establish.** Next, discourse verbs refer to any activities related to speech or writing. Some of the discourse verbs are **report, describe, suggest, recommend,** and **conclude.** For the last group, cognition verbs are reporting verbs referring to mental activities.

These verbs include **believe, consider, think, assume, and recognize.** This classification is useful for writers when choosing a reporting verb appropriate to the cited information.

Over the last 50 years, linguists have been greatly interested in using corpus as a tool in language studies.[5] A corpus is a collection of written or spoken texts that represent authentic examples of language in use. A corpus-based research has been conducted in various fields including medicine.[6-11] For example, Nwogu used corpus to study the structures and functions of medical research papers.[6] Wang et al.[7] developed a Medical Academic Word List (MAWL) from online medical research articles. In 2007, a corpus-based study was conducted to explore syntactic structures of medical research article titles.[8]

As English is increasingly important in medical communication worldwide, English is regarded as the international language of medicine.[12] Most international journals accept only research articles published in English. In Thailand, although authors can submit Thai manuscripts, some national journals also require manuscripts in English. Some journals will accept a Thai research article with an English abstract. This emphasizes the importance of English in medical research writing at both national and international levels. Several studies point out that authors who are non-native English speakers face difficulties concerning writing English research articles.[13-15] In addition, English knowledge may affect linguistic characteristics of English manuscripts written by authors who are non-native English speakers Moreover, although manuscripts are written in English and related to medical field, different contexts may affect the writing method that the authors use when referring to previous studies. However, there has to date been no contrastive study of English research articles published in international and Thai medical journals.

Therefore, this study aims to explore the differences in the use of reporting verbs between medical research article introductions published in the international and Thai medical journals using a corpus-based approach

The results will be valuable to medical researchers aiming to publish their manuscripts in national and international journals. Besides, the data from this study can also be used as a guide for teachers of medical writing as well as those developing learning materials and courses.

Materials and Methods

In this study, two comparable corpora were compiled from 50 medical research article introductions, published in the English language during 2005-2009. The research articles in this study had to be from original research articles. The introduction section of each article was examined, as reporting verbs are more frequently used here than in other sections of a paper.

The criteria for selecting medical journals was based on representivity, reputation, and accessibility.[6] The list of international medical journals is the same as those of previous corpus-based medical discourse studies.[6, 16] With regard to the Thai journal corpus, the journals had to be representative for the national level. Although there are a considerable number of journals published in Thailand, some journals are identified as international journals; while some are identified as national journal. Thus, to make sure that the Thai corpus consisted of only national journals, only journals categorized as approved national journals by the Office of the Higher Education Commission were included in this study.[17]

The international corpus consisted of 25 introductions from 5 international peer-reviewed medical journals. These journals chosen were: **The Lancet**, **The British Medical Journal**, **The New England Journal of Medicine**, **The Journal of Clinical Investigation**, and **The Journal of the American Medical Association**. For the Thai corpus, 25 introductions from 5 Thai peer-reviewed medical journals were selected. These journals were **Thai Journal of Hematology and Transfusion Medicine**, **Thai Journal of Health Research**, **Srinagarind Medical Journal**, **Songklanagarind Medical Journal**, and **Thammasat Medical Journal**. The general information of both corpora is shown in Table 1.

Table 1: The characteristics of the international and Thai corpora

Characteristic	International corpus	Thai corpus
Total number of introductions	25	25
Average number of paragraphs per introduction	3.52	2.76
Average number of sentences per introduction	15.00	15.44
Average number of words per introduction	387.00	344.36
Total number of words in the corpus	9,675	8,609

Table 2: Frequency of reporting verbs in two corpora

Corpus	Frequency of occurrence	Total words in corpus	Frequency of occurrence per 1,000 words
International	122	9,675	12.61
Thai	85	8,609	9.87

Table 3: Top 5 reporting verbs in two corpora

Rank	International corpus		Thai corpus	
	Reporting verb	Frequency of occurrence per 1,000 words	Reporting verb	Frequency of occurrence per 1,000 words
1	show	2.17	show	1.86
2	suggest	1.76	report	1.74
3	report	0.93	find	1.16
4	find	0.62	demonstrate	0.81
5	think	0.52	associate	0.46
			study	0.46

After the corpus compilation, all reporting verbs were identified and categorized into 3 types: experimental, discourse and cognition verbs.[4] To compare the results from two corpora accurately, the frequencies of occurrence were normalized to a basis per 1,000 words. The frequencies of occurrence and the list of reporting verbs identified from both corpora were compared and the differences were examined.

Results

Twenty-five international research article introductions (100%) used reporting verbs; while reporting verbs were used in 21 Thai research article introductions (84%). Regarding frequency of occurrence, the international corpus had a higher frequency of occurrence of reporting verbs than the Thai corpus (12.61 per 1,000 words vs. 9.87 per 1,000 words) as shown in Table 2.

The 5 most prevalent reporting verbs in the international corpus were **show**, **suggest**, **report**, **find** and **think**. In the Thai corpus, the 6 most prevalent reporting verbs included **show**, **report**, **find**, **demonstrate**, **associate** and **study** (The verbs "associate" and *"study"* were in the same rank.). **Show, report** and **find** were frequently used in both corpora (Table 3)

Forty reporting verbs were identified from international research article introductions; whereas only 24 reporting verbs were identified from Thai research article introductions, as shown in Figure 1. In term of the categories of reporting verbs, both international and Thai medical journals used experimental verbs in the highest percentage (52.50% and 50.00%, respectively). Discourse verbs were used in the second rank (37.50% and 41.67%, respectively) and cognition verbs were used in the lowest percentage (10.00% and 8.33%, respectively).

For the first category, 21 experimental verbs were found in the international research article introductions; while only 12 experimental verbs were identified in the Thai research article introductions. Nine experimental verbs found in both corpora included **show, find**, **demo strate**, **associate**, **identify**, **prove**, **reveal**, **conduct**, and **observe** (Table 4). Twelve experimental verbs were found only in the international corpus; whereas 3 experimental verbs were found only in the Thai corpus.

As shown in Table 5, the international research article introductions used more discourse verbs than the Thai research article introductions. Eight discourse verbs used in both corpora were **suggest**, **report**, **recommend**, **provide**, **conclude**, **describe**, **indicate**, and **predict**. Seven discourse verbs were found only in the international corpus; while 2 discourse verbs were found only in the Thai corpus.

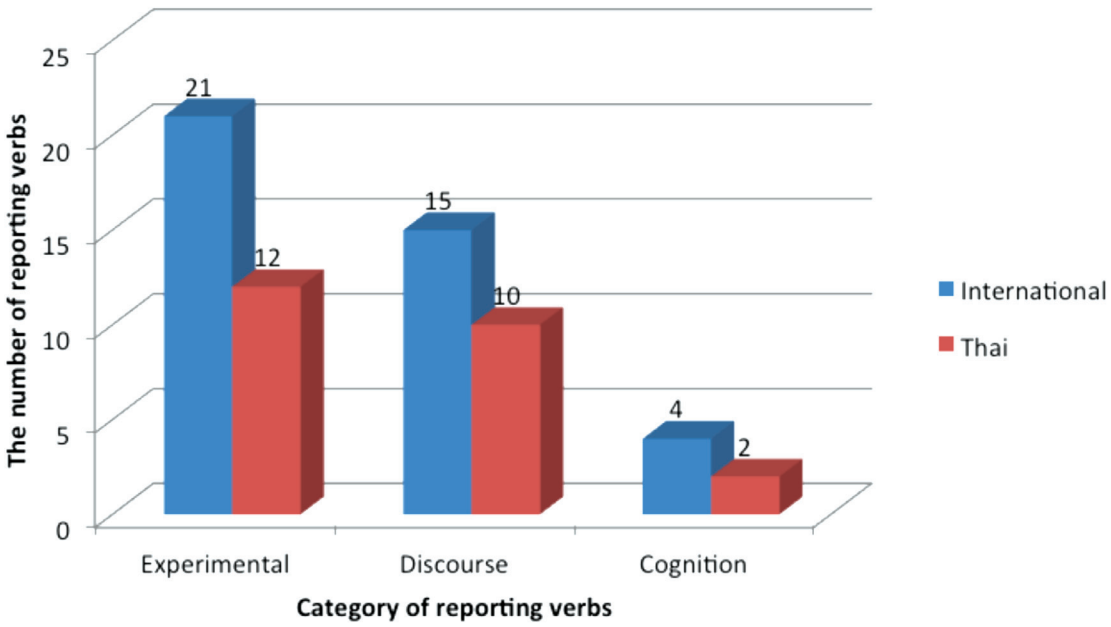

Figure 1: *The number of reporting verbs found in both corpora in each category*

Table 4: Experimental verbs in both corpora (listed according to the frequency of occurrence)

Experimental verbs		
Both corpora	Only international corpus	Only Thai corpus
show	detect	study
find	compare	assess
demonstrate	estimate	correlate
associate	evaluate	
identify	investigate	
prove	see	
reveal	analyze	
conduct	attempt	
observe	establish	
	illustrate	
	perform	
	set up	

Table 5: Discourse verbs in both corpora (listed according to the frequency of occurrence)

Discourse verbs		
Both corpora	Only international corpus	Only Thai corpus
suggest	agree	document
report	ascribe	put forward
recommend	discount	
provide	emphasize	
conclude	note	
describe	say	
indicate	support	
predict		

Table 6: Cognition verbs in both corpora (listed according to the frequency of occurrence)

Cognition verbs		
Both corpora	Only international corpus	Only Thai corpus
focus on	think	none
believe	consider	

Table 6 shows that 2 cognition verbs, **focus on** and **believe**, were found in both corpora; while **think** and **consider** were found only in the international corpus. No cognition verb was found only in the Thai corpus.

From both corpora, 207 sentences using reporting verbs can be used as examples for practice of research writing. They represent real use of reporting verbs in authentic documents. All these sentences would be beneficial for novice researchers as a guide to start writing their manuscripts. Examples of sentences using three prevalent reporting verbs in top 5 lists of both corpora are shown in Table 7. The examples vary in terms of tense and voice.

Table 7: Examples of sentences using reporting verbs, show, report and find, from both corpora

Reporting verb	Corpus	Example
Show	International	*Earlier studies have shown community occupational therapy given in the home can improve the functional independence of patients with dementia and decrease the burden on the care giver.* (Sentence 1)
		Aspirin started soon after acute MI and continued for a few weeks has been shown to reduce 1-month mortality by about a quarter and the risks of non-fatal reinfarction and stroke by about half. (Sentence 2)
		In this setting, torcetrapib not only increased levels of HDL cholesterol and apolipoprotein A-I but also decreased levels of LDL cholesterol and apolipoprotein B-100 (the latter especially at higher doses) and also showed favorable effects on increasing the size of both HDL and LDL particles. (Sentence 3)
	Thai	*One study showed that music significantly reduced the sensation of labor pain and the distress of labor pain.* *(Sentence 4)*
		a) Several comparative studies, both in vitro and in vivo, in animals and in human, have been shown that lenograstim is more active than filgrastim on a weight-by-weight basis. *b) Several comparative studies, both in vitro and in vivo, in animals and in human, have shown that lenograstim is more active than filgrastim on a weight-by-weight basis.* *(Sentence 5)*
	Thai	*It has been shown that Bifidobacterium bifidum and Lactobacillus acidophilus stimulate the systemic immune response (macrophage function and number of immunoglobulin secreting cells) as well as the local immune response (IgA secretion into the intestine).* *(Sentence 6)*
Report	International	*Studies in various countries have reported long-term rates of event-free survival (EFS) of 28–45%.* *(Sentence 7)*
		In a recent review, Lievense et al reported that radiological features were the main mediators of progression of hip osteoarthritis; however, all the included studies had a small study population, follow-up was short, and the studies were hospital based. *(Sentence 8)*
		Furthermore, opportunistic infections of all etiologies have been reported in such patients. *(Sentence 9)*
	Thai	*Amongst type 2 DM, plasma total homocysteine (tHcy) levels in patients with macrovascular complications have been reported to be higher than in those without and in healthy non-diabetic controls.* *(Sentence 10)*

Reporting verb	Corpus	Example
		In 1998, Kuldip, et al. had reported that the optimal dose of vaginal misoprostol for pre-abortion cervical priming was 400 micrograms and its efficacy was dose-dependent. *(Sentence 11)* *It has been reported that 40-50% of infertility is due to a male factor.* *(Sentence 12*
Find	International	*A systematic review found non-pharmacological interventions to produce effect sizes in behaviour similar or larger to those seen with cholinesterase inhibitors, the currently available drug treatment, but without any side effects.* *(Sentence 13)* *Firstly, the cerebral cortex from fetuses with Down's syndrome was found to have increased activity of superoxide dismutase without a compensatory increase in glutathione peroxidase activity.* *(Sentence 14)* *Notably, two epidemiology studies among older individuals have found a dose-response relationship between lower extremity function and serum 25(OH)D concentrations, with one study identifying a threshold of 50 nmol/l for optimal function.* *(Sentence 15)*
	Thai	*In Japan, Kohno found that low dose of rhG-CSF (2 μg/kg or 50 μg/m2 of lenograstim) enables the efficient collection of peripheral blood stem cells after disease-oriented conventional dose chemotherapy in breast cancer patients.* *(Sentence 16)* *a) Each 5 μmol/l increment of tHcy after adjustment for the others known CVD risk factors has found to increase the risk of coronary events by 28 % with the hazard ratio of 1.28.* *b) Each 5 μmol/l increment of tHcy after adjustment for the others known CVD risk factors has been found to increase the risk of coronary events by 28 % with the hazard ratio of 1.28.* *(Sentence 17)* *a) According to a health status and exercise survey of 7,763 elders from 12 provincials public health offices and 1 Bangkok metropolitan public health office, osteoarthritis/rheumatoid arthritis/joint pain were found in 26.4% of the elderly, muscle fatigue & pain were found 18.6%, within 1 month prior to survey muscle fatigue & pain in 23.9% and osteoarthritis/rheumatoid arthritis/joint pain for 22.7%.* *b) According to a health status and exercise survey of 7,763 elders from 12 provincials public health offices and 1 Bangkok metropolitan public health office, osteoarthritis/rheumatoid arthritis/joint pain was found in 26.4% of the elderly, muscle fatigue & pain was found 18.6%, within 1 month prior to survey muscle fatigue & pain in 23.9% and osteoarthritis/rheumatoid arthritis/joint pain for 22.7%.* *(Sentence 18)*

Discussion

This contrastive analysis demonstrated that authors of the international medical journals used a wider variety of reporting verbs than those of the Thai medical journals. Additionally, the frequency of occurrence of reporting verbs in the international corpus was higher than the Thai corpus. These findings are similar to an investigation of lexical bundles used by native and non-native English speakers.[18] More varied lexical bundles were found in academic essays written by native speakers than those of non-native speakers. Thus, the lack of language knowledge may be the cause of this limited reporting verb capacity of the authors of the Thai corpus. This also affects variety of verb choices in writing a research article.

Moreover, wrong grammatical usage of reporting verbs was found in the Thai corpus. Some of these mistakes are presented in Sentence 5a, 17a, and 18a in Table 7. The correct versions of these sentences are shown in Sentence 5b, 17b, and 18b, respectively. From this wrong usage, we can see that the Thai authors tend to make mistakes in passive voice (Sentence 5a and 17a) and subject-verb agreement (Sentence 18a) when using reporting verbs. According to an error analysis of Thai undergraduate writing[19], error in passive voice was found with the highest percentage (80.55%) comparing to other grammatical errors including participial phrase (42.85%), relative clause (49.68%), and subject-verb agreement (5.77%). These findings demonstrate that passive voice is a highly confusing grammatical point for Thais.

Thep-Ackrapong[20] points out that the differences in passive voice structure of English and Thai cause Thai students to make a number of errors in their writing. English passive voice is recognized by using verb to be and the past participle; while Thai passive voice is interpreted by its contextual clues because there is no comparable change in the form of the Thai verb. Error in subject-verb agreement can also be explained by the differences in the use of Thai and English verb form. Unlike Thai, an English verb has to agree with its subject. Despite having learnt the rule, Thais still make the subject-verb agreement error due to first language interference. These differences explain the grammatical mistakes Thai authors make in their articles.

Scully and Jenkins[21] note that some manuscripts submitted from non-English speaking countries may be written in poor English, below the expectations of a scientific publication. They recommend the authors use automated language checking tools and professional language editing services before submission. Also, Iverson[22] suggests that authors should ask for help from professional editors or their peers. According to Breugelmans and Barron[23], in-house medical communications centers provide useful language supports for both native and non-native speaking authors. This can be seen from the Mayo Clinic Section of Scientific Publications and the International Medical Communications Center of Tokyo Medical University. They also emphasize that the collaboration between clinicians and language professionals produce the best manuscripts. Besides, several institutions have developed training program to increase the authors' knowledge and skills in research writing. For instance, the UCSF Neurological Surgery Biomedical Publications Program was designed to help their residents write better research reports.[24] This kind of support can help improve the quality of submitted manuscripts.

Among three categories, experimental verbs were most frequently used in both corpora. This finding accords with the finding of Thomas and Hawes.[4] This may result from the characteristic of the medical field. As medicine is a scientific discipline, the concept and approach is experimental-based. Therefore, it is unsurprising that experimental verbs appeared in the corpora more than discourse and cognition verbs.

The differences in reporting verb use from this study provide useful information to research writers. Although a research article has standard four-section structures: Introduction, Methods, Results, and Discussion, the linguistic characteristics, such as reporting verbs, in these sections may vary in different journals. The international medical journals generally have more manuscripts submitted for publication than national journals, so the authors aiming to publish in high-ranked peer-reviewed journals must put in enormous effort in developing a high quality and convincing manuscript. Using appropriate reporting verbs to present the cited data is a strategy that medical researchers should employ to improve the quality of their writing. The non-native English speaking authors should seek help from professional language editors to ensure that their manuscripts meet the standard of written English. Moreover, medical writing teachers may use the reporting verbs and sentences collected in this study as parts of a useful vocabulary list or sentence examples for their students. Linguists who are interested in medical texts may extend this study to explore other linguistic characteristics of medical research articles.

Conclusion

Although reporting verbs in three categories were found in both corpora, the authors of the international medical journals used a wider variety of reporting verbs than those of the Thai medical journals. Additionally, the frequency of occurrence of reporting verbs in the international corpus was higher than the Thai corpus. Medical researchers, English teachers and materials developers should take these differences into account.

References

1. Zeiger M. Essentials of Writing Biomedical Research Papers. New York: Mcgraw-Hill, 1991.
2. Manske PR. Structure and Format of Peer-Reviewed Scientific Manuscripts. *The Journal of Hand Surgery* 2006; 31:1051-5.
3. Godfrey J. How to Use Your Reading in Your Essays. Basingstoke: Palgrave Macmillan, 2009.
4. Thomas S, Hawes TP. Reporting Verbs in Medical Journal Articles. *English for Specific Purposes* 1997;16:119-38.
5. Anthony L. Issues in the Design and Development of Software Tools for Corpus Studies: The Case for Collaboration. In: Baker P, editor. Contemporary Corpus Linguistics. London: Continuum, 2009.
6. Nwogu KN. The Medical Research Paper: Structure and Functions. *English for Specific Purposes* 1994;13:129-48.
7. Wang J, Liang S, Ge G. Establishment of a Medical Academic Word List. *English for Specific Purposes* 2008;27:442-58.
8. Wang Y, Bai Y. A Corpus-Based Syntactic Study of Medical Research Article Titles. *System* 2007;35:388-99.
9. Millar N, Budgell BS, Kwong A. Quantitative Corpus-based analysis of the Chiropractic Literature -A Pilot Study. *Journal of Canada Chiropractic Association* 2011;55:56-60.
10. Clugston M. An Analysis of Citation Forms in Health Science Journals. *Journal of Academic Language and Learning* 2008;2:A11-A22.
11. Banpho P. A Survey of Writing Techniques, Authorship, Tenses, Voices and Length of Opening Sentences of Medical Research Articles. *PASAA* 2004;35:69-87.
12. Maher J. The Development of English as an International Language of Medicine. *Applied Linguistics* 1986;7:206-18.
13. Mišak A, Marušić M, Marušić A. Manuscript Editing as a Way of Teaching Academic Writing: Experience from a Small Scientific Journal. *Journal of Second Language Writing* 2005;14:122-31.
14. Benfield JR, Howard KM. The Language of Science. *European Journal of Cardiothoracic Surgery* 2000; 18:642-8.
15. Cho DW. Science Journal Paper Writing in an Efl Context: The Case of Korea. *English for Specific Purposes* 2009;28:230-9.
16. Li L, Ge G. Genre analysis: Structural and Linguistic Evolution of the English-medium Medical Research Article (1985-2004). *English for Specific Purposes* 2009;28:93-104.
17. Office of the Higher Education Commission. List of Approved National/International Journals. (Accessed June 27, 2012, at http://www.research.chula.ac.th/rs_news/2554/files/304-9533.pdf.)
18. Ädel A. Recurrent Word Combinations in Academic Writing by Native and Non-Native Speakers of English: A Lexical Bundles Approach. *English for Specific Purposes* 2012;31:81-92.
19. Abdulsata P. An Error Analysis of Srinakharinwirot University Second-Year English Major Student Composition. M.A. Thesis, Srinakharinwirot. University, 2000.
20. Thep-Ackrapong T. Teaching English in Thailand: An Uphill Battle. *Journal of Humanities Parithat* 2005;27 :51-62.
21. Scully C, Jenkins S. Publishing in English for Non-native Speakers. *Oral Oncology* 2006;42:753.
22. Iverson C. US Medical Journal Editors' Attitudes Toward Submissions from Other Countries. *Science Editor* 2002;25:75-8.
23. Breugelmans R, Barron JP. The Role of In-House Medical Communications Center in Medical Institutions in Nonnative English-Speaking Countries. *Chest* 2008; 134:883-5.
24. Eastwood S, Derish PA, Berger MS. Biomedical Publication for Neurosurgery Residents: A Program and Guide. *Neurosurgery* 2000;47:739-48.

Differentiation between ruptured Baker's cyst and deep vein thrombosis (DVT)

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Keywords:
ruptured Baker's cyst, deep vein thrombosis, calf pain and swelling.

In cases of calf pain and swelling, diagnosis by physical examination alone may be difficult. Emergency physicians will need the history and duration of occurrence as well as routine laboratory findings to help them make the decisiom. Initial investigation may begin with ultrasound, followed by magnetic resonance imaging (MRI). We present a case report of using these systems step by step until the diagnosis was established.

Case Report

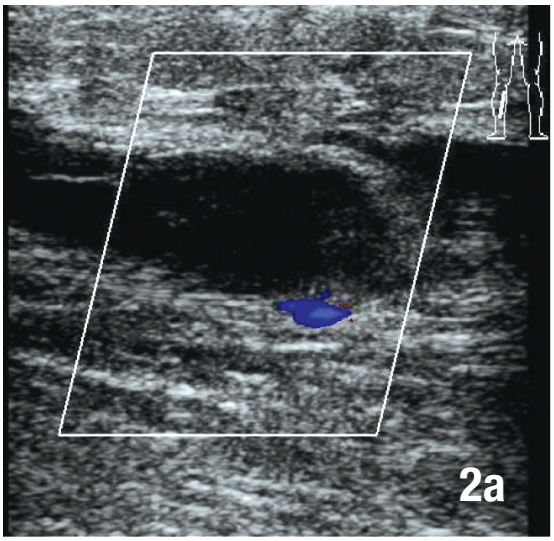
A 67-year-old man, presented to the emergency room (ER) with left knee, calf and ankle pain which developed 2 days prior to admission. His left foot was twisted after a car accident. He subsequently developed severe pain at left knee and leg.

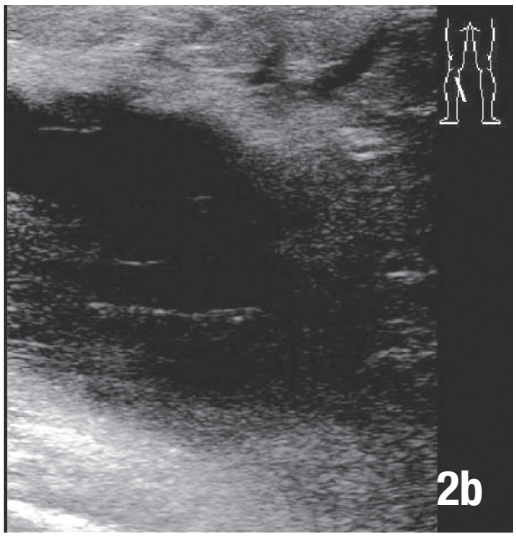
Physical examination

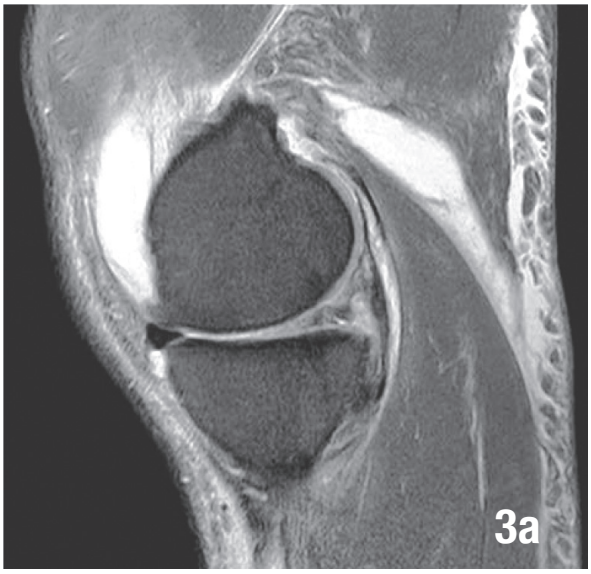
Temperature check revealed low grade fever (T 37.8°C), no dyspnea and normal breath sounds. Left knee was not swollen; ballottement test was negative, limited flexion and extension due to pain. The negative Lachman test indicated neither rips, tears nor palpable mass was detected. Left calf was mildly swollen, and tender. No pain or resistance in the calf was observed during passive ankle dorsiflexion. Left ankle was mildly swollen and tender but it was full range of motion (Figure 1a-b).

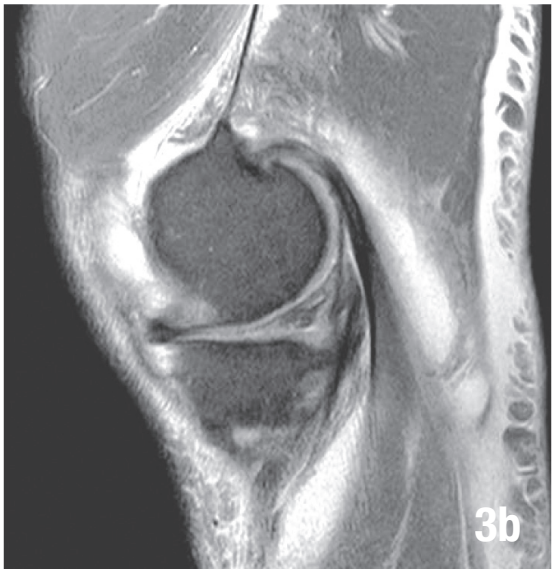

1a


1b









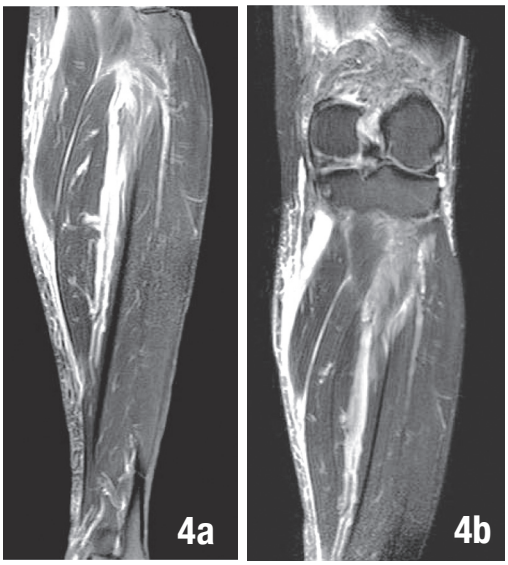
Investigations

Routine laboratory test was unremarkable. The clinical differential diagnosis was cellulitis of left calf and deep vein thrombosis (DVT). Hemocultures were taken and intravenous antibiotics (Rocephin® and Clindamycin®) were administered immediately.

Ultrasound of left leg revealed a echogenic mass at popliteal fossa (Figure 2a). The popliteal vein was compressed by a cystic mass (Figure 2b).

Axial proton density weighted MRI with fat saturation (Figure 3a-b) revealed high signal intensity fluid in the popliteal cyst (Baker's cyst) which was located between medial head of the gastrocnemius muscle and the semimembranosus tendon. There was extension of high signal-intensity fluid inferiorly from the popliteal cyst which surrounded the medial aspect of medial head of gastrocnemius muscle. These fluids dissected subcutaneous tissue of medial aspect of calf and fascia of medial head of gastrocnemius muscle.

Coronal proton density weighted MRI with fat saturation of left knee (Figure 4a) revealed high signal-intensity fluid dissecting subcutaneous tissue of medical aspect of left calf and downward along fascia of medical head of gastrocnemius muscle toward ankle. The signal intensity of gastrocnemius muscle is intact; no atrophic change is noted. Sagittal protein density-weighted MR image with fat saturation of left knee (Figure 4b) shows high signal-intensity fluid extending inferiorly from the popliteal cyst. Continuation of fluid is seen within subcutaneous tissue of posterior aspect of left knee joint. Dissecting fluid is also extending down toward the ankle joint, moderate tear of posterior horn of medical meniscus is also demonstrated on this study.



Hospital course

Symptomatic treatment was started which included physical modalities such as local heat, analgesics, compression, bandages, and close observation. Hemocultures were positive for gram-positive cocci, so IV antibiotics were continued for 1 week. The fever subsided after 1st day of admission; the knee and calf pain swelling were improved. The patient could ambulate on the 3rd day of admission.

Discussion

Causes of calf swelling and related pain include muscular strain, cellulitis, fasciitis, thrombophlebitis, Baker's cyst rupture or rupture of plantaris tendon, compartment syndrome, varicosis, popliteal aneurysm rupture or even neural tumor or malignant histiocytoma. The emergency physician is usually the first person to observe the patient presenting with calf pain and swelling. The physician should examine the leg completely as follows: where is the point of tenderness? Is swelling is localized or generalized? What about skin color; is there any fever? Is there any history of trauma? Do a Diagnostic Tap: is there any serous fluid or blood? The physical examination and lab findings may not be conclusive. In such cases then, ultrasonic scan and MRI can be essential to the definite diagnosis as above mentioned in our case.

The history and duration occurrence may be taken into consideration as well. However though the history of trauma may confirm the diagnosis, minor trauma may not be recognized.

The physical examination in general cannot differentiate a ruptured Baker's cyst from DVT.[1] In rare cases, a Baker's cyst rupture may develop a crescent shaped hemorrhagic sign at the malleolar region. The ultrasonic scan is the initial investigation to evaluate these symptoms. If the diagnostic tap shows hemorrhage, it may indicate ruptured Baker's cyst rather than DVT. The next investigations to differentiate between these entities are duplex and conventional ultrasound. Ward EE et al[2] commented that sonographic detection of Baker's cyst is 100% accurate when fluid is identified between the semimembranous and medical gastrocnemius tendons, in communication a posterior knee cyst. Not all causes though could be demonstrated well by ultrasound, so further study would be MRI which will demonstrate ruptured Baker's cyst and the extent of the disease. The gold standard to demonstrate ruptured Baker's cyst is arthrography. In any case, ruptured Baker's cyst as opposed DVT should be diagnosed definitely before the start of treatment since the treatment is completely different for each.

Conclusion

The diagnosis of calf pain and swelling is difficult to diagnose by history and physical examination alone. Many differential diagnoses are possible. To distinguish between ruptured Baker's cyst vs. DVT requires both conventional and duplex ultrasonic scan and finally MRI for a definite diagnosis as shown by our case.

References

1. Robert SR. Distinguishing Baker's cyst from DVT. *Emergency medicine news* 2003;25:14-6.

2. Ward EE, Jacobson JA, Fessell DP, et al. Sonographic Detection of Baker's Cysts Comparison with MR Imaging. *AJR* 2001;176: 373-80.

Case Report

Improved angiographic findings in a high risk acute coronary syndrome patient after modest weight reduction, regular exercise and medication: *A case report and literature review*

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Keywords:
secondary prevention, exercise, angiographic regression, diet, atherosclerosis, High risk acute coronary syndrome

Case report

A 55-year-old, morbidly obese man body weight (BW) of 104 kg, body mass index (BMI) of 30.5 kg/m^2 with known history of type 2 diabetes mellitus, hypertension, dyslipidemia and primary hypothyroidism, presented with acute chest pain and heart failure in 2007. Frank pulmonary edema and cardiomegaly were documented from admission chest film (Figure 1). The electrocardiogram (ECG) (Figure 2) showed sinus tachycardia, left atrial enlargement, tall R in V2 with ST depression in V2-4, Q wave and mild ST segment elevation in inferior leads. The cardiac enzymes were elevated, troponin T (TnT) of 1.84 ng/ml, CK-MB of 94.15 ng/ml. Echocardiography revealed severe hypokinesia of antero-apical-lateral, infero-posterior wall, causing low left ventricular ejection fraction (LVEF) of below 0.30. After administration of aspirin, clopidogrel, heparin and glycoprotein IIb IIIa antagonist, he was referred for emergent coronary angiography.

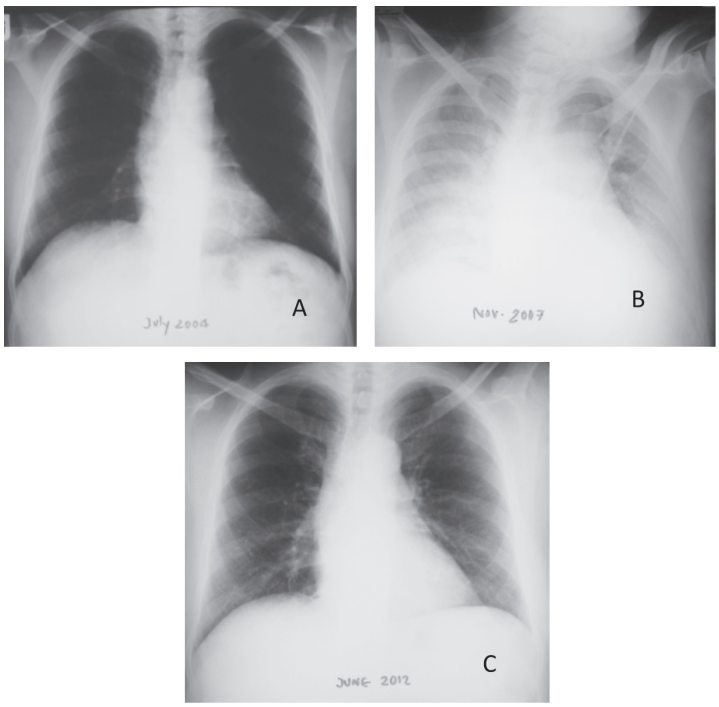

Figure 1: *Chest film shows the baseline normal heart size in 2004 (A). Cardiac enlargement and full blown pulmonary edema in 2007 is shown in (B). Reduction of heart size is noted in 2012 (C).*

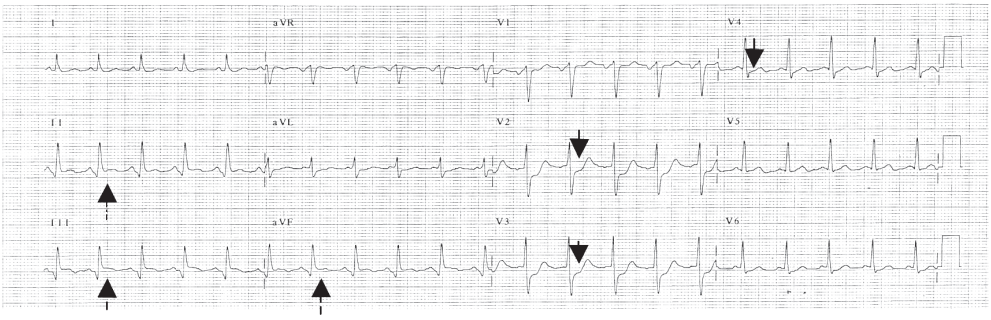

Figure 2: *The first ECG in 2007 showed sinus tachycardia, 124/min, early transition (tall R in V2) with depressed ST segment in V2-4 (black arrow). Q wave and mild ST segment elevation (dashed arrow) was observed in inferior leads.*

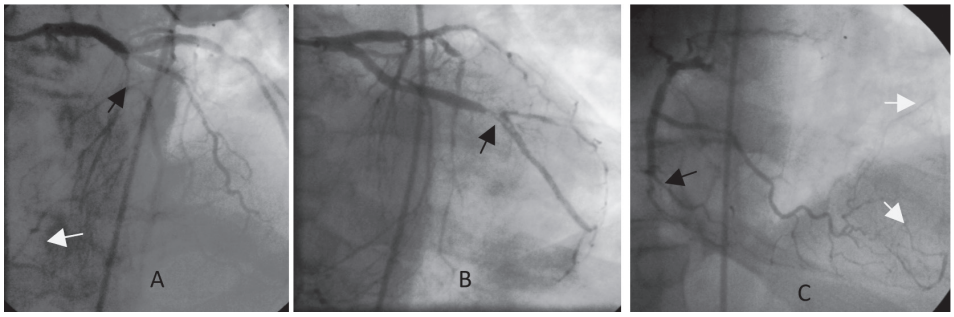

Figure 3: *The occluded proximal LAD (A, black arrow) and the RCA (C, black arrow) are illustrated. Collateral supply from the LAD and Cx arteries to distal part of RCA (A, white arrow) and from RCA to distal part of LAD (C, white arrows) suggested remote obstruction of both vessels. The thrombus containing lesion in mid Cx/OM artery (B) was likely the culprit lesion*

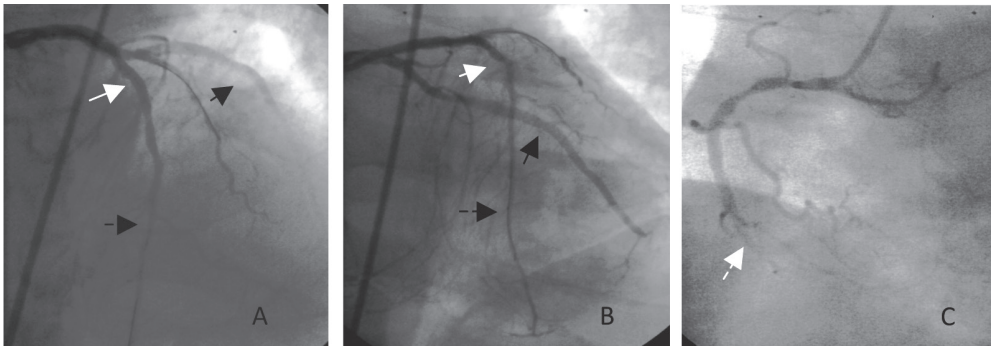

Figure 4: *Final results of stent implantation in the Cx/OM (A&B, black arrow) and the LAD arteries (A&B, white arrow) were illustrated. The diffuse small irregular lumen of the distal LAD artery (A&B, dashed black arrow) was also noted. The old occluded RCA (C, white dashed arrow) was left for medication.*

Emergent coronary angiogram (Figure 3) illustrated severe 3-vessel coronary artery disease (CAD) with two totally occluded vessels, the proximal left anterior descending (LAD) and the dominant right coronary artery (RCA). Collateral supply from the left coronary artery to RCA and vice versa was noted suggesting a chronic occlusion of these arteries. In addition, there was a thrombus containing lesion, causing subtotal stenosis of the mid part of circumflex (Cx) artery which caused this event.

To support the depressed left ventricle, an intra-aortic balloon counter-pulsation (IABP) was performed and did improve his condition. The heart rate decreased from over 120 to 108 bpm. Coronary bypass surgery (CABG) was recommended to the patient and his family members. All of them insisted to have emergent coronary angioplasty for this critical event. Balloon dilatations, following by metallic stents implantation were successfully performed, first at the mid Cx/OM and later at proximal LAD arteries (Figure 4 A-B). The chronically occluded RCA (Figure 3 C) was left for medication. After intervention, he recovered well and was discharged home on the 7th day. The home medication included aspirin, clopidogrel, statin, eltroxin, diuretic, anti-diabetic, angiotensin converting enzyme inhibitors and beta-blockade. The elective CABG surgery was recommended whenever he had recurrent ischemic symptoms, either spontaneous or after stress test induction

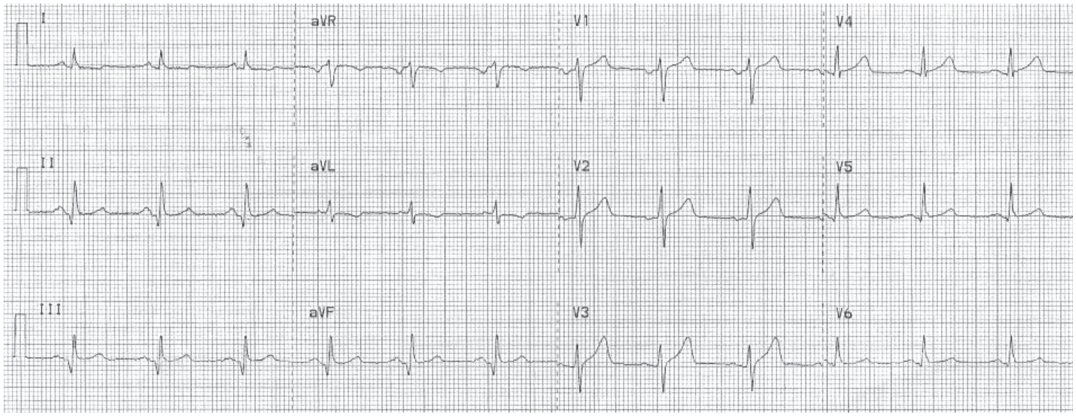

Figure 5: *The ECG in 2012 shows no new ischemic changes. Both Q wave with mild ST elevation in inferior leads and subtle ST depression, <0.5mm, in leads I and aVL are not different from 2007 study.*

Table 1: Most of his biochemical profiles improved from 2007-2012

Parameter	Target	2007	2008	2009	2010	2011	2012	Average 5 years
BW (Kg)	86	104	99.6	93	95.1	98	97.5	96.6
BMI	<25	30.58	29.1	27.2	27.8	28.6	28.5	28.2
BP (mmHg)	<130/80	155/119	135/86	122/80	134/82	137/88	120/70	130/81
HbA_1C (%)	<6.5	10.6	NA	8.6	8.3	NA	8.4	8.4
FBS (mg/dl)		FBS 209		FBS 180	FBS128	FBS 126		
T.Chol (mg/dl)	<200	256	131	122	149	121	145	133.6
TG (mg/dl)	<150	203	150	187	179	154	174	168
LDL-C (mg/dl)	<70	182	65	52	82.9	67	74.1	68.2
HDL-C (mg/dl)	>40	33.6	NA	33.2	39.7	36.9	NA	36.6

BMI=body mass index FBS=fasting blood glucose T.Chol = total cholesterol TG=triglyceride,
LDL-C=Low density cholesterol HDL-C=high density cholesterol NA= not available

After being discharged, he intentionally changed his life-style. As a vegetarian, he reduced multiple meals to twice a day. Under his wife's care, no fried, salty food and no late dinner beyond 19.00 were allowed. He regularly walked, for 30-45 minutes, nearly every day, and consistently took all medication. His dedication resulted in declining of BW, at least 0.5 kg/month. By the year 2009, his BW had decreased 10.5 %, from 104 to 93 kg. The total cholesterol was reduced from 256 to 122 mg/dl. The LDL-C reduced from 182 to 52 mg/dl. The HDL-C increased from 33.6 to 36.9 mg/dl in 2010 (Table 1).

In 2012, he had a brief episode of post-prandial epigastric discomfort, lasting for only few minutes, and decided to come for a checkup. ECG (Figure 5) showed sinus rhythm (75 bpm) and unchanged pattern of inferior Q wave and subtle (< 0.5 mm) ST depression in leads I, aVL. Echocardiogram showed eccentric LVH, normal wall motion except posterior wall hypokinesia. The LV systolic function increased from below 0.30 to 0.57. However, the TnT was mildly elevated, 0.093 ng/ml, so he was referred for repeat coronary angiography.

Coronary angiogram showed the well-patent stented LAD and Cx arteries with no re-stenosis, see Figure 6. No new lesion had developed. Although the proximal RCA lesion was unchanged, the occluded mid vessel was re-canalized (Figure 6C). This allowed a successful balloon dilatation and stent implantation of the distal RCA (Figure 6D). The patient was discharged home with no complication.

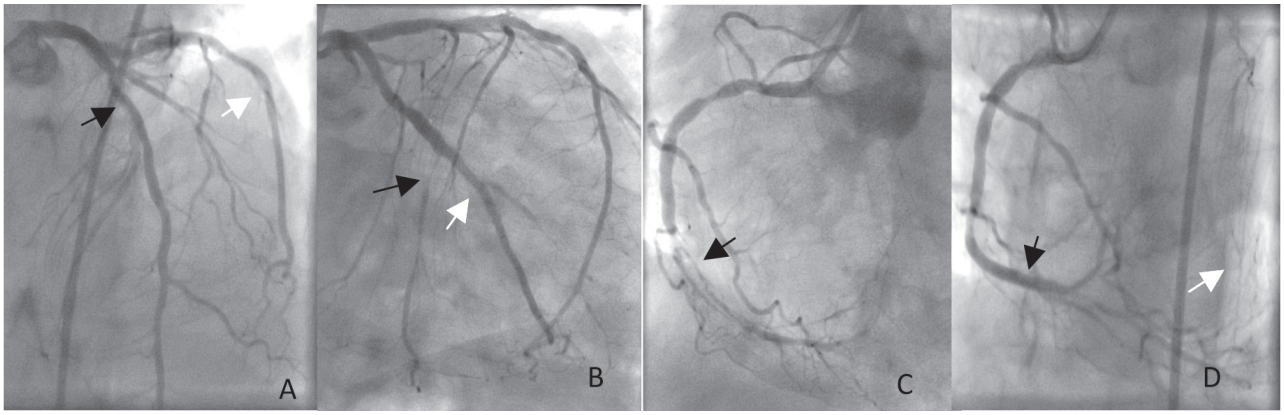

Figure 6: *The stented LAD (A, black arrow) and Cx/OM arteries (A&B, white arrow) were patent with no restenosis. The occluded distal Cx (B, black arrow) and RCA (C, black arrow) were spontaneously re-canalized. PTCA with stent implantation of the RCA (D, black arrow) was performed. Increased collateral supply from RCA to distal Cx artery (D, white arrow) was noted after stent implantation*

Discussion

The high mortality candidate

The presence of myocardial infarction, heart failure and poor left ventricular systolic function (EF below 30%) placed our case in a high-fatality subset. According to the Global Registry of Acute Coronary Events (GRACE) study, the calculated risk score was high as 181 and the predicted in-hospital mortality was 9%.[1] The GRACE score over 140 indicated urgent (within 24 hours) coronary angiography and revascularization as recommended by the current European Society of Cardiology (ESC), the European Association for Cardio-Thoracic Surgery (EACTS)[2] and American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) 2011 guidelines.[3] The angiography in 2007 (Figure 3) clearly explained the 1st ECG manifestations. The well-developed collateral supply to the LAD and RCA not only nourished the underlying ischemic but viable myocardium but also indicated the remote occlusion of these two arteries. The recent thrombus-containing lesion in the mid Cx artery compromised the collateral flow to inferior wall causing re-elevation ST segment of the inferior wall and ST depression in pre-cordial leads. With severely stenotic lesions in all three coronary arteries, the calculated SYNTAX score[4] was 28.5. This intermediate score (ranging from 23-32) predicted a non-significant but higher major adverse clinical events (MACE) at 12 months if he underwent revascularization by percutaneous coronary intervention (PCI) with drug eluting stent (DES), as opposed to the MACE of coronary bypass surgery (CABG), 16.6% vs. 11.7%, $p = 0.1$.[4] Nevertheless, in accordance with the family's wishes, bridging PCI with metallic stent implantations of the LAD and the Cx arteries was successfully performed. He recovered well and was discharged home within 7 days. The estimated 6-month mortality by GRACE score, was 13% and the rate of death or myocardial infarction (MI) was high as 40%.[1] Although an elective CABG was strongly recommended for better long-term outcome, he did well with no recurrent chest pain for five years.

Benefits of diet, exercise, and weight reduction in CAD cases

Being overweight (BMI > 25-29.9) and obese (BMI > 30) increases cardiovascular disease development and its mortality[5,6] as presented in our case. Obesity flourished metabolic syndrome[7] produces pro-inflammatory cytokines[8], furnishing pro-thrombotic states[9] and accelerates atherosclerosis. Reduction of initial body weight by 5-10% has been shown to improve cardiovascular risk factors and other health benefits.[10] This modest body weight reduction can be achieved by combining dietary control and regular exercise.[11]

Regular aerobic exercise decreases myocardial oxygen demand[12], increases coronary flow to microcirculation and improves endothelial function.[13] Exercise-based cardiac rehabilitation has been associated with improvement of cardiovascular risk profiles and reduction of all-cause, cardiovascular mortality.[14,15] Current secondary prevention guidelines recommend a moderate intensity of physical activity, for at least 30 minutes, continuously or intermittently (preferably 60 minutes) at least 5 days/week.[16]

Along with walking 30-45 minutes a day, our patient reduced multi-meals vegan diet to twice a day. Generally a vegetarian diet contains less energy, lower percentage of fat and cholesterol but is richer in fiber and folate content if compares with a regular mixed diet.[17] The inverse relation between fruit, vegetable and fiber consumption and myocardial infarction has been observed in a large

Italian epidemiologic study of 46,693 subjects.[18] In one single blind randomized control trial of 406 post-MI Indian patients, the vegetarian assigned group was associated with a significant reduction of total cardiac events including fatal or non-fatal MI and sudden death when compared with the regular diet assigned cases.[19] The benefit of low-fat vegetarian diet and intensive lifestyle modification including aerobic exercise had been shown to provide more atherosclerosis regression when compared to the control group.[20] By 2009, our patient achieved 10% BW reduction (from 104 to 93 kg; BMI decreased from 30.58 to 27.2 kg/m^2). His enlarged heart size reduced (Figure 1C) and LVEF became normalized.

An improved angiographic finding in 2012

The very brief episode in 2012 was less convincing for myocardial ischemia. The admission ECG showed no new ischemic changes on top of the old findings in inferior and high lateral leads. Echocardiogram showed improved LV systolic function with normal LVEF of 0.57. While other abnormal wall motion became normalized, hypokinetic posterior wall persisted. This was not surprising since the RCA was occluded for at least five years. However, the mildly elevated TnT, 0.09 ng/ml, indicated repeat angiographic study in patient with known 3-vessel CAD. It was interesting that there was no significant restenosis in all stented arteries and no new lesion was observed. The improvement in luminal diameter of the distal LAD was quite impressive, as much as the re-canalized distal Cx (6B) and the mid RCA (6C) since more progressive lesions would be expected in most diabetic CAD patients. Owing to the small luminal size of the distal Cx, the only intervention was performed in the mid RCA (7D).

Atherosclerosis regression and mortality reduction

Retardation[21,22] and regression of the atherosclerotic process[23-30] by angiography had been formerly reported in CAD patients treated with lipid lowering agents[23,26,27,30] and life-style modification (i.e. physical exercise and low-fat diet).[24,28,29,31] Angiographic regression although occurred in modest degree, 3- 10% of diameter stenosis, had been consistently observed[23-30] and associated with reduction of clinical events.[26,31] However, reduction of both clinical events and mortality had been only shown in the large trials with cholesterol lowering drugs studies.[32-36] For example, in 4S studies, there was a 42% reduction in coronary deaths and a 37% reduction in cerebrovascular events in patients treated with simvastatin in comparison with a placebo treated group.[32] Recently, plaque regression has been confirmed by a series of cross sectional studies of intravascular ultrasound imaging with simvastatin[37], rosuvastatin[38,39] and atorvastatin.[39] In ASTEROID trial, patients treated with rosuvastatin 40 mg/day achieved significant plaque regression from 64-78% and the mean LDL-C level achieved in this study was 61 mg/dl.[38] This result supported the recommended target for lowering the LDL-C in known CAD cases to below 70 mg/dl.[40] Along with BW reduction, our patient's lipid profiles consecutively improved as listed in Table 1. Total cholesterol decreased from 256 mg/dl to 122 mg/dl and the average LDL-cholesterol over the past five years was 68.1 mg/dl. The HDL cholesterol increased from 33.6 to 39.7 mg/dl in 2010. All of these parameters contributed to the angiographic improvement in 2012.

Conclusion

We presented a high risk acute coronary syndrome case with multiple coronary risk factors who had angiographic improvement of coronary stenosis after five years of combined medication and life style modification. Although we did not perform a comparative analysis with digital angiographic measurement, it was clear that there was no new lesion formation observed and two occluded arteries were re-canalized. This case reminds us about the significant role of modest aerobic exercise, controlling diet and good compliance in medication which is the core recommendation in current secondary CAD prevention.

References

1. Eagle F KA, Gore JM, Sleg PG, et al. The Global Registry of Acute Coronary Events 1999 to 2009-GRACE. *Heart* 2010;96:1095-101.
2. Wijns W, Kolh P, Danchin N, et al. Guidelines on myocardial revascularization. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2010;31:2501-55.
3. Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA Focused Update of the Guidelines for the Management of Patients with Unstable Angina/ Non-ST Elevation Myocardial Infarction (Updating the 2007 Guideline): A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines Developed in Collaboration With the American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Am Coll Cardiol* 2011;57;1920-59.
4. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360:961-72.
5. De Gonzales B, Hartge P, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. *N Engl J Med* 2010;363:2211-9.

6. Zheng W, McLerran DF, Rolland B, et al. Association between body mass index and risk of death in more than 1 million Asians. *N Engl J Med* 2011;364:719-29.
7. Park YW, Zhu S, Palaniappan L, et al. The metabolic syndrome: prevalence and associated risk factor findings in the U.S. population from the Third National Health and Nutrition Examination Survey, 1988–1994. *Arch Intern Med* 2003;163:427-36.
8. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr* 2004;92:347-55.
9. Juhan-Vague I, Alessi MC, Mavri A, et al. Plasminogen activator inhibitor-1 inflammation, obesity, insulin resistance and vascular risk. *J Thromb Haemost* 2003;1:1575-9.
10. Goldstein DJ. Beneficial health effects of modest weight loss. *Int J Obes Relat Metab Disord* 1992;16:397-415
11. Grundy SM, Cleeman JI, Daniels SR, et al. American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation* 2005;112:2735-52.
12. Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001;104:1694-1740.
13. Segasothy M, Phillips PA. Vegetarian diet; panacea for modern lifestyle disease? *Q J Med* 1999;92:531-44.
14. Linke A, Erbs S, Hambrecht R. Effects of exercise training upon endothelial function in patients with cardiovascular disease. *Front Biosci* 2008;13:424-32.
15. Thompson PD, Buchner D, Pina IL, et al. For the American Heart Association. Exercise and physical activity in the prevention and treatment of atherosclerotic cardiovascular disease: a statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity). *Circulation* 2003;107:3109-16.
16. Leon AS, Franklin BA, Costa F, et al. Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in collaboration with the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2005;111:369-76.
17. Smith SC Jr, Allen J, Blair SN, et al. AHA/ACC guideline for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart Lung, and Blood Institute. *Circulation* 2006;113:2363-72.
18. Vecchia CL, Decarli A, Pagano R. Vegetable consumption and risk of chronic disease. *Epidemiology* 1998;9:208-10
19. Singh RB, Rastogi SS, Veram R, et al. An Indian experiment with nutritional modulation in acute myocardial infarction. *Am J Cardio*l 1992;69:879-85.
20. Ornish D, Scherwitz LW, Billings JH, et al. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998;280:2001-7.
21. Brensike JF, Levy RI, Kelsey SF, et al. Effects of therapy with cholestyramine on progression of coronary atherosclerosis: Results of the NHLBI type II coronary intervention study. *Circulation* 1984;69:313-24.
22. MAAS Investigators. Effects of simvastatin on coronary atheroma. *Lancet* 1994;344:633-38.
23. Blankenhorn DH, Nessim SA, Johnson RL, et al. Beneficial effects of combine colestipol-niacin therapy on coronary atherosclerosis and coronary venous bypass graft. *JAMA* 1987;257:3233-40.
24. Ornish DM, Scherwitz LW, Brown SE, et al. Can lifestyle changes reverse atherosclerosis? *Lancet* 1990; 336:129-33.
25. Gould KL, Ornish D, Kirkeeide R, et al. Improve stenosis geometry by quantitative coronary arteriography after vigorous risk factor modification. *Am J Cardiol* 1992; 69:845-53.
26. Brown GB, Albers JJ, Fisher LD, et al. Regression of coronary artery disease as a result of intensive lipid lowering therapy in men with high level of apolipoprotein B. *New Engl J Med* 1990;323:1289-98.
27. Kane JP, Malloy MJ, Ports TA, et al. Regression of coronary atherosclerosis during treatment of familial hypercholesterolemia with combined drug regimens. *JAMA* 1990;264:3007-12.
28. Schuler G, Hambrecht R, Schlierf G, et al. Myocardial perfusion and regression of coronary artery disease in patients on a regimen of intensive physical exercise and low fat diet. *J Am Coll Cardiol* 1992;19:34-42
29. Schuler G, Hambrecht R, Schlierf G, et al. Regular physical exercise and low fat diet: effects on progression of coronary artery disease. *Circulation* 1992;86:1-11.
30. Blankenhorn DH, Azren S, Kramsch DM, et al. Coronary angiographic changes with lovastatin therapy. *Ann Intern Med* 1993;119:969-76.
31. Haskell WL, Alderman EL, Fair JM, et al. Effects of intensive multiple risk factor reduction on coronary atherosclerosis and clinical cardiac events in men and women with coronary artery disease: the Stanford Coronary Risk Intervention Project (SCRIP). *Circulation* 1994;89:975-90.
32. Scandinavian Simvastatin Survival Study (4S). Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease. *Lancet* 1994; 344:1383-89.
33. Shepherd J, Cobbe SM, Ford I, et al. For the West of Scotland Coronary Prevention Study Group. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *New Engl J Med* 1995;333:1301-07.
34. Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol. *N Engl J Med* 1996;335:1001-9.
35. The Long-term Intervention with Pravastatin in Ischemic

Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *N Eng J Med* 1998;339:1349-57.
36. Pedersen TR, Faergerman O, Kastelein JJ, et al. High-dose atorvastatin vs. usual dose simvastatin for secondary prevention after myocardial infarction; the IDEAL study: a randomized control trial. *JAMA* 2005; 294:2437-45.
37. Jensen LO, Thayssen P, Pedersen KE, et al. Regression of Coronary Atherosclerosis by Simvastatin: A Serial Intravascular Ultrasound Study. *Circulation* 2004;110: 265-70.
38. Nissen SE, Nichols SJ, Sipahi I, et al. Effect of Intensive compared with moderate lipid lowering therapy on progression of coronary atherosclerosis: the ASTEROID trial. *JAMA* 2006;295:1556-65.
39. Nicholls SJ, Ballantyne CM, Barter PJ, et al. Effect of Two Intensive Statin Regimens on Progression of Coronary Disease. *N Engl J Med* 2011;365:2078-87.
40. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Force of the European Society of cardiology and Other Societies on cardiovascular Disease prevention in clinical Practice. *Eur Heart J* 2012;33:1635-701.

Clinical benefits of therapeutic hypothermia after in-hospital cardiac arrest with surface cooling method in Phyathai 2 Hospital: Two cases report

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Keywords:
therapeutic hypothermia, in-hospital cardiac arrest, surface cooling

Therapeutic hypothermia is a standard recommended treatment for patients after out-of-hospital cardiac arrest. However, clinical benefits of therapeutic hypothermia for patients with in-hospital cardiac arrest have not yet been approved. The present report aims to demonstrate clinical benefit of therapeutic hypothermia in patients with in-hospital cardiac arrest at the Phyathai 2 Hospital.

We reported two cases of patients who were treated with therapeutic hypothermia after in-hospital cardiac arrest. Surface cooling method with Arctic Sun® system was applied in both cases. Core temperature curve and serial laboratory parameters are reported.

Case report# 1

A 65-year-old man with non-insulin-dependent diabetes mellitus (NIDDM), hypertension, dyslipidemia was admitted to the Intensive Care Unit (ICU) because of acute inferior wall type of myocardial infarction with right ventricular infarction. Coronary angiogram showed triple vessels stenosis. Coronary Artery Bypass Graft operation was planned. Unfortunately, cardiac arrest due to ventricular tachycardia developed. After the first successful resuscitation, cardiac arrest due to ventricular tachycardia developed again. However, restoration of spontaneous circulation was achieved after the second resuscitation. He was sent to operating room with Glasgow Coma Scale of $E_1V_TM_1$. Therapeutic hypothermia was started during the operation. The core temperature was 34.8°C when he came back from operating room. Therapeutic hypothermia with surface cooling method by Arctic Sun™ machine was continued. Core temperature was assessed via esophageal route. It took 45 minutes to bring core temperature down to the target of 33°C. Shivering was treated with pethidine and midazolam. The target temperature was sustained for 24 hours. Then, he was re-warmed at rate of 0.2°C per hour until core temperature reached 37°C (as shown in Figure 1). Some clinical parameters are shown in Table 1 and serial basic laboratory data is shown in Table 2.

Post-anoxic myoclonus with electro-clinical seizure was treated with multiple antiepileptic agents. Hemodialysis was initiated during hypothermic procedure for treatment of post-anoxic renal insufficiency. His condition gradually improved including recovery of renal function at 5 weeks of ICU care. He was transferred to a general ward with a tracheostomy tube. One month later, he was alert and able to follow one step commands. After 4 months of hospital rehabilitation program, he regained some motor and cognitive functions. He was able to maintain sitting position on the bed, follow some simple verbal commands, pronounce some words, and swallow pureed food. Finally, he was transferred to another hospital for long term rehabilitation.

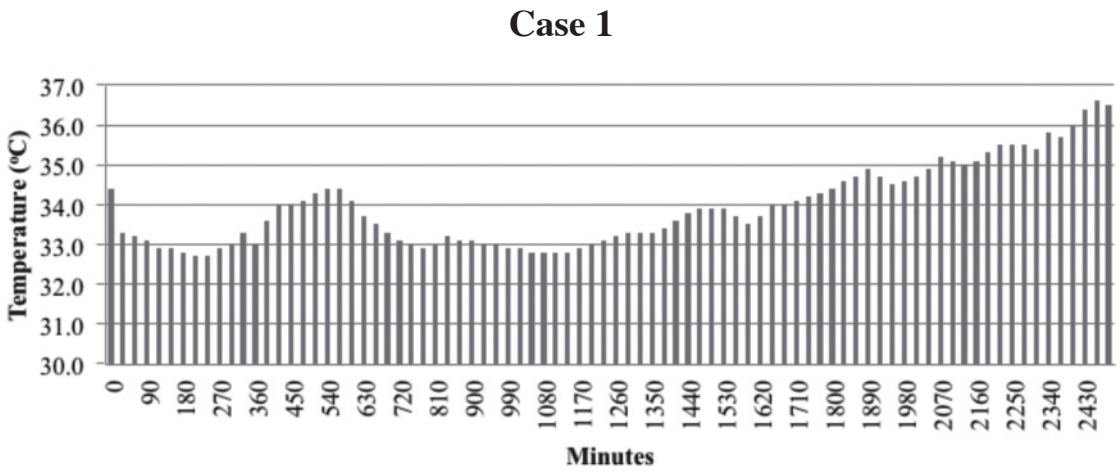

Figure 1: *The temperature curve of case 1*

Table 1: Baseline parameter of cases

Parameter	Case 1	Case 2
Initial Core Temperature	34.4°C	35.2°C
Initial Blood Pressure	88/31 mmHg	193/70 mmHg
Oxygen Saturation	93%	99%
EKG after ROSC*	Normal sinus rhythm with Ventricular Tachycardia	Atrial Fibrillation
Initial Glasgow Coma Score	3 ET	5 ET
Baseline Arterial Blood Gas		
pH	7.103	7.404
pO_2	105.5	587.2
pCO_2	40.1	36.1
HCO_3	12.3	22.1

*ROSC = return of spontaneous circulation

Table 2: Laboratory data of case # 1.

Laboratory	initial	12 hrs	24 hrs	48 hrs	72 hrs
CBC					
WBC cell/mm^3	20,850	22,710	23,570	22,790	26,960
Platelets cell/mm^3	166,000	134,000	65,000	29,000	34,000
PT/PTT	28.2/59.9	ND	24.9/42	24.4/42.7	17.7/ND
BUN (mg/dl)	22.1	33.7	ND	ND	69.2
Cr (mg/dl)	1.68	2.99	3.78	ND	5.32
Na^+ (mEq/l)	136	152	150	143	136
K^+ (mEq/l)	3.7	3.0	3.7	3.6	4.0
CO_2 (mEq/l)	15	17	29	29	23
CPK (mg/dl)	2,336	6,940	9,807	ND	ND
CK/MB (mg/dl)	9.080	58.3	116.3	138.3	ND
Troponin T	7.48	>10	>10	>10	ND
Glucose (mg/dl)	164	157	114	154	198

Case report # 2

A 66-year-old woman with NIDDM, hypertension, coronary artery disease and chronic kidney disease came in for regular twice-a-week hemodialysis. Cardiac arrest due to ventricular fibrillation developed during dialysis at Dialysis unit. Advanced cardiopulmonary resuscitation (PCR) was started immediately.

Restoration of spontaneous circulation was achieved after 20 minutes of CPR. She was sent to ICU and still remained unconsciousness with Glasgow Coma Scale of $E_1M_4V_T$. Arrhythmia was controlled with xylocaine treatment. Therapeutic hypothermia with surface cooling method by Arctic Sun™ machine was started. Esophageal temperature probe was placed for core temperature measurement. It took 4 hrs. 30 mins. to bring core temperature down to the target of 33°C. Shivering was found but successfully treated with pethidine and midazolam. The target temperature was sustained for 12 hrs. Then, she was re-warmed at rate of 0.15°C per hour until core temperature reached 37°C (as shown in Figure 2). Some clinical parameters are shown in Table 1 and serial basic laboratory data is shown in Table 3. Sedative drugs were gradually tapered down during re-warming phase. The patient regained consciousness and Glasgow coma score was raised to 10T ($E_4M_6V_T$) after re-warming. She was extubated 5 days later after AICD implantation. Her motor and cognitive function fully recovered. She was discharged from hospital one week later. Currently, she continues to come in regularly for hemodialysis.

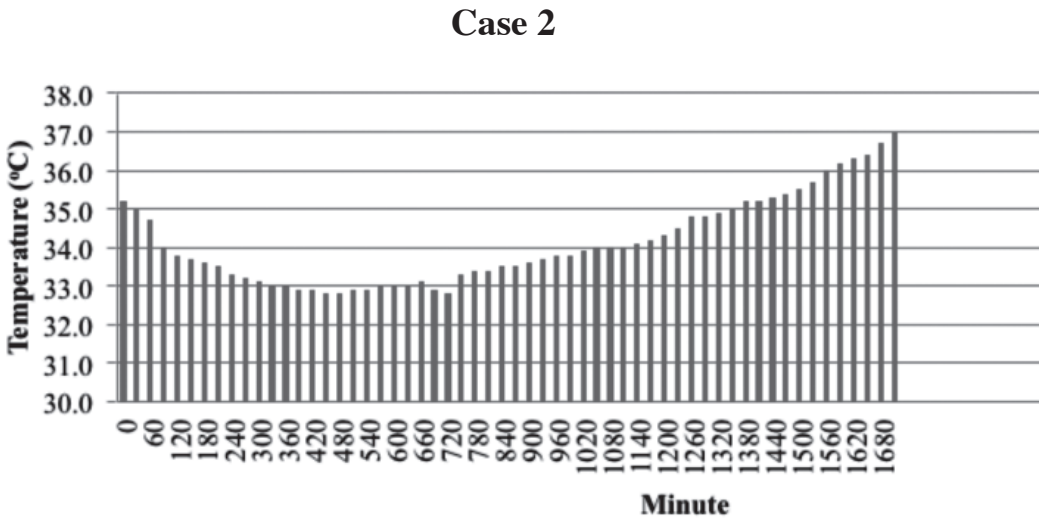

Figure 2: *The temperature curve of case 2*

Table 3: Laboratory data of case # 2.

Laboratory	initial	12 hrs	24 hrs	48 hrs	72 hrs
CBC					
WBC cell/mm^3	13,490	ND	ND	ND	ND
Platelets cell/mm^3	330,000	ND	ND	ND	ND
PT/PTT	10.5/18.1	ND	ND	ND	ND
BUN (mg/dl)	33	45.8	ND	ND	ND
Cr (mg/dl)	5.18	6.2	ND	ND	ND
Na^+ (mEq/l)	128	129	128	130	125
K^+ (mEq/l)	4.3	4.3	4.2	4.5	4.8
CO_2 (mEq/l)	15	23	22	22	23
CPK (mg/dl)	255	ND	ND	ND	ND
CK/MB (mg/dl)	8.930	ND	ND	ND	ND
Troponin T	0.637	ND	ND	ND	ND
Glucose (mg/dl)	119	130	156	164	125

Discussion

Therapeutic hypothermia after cardiac arrest has been the Class 1 recommendation by International Liaison Committee on Resuscitation since 2003.[1] In October 2010, the American Heart Association announced the class 1 recommendation for therapeutic hypothermia after cardiac arrest in part 9 of the guidelines for cardiopulmonary resuscitation and emergency cardiovascular care.[2] The evidence of clinical benefit of therapeutic hypothermia after cardiac arrest derived from two major studies from Europe and Australia.[3, 4] From pooled data analysis of therapeutic hypothermia in out-of-hospital cardiac arrest, one in six patients are helped by having neurological intact survival (number-needed-to-treat [NNT] = 6).[5] Therapeutic hypothermia after cardiac arrest has been successfully implemented in many countries, including some countries in Asia.[6-8] It is also however true to say that there is some controversy over the clinical benefits.[8-9] One retrospective study reported no neurological benefit of therapeutic hypothermia in non-shockable patients with in-hospital cardiac arrest.[10] As yet, therapeutic hypothermia after cardiac arrest is not well established in Thailand.

Several methods of therapeutic hypothermia have been tested. Surface and Endovascular Cooling methods are reliable. These two methods are the most commonly used for therapeutic hypothermia. Surface cooling is less invasive than endovascular method. Surface cooling provides an acceptable hypothermic efficacy. For these reasons, surface cooling is most commonly as the initial method for therapeutic hypothermia after cardiac arrest.[11] However, multimodality methods may be necessary to facilitate achievement of temperature target.[12] Shivering is the last resort defense mechanism to prevent hypothermia. To bring the core temperature down to target, shivering needs to be effectively defeated.[13] Pethidine or Meperidine raises shivering threshold. Pethidine is commonly available worldwide, therefore, is generally used to reduce shivering.[14] Therapeutic hypothermia has not yet been approved as a standard treatment of in-hospital post-cardiac arrest patients. Our initial experience of therapeutic hypothermia after in-hospital cardiac arrest with surface cooling method implies feasibility of its use in clinical practice and clinical benefits are also demonstrated in our patients. However, further clinical study is needed to confirm its clinical benefit in worldwide patients with in-hospital cardiac arrest.

Conclusion

This initial experience of therapeutic hypothermia after in-hospital cardiac arrest with surface cooling method possibly implies clinical benefit and feasibility of its use in clinical practice.

References

1. Nolan JP, Morley PT, Vanden Hoek TL, et al. Therapeutic hypothermia after cardiac arrest: an advisory statement by the advanced life support task force of the International Liaison Committee on Resuscitation. *Circulation* 2003;108:118-21.
2. Peberdy MA, Callaway CW, Neumar RW, et al. Part 9: post-cardiac arrest care: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122: S768-86.
3. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med* 2002;346: 549-56.
4. Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med* 2002;346:557-63.
5. Arrich J, Holzer M, Herkner H, et al. Hypothermia for neuroprotection in adults after cardiopulmonary resuscitation. In: Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd; 2009.
6. Bro-Jeppesen J, Kjaergaard J, Horsted TI, et al. The impact of therapeutic hypothermia on neurological function and quality of life after cardiac arrest. *Resuscitation* 2009;80:171-6.
7. Kim Y-M, Kim J-H, Park K-N. Use of therapeutic hypothermia after cardiac arrest: A survey of the society of critical care medicine in South Korea. *Resuscitation* 2009;80:836.
8. Skulec R, Truhlar A, Knor J, et al. Broad implementation of therapeutic hypothermia after cardiac arrest--Mission possible. *Resuscitation* 2010;81:779-80.
9. Sandroni C, Nolan J, Cavallaro F, et al. In-hospital cardiac arrest: incidence, prognosis and possible measures to improve survival. *Intensive Care Medicine* 2007;33:237-45.
10. Kory P, Fukunaga M, Mathew JP, et al. Outcomes of mild therapeutic hypothermia after in-hospital cardiac arrest. *Neurocrit Care* 2012;16:406-12.
11. Alzaga AG, Cerdan M, Varon J. Therapeutic hypothermia. *Resuscitation* 2006;70:369-80.
12. Kamarainen A, Virkkunen I, Tenhunen J, et al. Induction of therapeutic hypothermia during prehospital CPR using ice-cold intravenous fluid. *Resuscitation* 2008; 79:205-11.
13. Mahmood MA, Zweifler RM. Progress in shivering control. *J Neurol Sci* 2007;261:47-54.
14. Mokhtarani M, Mahgoub AN, Morioka N, et al. Buspirone and meperidine synergistically reduce the shivering threshold. *Anesth Analg* 2001;93:1233-9.

The new Lumbar Spinal Fusion technique: Minimally Invasive Trans-psoas approach (Direct Lateral Interbody Fusion (DLIF®)) and a preliminary report of clinical and radiographic success in Bangkok Spine Academy

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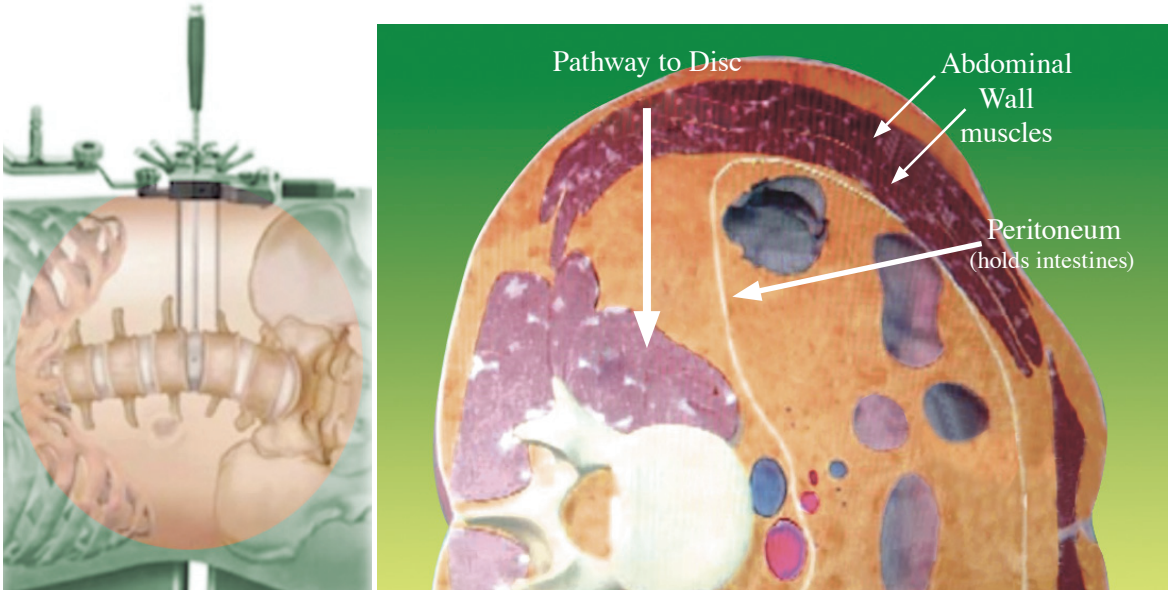
Keywords:
DLIF, direct lumbar interbody fusion, minimally invasive trans-psoas approach, spine surgery

OBJECTIVE. To study the preliminary results in 12 cases who underwent Direct Lateral Interbody Fusion (DLIF) in Bangkok Spine Academy.

MATERIALS AND METHODS. The study of the preliminary results and retrospective chart review of collected clinical and radiographic outcomes in 12 patients who underwent Direct Lateral Interbody Fusion L1-L5 as a treatment for degenerative disc disease, degenerative scoliosis and/or degenerative spondylolisthesis. Clinical outcomes measured include Visual Analog Scale (VAS) and Radiographic outcome.

RESULTS. Twelve patients underwent DLIF between February and July, 2012 with altogether twenty intervertebral disc levels treated. Most cases had indications of back pain with radiation to leg from nerve root compression. Two cases (16.6%) were back pain from a single level severe disc degeneration with signs of instability and unresolved by non-surgical treatment. Five cases (41.7%) were diagnosed with degenerative scoliosis and the other 5 (41.7%) were degenerative spondylolisthesis who did not respond to non-surgical treatment. Mean operative time was 70.6 (±17.7) minutes (mean ± standard deviation). Minimal surgical duration was 41.7 minutes for each level and maximum 110 minutes. Intraoperative blood loss averaged 81.7 mL. Initial pain scores in patient-reported questionnaires (VAS back, VAS legs) showed fast and lasting pain relief and improvement in daily activities. Mean VAS back scores decreased from 5.3 to 0.4. For leg pain assessment, mean VAS scores decreased from 6.3 to 0.3. at the 2 weeks visit. There was a mean correction of 7.9 to 3.2 degrees in segmental coronal plane in all instrumented levels. There was significant change in the overall coronal plane alignment of the lumbar spine. Increasing disc height at middle column 7.0 mm. There were no intraoperative complications. The bleeding during operation was much less than conventional surgery. Neurological examinations showed one patient to have Psoas weakness with anterior thigh numbness, both conditions resolving within 2 weeks.

CONCLUSION. This preliminary short term report of DLIF at Bangkok Spine Academy shows as satisfactory and consistent results as other mini-opened transposes approaches. The benefits of this procedure are reducing leg and back pain, less blood loss, minimized soft tissue injury, wide safety margin of inadvertent complications, especially nerve root injuries, thus less likelihood for long term complications and for lumbar degenerative spine in cases of decompression and fusion.



1a **1b**

Figure 1a-b: *Shows the new lateral trans-psoas approach may be achieving the advantage of lumbar spinal fusion. The retractor passes through loose retroperitoneal space directly to that which needs fusion.*[5]

The true lateral trans-psoas lumbar interbody fusion procedure is a modification of the retroperitoneal approach to the lumbar spine, which uses a tubular dilator/retractor system and was first reported in the literature by Ozgur, et al. in 2006.[1-4] Other terms commonly used to refer to this technique include lateral lumbar interbody fusion, lateral transpsoas interbody fusion (Figure 1a-b), direct lateral interbody fusion (DLIF®, Medtronic Sofamor Danek, Inc., Memphis, TN, USA) and extreme lateral interbody fusion (XLIF®; Nuvasive, San Diego, CA, USA). DLIF and XLIF are different in their instrumentation/ retractor systems, but not in their approach. Even though these minimally invasive lumbar fusion technologies are new and have limited literature reporting on outcomes, this procedure continues to gain popularity among spine surgeons in several countries. Most of the reports show impressive results in clinical and radiographic terms, with few complications. Especially in patients with multilevel degenerative discs which have to be corrected, as in degenerative scoliosis, the advantages of this procedure seem to be clear.

Compared with anterior lumbar procedures (ALIF), DLIF shows superiority in terms of not requiring an access surgeon, eliminating the need to violate or retract the peritoneum and obviating the need for great vessel mobilization.[6] It also eliminates the risk of retrograde ejaculation[7] in males due to inadvertent superior hypogastric nerve plexus disruption during anterior approach procedure and there is reduced incidence of ileus post operation.

One of the major advantages of DLIF is the fact that the supporting back muscle is still intact. The lack of need for bony resection on the posterior column when compared with posterior fusion means that the posterior ligamentous complex *("the tension band of spinal column")* is still functioning during body flexion and extension (which may reduce the chance of adjacent problem). The intact anterior and posterior longitudinal ligament on vertebral column allows the cage to be fixed in the center of body and for better correction of spine in sagittal and coronal alignment, preventing dislocation of the graft and cage, reducing blood loss and operative time (as compared to other approaches in many reports), and reduced postoperative hospital stay and analgesic requirements.

In our center (Bangkok Spine Academy), the DLIF operation has been commenced since February, 2012 (Figure 2). For the purpose of this article, we would discuss the indications and candidates for this operation, the surgical steps, and include preliminary results of the first 12 cases with details of blood loss, complications, radiographic evaluation and early clinical outcome.

Materials and Methods

Indications and surgical candidates

Trans-psoas lateral interbody fusion has the same surgical indication as posterior lumbar decompression or spinal fusion in patients who have axial back pain and/ or radicular leg pain. For example, patients who have

Figure 2: *The occasion of the first operative demonstration of DLIF technique in Thailand on February 17, 2012 at Bangkok Spine Academy, Bangkok Hospital. The surgeon who was invited to perform this operation is on the middle, Dr. Robert Watkins, Jr. from Marina Spine Center, Los Angeles, USA.*

axial back pain from degenerative disc disease, which requires total removal of the disc and segmental spinal fusion or the patient who has **leg pain from spinal stenosis** due to segmental disc degeneration and ligamentum flavum thickening. Especially those who have disc bulging or collapse that are responsible for corresponding foraminal and lateral recess stenosis (but excluding central canal stenosis) are good candidates for this procedure. The total disc removal and space distraction by the cage will open the foramen and both lateral recess directly. L**umbar spondylolisthesis** *"slipped vertebra"* grade 1 and 2 with or without nerve root compression are also the candidate for this procedure. The large intervertebral DLIF cage that was inserted into the disc space will distract the disc height and also the automatic reduction of the slipped vertebra in to normal sagittal alignment and also indirect decompression of the nerve root within spinal canal and its foramen. Lumbar segmental instability such as **degenerative scoliosis** is also the candidate for direct lateral interbody fusion. By this surgery, the segmental coronal tilting automatically reduces due to the insertion of the large intervertebral DLIF cage and when done multilevel, the abnormal global coronal alignment will correct into acceptable balance. Furthermore, it can decompress the neural canal and foramen indirectly in each level to eliminate patient leg pain.

The contraindications of direct lateral interbody fusion technique are congenital spinal canal stenosis, patients who have severe osteoporosis and auto-fusion in between each level that cannot be separated. All L1-2, L2-3, L3-4 disc spaces and the majority of L4-5 discs (lying higher than the bony iliac crest level) are candidates for the procedure. For L4-5 and L5-S1 (lying below the iliac crest level) the procedure is contraindicated.

Patient selection

The enrolled patients in this study had the indication for spinal fusion and/or spinal decompression. All had lesions from L1 to L5 without symptomatic lesion at L5/S1.

Indications
1. Degenerative spondylolisthesis
2. Degenerative Scoliosis
3. Degenerative disc disease (DDD)
4. Spinal stenosis with foramina stenosis
5. All cases who failed conservative treatment such as medication, physiotherapy and/or injection.

Contraindications
1. Severe spinal canal stenosis with congenital narrowing,
2. Severe Spondylolisthesis more than grade 2
3. Very low seated L4-5 disc
4. Prior abdominal and retroperitoneal surgery

During preoperative consultation, each patient was informed of all the surgical options. A complete discussion and description of the approach technique was described to all patients interested in this procedure.

Study design

Data for this study was obtained through retrospective chart reviews and concurrent follow-up of patients who underwent DLIF surgery by a single spine surgeon (T.B.) at Bangkok Spine Academy. Outcome data were obtained prospectively preoperatively and at each visit postoperative through self-administered questionnaires. The roentgeno graphic data was obtained and calculated by another orthopedic doctor (K.J.).

The clinical charts were reviewed to identify the complications and outcomes. Chart review included compilation of demographics (age, gender), symptoms and diagnosis, surgical details (levels treated, instrumentation used, blood loss, operative time, complications), hospital stay, additional procedures, results of physical exams, late-occurring complications and patient complaints, prospectively collected back and leg pain scores (Visual Analog Scale, VAS). The radiographic measurements were taken before and after the operation to assess change in the sagittal and coronal plane alignment of the individual operated disc level, overall lumbar spine, and lumbar scoliotic curves. The radiographs were also analyzed for vertebral fracture, end plate indentation, correction of sagittal and coronal plane, vertebral slip correction in sagittal and coronal plane in each level, nerve root injury, implant malposition, wounds and other possible complications.

Surgical technique

Under general anesthesia, the patient is prepared in the same manner as normal spine surgery. The IV line and urinary catheter are placed. The needle recording electrodes are placed in the innervated muscles in the legs to monitor the affected nerve roots during the procedure, then patient is transferred to operating table and placed in a true 90 degree right lateral decubitus position with the left side elevated and taped in this secured position, bending laterally in such a way as to increase the distance between the iliac crest and the rib cage, making sure the patient's hip is in flexion position for relaxing the psoas muscle and nerve. A cross-table anterior-posterior (AP) image helps to confirm the true 90 degree position (Figure 3).

After aseptic treatment of the skin, AP and lateral fluoroscopic images are used to identify the lumbar disc's mid-position. A marking point is made on the patient's lateral side, overlying the center of the affected disc space. Through this mark, a small incision will be created transversely. The surgeon uses his finger to perform blunt dissection, passing through a lateral abdominal muscle. The layer of muscles are spitted along their fibers until the surgeon's finger can pass the transversus abdominis fascia, then the fat tissue in retroperitoneal space is exposed. The peritoneum and its visceral content are protected and retracted anteriorly with the angle retractor. The retroperitoneal space is bluntly dissected in straight direction until the anterior surface of psoas muscle is exposed (Figure 4).

After the fluoroscope is checked for the correct level, the PAK probe (NIM® X-PAK Probe: connected to the electrophysiological monitoring and using triggered and free running electromyography) is introduced directly into the target disc, making sure the abdominal contents are not in the way. This monitoring method is used to

Figure 3: *Shows the position of the patient for DLIF procedure; mostly on the right lateral decubitus. The table is positioned at maximum bending to keep lumbar intervertebral disc opened.*

Figure 4: *Shows the approach performed by bluntly dissection on the left flank. The finger is passed anterior to the psoas muscle until reaching the tip of spinous process. Make sure the abdominal content and peritoneum are retracted to the front.*

reduce the risk of injuries to the lumbosacral plexus when accessing the disc space through the psoas muscle. After the PAK probe is in the correct position, the guide wire is introduced into the target disc.

The probe is removed, and then sequential dilators are introduced into the psoas muscle in the direction of guide wire, attached directly to the lateral aspect of disc. The ball tip EMG probe (NIMS-Spine ball tip probe) is used to check the final dilator. Make sure there is no lumbosacral plexus nearby this dilator (Figure 5a-b). After that, the proper DLIF retractor can be inserted through the psoas muscle and fixed.

After the dilator is removed, the position of this retractor can be checked by fluoroscope, both AP and Lateral. The ball tip EMG probe is used to check the lumbosacral plexus in all the areas of tubular retractor. After the light illumination fiber optic is attached, the surgical field inside the tube should be inspected to ensure that there are no neural structures in direction of working area. The bleeding is stopped by the bipolar coagulator.

5a **5b** **5c**

Figure 5a: *Shows the sequential dilator (5a) is bluntly passed through the retroperitoneal approach directly to the intervertebral disc until reaching maximal size.*

Figure 5b-c: *The tubular retractor is securely placed in the tract of dilator. Then expose the intervertebral disc. The exposure is around 1 inch diameter; use intra-operative neuromonitoring to make sure it is safe and will not cause nerve injury (Figure 6).*

Figure 6: *Shows the intra-operative neuromonitoring in use to evaluate the lumbosacral plexus, making sure the neural structure is safe from interference by instruments*

The intervertebral disc is opened as a rectangular window, like the size of cage. The disc material is removed by a disc punch. A Cobb elevator is used to separate the disc material and cartilaginous end plate from bony end plate of vertebral body. Under fluoroscopic control using AP imaging (Figure 6a), the Cobb elevator is used to release the annulus on the contralateral side and cross just beyond the disc space. The end plates are then meticulously prepared with the disc shaver, rasps and curettes until the bone is bleeding in order to have a good fusion bed.

We use several serial trial spacers to elevate and trial for the correct size of the implant, as compared to the normal disc. After the final trial, the correspondingly sized DLIF cage (Clydesdale cage, Sofamor Danek, USA) was filled with bone graft/bone graft substitute extender and/or biologic material. (rhBMP-2 *"infuse®"* or demineralized bone graft *"Grafton®"*) see figure 7. We then inserted the implant and impacted it into the disc space to the correct position under fluoroscope guidance (Figure 8c-d).

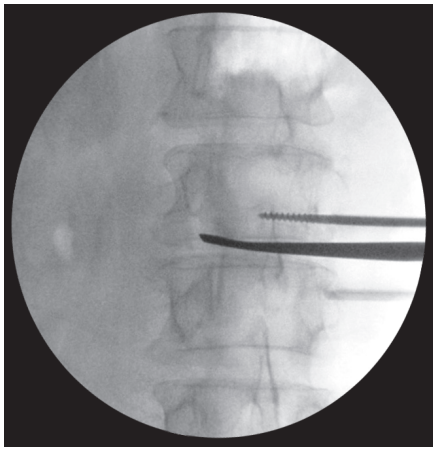


Figure 6a: *Shows the exposed intervertebral disc and disc material is totally removed using the Cob elevator and Curette.*

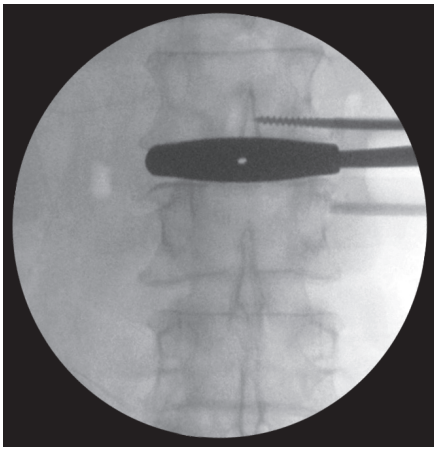


Figure 6b: *Shows serial trial spacer inserted into intervertebral disc space to the correct size and position. Make sure it's well fitted with the vertebrae and distract the spinal column to the normal alignment.*

Figure 7: *The DLIF cage compared to the size of Thumb. Note this cage is bigger than the cage used in posterior approach such as TLIF or PLIF, so the biomechanics support the body weight better. Note the white material inside this cage is the bone forming agent "rhBMP-2 (infuse®)".*

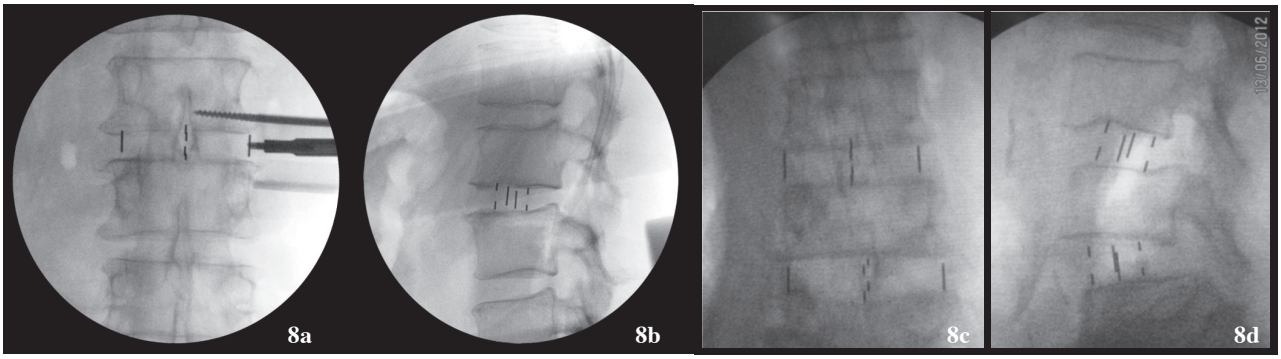


Figure 8a-b: *Shows the intervertebral cage (DLIF cage) as finally inserted into the space and checked under fluoroscopy under AP and Lateral fluoroscope views. Note the minimal breaching of the superior end plate that is almost asymptomatic.*

Figure 8c-d: *Shows two levels of DLIF where cage is in proper position. Note the slippage of vertebra is markedly improved and the intervertebral space is nicely distracted.*

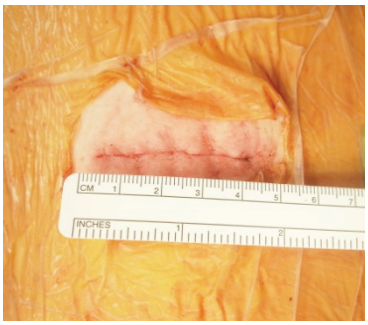


Figure 9: *Shows the size of flank wound after finish DLIF operation is 3-4 cm. One incision can account for 2 levels being fused, meaning this operation is indeed minimally invasive. No need for any drainage from this wound.*

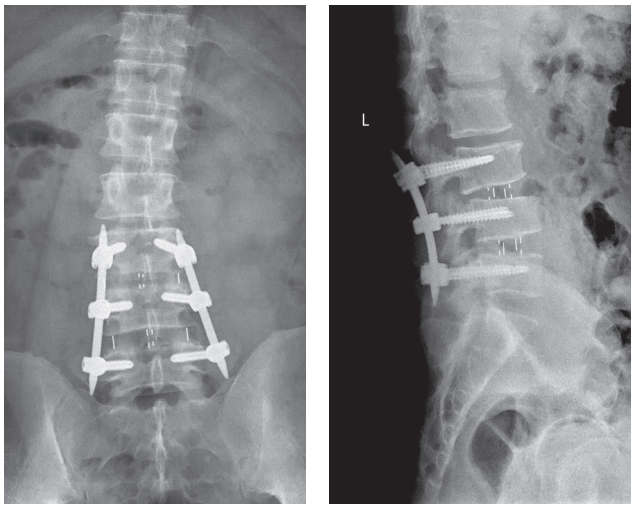


Figure 10: *Shows after DLIF procedure is finished. The augmentation with posterior pedicular screws by percutaneous method is recommended for maximal stability of the vertebral column.*

Some literature reported performing stand-alone DLIF procedures, but we made sure that we augmented the stability of the vertebral segment in all of our patients by percutaneous pedicle screws insertion (Sextant®: Medtronic Sofamor Danek for 1 level fusion and Apollo®: Orthopesia Co., Thailand for 2 or more levels), in order to achieve maximal stability.

Results

Demographic and Clinical Data

All patients had DLIF procedure performed for lumbar degenerative disc disease, spondylolisthesis, or Adult scoliosis. Most cases had indications of back pain with radiation to the leg from nerve root compression. Two cases (16.6%) had back pain only from single level severe disc degeneration with sign of instability and unresolved by non-surgical treatment. Five cases (41.7%) were diagnosed of degenerative scoliosis and another five (41.7%) had degenerative spondylolisthesis that did not respond to non-surgical treatment.

As for the distribution of age and gender, male and female were equal. The average age was 60 years old, (range:37 to 82).

The level of spine that was affected and operated on included L1-2 disc space to L4-5. The spinal levels that were mostly operated on were L4-5 and L3-4 respectively.

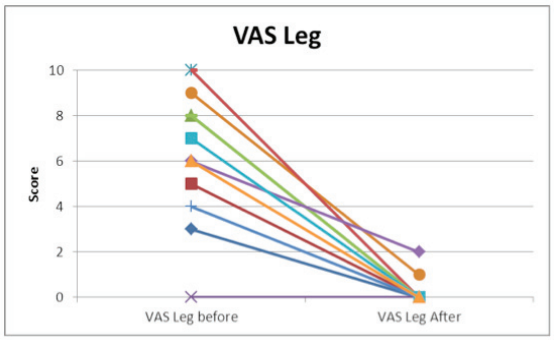
Mean VAS before surgery was 6.3 for leg pain and 5.3 for back pain. Some patients had only one symptom, either back or leg pain.

Because of the preliminary report of DLIF operations in our center, the Oswestry Disability Score that has been collected before operation and then compared with post operative status at 6 weeks, 3 months and 6 months are not yet completed.

Demographic and Clinical Data are shown in Table 1.

Table 1: Demographic and Clinical Data.

Parameter	Mean	Min / Max
Patients (n)	12	
Male	6 (50%)	
Female	6 (50%)	
Age(years)	59.7 (13.1)	37 / 82
Pre-op VAS leg	6.3 (3.0)	0 / 10
Pre-op VAS back	5.3 (3.3)	0 / 10
Diagnosis		
Degenerative Disc Disease	2 (16.6%)	
Degenerative Scoliosis	5 (41.7%)	
Degenerative spondylolisthesis	5 (41.7%)	
Spine levels		
L1-2	2 (10%)	
L2-3	4 (20%)	
L3-4	6 (30%)	
L4-5	8 (40%)	



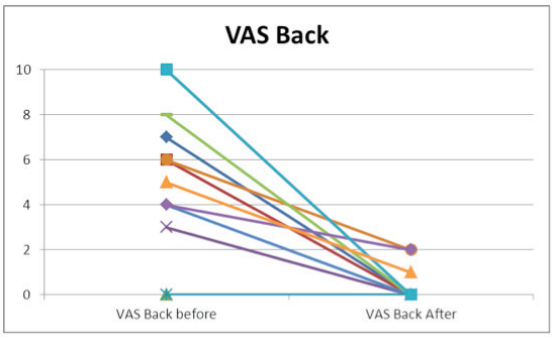
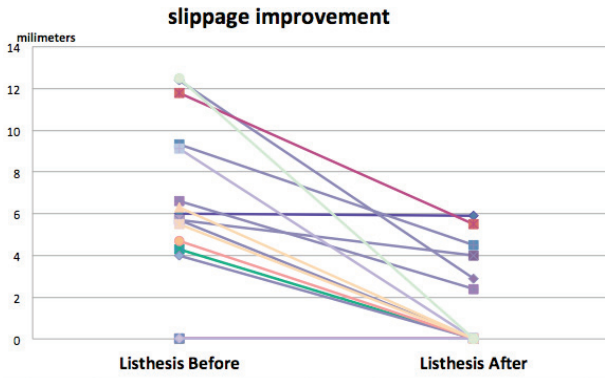
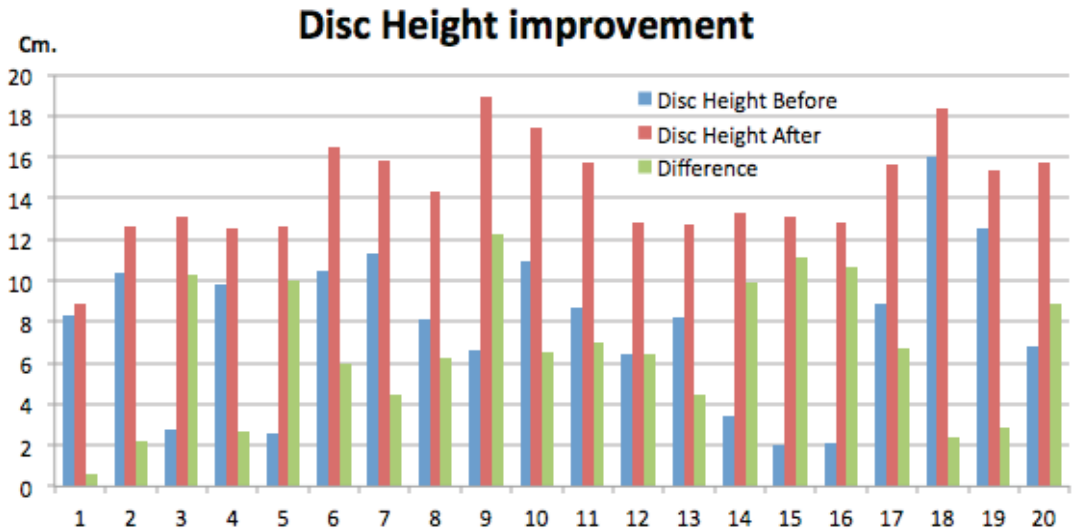


Table 2: Radiological parameters.

Parameter	Mean	Min / Max
Improvement disc height (mm.)	7.0 (±3.0)	1.0 / 12.0
Improvement in coronal angle (degree)	4.5 (±5.6)	0.7 / 21.1
Improvement in slip distance (mm.)	4.0 (±4.0)	0.0 / 12.0





Operative and Clinical outcome

Surgical duration was measured by skin to skin time. Mean operative time was 70.6 (±17.7) minutes (mean ± standard deviation). Minimal surgical duration was 41.7 minutes for each level and maximum 110 minutes. The operative time seemed to be faster after we passed the second case. Intraoperative blood loss averaged 81.7 (±27.6) mL. Minimum blood loss for each level was 30 mL. and maximum was 130 mL. Blood loss mostly occurred during vertebral end plate preparation.

There were no intraoperative complications. The bleeding during operation was much less than conventional surgery. Because of the nature of this operation is indirect reduction, the intra-operative complication that comes from opened surgery such as dura tear does not exist. Neurological examinations showed one patient developed Psoas weakness with anterior thigh numbness, both conditions resolved within 2 weeks.

Clinical scores in patient-reported questionnaires (VAS back, VAS legs) showed fast and lasting pain relief and improvement in daily activities. Mean VAS back scores decreased from 5.3 (3.3) to 0.4 (0.8). For leg pain assessment, mean VAS scores decreased from 6.3 (3.0) to 0.3 (0.6) at the 2 weeks visit.

Radiographic outcome

There was a mean correction of 7.9 to 3.2 degrees in segmental coronal plane in all instrumented levels. There was significant change in the overall coronal plane alignment of the lumbar spine. Increasing disc height at middle column 7.0 (0.3) mm.

Discussion

Low back pain is very common. Even though much back pain comes from non specific problems, many conditions still need to be treated by surgical intervention, for example, neurological compression by pathological structures of lumbar spine such as disc herniation or back pain due to degeneration or instability of the vertebral segments. The most common surgical intervention for neurological compression is surgical decompression, or *"laminectomy"* procedure[9-11] but half of the cases need a more complicated procedure known as *"spinal fusion"* to eliminate segmental instability, reduce back pain, maintain spinal canal in such a way as nerves do not get compressed despite different body positions used in daily life activities. Spinal fusion can also improve spinal alignment for normal human posture.

Lumbar spinal fusion has been recognized as a treatment option for symptomatic spinal instability, spondylolisthesis, and degenerative scoliosis. The aim of fusion is to reduce back pain by reducing the motion of segments; the higher the fusion and possibility of achieving a better fusion rate, the better the patient satisfaction. When spinal fusion technique first began to be used, it was non-instrumented and bone was grafted on the posterior surface of lumbar spine (Figure 10). However, we now know that the non-instrumented spinal fusion rate is less than that achieved from anterior interbody fusion. (Figure 11).[11-14]

Figure 10: *Shows how to do posterior fusion by placing the ship bone graft posteriorly. The biomechanics, rate of fusion, stability was acceptable but inferior to fusion from anterior.*

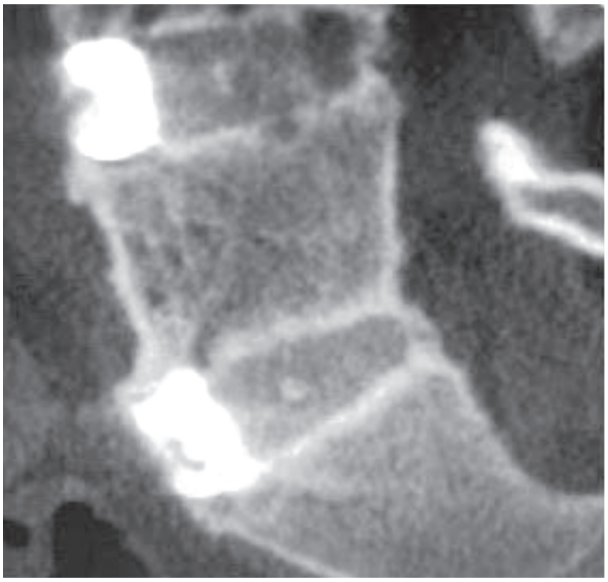


Figure 11: *Anterior lumbar interbody fusion (ALIF) shows the complete fusion at L45 AND l5-S1. Anteriorly fusion shows superiority in terms of biomechanics, rate of fusion, stability and alignment when compared posterior fusion.*

Spinal fusion technologies have continued to develop and improve, from non instrumented fusion that has a limited improvement of spinal alignment to instrumented spinal fusion that can improve both fusion rate and spinal segmental alignment.[11-19] Most surgeons agree that the spinal fusion in the anterior column of spine is better than posterior fusion, as regards fusion rate, ability to keep the segment in normal spinal alignment with both coronal and sagittal balance. Including the overall clinical outcome, anterior column fusion shows a superior result. The only problem of anterior fusion is the difficulty in approach from the anterior abdominal wall and the accessibility through the great vascular bundle in front of the vertebral column (Figure 12).[19-22, 25-26]

Thus the development of *"anterior fusion from the posterior"*, PLIF (Posterior Lumbar Interbody Fusion) or TLIF (Transforaminal Lumbar Interbody Fusion), which achieve the benefits of anterior column fusion but eliminate the difficulties of anterior approach (Figure 13). The surgeon can do anterior fusion from the small opening site at posterior wall of intervertebral disc during posterior decompression and discectomy. The ship bone graft is impacted in the space and the disc height can be restored by small *"cage"* instruments before the spinal segment is held by inter-pedicular screw constructs.

Nevertheless, the posterior approach to anterior column fusion (PLIF, TLIF) is not without drawbacks. The scarring on the back site, continued chronic back pain, back muscle denervation, excessive blood loss, iatrogenic excessive removal of stabilizing bone and ligament structures and also increased post operative pain have all been reported. The overall spinal correction results by PLIF and TLIF are still limited in their ability to restore disc height, or improve the sagittal and coronal alignment. Furthermore the success rate of fusion is also affected by the size limits of bone graft and cage that can be inserted in the small annular hole.[23-24]

As spinal surgery evolves to *"minimally invasive technologies"*[2-5] (Figure 14), the primary goals are to minimize paraspinal muscle retraction and dissection in order to reduce blood loss and post operative pain, accelerate recovery period and improve clinical outcomes. Yet because of the nature of the technique, a multilevel posterior approach needs longer incision, longer muscle denervation, longer destruction on the posterior bone structure for decompression, which means the minimal invasive purpose or ideal may not always be achieved.

The nature of posterior decompression itself also has some drawbacks. The necessity for laminar bone removal in both PLIF, TLIF and also in conventional wide laminectomy can cause problems. The risk of direct neural injury when the laminar roof is removed, the risk of late fibrosis around the neural structure or the iatrogenic disruption of posterior stabilization structures during directed decompression can all be a cause of problems in the future.

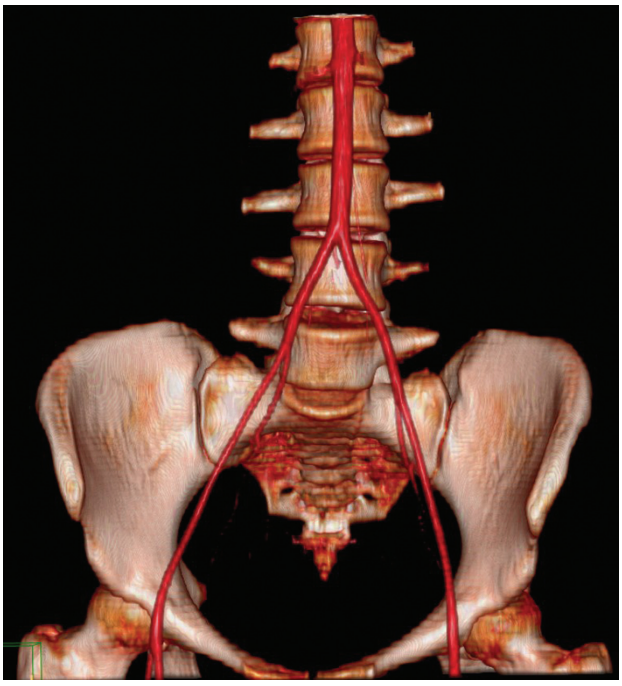


Figure 12: *Show the inferiority of anterior fusion technique is the difficulty in access through the great blood vessels in front of the vertebra. The injuries of these vessel can cause catastrophic complications.*

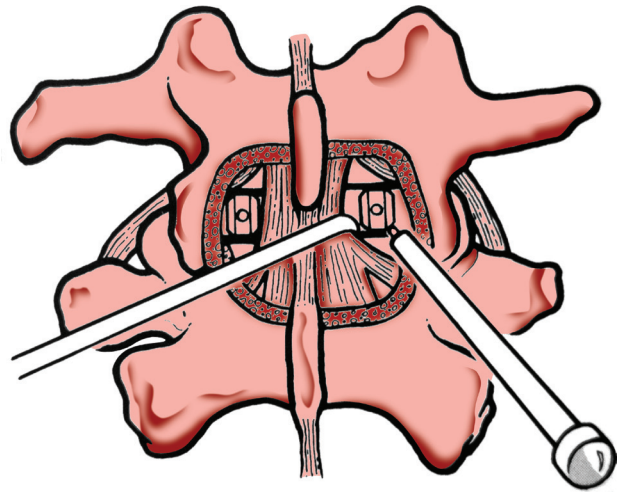


Figure 13: Show the anterior column fusion as made by posterior approach (as in the procedures "PLIF" - posterior lumbar interbody fusion and "TLIF" Transforaminal lumbar interbody fusion). Note the surgeon needs to open the spinal canal and works nearby nerve roots that can cause neural injury. Note also the small cage size inserted from the back, which needs to carry the whole body weight.

Due to the considerations mentioned above, spine specialists look forward to the ideal operation that will achieve goal of nerve decompression and best fusion results within minimally invasive strategy. The anterior column fusion has better outcomes in term of fusion rates but greater risks of serious complication. For minimally invasive anterior spinal fusion, various minimal invasive techniques have been developed such as Anterior Lumbar Interbody Fusion (ALIF) including laparoscopic, endoscopic and mini-open approaches but these all require a steep learning curve for surgeons and continue to have potential for serious complications.[7]

The trans-psoas lumbar interbody fusion procedure is a modification of the retroperitoneal approach to the lumbar spine using a tubular dilator/retractor system coming in the same indication of ALIF. The lateral transpsoas approach is a modification of the anterior retroperitoneal approach to the lumbar spine. The technique was first presented in 2001 by Pimenta1 in VIII Brazilian Spine Society Meeting. After that, several reports have detailed the technique, the safety of the approach, and the clinical benefits

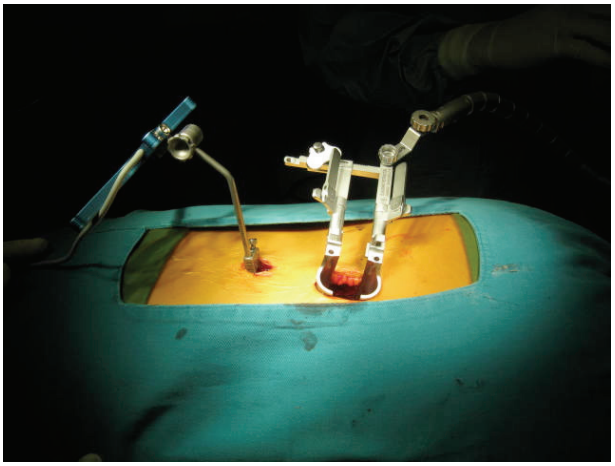


Figure 14: *Shows MIS TLIF Minimal invasive decompression and interbody posterior fusion. Even though soft tissue is protected by the tubular retractor for the minimal invasive means but the posterior intervertebral cage is smaller size when compare to DLIF and ALIF, so the technique is inferior in terms of biomechaics and fusion rates*

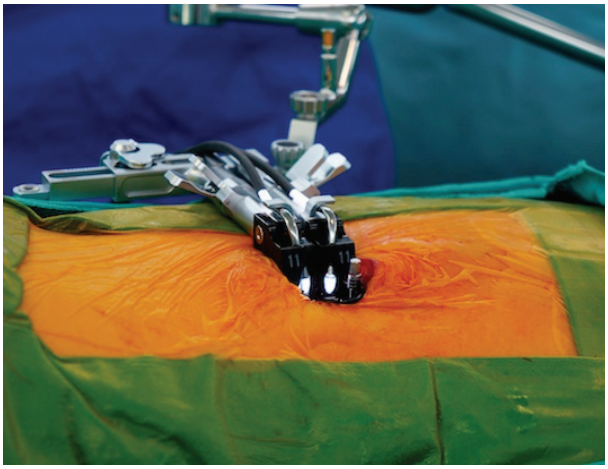


Figure 15: *Shows MIS DLIF Minimal invasive interbody fusion from lateral approach. The portal is made by slightly smaller size tube that passes to the retroperitoneal space. It can provide space enough for placing a bigger cage inside when compared to MIS TLIF.*

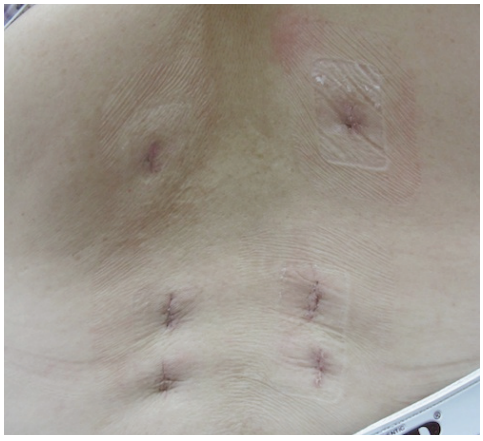


Figure 16: *Shows the posterior wound scars after 1 level DLIF operation and 4-percutaneous screws fixation. Note the wound is much smaller than conventional posterior opened fusion surgery. That means DLIF has less pain, faster recovery and this technique can provide better biomechanics and fusion rates.*

The advantages include elimination of great vessel mobilization thus reduction in the risk of vascular injuries and elimination of the risk of superior hypogastric plexus injuries that may cause retrograde ejaculation. Wright[28] reported the outcomes of 145 cases in the United States; only 5 cases had transient hip flexor weakness. No visceral or vascular injuries and mean blood loss was 88 cc. Most of the literature reports minimal blood loss, less muscle and soft tissue destruction leading to early return to normal ability. The anterior larger cage has a big surface on which to create a better fusion when compared to posterior anterior fusion back (TLIF-PLIF). The transpsoas lumbar interbody fusion procedure is particularly useful in degenerative scoliosis condition. The large DLIF cage can reduce the coronal deformity in scoliosis patient by ensuring full bilateral end plate coverage by the DLIF cage. The minimal blood loss for this surgery increases the benefit in scoliosis in elderly. Anand et al.[2] reported the mean blood loss for anterior procedure within 2-8 level scoliosis correction was only 163 cc. Finally, the procedure is relatively straight forward which makes the surgeon have a shorter learning period before being able to perform it, step by step, with less variation in each patient.

Our preliminary results show the conformity of this minimal invasive procedure. Because the procedure is straightforward, our surgeons have been able to see acceptable results as reported elsewhere in the literature. Pre-operative VAS leg pain from nerve root compression has rapidly declined even during a short follow up period. Most of our patients could ambulate by post-operative day 2-3. There were no cases where we failed to reduce radicular leg pain or back pain in a short period of surgery. The most common reported complication in other series is transient hip numbness or pain, which we also found, but it is transient and resolved within a short period of follow up. Due to the minimal disruption of back muscle and elimination of destruction of posterior vertebral structure, together with the better biomechanics of anterior vertebral column support, this procedure shows out-standing benefits in multiple level corrections such as in scoliosis, over the traditional opened posterior fusion procedure.

The radiographic result in this report shows the success in correction of coronal (scoliosis) angle. Every disc space increased in disc height; i.e. increasing the diameter of the neural foramen respectively. Therefore, this procedure should be useful particularly in L1-L5 foraminal narrowing, which is one of the pathological patterns that is difficult to solve by traditional posterior approach, especially at higher lumbar levels. The reduction in slipped distance (degree of slip) may come from the ligamentotaxis property of intact anterior and posterior longitudinal ligament in that disc level, resulting in a widening of the central spinal canal of that slipped vertebrae, without the need of direct removal of laminar and posterior ligament. That is why this procedure is also indicated in the patient with spondylolisthesis which is not more than grade 2 slipped.

Limitations of this preliminary report include the heterogeneity of our patient population. This study has a mix of patient demographics, pathologies. Scoliosis cases may not be expected to have the same results as spondylolisthesis or DDD. However, the average results demonstrate that good outcomes may still be generalized over a wide variety of patients. The one interesting indicator that we are following but cannot yet report in this study is the Oswestry disability score at pre-operative, 3 month, 6 month and at 1 year and the success of fusion rate because of the short time follow up. That data result will be very interesting and will be reported in the near future.

Conclusion

This preliminary short term report of DLIF at Bangkok Spine Academy shows satisfactory consistent results as other mini-opened transposes approaches. The benefits of this procedure are reducing leg and back pain, less blood loss, minimized soft tissue injury, wide safety margin of inadvertent complication especially nerve root injuries, less likelihood for long term complications and for lumbar degenerative spine in cases of decompression and fusion.

This procedure has a lot of potential to be more widely used in the near future.

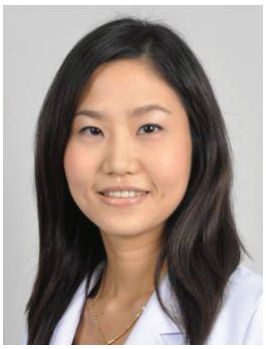
References

1. Ozgur BM, Aryan HE, Pimenta L, et al. Extreme lateral interbody fusion (XLIF): a novel surgical technique for anterior lumbar interbody fusion. *Spine J* 2006;6:435-43.
2. Anand N, Baron EM, Thaiyananthan G, et al. Minimally invasive multilevel percutaneous correction and fusion for adult lumbar degenerative scoliosis a technique and feasibility study. *J Spinal Disord Tech* 2008;21:459-67.
3. Marotta N, Cosar M, Pimenta L, et al. A novel minimally invasive presacral approach and instrumentation technique for anterior L5-S1 intervertebral discectomy and fusion: technical description and case presentations. *Neurosurg Focus* 2006;20:E9.
4. Pimenta L, Diaz RC, Phiilips FM, et al. XLIF® for lumbar degenerative scoliosis: outcomes of minimally-invasive surgical treatment out to 3 years post-op.

Seattle, WA: North American Spine Society, 2006.
5. Baker JK, Reardon PR, Reardon MJ, et al. Vascular injury in anterior lumbar surgery. *Spine* 1993;18:2227-223
6. Flynn JC, Price CT. Sexual complications of anterior fusion of the lumbar spine. *Spine* (Phila Pa 1976) 1984;9:489-92.
7. Brau SA. Mini-open approach to the spine for anterior lumbar interbody fusion: description of the procedure, results and complications. *Spine J* 2002;2:216-23.
8. Kaiser MG, Haid RW Jr, Suba ch BR, et al. Comparison of the mini-open versus laparoscopic approach for anterior lumbar interbody fusion: a retrospective review. *Neurosurgery* 2002;51:97-103; discussion 103-5.
9. Chen, MPP*, Tong KB, Laouri M. Surgical treatment patterns among Medicare beneficiaries newly diagnosed with lumbar spinal stenosis. *The Spine Journal* 2010;10 :588-94.
10. Weinstein JN, Tosteson TD, Lurie JD, et al. Surgical versus nonsurgical therapy for lumbar spinal stenosis. *N Engl J Med* 2008;358:794-810.
11. Gibson JN, Waddell G. Surgery for degenerative lumbar spondylosis: updated Cochrane Review. *Spine* 2005;30: 2312-20.
12. Angus S. Don, FRACS, Eugene Carragee, MD. A brief overview of evidence-informed management of chronic low back pain with surgery. *The Spine Journal* 2008; 8:258-65.
13. Bridwell KH, Sedgewick TA, O'Brien MF, et al. The role of fusion and instrumentation in the treatment of degenerative spondylolisthesis wi th spinal stenosis. *J Spinal Disord* 1993;6:461-72.
14. Hercowitz HN, Kurz LT. Degenerative lumbar spondylolisthesis with spinal stenosis. A prospective study comparing decompression with decompression and intertransverse process arthrodesis. *J Bone Joint Surg Am* 1991;73:802-8.
15. Fischgrund JS, Mackay M, Herkowitz HN, et al. 1997 Volvo Award winner in clinical studies. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective, randomized study comparing decompressive laminectomy and arthrodesis with and without spinal instrumentation. *Spine* 1997;22:2807-12.
16. Mardjetko SM. Connolly P J, Shott S. Degenerative Lumbar Spondylolisthesis: A Meta-Analysis of Literature 1970-1993. *Spine* 1994;19:2256-65.
17. Kwon B, Katz JN, Kim DH, et al. A review of the 2001 Volvo Award Winner in Clinical Studies. Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish lumbar spine study group. Spine 2006;31:245-9.
18. Gupta MC: Degenerative scoliosis. Options for surgical management. *Orthop Clin North Am* 2003;34:269-79.
19. Islam N, Wood KB, Transfeldt EE, et al. Extensions of fusions to the pelvis in idiopathic scoliosis. *Spine* 2001;26:166-73.
20. Shapiro GS, Taira G, Boachie-Adjei O. Results of surgical treatment of adult idiopathic scoliosis with low back pain and spinal stenosis: a study of long-term clinical radiographic outcomes. *Spine* 2000;28:358- 63.
21. Swan J, Hurwitz E, Malek F, et al. Surgical treatment for unstable low-grade isthmic spondylolisthesis in adults: a prospective controlled study of posterior instrumented fusion compared with combined anterior-posterior fusion. *Spine J* 2006;6:606-14.
22. Chen DF, Fay LA, Lok J, et al. Increasing neuroforaminal volume by anterior interbody distraction in degenerative lumbar spine. Spine 1995;20:74-9.
23. Ricardo SG. Umeta, Avanzi O. Techniques of lumbar-sacral spine fusion in spondylosis: systematic literature review and meta-analysis of randomized clinical trials. *The Spine Journal* 2001;11:668-76.
24. Chad D. Cole, Todd D. McCall. Comparison of low back fusion techniques: transforaminal lumbar interbody fusion (TLIF) or posterior lumbar interbody fusion (PLIF) approaches. *Curr Rev Musculoskelet Med* 2009; 2:118-26.
25. Christensen FB, Hansen ES, Eiskjaer SP, et al. Circumferential lumbar spinal fusion with Brantigan cage versus posterolateral fusion with titanium Cotrel-Dubousset instrumentation: a prospective, randomized clinical study of 146 patients. *Spine* 2002;27:2674-83.
26. Fritzell P, Hagg O, Wessberg P, et al. 2001 Volvo Award Winner in Clinical Studies: Lumbar fusion versus nonsurgical treatment for chronic low back pain: a multicenter randomized controlled trial from the Swedish Lumbar Spine Study Group. *Spine* (Phila Pa) 1976 ;26:2521-32; discussion 2532-24.
27. Rodgers WB, Cox CS, Gerber EJ. Early complications of extreme lateral interbody fusion in the obese. *J Spinal Disord Tech* 2010 Jan 15.
28. Wright N. XLIF- the United States Experience 2003-4. International Meeting on Advanced Spinal Techniques Banff Alberta, Canada, 2005.

Case Report

Arrhythmogenic Right Ventricular Dysplasia (ARVD) Diagnosis In The Elderly



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Keywords:
ARVD, arrhtythmia, right ventricular dysplasia

Arrhythmogenic right ventricular dysplasia (ARVD) is a type of nonischemic cardiomyopathy which primarily involves the right ventricle (RV). ARVD is considered a major cause of sudden death in young adults, mainly in the age group under thirty years old and is rarely found in the elderly. Males are predominantly affected.[1-3] ARVD has been proposed as a genetic inherited disease with autosomal dominant and various penetrance patterns.[4, 5] ARVD is pathologically characterized by fibro-fatty or fatty replacement of the right ventricular myocardial tissue. The fatty form is presented by almost complete replacement without endocardial thinning and found almost exclusively on the RV myocardium. The fibro-fatty replacement is defined as a fatty replacement with endocardial thinning less than 3 mm thickness[6]. The fibro-fatty replacement is considered a source of electrical instability of the RV in the form of ventricular arrhythmias with left bundle branch block morphology.[2, 7] Many theories were proposed to explain the etiology and pathogenesis of ARVD such as apotosis or programmed cell death theory which leads to myocardial cell loss followed by fibro-fatty replacement and causes the RV increased vulnerability to life threatening arrhythmias.[2] The most common triangle effected areas of the RV which are the sites of fatty and fibro-fatty replacement are the right ventricular inflow (sub-tricuspid area) and outflow tract including the RV apex.[8] The fatty replacement can involve areas of the left ventricle (LV), the interventricular septum is spared in most cases. [9] The ARVD patient may present with a wide clinical spectrum, frequently asymptomatic with ectopic beat until sudden cardiac death. The typical clinical presentation is palpitation from ventricular arrhythmia, with left bundle branch block (LBBB) pattern which may be captured on electrocardiogram or holter monitoring.[2, 10] Other typical electrocardiographic signs are the epsilon wave and prolonged QRS complex (>110 msec) with the absence of complete right bundle branch block (RBBB) in precordial lead V1-V3 of twelve -lead ECG. Because of wide range of clinical presentation of ARVD, the original criteria for ARVD diagnosis was proposed in the year 1994[11]:

1. Global or regional systolic dysfunction and structural alterations of the RV (i.e. heart wall motion and changes to the heart muscle size and shape).
2. Tissue characterization as fatty or fibro-fatty replacement of the RV myocardial wall.
3. Electrical conduction abnormality (repolarization and depolarization abnormality).
4. Arrhythmias.
5. Family history of premature sudden death.

However, no single characteristic finding has been proved as a pathognomonic sign of ARVD. With regard to the original criteria, to diagnose ARVD requires either 2 major criteria or 1 major and 2 minor criteria or 4 minor criteria Table 1 below. Relying on the original diagnostic criteria for ARVD which was published and established in 1994 as shown, meant that ARVD would be diagnosed when the clinical conditions reach the overt stage therefore the early stage of ARVD would not be discovered. **T**he new criteria for ARVD diagnosis was proposed in 2010 by Dr Frank Marcus and colleagues.[12] This new criteria divided the possibility for being diagnosed an ARVD into three stages; ***Definite ARVD***: 2 Major or 1 major and two minor or 4 minor criteria from different categories, ***Borderline ARVD***: 1 major and 1 minor, 3 minor criteria from different categories, ***Possible ARVD***: 1 major or 2 minor criteria from different categories. Some other characteristic findings were introduced to the revised criteria, to increase the diagnostic sensitivity.

Table 1: The diagnostic criteria for ARVD

The 1994 Task Force Report on ARVD diagnosis[11]	The Revised criteria for ARVD diagnosis[12]
Major Criteria	***Major criteria***
Right ventricular (RV) dysfunction and structure	**RV systolic function and structure**
Severe dilatation and reduction of RV ejection fraction with little or no LV impairment	*By 2D echo :* Regional RV akinesia, dyskinesia or aneurysm and one of the following (end diastole): PLAX RVOT ≥ 32 mm, PSAX RVOT ≥ 36 mm, Or fractional area change ≤ 33%
Localized RV aneurysms	*By MRI :* Regional RV akinesia, dyskinesia or aneurysm or dyssynchronous RV contraction and one of the following: Ratio of RV end-diastolic volume to BSA ≥ 110 mL/m2 (male) or ≥ 100mL/m2 (female) or RV ≤ 40%
Severe segmental dilatation of the RV	*By RV angiography :* Regional RV akinesia, dyskinesia or aneurysm
Tissue characterization	**Tissue characterization :** Residual myocytes < 60% by morphometric analysis (or <50% if estimated), with fibrous replacement of the RV free wall myocardium in ≥ 1 sample, with or without fatty replacement of tissue on **endocardial biopsy**
Fibrofatty replacement of myocardium on endomyocardial biopsy	
Conduction abnormalities	**Repolarization abnormality :** Inverted T waves in right precordial leads (V1, V2, and V3) or beyond in individuals >14 years of age (in the absence of complete right bundle – branch block QRS ≥ 120 ms)
Epsilon waves in V1 - V3.	**Depolarization abnormality :** (reproducible low-amplitude signals between end of QRS complex to onset of the T wave in the right precordial leads (V1-V3) or
Localized prolongation (>110 ms) of QRS in V1 - V3	**Arrhythmia :** Nonsustained or sustained ventricular tachycardia of left bundle branch morphology with superior axis (negative or indeterminate QRS in leads II, III, and a VF and positive in lead aVL)
Family history	**Family history :** ARVD/C confirmed in the first degree relative who meets current Task Force criteria or ARVD/C confirmed pathologically at autopsy or surgery in the first degree relative or identification of a pathogenic mutation categorized as associated or probably associated with ARVD/C in the patient under evaluation
Familial disease confirmed on autopsy or surgery	

The 1994 Task Force Report on ARVD diagnosis[11]	The Revised criteria for ARVD diagnosis[12]
Minor Criteria	***Minor criteria***
RV dysfunction and structure	**RV systolic function and structure**
Mild global RV dilatation and/or reduced ejection fraction with normal LV	By 2D echo : Regional RV akinesia, dyskinesia or aneurysm and one of the following (end diastole): PLAX RVOT ≥ 29 to < 32 mm, PSAX RVOT ≥ 32 to < 36 mm, Or fractional area change ≥ 33% to ≤ 40%
Mild segmental dilatation of the RV	By MRI : Regional RV akinesia, dyskinesia or aneurysm or dyssynchronous RV contraction and one of the following ; Ratio of RV end-diastolic volume to BSA > 100 to ≤ 110 mL/m2 (male) or ≥ 90 to ≤100mL/m2 (female) or RV≥ 40 to ≤45 %
Regional RV hypokinesis	By RV angiography : Regional RV akinesia, dyskinesia or aneurysm
Conduction abnormalities	**Tissue characterization :** Residual myocytes 60% to 75% by morphometric analysis (or 50% to 65% if estimated), with fibrous replacement of the RV free wall myocardium in ≥ 1 sample, with or without fatty replacement of tissue on endocardial biopsy
Inverted T waves in V2 and V3 in an individual over 12 years old, in the absence of a right bundle branch block (RBBB)	**Repolarization abnormality :** Inverted T waves in leads V1 and V2 in individuals > 14 years of age (in the absence of complete right bundle – branch block) or in V4, V5, or V6 or inverted T waves in leads V1-V4 individuals > 14 years of age in the presence of complete right bundle branch block
Late potentials on signal averaged ECG.	**Depolarization abnormality :** late potential by SAECG (signal average ECG in ≥ 1 of 3_parameters in the absence of a QRS duration of ≥ 110 ms on the standard ECG, Filtered QRS duration (fQRS) ≥ 114 ms, Duration of terminal QRS < 40 micro V (low amplitude signal duration) ≥ 38 ms, Root –mean-square voltage of terminal 40 ms ≤ 20 micro V, terminal activation duration of QRS ≥ 55 ms ≤ 20 micro V or Terminal activation duration of QRS ≥ 55 ms measured from the nadir of the S wave to the end of the QRS, including R' in V1, V2, or V3, in the absence of complete right bundle-branch block
Arrhythmia : Ventricular tachycardia with a left bundle branch block (LBBB) morphology	**Arrhythmia :** Nonsustained or sustained ventricular tachycardia of RV outflow configuration , left bundle branch morphology with inferior axis (positive QRS in leads II, III, and aVF and negative in lead aVL) or of unknown axis or > 500 ventricular extrasystoles per 24 hours (holter)
Frequent PVCs (> 1000 PVCs / 24 hours)	
Family history	**Family history :** History of ARVD/C in a first degree relative in whom it is not possible or practical to determine whether the family member meets current Task Force criteria or premature sudden death (<35 years of age) due to suspected ARVC/D in the first – degree relative or ARVD/C confirmed pathologically or by current Task Force Criteria in second-degree relative
Family history of sudden cardiac death before age 35	
Family history of ARVD	

Case Report

A 74-year-old Thai monk, with history of post endarterectomy of the left carotid artery, came to the hospital with vertigo and chronic fatigue. Physical examination was unremarkable. Twelve leads ECG revealed localized widening QRS wave of complete right bundle branch block in precordial lead V1 and widening of QRS complex with Osborn wave in precordial lead V2-V3 and no sign of ischemic change. Echocardiography revealed moderate RV systolic dysfunction (RVEF = 45.0%) with moderate hypokinesia of the RV apex. Multi-slice Computed Tomography for coronary artery revealed normal study. The patient was sent to MRI center for cardiac MRI to find out the cause of right ventricular dysfunction. Cardiac MRI with gradient echo CINE technique revealed normal size of the RV and hypokinesia of the right ventricular apex on horizontal long axis view images. Fatty replacement in right ventricular myocardial tissue was demonstrated on the T1W black blood MRI images which is compatible with the result of cardiac MRI by spin echo T2W BB with fat suppression technique. By delayed contrast (gadolinium) enhancement MRI study, myocardial contrast enhancement of both ventricles was not demonstrated. This patient was diagnosed as a borderline ARVD by the result of MRI examination met one major criterion and one minor criterion of ARVD diagnosis in different categories according to the original criteria.

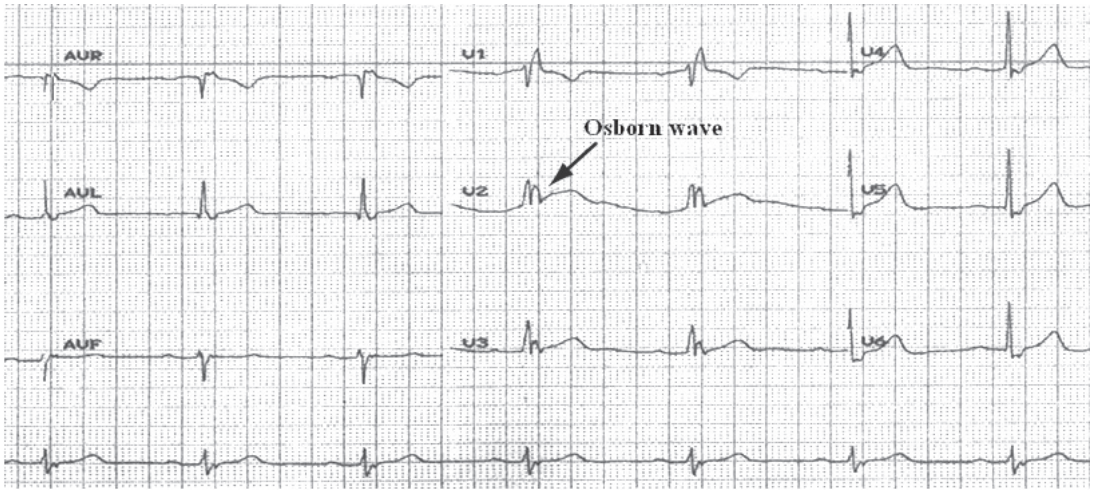

Figure 1: *Demonstration of widening QRS complex of complete right bundle branch block in lead V1, widening QRS complex with Osborn wave in lead V2-V3*

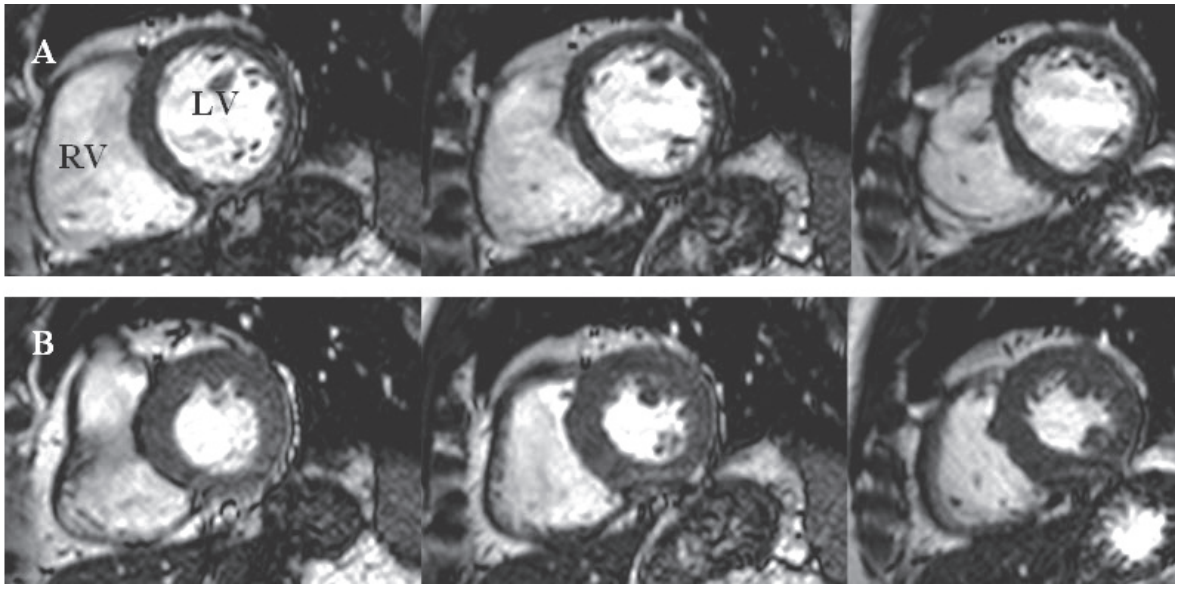

Figure 2: *Gradient echo CINE MRI images on short axis view reveal moderate RV systolic function with mild global hypokinesia (RVEF = 45.0%, normal = 54-78%). Series A: diastolic phase; Series B: systolic phase*

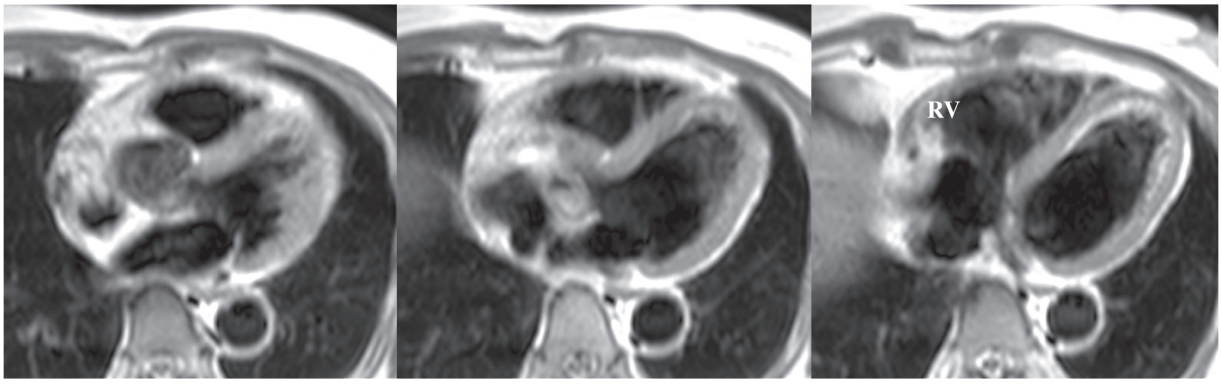

Figure 3: *T1W black blood MRI images reveal fibro-fatty replacement (myocardial tissue = gray intensity, fatty = white band) at the RV apex (in box)*

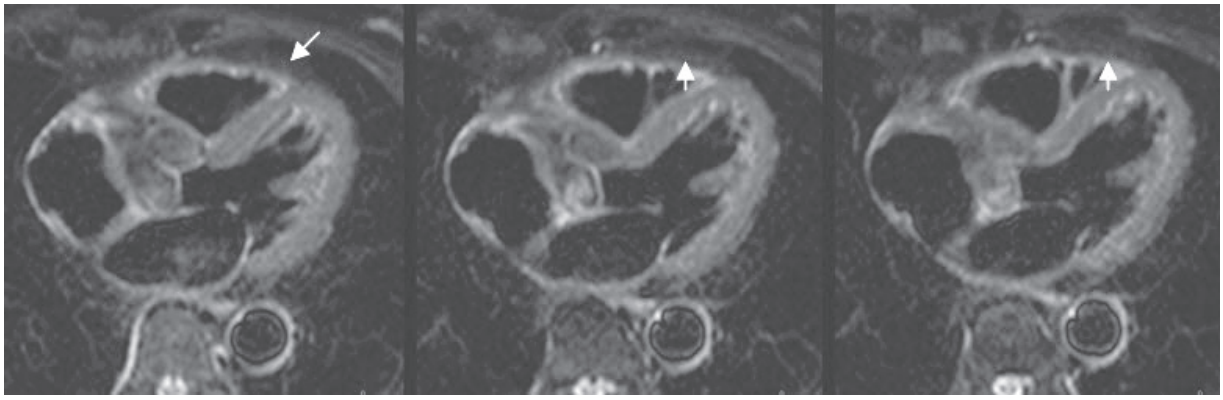

Figure 4 : *T2W black blood fat suppression MRI reveal hypointensity of fat which replaced RV myocardium tissue (gray intensity, white arrow) which was compatible with the white band of fatty replacement as shown on T1W black blood images*

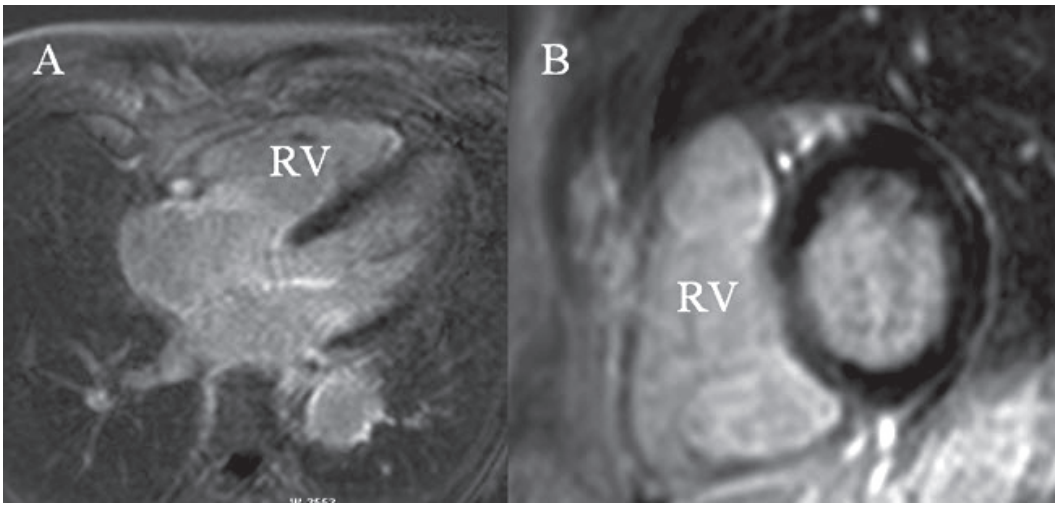

Figure 5 : *MRI with Delayed contrast enhancement technique revealed no myocardial contrast enhancement of the left ventricle and right ventricle. A: Horizontal long axis view, B: short axis view of both ventricles*

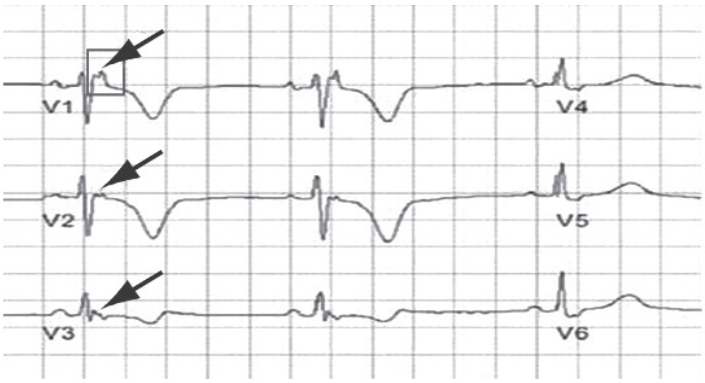

Figure 6: *Demonstration of the epsilon wave character in precordial lead V1-V3 (arrow)*

Discussion

1. Case report

In this article, we describe a borderline ARVD in an elderly patient older than 65 years. The clinical signs of the patient obtained from CMRI met one major criteria of tissue characterization as fatty replacement in the RV myocardial tissue and one minor criteria of RV dysfunction with apical RV hypokinesia regarding to the original criteria (1994). Although ARVD is considered a disease of young adult with mean age less than 30 years and rarely occurs in the elderly (more than 65 years)[13], however, to diagnose ARVD in both young adult and elderly groups follows the same criteria. Therefore, ARVD should be considered individually in line with supporting evidences. The typical clinical presentations are often palpitation from ventricular arrhythmia or near syncope or even sudden cardiac death. ARVD should be taken into account in case of ventricular arrhythmia of the right heart without other overt myocardial diseases. The electrocardiographic signs of our patient were CRBBB with T wave inversion in precordial lead V1 and widening QRS complex with Osborn wave in precordial lead V2-V3, which were not matched for the typical characteristic findings of the ARVD. Osborn waves were positive deflections occurring at the junction between the QRS complex and the ST segment where the S point, also known as the J point, has a myocardial infarction-like elevation [These waves were described in 1953 by JJ Osborn]. Osborn wave is often found in case of hypotemperature (< 32 °C), hypercalcemia, brain injury, vasospastic angina or ventricular fibrillation[14]. Epsilon wave which is one of the typical sign of the ARVD and is found about 33% in ARVD patient (Khurram N et al[15] 2004). This is described as a terminal notch in the QRS complex. The epsilon wave is more often seen on signal averaged ECGs and occasionally observed on twelve lead ECG. The electrocardiographic sign of right bundle branch block was found in around 17% of ARVD cases (Jain R et al.[16] 2009). Complete right bundle branch block (CRBBB) on precordial lead has been introduced into the minor subgroup of revised criteria (2010) as a character of CRBBB with T wave inversion on precordial lead V1-V4 but T wave inversion on precordial lead V1-V3 without CRBBB is classified as a characteristic finding in major subgroup of abnormal repolarization abnormality regarding to both original and revised criteria for ARVD diagnosis. Normally, this character may be seen in less than 3% in normal healthy heart.[17, 21] Although ARVD is characterized by the fatty replacement in the RV myocardium but it is not the hallmark of ARVD. Fatty replacement in the RV myocardium is classified as one only of the characteristic findings of major criteria for ARVD diagnosis. Significant fatty infiltration of the RV is observed in more than 50% of normal heart in elderly people[18] but in typical cases with presence of VT with LBBB pattern a high percentage of fatty replacement is not found.[19] Fatty and fibro-fatty replacement in the RV myocardial tissue can be characterized by using MRI and endomyocardial biopsy. MRI is a good alternative modality for RV tissue characterization. The sensitivity of the use of spin echo T1W bb MRI for characterization of the fatty replacement was not high (67%) and the specificity was of 100%[18] hence the presence of fatty replacement of the RV myocardium should be considered as a diagnostic factor when using with other indicative clinical characters for ARVD diagnosis and the absence of fatty replacement in the RV myocardium in highly suspicious cases does not rule out ARVD.

2. MRI and ARVD assessment

Imaging techniques for ARVD assessment include echocardiography, conventional RV angiography and Magnetic Resonance Imaging. Echocardiography and RV angiography are very good at RV structure and function assessment but these imaging techniques have the limitation of spatial resolution to characterize the typical fatty and fibro-fatty replacement of the RV myocardium. Only Magnetic resonance imaging (MRI) is a promising tool for evaluation anatomy and function of the right ventricle and is frequently used to characterize fatty replacement on the RV myocardial wall.[20,21] ARVD diagnosis frequency has demonstrably increased since MRI became established

in use for ARVD diagnosis.[22] MRI can demonstrate the typical characters which are proposed in both major and minor criteria in terms of RV systolic dysfunction and structural changes including RV myocardial tissue characterization. Gradient echo CINE MRI technique is used to demonstrate the RV structure and to assess the RV systolic function. RV systolic function assessment was done by using semi-manual delineation of the endocardial lining of the RV in every slice from basal to the apex (on short axis view of Gradient echo CINE MRI images) of in both diastole and systole. The RV ejection fraction was calculated by computerized program on the work station. Some special MRI techniques are used for ARVD diagnosis. The spin echo T1W BB MRI technique is used to characterize the fatty replacement on the RV myocardial tissue. The fatty replacement on the RV myocardial tissue is presented as hyperintensity signal tissue band with irregular demarcation on the intermediate intensity signal RV myocardial tissue. The spin echo T2W bb MRI with fat suppression technique may be used to confirm the result of ordinary T1W bb MRI by producing of the hypointensity signal of fatty replacement which is compatible with the hyperintensity signal of fat which is seen on the ordinary T1W bb images. Delayed contrast enhancement study MRI is used to detect myocardial fibrosis in both right and left ventricular myocardium. Although MRI has proved to permit myocardial fibrosis characterization in the left ventricle, however it may also produce uncertain results in the RV because RV has thinning myocardium and may be confusing with fat signal[20,23] and may be missed due to very small area of fibrosis. To document fatty replacement on the RV myocardial tissue on MRI image, eye visualization methods are used, therefore varying experience among the interpreters may cause uncertain accuracy in ARVD diagnosis using MRI.

3. Diagnostic criteria

Although the original 1994 criteria are too rigid to detect the early stages of ARVD yet it allows the true typical case to be detected with very high accuracy. The revised 2010 criteria were created with improved sensitivity and preserved specificity, aiming for early evaluation the non-overt stage group. As regards the original criteria, MRI was allowed as a tool for fatty or fibro fatty replacement characterization but it is not for the revised criteria. As a matter of fact. the standard of reference for the diagnosis ARVD is based on histologic demonstration of fatty or fibro-fatty replacement of the RV myocardium by autopsy or surgery. However, endomyocardial biopsy which is used for tissue characterization according to the revised criteria lacks sufficient sensitivity to diagnose ARVD because of sampling errors.[22] Therefore, to confirm diagnosis by endomyocardial biopsy is not recommended. For assessing the development of disease in the first relatives of patients with ARVD, non-invasive testing should be taken into consideration as an alternative following the revised criteria.

Conclusion

No single criterion has been proved to be used alone for ARVD diagnosis because ARVD has various clinical presenting signs. Diagnosis ARVD in both young adult and elderly use the same diagnostic criteria. To assess the risk of the first relative of ARVD patient can follow the revised criteria using noninvasive test. Ventricular arrhythmia with left bundle branch block pattern, fatty or fibro-fatty replacement and RV systolic dysfunction with regional aneurysm are the typical characters which are often found in true ARVD case. Positive MRI finding of fatty replacement in RV myocardium can be found in normal healthy heart and, in the opposite, negative MRI findings of fatty replacement in highly suspicious case does not rule out ARVD. RV disorder conditions such as myocarditis or sarcoidosis which may present clinical features which mimic ARVC must be excluded in suspicious ARVD cases. Although CMRI is the tool that provides the most important anatomic, functional and histologic clues for ARVD diagnosis within a single study, the degree of variability among the MRI interpreters may, as aforementioned, be related in part to their experience with CMR diagnosis of ARVD, especially in fatty replacement characterization and identification.

References

1. Lahtinen AM, Lehtonen E, Marjamaa A, et al. Population-prevalent desmosomal mutations predisposing to arrhythmogenic right ventricular cardiomyopathy. *Heart Rhythm* 2011;8:1214-21.
2. Basso C, Thiene G, Corrado D, et al. Arrhythmogenic right ventricular cardiomyopathy. Dysplasia, dystrophy, or myocarditis?. *Circulation* 1996;94:983-91.
3. Braunwald E, Libby P, Zipes DD. Heart Disease: A Textbook of Cardiovascular Medicine. 6th ed. WB Saunders 2001: 324-4, 863-89, 2052-6.
4. Ahmad F, Li D, Karibe A , et al. Localization of a gene responsible for arrhythmogenic right ventricular dysplasia to chromosome 3p23. *Circulation* 1998;98: 2791-5.
5. Rampazzo A, Nava A, Danieli GA, et al. The gene for arrhythmogenic right ventricular cardiomyopathy maps to chromosome 14q23-q24. *Hum Mol Genet* 1994;3:959-62.
6. Thiene G, Nava A, Corrado D, et al. Right ventricular cardiomyopathy and sudden death in young people.

N Engl J Med 1988;318:129-133

7. Basso C, Calabrese F, Corrado D, et al. Postmortem diagnosis in sudden cardiac death victims: macroscopic , microscopic and molecular findings . *Cardiovascular Research* 2001;50:290-300.
8. Fontaine G, Fontaliran F, frank R. Arrhythmogenic right ventricular cardiomyopathies:clinical forms and main differential diagnoses (editorial). *Circulation* 1998;97: 1532-5.
9. Richardson P, McKenna W, Bristow M. Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies. *Circulation*. 1996;93:841-2.
10. Gorrado D, Fonteine G, Marcus FI, et al. Arrhythmogenic right ventricular dysplasia cardiomyopathy : need for an international registry: *Circulation* 2000; 101: 101-6.
11. McKenna WJ, Thiene G, Nava A, et al. Diagnosis of arrhythmogenic right ventricular dysplasia cardiomyopathy. *Br Heart J* 1994;71:215-8.
12. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic Right Ventricular Cardiomyopathy/ Dysplasia : Proposed Modification of the Task Criteria. *Circulation* 2010;121:1533-41.
13. García-Quintana A, Ortega-Trujillo JR, Fernández-Aceytuno AM . Arrhythmogenic Right Ventricular Dysplasia in the Elderly. *Rev Esp Cardiol*. 2007;60:87-9
14. Marx, John. Rosen's emergency medicine: concepts and clinical practice 7th edition. Philadelphia, PA: Mosby/ Elsevier 2010:1869.
15. Khurram N, Bomma C, Tandri H, et al. Electrocardio graphic features of Arrythmogenic Right Ventricular Dysplasia/Cardiomyopathy According to Disease Severity: A Need to Broaden Diagnostic .*Circulation* 2004;110:1527-34.
16. Jain R, Dalal D, Daly A, et al. Electrocardiographic features of arrhythmogenic right ventricular dysplasia. *Circulation* 2009;120:477-87.
17. Khan A, Mittal S, Sherrid MV. et al. ARVD: from genetic to treatment. *Anadolu Kardiyol Derg* 2009;9:24-31.
18. Burke A, Farb A, Tashko G, et al. Arrhythmogenic Right Ventricular cardiomyopathy and fatty replacement of the right ventricular myocardium: are they different disease? *Circulation* 1998;97:1571-80.
19. Metha D , Davies MJ , Ward DE, et al. Ventricular tachycardia of right ventricular origin: markers of subclinical right ventricular disease. *Am Heart J* 1994; 127:360-6.
20. Frank I. Marcus, William J. et al. Diagnosis of Arrhythmogenic Right Ventricular Cardiomyopathy/ Dysplasia. Proposed Modification of the Task Force Criteria. *Circulations* 2010;121:1533-41.
21. Ricci C, Longo R, Pagnan L, et.al. Magnetic resonance imaging in right ventricular dysplasia. *Am J Cardiol* 1992;70:1589-95.
22. Corrado D, Basso C, Thiene G. Arrhythmogenic right ventricular cardiomyopathy : diagnosis , prognosis , and treatment. *Heart* 2000;83:588-95.
23. Tandri H, Saranathan M, Rodrigue Z, et al. Noninvasive detection of myocardial fibrosis in arrhythmogenic right ventricular cardiomyopathy using delayed enhancement magnetic resonance imaging : *J Am Coll Cardiol* 2005; 45:98-103.

Review Article

Management of Colorectal Cancer with Hepatic Metastasis

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Keywords:
colorectal cancer, CRC, hepatic metastasis, tumor resection

Colorectal cancer has become one of the leading causes of cancer-related death worldwide. In Thailand, colorectal cancer (CRC) was the most commonly reported gastrointestinal malignancy by the National Cancer Center in 2010. It is the second most commonly diagnosed malignancy in men after lung cancer and in women after breast and cervical cancer.[1] Median survival of stage IV CRC without any kind of treatment has been reported to be around 5 to 6 months.[2, 3] The liver appears to be the most common organ of distant metastatic spread from colorectal cancer. Approximately 25% of patients present with synchronous disease and an additional 30% to 40% will develop hepatic metastases during the course of their disease.[4] In addition, liver metastases are found in over 50% of patients who die from CRC and hepatic involvement is the most implicated reason for their death.[5] This review will attempt to give an overview of the treatment alternatives in CRC patients with liver metastasis, with a focus on the updated rationales as well as controversial and current trends in the multidisciplinary approach.

Preoperative hepatic assessment using appropriate hepatic imaging is a crucial step to achieve the most beneficial treatment outcomes. Identifying the best imaging modality to determine hepatic metastasis has been the subject of many studies. Ward, et al.[6] performed the prospective evaluation of hepatic imaging studies in the detection of colorectal metastasis including an intravenously administered lipid contrast agent that enhances liver parenchyma on computed tomography (CT) scans (EOE-CT), arterial portography (AP-CT), delayed CT scanning (DS-CT), T1- and T2-weighted magnetic resonance imaging (MRI) (T1-MRI, T2-MRI). The authors demonstrated that the T1-MRI examination proved to be the best hepatic imaging study in the detection of colorectal metastases. More recent meta-analysis from the Netherlands group[7] performed a systematic review to obtain the sensitivity estimates of CT, MRI and fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET) for detection of colorectal liver metastases. Sixty one relevant articles were included. They reported that FDG PET was the most accurate modality by showing the most sensitivity estimates on both per-patient basis and per-lesion basis. Moreover, the study performed by Engledow et al.[8] which enrolled 64 consecutive patients with CRC liver metastases demonstrated that the addition of PET/CT scans led to management changes in over one-third of the patients. Using PET/CT scans, they were able to find the disease upstaging in 20 patients (31%) and downstaging in two patients (3%).

Whether or not to perform preoperative biopsy of detected suspected liver lesion is still the subject of debate. The survival after liver resection was substantially diminished compared with well matched patients in whom no biopsy or fine needle aspira-

tion cytogy (FNAC) had been attempted.[9] Jones et al.[10] analyzed 598 consecutive patients undergoing radical resection of colorectal liver metastases between 1986 and 2003. The authors examined specifically the 90 patients in whom diagnostic biopsy had been performed before the referral. Tumor seeding at the site of biopsy was histologically confirmed in 17 patients (19%). The authors also found that biopsy of liver metastases conferred significant poorer long-term survival on patients after liver resection (p = 0.008). They concluded that preoperative liver biopsy was not justified in patients with potentially resectable disease. This finding has been confirmed by other studies.[11, 12] Consultation with a specialist hepatobiliary surgical team is recommended before a *"tissue diagnosis"* is attempted in such patients.[9]

Among the current treatment alternatives for CRC with liver metastasis, hepatic resection has been established as the standard therapy offering a chance for cure for well-selected resectable metastases, over the last two decades[13] Many studies have shown that resection offers the only chance of long-term survival and cure in highly-selected patients.[14-17] Robertson et al.[18] reported long term outcomes after hepatic resection in an national experience study that analyzed Medicare enrollees (age > 63 years old) who were admitted to hospital in the United States of America between January, 2002 and December, 2004. A total of 306,061 patients were diagnosed with colorectal cancer, 3,957 patients with liver metastasis were identified and underwent hepatic resection. The 5-year survival rate was 25.5%. The authors concluded that subgroups at high risk for worse outcomes included the extreme elderly and those undergoing synchronous colon and hepatic resection. Other reports also demonstrated similar findings, whereby poorer long term outcomes were associated with synchronous liver metastases as compared to metachronous liver metastases.[19, 20] However, a better long term outcomes were demonstrated in an earlier report by a group of surgeons from Johns Hopkins Hospital in 2002.[17] Over a 16-year period, 226 patients undergoing curable liver resection for CRC with liver metastasis were reviewed. The median survival was 46 months, and a 5-year survival rate was 40%. They found significantly better overall and disease-free survival in the recent time period when compared with the earlier period; 58% (133 patients, 1993-1999) vs. 31% (93 patients, 1984-1992). The authors also pointed that the independent factors associated with improved survival included number of metastatic tumor < 3, negative resection margin, and carcinoembryonic antigen (CEA) < 100 ng/mL. Comparisons were made between time periods, only resection type (anatomical vs. non-anatomical), and the use of intra-operative ultrasound differed between the early and recent time periods. In addition, more effective peri-operative medical antitumor therapy (e.g. chemotherapy) and better patient selection were also responsible for significant improvement in long term outcomes. Most studies suggest poor prognostic indicators including extrahepatic disease, 4 or more lesions, bilateral lesions, and a surgical margin less than 1 cm; therefore, these factors were long considered relative contraindications to hepatectomy. In contrast, more recent research suggests that a wider range of patients may benefit from liver resection.

Several published literature has described factors identified as predictors for long term survival after hepatic resection. Wagner et al.[21] reported in 1984 that differences in survival depend on the extent of liver metastases-patients with solitary metastasis have a median survival of 21 months, those with unilobar oligometastases have a median survival of 15 months, and those with widespread bilobar disease have a median survival of less than 12 months. Nordlinger et al.[16] proposed a simple prognostic scoring system to select patients who were likely to benefit from surgery. Data from 1,568 patients with resected liver metastasis from CRC were analyzed with multivariate analysis. The authors found independent predictors of overall survival after hepatic resection included age, primary tumor stage, disease free interval of less than 12 months, preoperative CEA levels, number and size of metastatic tumors, and presence of extrahepatic disease. Furthermore, the surgical resection margin is also considered to be one of the important prognostic factors. A consensus stated that surgical margin positivity results in a worse outcome as compared to the patients with negative resection margins, however the extent of negative margins remains controversial. A recent meta-analysis performed using 18 studies by Dhir et al.[22] demonstrated the result of a total of 4,821 CRC with liver metastasis patients undergoing hepatic resection with negative resection margin to determine whether negative resection margins of 1 cm or more confer any survival advantage over negative resection margin of less than 1 cm. The authors concluded that among patients undergoing hepatic resection for colorectal cancer with liver metastasis, a negative margin of 1 cm or more conferred a survival advantage when compared with sub centimeter negative margins (46% vs. 38%; OR = 0.773; 95% CI, 0.638-0.938; p = 0.009). Other authors have however concluded that the width of negative margin has no influence on the outcome.[23-26] Gomez et al.[27] recently failed to identify a relevant prognostic scoring system to predict the patient outcomes following hepatic resection. They found that the published studies had been inconsistent in identifying these variables as independent predictors of survival on multi-variable analyses in different datasets, which suggested that certain prognostic variables may be more significant in certain patient groups. The explanation for this observation may involve suboptimal number of patients, limitation of the data available for analysis, and an insufficient follow up.

Despite an improvement in preoperative imaging, better surgical resection together with modern chemo-

therapy, up to two-thirds of patient's still experience recurrence of the disease which is most commonly found in the liver and lungs after hepatectomy.[28-36] Adequate surveillance protocols after hepatic resection are essential which should (ideally) be designed for each individual patient depending on the risks of recurrence. Many researchers had been investigating prognostic scoring systems to predict recurrence.[14, 16, 22, 27, 37] However there is currently no standard prognostic scoring system that has been generally accepted. Apart from the potential risk factors to predict recurrences, cost benefit analysis must also be carefully considered to determine the frequency of radiological imaging. The fact is that the first two years following hepatic resection have been recognized as when the disease is most likely to recur.[15] Bhattacharjya et al.[38] proposed an intensive follow up after hepatic resection using serial tumor marker estimations and contrast-enhanced CT of the chest and abdomen. This prospective study of 76 consecutive patients undergoing potentially curative resections of colorectal liver metastases was performed in a single unit where all the patients were followed up with a protocol of 3 monthly CEA and carbohydrate antigen 19-9 estimations and contrast-enhanced spiral CT of the chest, abdomen and pelvis for the first 2 years following surgery and 6 monthly thereafter. The median period of follow-up was 24 months (range 18–60). Nineteen patients developed isolated liver recurrence, of which 8 developed within 6 months of liver resection and none of which were resectable. Five of the 11 recurrences (45%) after 6 months were resectable. The authors found that the use of computerized tomography (CT) scan or tumor markers alone would have failed to demonstrate early recurrence. A combination of tumor markers and CT scan detected significantly more ($p < 0.05$) recurrence than either modality alone. They concluded that the tumor markers and CT scan should be used in combination in the follow-up of patients with resected colorectal liver metastases.

Patients with disease recurrence following resection of liver metastasis were considered to have poor prognosis. With development in hepatobiliary surgery, nowadays repeated liver resection can be offered with curative intent in properly selected patients with recurrent hepatic metastatic disease. Several reports have demonstrated a 5-year survival following repeat hepatic resection of up to 45%[39,40]; however the efficacy in 5-year survival typically decreases with each resection.[41] It is also recommended to preserve of at least two contiguous liver segments with adequate vascular inflow/outflow, biliary drainage, and an adequate hepatic remnant as defined as greater than 20-25% in a healthy liver.[42] The benefit of adjuvant chemotherapy following complete surgical resection among CRC with liver metastasis remains inconclusive and requires further evaluation. Nevertheless some published data supports the superiority of this adjuvant chemotherapy.[43, 44] Kemeny et al.[45] conducted an intergroup study of 109 CRC patients with one to three potentially resectable liver metastases. Fifty and six patients were randomized to receive surgery alone (control group). Fifty and three patients underwent surgical resection followed by adjuvant chemotherapy which was postoperative hepatic arterial floxuridine combined with intravenous continuous-infusion fluorouracil. They found that 4-year recurrence-free rate was 25% for the control group and 46% for the chemotherapy group ($p = 0.04$). The 4-year liver recurrence-free rate was 43% in the control group and 67% in the chemotherapy group ($p = 0.03$). The median survival of the 75 assessable patients was 49 months for the control arm and 63.7 months for the chemotherapy arm ($p = 0.60$). The authors stated that adjuvant intra-arterial and intravenous chemotherapy was beneficial in prolonging time to recurrence and preventing hepatic recurrence after hepatic resection of CRC. Furthermore, the presence of extrahepatic disease at the time of surgery is independently associated with a poorer prognosis.[41] The resection of concurrent pulmonary and hepatic metastases can also be undertaken in highly selected patients and still yield 5-year survival rates at or above 50%.[46] However, the outcomes have been poor for lymph node metastatic involvement; hence surgical resection in this group of patients is contraindicated. The survival benefit from surgical resection can be expected in younger patients whose lymph node metastasis response to or stabilized by neoadjuvant chemotherapy.[47]

To date, there is no strong evidence to support the use of neoadjuvant chemotherapy in resectable liver lesion. Current reports demonstrated that even with the best chemotherapy regimen, 20% of the patients had disease progressed while 50% of the patients experienced partial response.[48] Neoadjuvant chemotherapy on the other hand is recommended for those patients who have unresectable liver lesions. This will enhance the chance of curative resection. One study[49] analyzed 701 consecutive patients with unresectable liver metastases who were treated with neoadjuvant chemotherapy and found that 13.5% of these patients were resectable on the reevaluation. In addition, the authors also demonstrated that 5-year survival rates were 60% for large tumors, 49% for ill-located lesions, 34% for multinodular disease and 18% for liver metastases with extrahepatic disease. A more recent study from a North Central Cancer Treatment Group[50] described that after a median of 6 months of chemotherapy, 60% of the patients had tumor reduction by serial imaging, and 40% underwent curative liver resection. This concurs with the findings of other studies.[51] Nordlinger et al.[52] performed an interesting intercontinental (Europe, Australia, and Hong Kong) study recruiting 364 patients (78 hospitals) with histologically proven colorectal cancer and up to four liver metastases. Patients were randomly assigned to either six cycles of FOLFOX4 before and six cycles after surgery (182 patients) or to surgery alone (182 patients). In the

perioperative chemotherapy group, 151 (83%) patients were resected after a median of six (range 1-6) preoperative cycles and 115 (63%) patients received a median six (1-8) postoperative cycles. 152 (84%) patients were resected in the surgery group. The absolute increase in rate of progression-free survival at 3 years was 7.3% (from 28.1% to 35.4%, $p = 0.058$) in randomized patients; 8.1% (from 28.1% to 36.2%, $p = 0.041$) in eligible patients; and 9.2% (from 33.2% to 42.4%, $p = 0.025$) in patients undergoing resection. The authors concluded that perioperative chemotherapy with FOLFOX4 was compatible with major liver surgery and reduced the risk of events of progression-free survival in eligible and resected patients. The efficacy of a regimen can be enhanced to induce sufficient tumor regression to permit R0 resection by combining targeted agents.[53-56] The most recent study published in 2012 by Bokemeyer et al.[53] analysing the pooled radomized clinical trials (CRYSTAL and OPUS) of 845 patients with KRAS wild-type tumors. The authors demonstrated a significant improvement in overall survival ($p = 0.0062$), progression-free survival ($p < 0.001$) and overall-recurrent rates ($p < 0.0001$) in cetuximab combined with chemotherapy group. They also confirmed that the consistency of the benefit obtained across all efficacy end-points from adding cetuximab to first-line chemotherapy in patients with KRAS wild-type metastatic CRC. Folprecht et al.[57] described that chemotherapy with cetuximab yielded high response rates compared with historical controls, and led to significantly increased resectability in multicenter (17 centers in Germany and Austria) randomized trial of 111 patients. Patients with non-resectable liver metastases (technically non-resectable or > 5 metastases) were randomly assigned to receive cetuximab with either FOLFOX6 (oxaliplatin, fluorouracil, and folinic acid) or FOLFIRI (irinotecan, fluorouracil, and folinic acid). The study showed the increase of resectability rates from 32% at baseline to 60% after chemotherapy ($p < 0.0001$). Perioperative chemotherapy can be administered in selected patients in order to improve long term treatment outcomes.[52] Furthermore, the addition of targeted agents had also shown significantly increase in resectability of the CRC with liver metastases.[53, 57]

While surgical resection is considered the gold standard for the treatment of CRC with liver metastases, other alternatives which also have an impact on survival such as radiofrequency ablation[58], cryotherapy and other ablative therapy[59] may be indicated for those patients who are not surgical candidates for various reasons, such as the lesion being anatomically ill-located, the functional hepatic reserve after a resection being insufficient, the patient's co-morbidities inhibiting a major operation, or presence of extrahepatic metastases, all of which can further decrease the likelihood of cure. Radiofrequency ablation (RFA) produces localized tumor destruction by generating a high-frequency alternating current which converses to heat that subsequently evaporates intracellular water and leads to irreversible cellular changes, including intracellular protein denaturation, melting of membrane lipid bilayers, and coagulative necrosis of individual tumor cells. It has been applied in metastatic CRC to reduce the survival gap between resectable and unresectable disease. The first randomized study on the efficacy of RFA reported by a group from the Netherlands[60] randomly assigned 119 patients with non-resectable CRC liver metastases between systemic treatment (n = 59) or systemic treatment plus RFA (±resection) (n = 60). 30-month overall servival (OS) rate was 61.7% for combined treatment, and 57.6% for systemic treatment. Progression-free survival rate at 3 years for combined treatment was 27.6% compared with 10.6% for systemic treatment only ($p = 0.025$). The authors suggested that RFA plus systemic treatment resulted in significant longer progression-free survival; however the effect of RFA on overall survival remains uncertain. Although RFA has been established as a safe, well tolerated, easily repeated and less invasive procedure[61, 62], Wu et al.[58] again stated in the meta-analysis of 647 patients from 17 studies that hepatic resection was related to superior long term outcomes when compared to RFA in the treatment of CRC liver metastases. On the other hand, cryotherapy uses extremely low temperatures to destroy malignant tissue. A retrospective study conducted by Rivoire et al.[63] reviewed 131 patients with unresectable CRC liver metastases. After 3-6 months of systemic chemotherapy, 57 patients were considered candidates for curative liver resection. Surgery alone was performed in 33 patients (25%) or cryotherapy associated with resection in 24 patients (18%). After a median follow-up of 48 months were similar in both groups: 37% in the resection group and 36% in the cryotherapy plus resection group. They noted that the combination of neoadjuvant chemotherapy, cryotherapy, and liver resection constitutes promising treatment outcomes for patients with advanced CRC with liver involvement.

A new tissue ablation technique, irreversible electroporation (IRE) which was first reported in the early seventies[64-67], is associated with an increase in cell membrane permeability after microseconds to milliseconds of the electrical fields (high-voltage direct current, up to 3 kV) are applied. The increase in membrane permeability is associated with the formation of nanoscale defects (pores) in the cell membrane. These changes in membrane permeability have led to the naming of the process *"electroporation"*. The defects (pores) do not reseal, and are known to cause *"irreversible electroporation"*. As a result, the eventual cell death occurs due to loss of the cell's homeostatic mechanisms.[68] Unlike other ablative techniques, IRE can ablate the tissue without thermal effects[69] and the extent of tissue ablation can be predicted with mathematical analysis[70], therefore IRE can be applied in those lesions adjacent to blood vessels in the liver; it also demonstrates a decrease in size of treatment zone as early as 1 month following treatment. Several ongoing studies using this novel technology will

soon provide more information on its safety and efficacy for future applications.

Summary

Even though surgical resection has become the optimal, indeed only treatment modality associated with long term survival in the CRC patient with liver metastasis, a multidisciplinary approach is essential to increase potentials for cure. The aims of liver resection are to remove all macroscopic disease, to achieve clear resection margins and to leave sufficient functioning liver. Multiple randomized control trials are ongoing to evaluate both conventional and newer approaches to improve the treatment outcomes.

References

1. Attasara P, Buasom R. Hospital - Based Cancer Registry. National Cancer Institute DoMS, Ministry of Public Health, editor. Bangkok: Ramthai Press Co.; 2009.
2. Labianca R, Beretta GD, Kildani B, et al. Colon cancer. *Crit Rev Oncol Hematol* 2010;74:106-33.
3. StatBite. At what stage are colorectal cancer patients diagnosed? *J Natl Cancer Inst* 2009;101:1114.
4. Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. *CA Cancer J Clin* 2005;55:10-30.
5. Foster JH. Treatment of metastatic disease of the liver: a skeptic's view. *Semin Liver Dis* 1984;4:170-9.
6. Ward BA, Miller DL, Frank JA, et al. Prospective evaluation of hepatic imaging studies in the detection of colorectal metastases: correlation with surgical findings. *Surgery* 1989;105:180-7.
7. Bipat S, van Leeuwen MS, Comans EF, et al. Colorectal liver metastases: CT, MR imaging, and PET for diagnosis--meta-analysis. *Radiology* 2005;237:123-31.
8. Engledow AH, Skipworth JR, Pakzad F, et al. The role of 18FDG PET/CT in the management of colorectal liver metastases. *HPB (Oxford)* 2012;14:20-5.
9. Jones OM, Rees M, John TG, et al. Biopsy of potentially operable hepatic colorectal metastases is not useless but dangerous. *BMJ* 2004 ;329:1045-6.
10. Jones OM, Rees M, John TG, et al. Biopsy of resectable colorectal liver metastases causes tumour dissemination and adversely affects survival after liver resection. *Br J Surg* 2005;92:1165-8.
11. Rodgers MS, Collinson R, Desai S, et al. Risk of dissemination with biopsy of colorectal liver metastases. *Dis Colon Rectum* 2003;46:454-8.
12. Ohlsson B, Nilsson J, Stenram U, et al. Percutaneous fine-needle aspiration cytology in the diagnosis and management of liver tumours. *Br J Surg* 2002;89:757-62.
13. Eadens MJ, Grothey A. Curable metastatic colorectal cancer. *Curr Oncol Rep* 2011;13:168-76.
14. Fong Y, Fortner J, Sun RL, et al. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg* 1999;230:309-18.
15. Scheele J, Stang R, Altendorf-Hofmann A, et al. Resection of colorectal liver metastases. *World J Surg* 1995;19:59-71.
16. Nordlinger B, Guiguet M, Vaillant JC, et al. Surgical resection of colorectal carcinoma metastases to the liver. A prognostic scoring system to improve case selection, based on 1568 patients. Association Francaise de Chirurgie. *Cancer* 1996;77:1254-62.
17. Choti MA, Sitzmann JV, Tiburi MF, et al. Trends in long-term survival following liver resection for hepatic colorectal metastases. *Ann Surg* 2002;235:759-66.
18. Robertson DJ, Stukel TA, Gottlieb DJ, et al. Survival after hepatic resection of colorectal cancer metastases: a national experience. *Cancer* 2009;115:752-9.
19. Manfredi S, Lepage C, Hatem C, et al. Epidemiology and management of liver metastases from colorectal cancer. *Ann Surg* 2006;244:254-9.
20. Tsai MS, Su YH, Ho MC, et al. Clinicopathological features and prognosis in resectable synchronous and metachronous colorectal liver metastasis. *Ann Surg* Oncol 2007;14:786-94.
21. Wagner JS, Adson MA, Van Heerden JA, et al. The natural history of hepatic metastases from colorectal cancer. A comparison with resective treatment. *Ann Surg* 1984;199:502-8.
22. Dhir M, Lyden ER, Wang A, et al. Influence of margins on overall survival after hepatic resection for colorectal metastasis: a meta-analysis. *Ann Surg* 2011;254:234-42.
23. Muratore A, Ribero D, Zimmitti G, et al. Resection margin and recurrence-free survival after liver resection of colorectal metastases. *Ann Surg Oncol* 2010;17:1324-9.
24. Pawlik TM, Scoggins CR, Zorzi D, et al. Effect of surgical margin status on survival and site of recurrence after hepatic resection for colorectal metastases. *Ann Surg* 2005;241:715-22.
25. Arru M, Aldrighetti L, Castoldi R, et al. Analysis of prognostic factors influencing long-term survival after hepatic resection for metastatic colorectal cancer. *World J Surg* 2008;32:93-103.
26. Vandeweyer D, Neo EL, Chen JW, et al. Influence of resection margin on survival in hepatic resections for colorectal liver metastases. *HPB (Oxford)* 2009;11:499-504.
27. Gomez D, Cameron IC. Prognostic scores for colorectal liver metastasis: clinically important or an academic exercise? *HPB (Oxford)* 2010;12:227-38.
28. Fortner JG. Recurrence of colorectal cancer after hepatic resection. *Am J Surg* 1988;155:378-82.
29. Hughes KS, Simon R, Songhorabodi S, et al. Resection of the liver for colorectal carcinoma metastases: a multi-institutional study of patterns of recurrence. *Surgery* 1986;100:278-84.
30. Fong Y, Cohen AM, Fortner JG, et al. Liver resection for colorectal metastases. *J Clin Oncol* 1997;15:938-46.
31. Bozzetti F, Doci R, Bignami P, et al. Patterns of

failure following surgical resection of colorectal cancer liver metastases. Rationale for a multimodal approach. *Ann Surg* 1987;205:264-70.
32. Topal B, Kaufman L, Aerts R, et al. Patterns of failure following curative resection of colorectal liver metastases. *Eur J Surg Oncol* 2003;29:248-53.
33. Metcalfe M, Mann C, Mullin E, et al. Detecting curable disease following hepatectomy for colorectal metastases. *ANZ J Surg* 2005;75:524-7.
34. Ueno H, Mochizuki H, Hashiguchi Y, et al. Predictors of extrahepatic recurrence after resection of colorectal liver metastases. *Br J Surg* 2004;91:327-33.
35. Mutsaerts EL, van Ruth S, Zoetmulder FA, et al. Prognostic factors and evaluation of surgical management of hepatic metastases from colorectal origin: a 10-year single-institute experience. *J Gastrointest Surg* 2005;9: 178-86.
36. Takahashi S, Inoue K, Konishi M, et al. Prognostic factors for poor survival after repeat hepatectomy in patients with colorectal liver metastases. *Surgery* 2003; 133:627-34.
37. Chua TC, Saxena A, Chu F, et al. Predictors of cure after hepatic resection of colorectal liver metastases: an analysis of actual 5- and 10-year survivors. *J Surg Oncol* 2011;103:796-800.
38. Bhattacharjya S, Aggarwal R, Davidson BR. Intensive follow-up after liver resection for colorectal liver metastases: results of combined serial tumour marker estimations and computed tomography of the chest and abdomen - a prospective study. *Br J Cancer* 2006;95:21-6.
39. Yamada H, Katoh H, Kondo S, et al. Repeat hepatectomy for recurrent hepatic metastases from colorectal cancer. *Hepatogastroenterology* 2001;48:828-30.
40. Nishio H, Hamady ZZ, Malik HZ, et al. Outcome following repeat liver resection for colorectal liver metastases. *Eur J Surg Oncol* 2007;33:729-34.
41. de Jong MC, Mayo SC, Pulitano C, et al. Repeat curative intent liver surgery is safe and effective for recurrent colorectal liver metastasis: results from an international multi-institutional analysis. *J Gastrointest Surg* 2009;13: 2141-51.
42. Charnsangavej C, Clary B, Fong Y, et al. Selection of patients for resection of hepatic colorectal metastases: expert consensus statement. *Ann Surg Oncol* 2006;13: 1261-8.
43. Kemeny N, Huang Y, Cohen AM, et al. Hepatic arterial infusion of chemotherapy after resection of hepatic metastases from colorectal cancer. *N Engl J Med* 1999;341:2039-48.
44. Kemeny N. Management of liver metastases from colorectal cancer. *Oncology (Williston Park)* 2006; 20:1161-76.
45. Kemeny MM, Adak S, Gray B, et al. Combined-modality treatment for resectable metastatic colorectal carcinoma to the liver: surgical resection of hepatic metastases in combination with continuous infusion of chemotherapy--an intergroup study. *J Clin Oncol* 2002;20:1499-505.
46. Headrick JR, Miller DL, Nagorney DM, et al. Surgical treatment of hepatic and pulmonary metastases from colon cancer. *Ann Thorac Surg* 2001;71:975-9.
47. Adam R, de Haas RJ, Wicherts DA, et al. Is hepatic resection justified after chemotherapy in patients with colorectal liver metastases and lymph node involvement? *J Clin Oncol* 2008;26:3672-80.
48. Giacchetti S, Perpoint B, Zidani R, et al. Phase III multicenter randomized trial of oxaliplatin added to chronomodulated fluorouracil-leucovorin as first-line treatment of metastatic colorectal cancer. *J Clin Oncol* 2000;18:136-47.
49. Adam R, Avisar E, Ariche A, et al. Five-year survival following hepatic resection after neoadjuvant therapy for nonresectable colorectal. *Ann Surg Oncol* 2001;8:347-53.
50. Alberts SR, Horvath WL, Sternfeld WC, et al. Oxaliplatin, fluorouracil, and leucovorin for patients with unresectable liver-only metastases from colorectal cancer: a North Central Cancer Treatment Group phase II study. *J Clin Oncol* 2005;23:9243-9.
51. Bismuth H, Adam R, Levi F, et al. Resection of nonresectable liver metastases from colorectal cancer after neoadjuvant chemotherapy. *Ann Surg* 1996;224:509-20.
52. Nordlinger B, Sorbye H, Glimelius B, et al. Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): a randomised controlled trial. *Lance*t 2008;371:1007-16.
53. Bokemeyer C, Cutsem EV, Rougier P, et al. Addition of cetuximab to chemotherapy as first-line treatment for KRAS wild-type metastatic colorectal cancer: Pooled analysis of the CRYSTAL and OPUS randomised clinical trials. *Eur J Cance*r 2012;48:1466-75.
54. Van Cutsem E, Verslype C, Beale P, et al. A phase Ib dose-escalation study of erlotinib, capecitabine and oxaliplatin in metastatic colorectal cancer patients. *Ann Oncol* 2008;19:332-9.
55. Falcone A, Masi G, Loupakis F, et al. FOLFOXIRI (irinotecan, oxaliplatin, and infusional 5FU/LV) in combination with bevacizumab (BV) in the first-line treatment of metastatic colorectal cancer (mCRC): A phase II study by the G.O.N.O. group. *J Clin Oncol* 2008;26:abstr 4031.
56. Garufi C, Torsello A, Tumolo S, et al. POCHER (preoperative chemotherapy for hepatic resection) with cetuximab (Cmab) plus CPT-11/5-fluorouracil (5-FU)/ leucovorin(FA)/oxaliplatin (L-OHP) (CPT-11-FFL) in unresectable colorectal liver metastases (CLM). *J Clin Oncol* 2009;27:abstr e15020.
57. Folprecht G, Gruenberger T, Bechstein WO, et al. Tumour response and secondary resectability of colorectal liver metastases following neoadjuvant chemotherapy with cetuximab: the CELIM randomised phase 2 trial. *Lancet Oncol* 2010;11:38-47.
58. Wu YZ, Li B, Wang T, et al. Radiofrequency ablation vs hepatic resection for solitary colorectal liver metastasis: a meta-analysis. *World J Gastroenterol* 2011;17:4143-8.

59. Pathak S, Jones R, Tang JM, et al. Ablative therapies for colorectal liver metastases: a systematic review. *Colorectal Dis* 2011;13:e252-65.
60. Ruers T, Punt C, Van Coevorden F, et al. Radiofrequency ablation combined with systemic treatment versus systemic treatment alone in patients with non-resectable colorectal liver metastases: a randomized EORTC Intergroup phase II study (EORTC 40004). *Ann Oncol* 2012.
61. Gillams AR, Lees WR. Radiofrequency ablation of colorectal liver metastases. *Abdom Imaging* 2005;30: 419-26.
62. Livraghi T, Solbiati L, Meloni F, et al. Percutaneous radiofrequency ablation of liver metastases in potential candidates for resection: the "test-of-time approach". *Cancer* 2003;97:3027-35.
63. Rivoire M, De Cian F, Meeus P, et al. Combination of neoadjuvant chemotherapy with cryotherapy and surgical resection for the treatment of unresectable liver metastases from colorectal carcinoma. *Cancer* 2002; 95:2283-92.
64. Coster HG. A quantitative analysis of the voltage-current relationships of fixed charge membranes and the associated property of "punch-through". *Biophys J* 1965;5:669-86.
65. Neumann E, Rosenheck K. Permeability changes induced by electric impulses in vesicular membranes. *J Membr Biol* 1972;10:279-90.
66. Crowley JM. Electrical breakdown of bimolecular lipid membranes as an electromechanical instability. *Biophys J* 1973;13:711-24.
67. Zimmermann U, Pilwat G, Riemann F. Dielectric breakdown of cell membranes. *Biophys J* 1974;14:881-99.
68. Rubinsky B, Onik G, Mikus P. Irreversible electroporation: a new ablation modality--clinical implications. *Technol Cancer Res Treat* 2007;6:37-48.
69. Davalos RV, Mir IL, Rubinsky B. Tissue ablation with irreversible electroporation. *Ann Biomed Eng* 2005; 33:223-31.
70. Edd JF, Horowitz L, Davalos RV, et al. In vivo results of a new focal tissue ablation technique: irreversible electroporation. *IEEE Trans Biomed Eng* 2006;53: 1409-15.

An introduction to evidence-based medicine

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Keywords:
EMB, evidence-based medicine

Evidence-Based Medicine (EBM) is about offering support to make the right decision in choosing the best treatment for our patients. Since it first appeared in top medical journals in 1992[1], EBM has revolutionized medical practice and infiltrated other disciplines (such as dentistry) along the way as a tool to support the decision-making process in the provision of medical care.

The British Medical Journal concluded in 2007 that EBM represents one of the most important medical milestones of the last 160 years, which is quite an accolade when one considers all the other medical advances that were made during that timeframe.[2]

But what exactly is EBM and how can it help inform clinical practice?

Evidence-based medicine defined

Evidence-based medicine aims to apply the best available evidence gained from the scientific method to medical decision making.[3] Evidence-based medicine was defined as *"the process of systematically finding, appraising and using contemporaneous research findings as the basis for clinical decisions"* in one of the earliest papers on the subject.[1]

One of the most well known actors in the field is David Sackett who has written extensively on the subject and is credited with coining the phrase **evidence-based medicine**. In a paper from the mid-1990s[4], he and his coauthors offered the following definition, *"Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients."*

In another publication, Sackett et al[5] make explicit reference to the role of patients, urging *"more thoughtful identification and compassionate use of individual patient's predicaments, rights and preferences in making clinical decisions about their care."*

As the concept evolved, later definitions of EBM place emphasis on its complementary character and the aim to improve clinical experience through the provision of better evidence.[3]

Practicing evidence-based medicine

Sackett et al[4] have previously written that *"the practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research."* The learning curves associated with performing different types of surgery[6] mean that senior surgeons tend to have better outcomes.[7]

Table 1: Example for five main factor question

Method	Description	Example answers from SPRINT trial[11]
Patients	What patient group?	Patients aged over 18 but under 65 with isolated, closed, comminuted, tibial shaft fractures
Intervention	What surgical treatment, procedure or implant are you interested in?	Reamed intramedullary nailing
Comparison	What is the comparison treatment?	Unreamed intramedullary nailing
Outcome	What outcomes are you interested in?	Complications measured by any secondary intervention
Time	At what point in time will you measure treatment success?	One year after injury

Sackett et al[5] summarized the key steps of practicing EBM as follows:

1. Convert the clinically important information needs (about diagnosis, prognosis, therapy and other clinical and health care issues) into clinically relevant and meaningful questions.
2. Track down, with maximum efficiency, the best evidence with which to answer these questions. (This information comes from the clinical examination, the diagnostic laboratory, from research evidence or other sources).
3. Critically appraise that evidence for both its validity (closeness to the truth) and usefulness (clinical applicability).
4. Consider the applicability of this appraisal to your patients.

Similar versions of these essential steps of EBM practice can be found throughout the EBM literature.[8-10]

Posing the clinical question

There are five main factors to consider when generating the clinical question. A simple way to help you frame it is to use the acronym PICOT (Patients, Intervention, Comparison, Outcome, and Time). The PICOT grid for therapeutic studies is given below, along with some example answers from the published SPRINT trial.[11] (Table 1)

Selecting the most important terms from your PICOT answers will give you the search words you will need for the next stage of practicing EBM.

Finding the literature

One of the most popular information sources is PubMed, which is free to search on. It can be directly accessed at: www.pubmed.gov. This comprehensive database of the life sciences with a concentration on biomedicine also has some full text papers available for free.

PubMed is a powerful tool with many options. To help you find the published medical literature you require, please visit the series of brief animated tutorials with audio to learn more. Click on the *'PubMed Tutorials'* link on the PubMed home page or go directly to: www.nlm.nih.gov/bsd/disted/pubmed.html

You can also find systematic reviews at The Cochrane Library: www.thecochranelibrary.com. Another popular service for biomedical records is Embase: www.embase.com - a subscription is required for this service. Don't forget the resource that is your colleagues too!

Study design and Levels of Evidence

Levels of evidence are a method of arranging studies into a hierarchy based upon the quality of the evidence they produce as a result of their study designs (Figure 1).

Levels of evidence provide a concise and simple appraisal of study quality. The essence of levels of evidence is that, in general, cohort studies where are there are 2 groups to compare are better than single arm studies, prospective studies are better than retrospective studies, and randomized studies are better than nonrandomized studies.

Levels of evidence should be used with caution as they only provide a rough guide to study quality and should not preclude a complete critical appraisal. In addition, Level I evidence may not be available for all clinical situations, in which case lower levels of evidence can still be valuable. An answer to a clinical question is found by analyzing all evidence of all grades. A single study does not provide a definitive answer.[12]

Although not shown in the diagram, the tip of the evidence iceberg is a meta-analysis. Examples of these can be found at www.cochranelibrary.com.

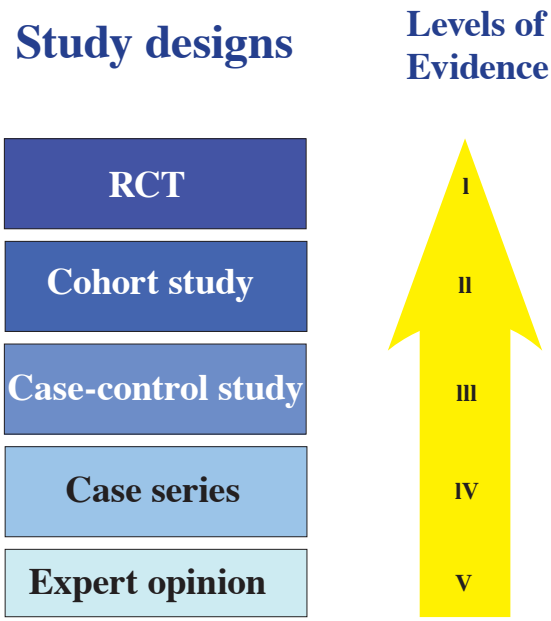

Figure 1: *Study designs and levels of evidence*

A meta-analysis is a systematic review of several Randomized Controlled Trials on the same subject but with more statistical power. What does this mean? If a sample size is too small, a study may not be able to detect differences in treatment effectiveness even if one treatment is truly superior to another. The ability to detect these differences is the statistical power of the study, which depends on the characteristics of the studied variables and on the sample size. Since we cannot change the characteristics of the variables we are studying, the only way to influence the power is to change the sample size. A larger sample size will bring more power to the study, and by combining several studies into a meta-analysis we can effectively achieve this.[13]

How important and applicable are levels of evidence in orthopedics?

Although rising, less than 5% of trials in the orthopedic literature are RCTs.[7] However, although they provide the highest level of evidence, an RCT is not always what is needed in orthopedics to answer a specific clinical question.[5, 14, 15] Glasziou et al describe some historical examples of treatments whose effects enjoyed wide acceptance on the basis of evidence drawn from case series or non-randomized cohorts (for example, ether for anesthesia).[16]

Assigning levels of evidence to studies published in the literature is also something relatively recent in orthopedics. The Journal of Bone and Joint Surgery, American Volume began running a quarterly *"Evidence-Based Orthopaedics"* section in 2000, which provided information on randomized trials published in a large number of other journals. Rating studies published in the journal with a level of evidence began in 2003. The Journal of Bone and Joint Surgery, American Volume, uses a model of five levels for each of four distinct study types (therapeutic, prognostic, diagnostic, and economic or decision modeling).[15]

The Journal of Orthopaedic Trauma introduced level of evidence rating for all therapeutic, prognostic, diagnostic and economic studies in March 2012.[17] In an acknowledgement of the established role that EBM now plays in orthopedics and trauma, the authors noted, *"the widespread use of the levels of evidence rating system in other orthopaedic journals and subspecialty meetings."*

However, despite the special challenges that EBM in orthopedics poses, there are ways to surmount these problems. While we obviously cannot blind the surgeon as to the treatment choice, patient and independent outcomes assessors can be blinded, a good example of how we can be creative in adapting standard research principles to suit the peculiarities of orthopedics.[18] Other proposed solutions include evaluating the learning curve using appropriate statistical techniques and a more precise definition of intervention to reduce the variations on operations that occur and impact upon surgical outcomes.[6]

Misclassification of fracture types often leads to a bias. Therefore, please be sure to use a validated fracture classification such as the Müller / AO Classification of Long Bones.

Appraising the literature

Critical appraisal is an integral part of Evidence Based Medicine. It should be done to try to identify methodological strengths and weaknesses in the literature. Therefore, evidence should be appraised for validity, importance and applicability to the clinical scenario.[19] Suitably critiqued, it allows the reader the opportunity to make an informed decision about the quality of the research evidence presented.

Critical appraisal checklists, which are a great help when interpreting scientific manuscripts, are available from the Centre for Evidence Based Medicine. Go to http://www.cebm.net/index.aspx?o=1913 for more information. The International Centre for Allied Health Evidence (iCAHE) also has a wide range of literature appraisal checklists from case studies to randomized controlled trials to download for free. Available at: www.unisa.edu.au/cahe/resources/cat/default.asp.

Incorporating the evidence into clinical practice

Having found the evidence and critically appraised the validity of the results, the most important question is whether the results are applicable to your patient. The benefits and limitations of applying the therapy should also be assessed.[7]

Sackett et al examine this issue across the range of clinically important needs.[5] For example, is a diagnostic test available at your hospital? Were the study patients in a prognostic study similar in profile to your patient? Are the patient's preferences satisfied by this particular treatment? It is also necessary to consider the level of patient compliance you can expect with a treatment regimen.

We hope that this article has piqued your interest in the world of Evidence-Based Medicine. However, as you learn and apply these and other EBM concepts, please always keep in mind that EBM can only ever inform your decision, it cannot make the decision for you.

References

1. Evidence-Based Medicine Working Group. Evidence-based medicine: a new approach to teaching the practice of medicine. *JAMA* 1992;268:2420-5.
2. Dickersin K, Straus SE, Bero LA. Evidence based medicine: increasing, not dictating, choice. *BMJ* 2007;334:10.
3. Timmermans S, Mauck A. The promises and pitfalls of evidence-based medicine. *Health Aff* 2005;24:18-28.
4. Sackett DL, Rosenberg WM, Gray JA, et al. Evidence based medicine: what it is and what it isn't. *BMJ* 1996; 312:71-2
5. Sackett DL, Richardson WS, Rosenberg W, et al. Evidence-Based Medicine-How to Practice & Teach EBM. New York: Churchill Livingstone, 1997.
6. McCulloch P, Taylor I, Sasako M, et al. Randomised trials in surgery: problems and possible solutions. *BMJ* 2002;324:1448-51.
7. Panesar SS, Philippon MJ, Bhandari M. Principles of evidence-based medicine. *Orthop Clin North Am* 2010; 41:131-8.
8. Chung KC, Swanson JA, Schmitz D, et al. Introducing evidence-based medicine to plastic and reconstructive surgery. *Plast Reconstr Surg* 2009;123:1385-9.
9. Straus SE, McAlister FA. Evidence-based medicine: a commentary on common criticisms. *CMAJ* 2000;163: 837-41.
10. Huić M. Evidence-based medicine and clinical practice. *Acta Medica Academica* 2008;37:29-37.
11. Study to Prospectively Evaluate Reamed Intramedullary Nails in Patients with Tibial Fractures Investigators, Bhandari M, Guyatt G, Tornetta P 3rd, Schemitsch EH, Swiontkowski M, Sanders D, Walter SD. Randomized trial of reamed and unreamed intramedullary nailing of tibial shaft fractures. *J Bone Joint Surg Am* 2008;90:2567-78.
12. Wright JG. A Practical Guide to Assigning Levels of Evidence. The Orthopaedic Forum. *J. Bone Joint Surg*. Am 2007;89:1128-30.
13. Hanson B, Kopjar B. Clinical studies in spinal surgery. *Eur Spine J* 2005;14:721-5.
14. Djulbegovic B, Guyatt GH, Ashcroft RE. Epistemologic inquiries in evidence-based medicine. *Cancer Control* 2009;16:158-68.
15. Wright JG, Swiontkowski MF, Heckman JD. Introducing levels of evidence to the journal. *J Bone Joint Surg Am* 2003;85:1-3.
16. Glasziou P, Chalmers I, Rawlins M, et al. When are randomised trials unnecessary? Picking signal from noise. *BMJ* 2007;334:349-51.
17. Slobogean G, Bhandari M. Introducing levels of evidence to the Journal of Orthopaedic Trauma: implementation and future directions. *J Orthop Trauma* 2012;26:127-8.
18. Helfet DL, Hanson BP. What's usable and what's missing in evidence-based medicine for fracture management. *Am J Orthop* 2011;40:450-1.
19. Karachi H, Samad K. A practical approach to evidence based medicine. *SAARC Jr., Anaesth* 2008;1:21-2.

Ceramic on Ceramic Bearings

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Keywords:
total hip replacement, ceramic on ceramic bearings, alumina matrix composite, squeaking sound, stripe wear, ceramic fracture

Metal on Polyethylene bearings have been widely used in total hip replacements for over 40 years. However there are still concerns about implant failures due to aseptic loosening and osteolysis, which occurs as a result of immune system responses triggered by the microscopic debris generated by normal wear and tear of the prosthetic joint.

Willert[1] suggest that Ultra-high monolecular weight polyethylene (UHMWPE) can be responsible for the formation of osteolysis occurring in areas around endoprosthetic implants, especially if greater amounts of this polymer's particles are released into the tissue.

In 1992, Amstutz et al.[2] discussed the factors leading to massive osteolysis, namely polyethylene wear debris induced osteolysis. Macrophages activated by phagocytosis of particulate wear debris are the key cells in this process. (Figure 1)

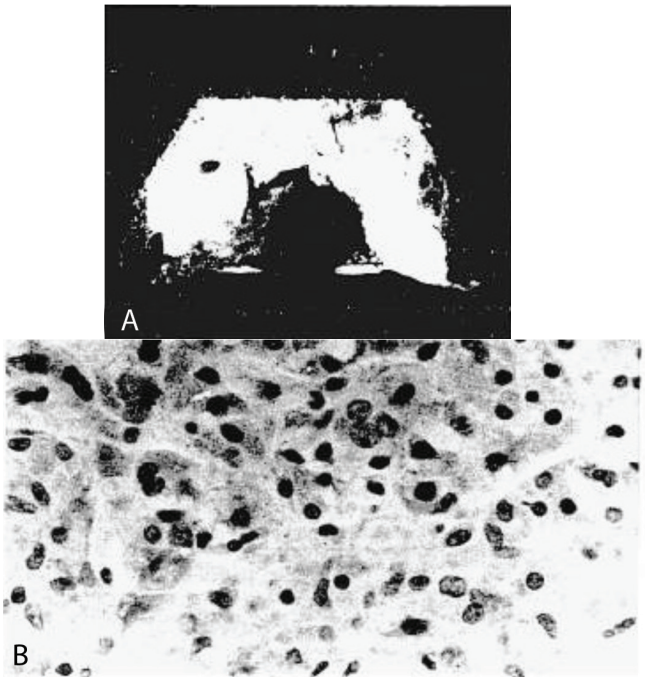

Figure 1 A-B: *(A) Retrieved titanium-alloy femoral porous-coated surface replacement bisected to show the replacement of bone by an invasive granulamalike tissue. This component failed after 50 months in an active 62-year-old man. (B) Histology of the tissue within the femoral head shows sheets of macrophages and giant cells, many with fine, intracellular metallic or UHMWPE debris. Lymphocytes are rarely seen in theses tissues. (Stain, toloidine blue; original magnification, X60.)*

Therefore, due to the most common cause of implant failure in Total Hip Replacement still being aseptic loosening from polyethylene wear debris, new bearing surfaces have been developed, such as ceramic on ceramic, in an attempt to reduce wear debris

Ceramic on Ceramic Bearings

Hard on Hard bearings (Ceramic on ceramic (COC) and Metal on metal) were developed because the long term outcome of Metal on non cross linked polyethylene was unsatisfactory due to the aforementioned extensive osteolysis from macrophage induced osteolysis.[2] Historically, the use of ceramic bearing was first introduced in April 1970 with Alumina-on-alumina bearings by Dr. Pierre Boutin[3] (Figure 2).

The advantage of ceramic on ceramic (COC) was shown by in vitro analysis to reduce wear debris particles that cause osteolysis[4,5] and Ceramic bearings made from Alumina have showed the lowest in vivo wear rates of any bearing couples.[6] The important property of ceramic that caused a lower wear rate was its being hydrophilic (Figure 3) Ceramic's hydrophilic properties facilitate an increased wettability of the surface because of the strong hydrogen bonds between the ceramic surface and synovial fluid that results in the synovial film being more uniformly distributed. In addition, ceramic has a greater hardness than metal and can be polished to a lower surface roughness (Figure 4). Lastly, ceramics have a high degree of Biocompatibility. Catelas et al.[7] reported in vitro studies show less macrophage reaction and decreased cytokine secretion when exposed to ceramic particles versus high-density polyethylene because of their small size, low volume, and inertness. These overall properties of ceramic create the lowest coefficient of friction and this bearings combination is the most likely to achieve true fluid film lubrication.[8]

***Figure 2**: Dr. Pierre Boutin (photograph courtesy of Laurent Sedel, MD)*

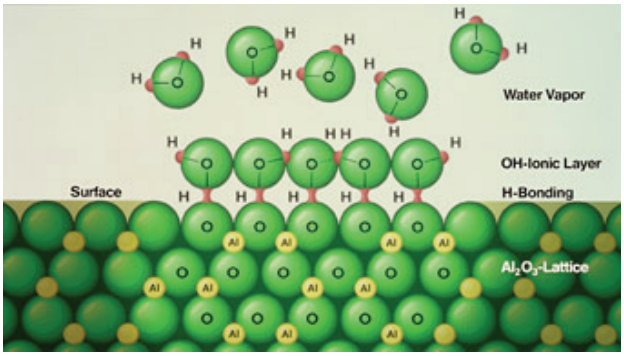

***Figure 3:** The strong hydrogen bond that forms between ceramic surfaces and synovial fluid give ceramic materials wetting properties that are superior to those of metal and polyethylene.*

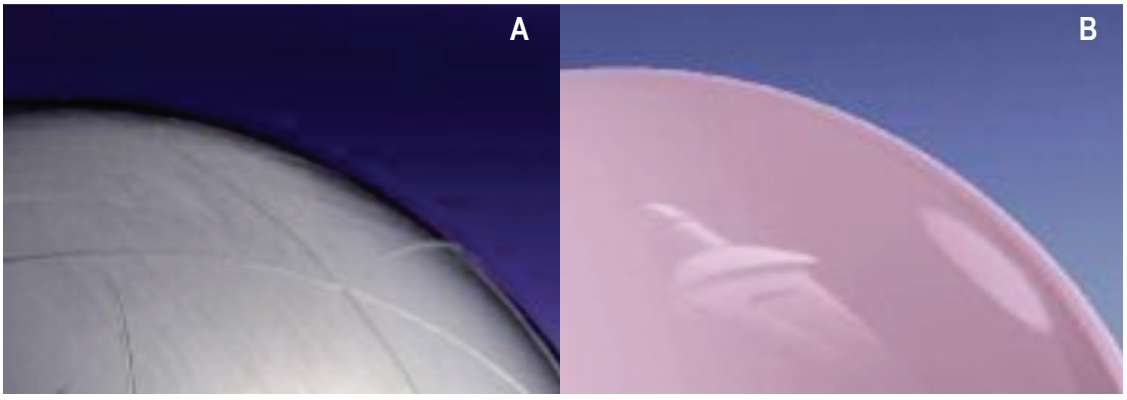

***Figure 4 A-B:** Shows no scratches on fourth Generation ceramics surface due to high degree of Hardness. (A) Scratched surface increases abrasion on surface of cup liners made of Polyethylene And Metal (CeramTec). (B) Only an unscratched smooth surface of the sort achieved in Fourth Generation ceramics enables optimal wetting, outstanding lubrication and minimal wear (CeramTec)*

However, the results of the early generation of COC were not promising due to poor design, inadequate material properties, and imperfect craftsmanship leading to catastrophic failures with ceramic fractures and excessive wear rate.

The first generations of COC were introduced between 1974 and 1988; at that time long sintering times resulted in large grained size material, which lead to decreased strength and crack propagation and thus a high incidence of ceramic fracture. The second generation of COC was developed between 1988 to 1994. Mixing micro-arc oxidation (CAO) and magnesium oxide (MgO) as sintering aids into the Alumina also limited the grain size, thus decreasing incidence of ceramic fracture. The Third Generation of COC was developed between 1994 to 2004. Improvements in manufacturing such as isostatic pressing, laser etching and proof testing resulted in a purer, denser ceramic with a small grain size, which reduced crack propagation and fracture.[9]

The mechanical properties of the three generations of ceramics are summarized in Table 1.[8]

The newest or fourth generation ceramic on ceramic design is Alumina-Matrix-Composite (AMC) or Biolox-Delta (Figure 5) which is composed of Alumina Oxide (approximately 75%), Zirconium Oxide, Chromium Oxide and other oxides. The combination of mechanical properties (fracture strength of Zirconia ceramic is approximately double that of alumina) and the good tribological properties of alumina ceramic make this an improved material for hip implants.

Surgical Grade Ceramics in Orthopaedics

Alumina Ceramics

Ceramics can be defined as inorganic non metallic materials compounded of a non metal and a metal. Alumina is a monophasic polycrystalline, very hard, stable and highly oxidized, with a high thermal conductivity coefficient, low bending stress and low resilience. The resultant material is in its highest state of oxidation, allowing thermodynamic stability, chemical inertness, and therefore excellent resistance to corrosion. The ionic structure of alumina ceramic creates a hydrophilic structure and fluid-film lubrication resulting in a higher wettability. In vitro studies show water is absorbed with high bond strength and that proteins quickly and completely cover the ceramic surface with a monolayer after surgical implantation; this phenomenon therefore improves lubrication of the joint. But Alumina ceramics are brittle because of excellent compression strength and bending strength is limited. Alumina ceramics can also break without warning signs due to low fracture toughness: ceramic has no possibility to deform without breakage.[11]

Table 1: The Changes in Grain Size and Burst Strength for Each Generation of Ceramic Manufacturing

Material Property	Generation I	Generation II	Generation III
Grain Size (μm)	4.2	3.2	1.8
Burst Strength (kN)	46	58	65

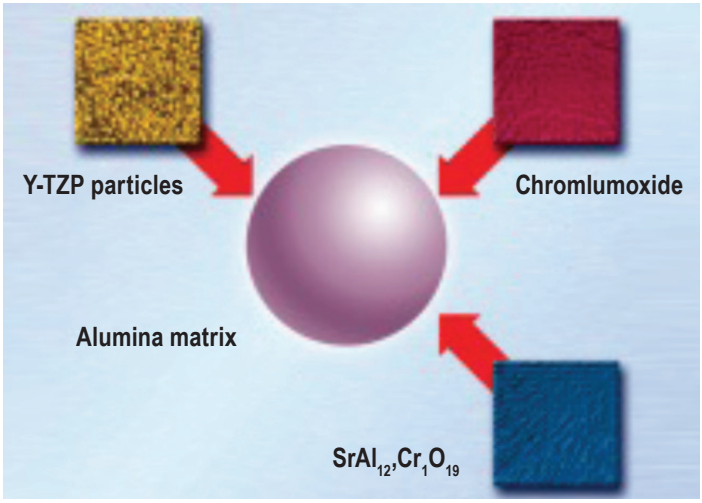

***Figure 5**: Composition of the alumina matrix composite (CeramTec)*

Zirconia Ceramic

Zirconia was introduced due to its higher fracture toughness and bending strength. However, pure zirconia is an unstable material exhibiting three crystalline phases: monoclinic, tetragonal, and cubic. The change between the three phases results in large volume changes and decreases the mechanical properties of the material considerably because of cracking on cooling. Adding oxides during the tetragonal phase stabilizes zirconia. Yttrium-stabilized tetragonal polycrystalline zirconia (Y-TZP) has a fine grain size and offers the best mechanical properties. The tetragonal phase that is the most resistant tends to transform into the monoclinic phase. This phenomenon explains the higher resistance of zirconia to shock but it also explains its lower sliding resistance properties and its unstable situation over time.[11] Another concern with Y-TZP is its hydrothermal stability. Because Y-TZP is destabilized during the process of steaming sterilization (causing surface roughness of zirconia due to hydrothermal transformation) these ceramics may also undergo slow degradation during long term implantation in the human body. This low temperature degradation is only significant after several years, but can still call the use of zirconia-on-zirconia bearings systems into question.[12]

Alumina-Matrix-Composite Ceramics (AMC)

Because of the brittleness of Pure Alumina ceramics and hydrothermal instability of Zirconia, it would seem that a composite of these materials with better mechanical properties would be the way to improve reliability of ceramics implants in orthopedics. De Aza et al.[13] studied crack growth resistance, comparing between 3 types of ceramics: alumina, zirconia and alumina-zirconia composite. They concluded that alumina-zirconia composites have a higher reliability than the monolithics due to the combined advantages of both alumina and zirconia. Alumina-zirconia nanocomposites with relative low zirconia content present similar hardness values to alumina but are not susceptible to hydrothermal instability.

Current concept of Aluminum-Matrix-Composite (AMC)

Ceramics are extremely hard, making them wear and scratch resistant however this also indicates a relatively high degree of brittleness, which led to failures in earlier designs. The new Ceramic design Alumina-Matrix-Composite has extremely high fracture toughness and is resistant to crack propagation results as the result of two strengthening mechanisms.

1. Airbag Function

The first toughening mechanism is dispersion of nano-sized, yttria-stabilized tetragonal zirconia particles in a stable, alumina matrix. These particles will be homogenously distributed and produce local pressure peaks in the area of crack which counteracts crack propagation and works like the airbag system in cars. (Figure 6)

2. Counteracting Crack Formation

The second strengthening mechanism is the result of in situ formation of platelet-shaped crystals in the oxide mixture. These platelets prevent cracking and crack propagation by deflecting the crack path and neutralizing crack energy. (Figure 7)

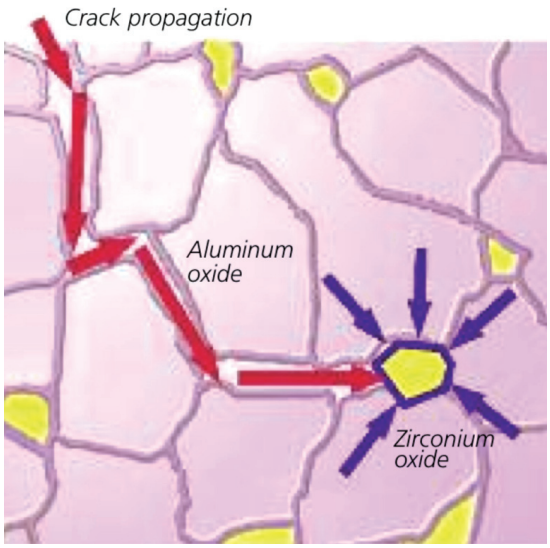

Figure 6: *The principle of conversion reinforcement: Zirconium oxide particles act like airbags by absorbing impacting forces. (CeramTec)*

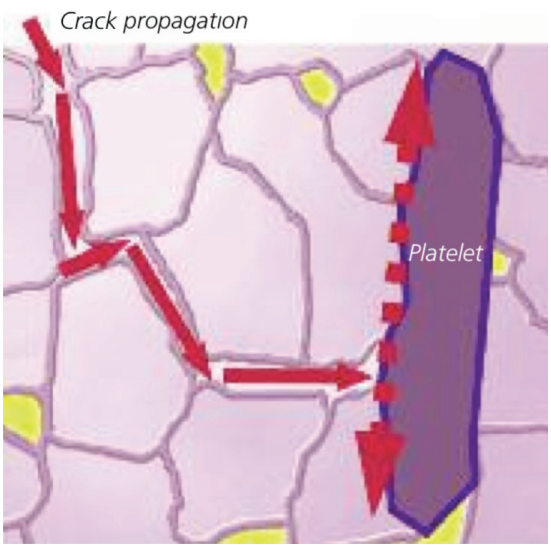

Figure 7: *The principle of platelet reinforcement: Platelet-shaped crystals block the propagation of cracks and thereby increase overall strength.*

Discussion

1. Squeaking Sounds

After improvements in ceramic manufacturing, the incidence of ceramic fracture decreased especially after third generation of ceramics. Over the last 5 years, the orthopedic community has been concerned with the noise of ceramic bearings, which was well documented with incidence varying from 1%-20.9%.[14-16] The squeaking noise was defined as a high-pitched noise audible to the human ear.

This disturbing, squeaking sound is like the sound of a new pair of shoes during walking and it annoys and worries patients. Mostly sound occurs during mid range of motion while weight bearing as in simulated stair climb.

The ten year follow up study by Chevillotte et al.[17] reported 100 Total hip replacements implanted with COC during November 1999 - December 2000; all hips used third generation ceramics (Biolox Forte, CeramTec). To determine the causes and consequences of squeaking, the patients were evaluated by questionnaire. Five patients (five Hips) reported the squeaking sound. The squeaking noise appeared at a mean of 66 months (4 to 85 months) post surgery with an incidence 2.2% at ten year follow up. The result showed more frequent squeaking sound found in hips in heavier ($p < 0.0008$) and taller males ($p < 0.0001$) and these result are in agreement with Walter[18] and Poggie.[19] Nevertheless, after 10 years of follow-up, patients with squeaking hip did not have any excessive wear, head fracture, cup or stem loosening, abnormal pain, or any limitation of their activities. Harris hip score and Postel-Merle d'Aubigné score were comparable. Squeaking did not disappear in the time but remained stable in intensity. Radiographic assessment did not found malpositioning of the cup in squeaking hips. They concluded that squeaking noise seem to be an isolated phenomenon with no consequence for functional result on longevity at ten years follow up.

In 2009, Chevillote et al.[20] reported a biomechanical in vitro study of COC bearings surface which intended to identify the potential contributing factors of Hip Squeaking. They used a custom-made hip stimulator to assess in vitro hip squeaking (Figure 8, 9). All Acetabulum Components were positioned in 45 degrees abduction and 20 degrees of anteversion. Eight conditions in two separate situations were applied to testing(Table 2 and Table 3).

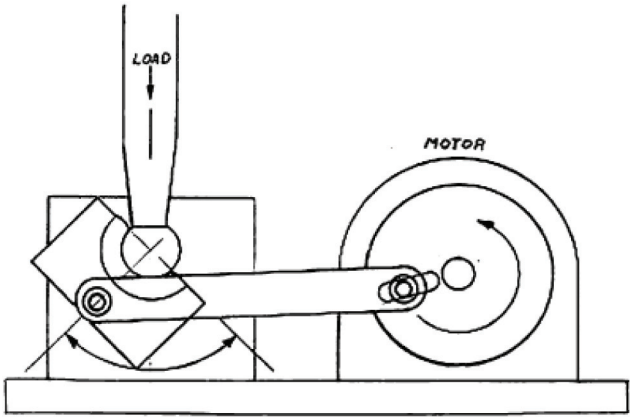

Figure 8: *A diagram of the custom-made testing device hip simulator*

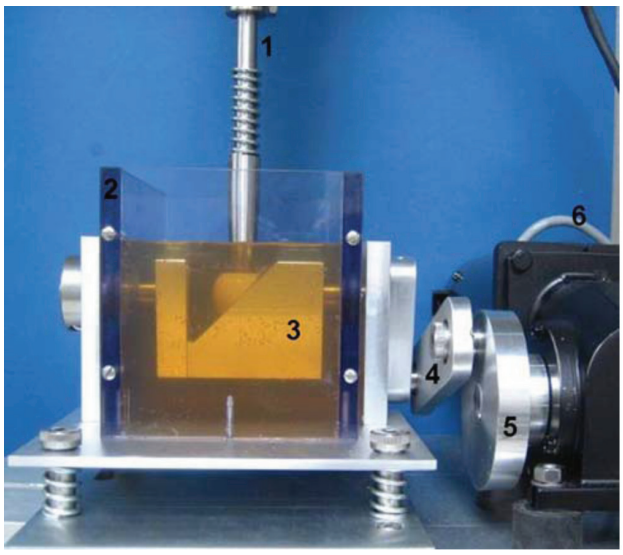

Figure 9: *A photograph of the custom-made device is shown.*
1 = Servo hydraulic testing machine
2 = box
3 = rotating table
4 = bar linkage
5 = rotating jig
6 = motor

Table 2: Situation without lubrication.

Conditions	Squeaking	Number of cycle for squeaking
Normal gait	√	2400
Normal gait (repeated same components)	√	300
High load	√	300
Stripe wear	√	Immediately
Stripe wear and high load	√	Immediately
Material transfer	√	Immediately
Edge wear	√	Immediately
Microfractures	√	4000

Table 3: Situation with lubrication

Conditions	Squeaking	Number of cycle for squeaking
Normal gait	0	2400
Normal gait (repeated same components)	0	300
High load	0	300
Stripe wear	0	Immediately
Stripe wear and high load	0	Immediately
Material transfer	√	Immediately; disappear after 30 cycles
Edge wear	0	Immediately
Microfractures	0	4000

Table 2's results show the squeaking sound was easily reproducible in all dry conditions, the squeaking noise was constant and did not disappear with time. In all these dry conditions, when a small amount of lubricant was added, the squeaking sound would disappear but if the lubricant was stopped, the squeaking would reappear and remain. Comparative to lubricated conditions, noise occurred only in material transfer condition (interposed of metal particles between head and liner). This suggested the exact etiology of squeaking is a disruption of fluid lubrication and this phenomenon occurs when the film fluid between the two surfaces in contact is disrupted. The researchers suggested this interruption most commonly results from metal particle transfer as a third body between COC.

Respeto et al.[21] reported the metal debris and stripe wear in four COC total hip replacements after revision surgery due to problems from squeaking noise.

Walter et al.[22] found bands of stripe wear in many ceramic heads after revision surgery without any previous squeaking problem So, in the conditions where there is a high risk to generate metal wear debris in COC hip replacement (such as neck rim impingement, malpostioning of acetabulum components, short neck design stem or some design of acetabular component with metal rim around the edge) the debris can interrupt the fluid film lubrication in COC Hip Replacement, resulting in squeaking noise. For the prevention of this disrupting sound the surgeon should pay attention to cup orientation and select the proper design of femoral stem and acetabulum cup.

2. Stripe wear

Stripe wear is the term used to describe the long, narrow area of damage seen on some femoral heads retrieved from alumina COC hip bearing couples. Stripe wear has been reported in first and second generation alumina bearings[23] However, there were also reports of stripe wear in third-generation alumina ceramic-on-ceramic bearings with well fixed and well positioned acetabular components.[24] (Figure 10)

Some literature reported produce stripe wear was due to edge effects in rigid ceramic-on-ceramic total hip arthoplasty.[26-28] When the hip was slightly subluxated during the swing phase of gait, the cup edge might create an inferior and somewhat equatorial stripe on the femoral head along with a circumferential stripe along the cup rim. During forced reduction at heel-strike, a superior and somewhat equatorial stripe would then be created on the head and the mating cup rim.[19](Figure 11).

Figure 10: *Third generation alumina ceramic-on-ceramic bearings with well fixed and well positioned acetabular components*

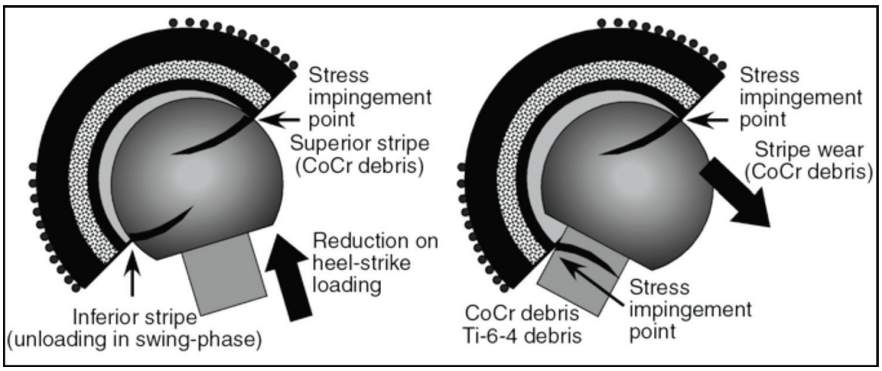

Figure 11: *During forced reduction at heel-strike, a superior and somewhat equatorial stripe would then be created on the head and the mating cup rim*

Nevelos et al.[30] proposed that microseparation of the bearing centers occurs during the swing phase of normal walking and that the subsequent edge loading with heel strike causes the stripe.

In an analysis of 16 retrieved third generation alumina COC bearings, the reseacher proposed that stripe wear was caused by edge loading between acetabular liner and femoral head ceramic component.[31] The pattern of wear stripes on the heads and liners showed that the majority do not occur with normal walking; instead they probably occur with edge loading when the hip is flexed such as in rising from a chair or climbing a high step. The mean volumetric wear rates of COC bearings in that study were 0.7 mm^3 per year (running-in). For the effect of alumina ceramic wear, in vitro study on the biologic activity of ceramic particles suggests that they will not be more destructive than polyethylene particles.[32] The wear particles produced by alumina ceramic on-ceramic bearings are not in the correct size range (0.1–1 micrometer) to stimulate macrophages to produce TNF. For this reason, volume of wear debris from stripe wear will neither be related to osteolysis nor to bearing failure.[31]

Ceramics Fracture

Total hip arthroplasty is often a successful orthopaedic surgical procedure. To improve longevity of prosthesis, many alternative bearings have been explored. One attractive choice is alumina ceramic-on-alumina bearings due to its properties of low friction, high wear resistance, and good biocompatibility. On the other hand, ceramic on ceramic bearings have problems of fracture of a ceramic head and/or liner. Many attempts were made to improve alumina material, that was associated with high rates of fracture as reported in the 1970s (Table 4).[32,33]

Table 4: Summary of the mechanical properties of the material used in ceramic-on-ceramic bearings over the past 40 years

property	Alumina 1970s	Alumina 1990s	Alumina/Zirconia composite 2000s
Bending strength (MPa)	400	580	1150
Fracture toughness (MPa m1/2)	4	4.3	8.5
Vickers Hardness HVQ (GPa)	20	20	19
Average grain size (μm)	7.2	1.8	0.6
Young's Modulus (GPa)	380	380	350
Hot isostatic pressing	no	yes	yes
Proof testing	no	yes	yes

Improvements of second-generation ceramics included purification of alumina powder, leading to smaller grain size. This, along with refined manufacturing, increased the density, resulting in decreased fracture rates to 0.014%.[34-36] Third generation fracture rates were reduced to 0.004%.[34-36] In the 2000s, the introduction of alumina/zirconia composite materials showed improvement in mechanical properties For this reason, the reported incidence of alumina femoral head fractures has decreased. The rate of fracture of femoral heads with this material is reported by the manufacturer to be 1 in 50,000.[37] In 2010, Lombardi et al.[38] reported atraumatic fracture of AMC femoral head. The analysis of the fractured alumina matrix composite femoral head demonstrated the surface roughness increased minimally from new condition (3 nm) to the main wear zone (5 nm) (Figure 12, 13).

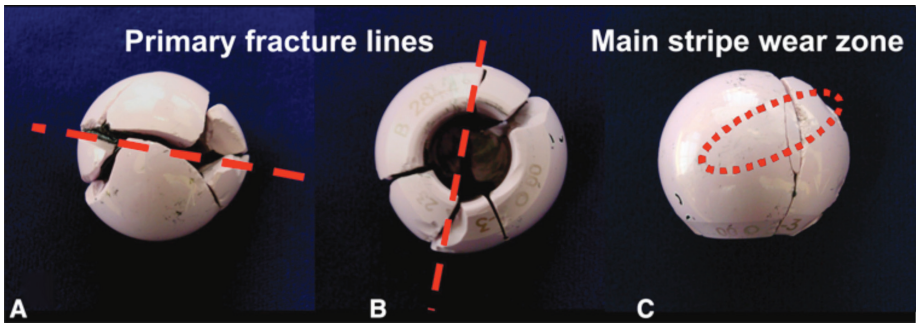

Figure 12A-C: *Overview of fracture fragment from a 28-mm delta from (A) polar view, (B) view of the base, and (C) side view of the stripe wear zone. The dominant fracture plane is indicated by dashed lines in the polar and basal views. The large stripe wear zone crosses over three of the fragments at the angle indicated by the dashed ellipse on the side view*

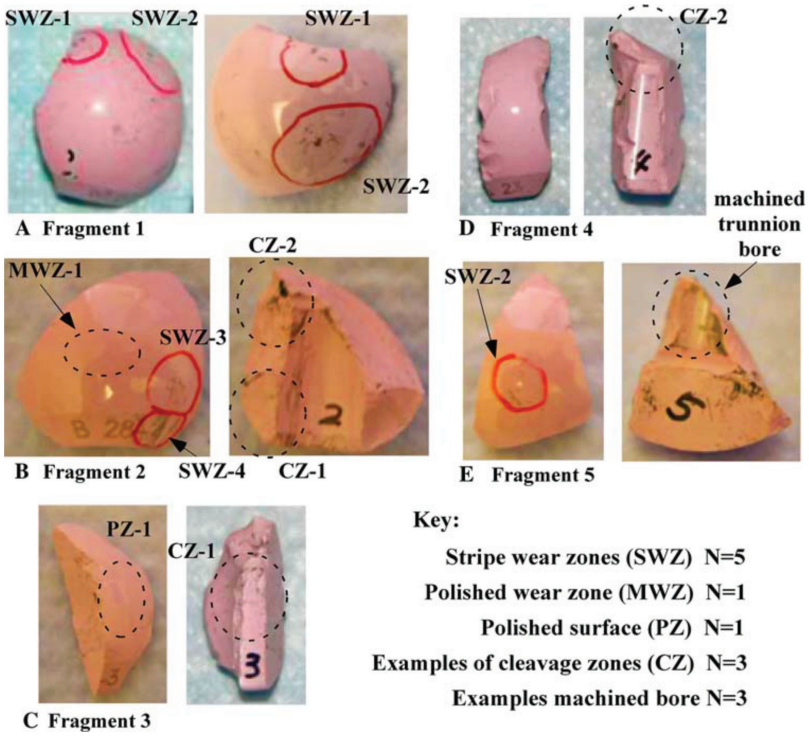

Figure 13A-E: *Photographs show five of the largest of seven fragments (A-E) from a fractured 28 mm 'Delta' ball. The circles indicate site of analysis for polished main wear zone (MWZ), stripe wear zones (SWZ), metal contamination, machined taper bore and fracture cleavage regions (CZ).*

Hamilton et al.[39] also reported the overall rate of post-operative ceramic liner fracture was 1.1% (two of 177). The authors presumes most liners failed as a result of eccentric or incomplete seating of the modular ceramic liner within the metal acetabular shell. Improper positioning and impaction may generate uncontrolled peak stresses in the ceramic, which may lead to fracture[40] (Figure 14).

Many predisposing factors for ceramic liner fracture were proposed such as microseparation trauma, and obesity.[41-43] Fractures apparently due to component impingement were explored.[40,44-46] There were reports that ceramics are vulnerable to fracture due to impact and from stress concentrations (point and line loading) such as those associated with impingement-subluxation.[47] The risk of ceramic femoral head fracture during impingement-subluxation was found to be highly site specific owing to the greatly higher tensile stress at the (edge-loading) egress site compared with that from neck-on-liner impingement (Figure 15).

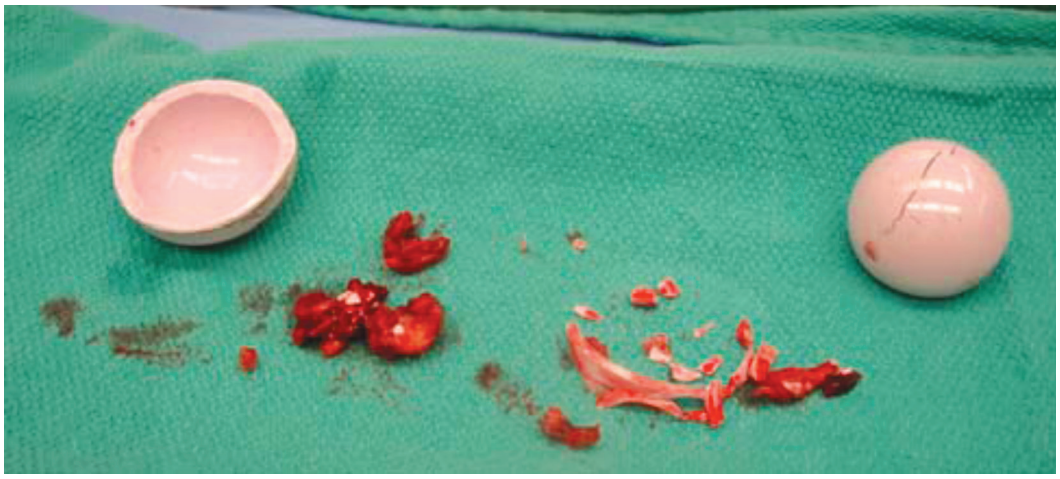

Figure 14: *The retrieved liner and head show the fractured rim of the liner and ceramic fragments retrieved from the wound.*

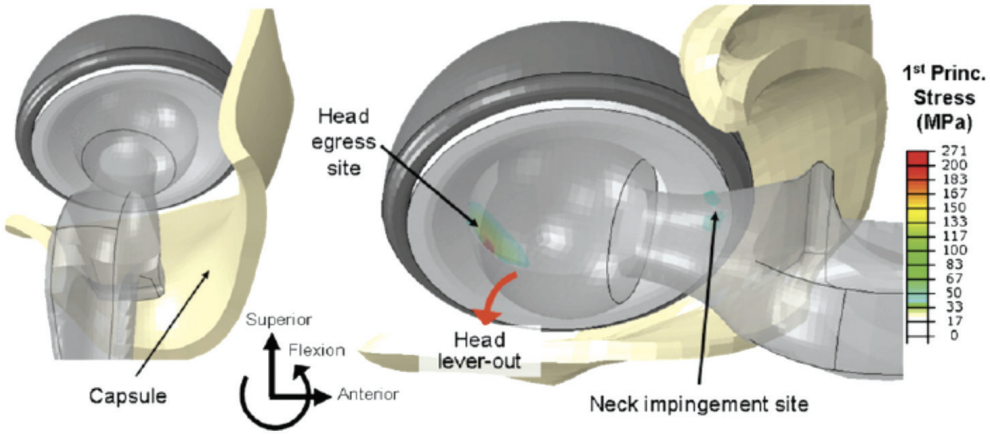

Figure 15: *Total hip arthoplasty impingement global FE model. Challenge motions began in full extension (left) and progressed through the prescribed hip angulation sequence, resulting in impingement (right).*

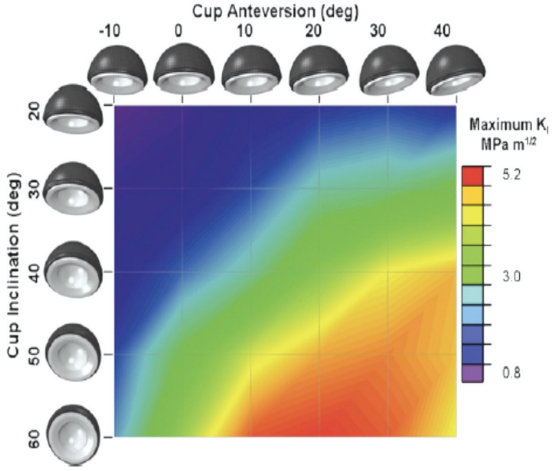

Figure 16: *Computed values of temporal-spatal maximum KI for the stoop challenge demonstrating fracture propensity sensitivity to both cup inclination and anteversion.*

Another interesting factor is cup position. The biomechanic study showed ceramic cup fracture propensity is presumably very sensitive to surgical cup positioning. Higher cup inclination and/ or cup anteversion angles gave rise to the higher values of tensile stress if/when subluxation-associated edge loading occurred (Figure 16). The study of the stress on cup position concluded that increased cup inclination and increased anteversion were found to elevate fracture risk. It is resonable to avoid impingement-subluxation, higher cup inclination and cup anteversion of ceramic bearing to reduce risk of ceramic bearing fracture.

Conclusion

The tribology properties of low friction, high wear resistance and good biocompatibility make ceramic material the most attractive in hip replacement surgery at the present time. In long term follow up after implantation,

the ceramic couple bearings show the lowest wear rate in many reports, which means low wear debris and less osteolysis.

Specific concerns about ceramics such as fracture, squeaking noise, and stripe wear are still topics of discussion among orthopedic surgeons. Significant advancements in manufacturing processes led to the production of alumina matrix composite ceramics that could eliminate the previous ceramics weaknesses. As for surgical factors, surgeons should perform operations with meticulous technique especially during positioning of the acetabulum component, and insertion of ceramics liner, and they check for any impingement or infolding of anterior-superior capsule, and check the hip tension to prevent hip laxity. These factors can all reduce complications from ceramic implants.

Otherwise, due to the continued high cost of ceramics implant (about double that of metal on polyethylene) it is suggested that good candidates for ceramics implants should be young, active, high demand patients that will need to use their new hip joints long term.

References

1. Willert HG, Bertam H, Buchhorn GH. Osteolysis in Alloarthroplasty of the hip: The role of ultra-high monolecular weight polyethylene wear particles. *Clin Orthop Relat Res* 1990;258:95-107.
2. Amstutz HC, Campell P, Kossovsky N, et al. Mechanism and clinical significance of wear debris induced osteolysis. *Clin Orthop Relat Res* 1992;276:7-18.
3. Boutin P. Total Arthroplasty of the Hip by Fritted Aluminum Prosthesis : Experimental study and 1st Clinical Applications. *Rev Chir Orthop Reparatrice Appar Mot* 1972;58:229-46.
4. Oonishi H, Clarke IC, Good V, et al. Alumina hip joints characterize by run-in wear and steady-state wear to 14 million cycles in hip-simulator model. *J Biomed Mater Res A* 2004;70:4.
5. Nevelos JE, Ingham E, Doyle C, et al. Wear of HIPed and non-HIPed alumina-alumina hip joints under standard and severe simulator testing conditions. *Biomaterials* 2001;22:2191-7.
6. Boutin P, Christel P, Dorlot JM, et al. The use of dense Alumina-alumina ceramic combination in total hip replacement. *J Biomed Mater Res* 1988; 22:1203-32.
7. Catelas I, Huk O, Petit A, et al. Flow cytometric analysis of macrophage response to ceramic and polyethylene particles: Effects of size, concentration, and composition. *J Biomed Mater Res* 1998;41:600-7.
8. Christel PS. Biocompatibility of surgical-grade dense polycrystalline alumina. *Clin Orthop Relate Res* 1992;282:10-8.
9. Bierbaum BE, Nairus J, Kuesis D, et al. Ceramic on Ceramic bearings in total hip replacement. *Clin Orthop Relate Res* 2002;405:158-63.
10. Hamadouche M, Sedel L. Ceramics in Orthopaedics. *JBJS* 82B:1095-9.
11. Hannouche D, et al. Ceramics in Total Hip Replacement. *Clin Orthop Relate Res* 2005;430:62-71.
12. Piconi C, Maccauro G. Zirconia as a ceramic biomaterial, a review. *Biomaterials* 1999;20:1-25.
13. A.H. De Aza, et al.Crack growth resistance of Alumina, Zirconia and Zirconia toughened Alumina ceramics for joint prosthesis. *Biomaterials* 2002;23:937-45.
14. Capello WN, D'Antonio JA, Feinberg JR, et al. Ceramicon-ceramic total hip arthroplasty: update. *J Arthroplasty* 2008;23:39-43.
15. Restrepo C, Parvizi J, Kurtz SM, et al. The noisy ceramic hip: is component malpositioning the cause? *J Arthroplasty* 2008;23:643-9.
16. Keurentjes JC, Kuipers RM, Wever DJ, et al. High incidence of squeaking in THAs with alumina ceramic-on-ceramic bearings. *Clin Orthop Relat Res* 2008;466:1438-43.
17. Chevillotte C, Pibarot V, Carret JP, et al. Hip squeaking: A 10 years Follow up Study. *J Arthroplasty* 2012;27: 1008-13
18. Walter WL, O'Toole GC, Walter WK, et al. Squeaking in ceramic-on-ceramic hips: the importance of acetabular component orientation. *J Arthroplasty* 2007;22:496-503.
19. Poggie RA, Turgeon TR, Coutts RD. Failure analysis of a ceramic bearing acetabular component. *J Bone Joint Surg Am* 2007;89:367-75.
20. Chevillotte C, Trousdale RT, Chen Q, et al. Hip Squeaking : A Biomechanical study of Ceramic-on-Ceramic Bearing Surfaces. *Clin Orthop Relat Res* 2010;468:345-50.
21. Restrepo C, Parvizi J, Kurtz SM, et al. The noisy ceramic hip: is component malpositioning the cause? *J Arthroplasty* 2008;23:643-9.
22. Walter WL, Insley GM, Walter WK, et al. Edge loading in third generation alumina ceramic-on-ceramic bearings: stripe wear. *J Arthroplasty* 2004;19:402-13.
23. Nevelos JE, Prudhommeaux F, Hamadouche M, et al. Comparative analysis of two different types of alumina-alumina hip prosthesis retrieved for aseptic loosen- ing. *J Bone Joint Surg Br* 2001;83:598.
24. Nevelos J, Ingham E, Doyle C, et al. Microseparation of the centers of alumina-alumina artificial hip joints during simulator testing produces clinically relevant wear rates and patterns. *J Arthroplasty* 2000;15:793.
25. Murali R, Bonar F, Kirsh G, et al. Osteolysis in Third-Generation Alumina Ceramic-on-Ceramic Hip Bearings With Severe Impingement and Titanium Metallosis. *J Arthroplasty* 2008;23:13-9.
26. Dorr LD, Zhinian W, Longjohn DB, et al. Total hip arthroplasty with use of the Metasul metalon-metal articulation: Four to sevenyear results. *J Bone Joint Surg Am* 2000;82:789-98.
27. Huo MH, Parvizi J, Gilbert NF. What's new in hip arthroplasty. *J Bone Joint Surg Am* 2006;88:2100-13.
28. Walter WL, Lusty PJ, Watson A, et al. Stripe wear and squeaking in ceramic total hip bearings. *Semin Arthroplasty* 2006;17:190-5.

29. Clarke IC, Manley MT. How do alternative bearing surfaces influence wear behavior? *J Am Acad Orthop Surg* 2008;16:S86-S93.
30. Nevelos J, Ingham E, Doyle C, et al. Microseparation of the centers of alumina-alumina artificial hip joints during simulator testing produces clinically relevant wear rates and patterns. *J Arthroplasty* 2000;15:793-5.
31. Walter WL, Insley GM, Walter WK, et al. Edge Loading in Third Generation Alumina Ceramic-on-Ceramic Bearings. *J Arthroplasty* 2004;19:402-13.
32. Fisher J, Stewart T, Tipper J, et al. Functional biological activity and osteolytic potential of wear debris generated in artificial hip joints. Presented at: IMechE 2000, June 13-15; London.
33 Willmann G. Ceramic femoral head retrieval data. *Clin Orthop Relat Res* 2000;379:22-8.
34. Rack R, Pfaff HG. A new ceramic material for orthopaedics. Procs 5th International CeramTec Symposium, February 2000.
35. Inzerillo CV, Garino JP. Alternative bearing surfaces in total hip arthroplasty. *J Southern Orthop Assoc* 2003;12: 106-11.
36. Mehmood S, Riyaz JH, Pandit H. Review of ceramic-on-ceramic total hip arthroplasty. *J Surg Ortho Adv* 2008;17:45-50.
37. Tateiwa T, Clarke IC, Williams PA, et al.Ceramic total hip arthroplasty in the United States: safety and risk issues revisited. *Am J Orthop* 2008;37:E26-31.
38. Pandorf T. How important it is to use clean taper fixations? Procs 13th International BIOLOX Symposium: Bioceramics and Alternative Bearings in Joint Arthroplasty, Edinburgh, 2009.
39. Lombardi AV Jr, Berend KR, Seng BE, et al. Delta ceramic -on-alumina ceramic articulation in primary THA: prospective, randomized FDA-IDE study and retrieval analysis. *Clin Orthop Relat Res* 2010;468:367-74.
40. Hamilton WG, McAuley JP, Dennis DA, et al. THA with Delta ceramic on ceramic: results of a multicenter investigational device exemption trial. *Clin Orthop Relat Res* 2010;468:358-66.
41. Min BW, Song KS, Kang CH, et al. Delayed fracture of a ceramic insert with modern ceramic total hip replacement. *J Arthroplasty* 2007;22:136-9 .
42. Sariali E, Stewart T, Mamoudy P, et al. Undetected fracture of an alumina ceramic on ceramic hip prosthesis. *J Arthroplasty* 2010;25:658.e1-5.
43. Hannouche D, Nich C, Bizot P, et al. Fractures of ceramic bearings: history and present status. *Clin Orthop Relat Res* 2003;417:19-26.
44. Poggie RA, Turgeon TR, Coutts RD. Failure analysis of a ceramic bearing acetabular component. *J Bone Joint Surg* 2007;89:367-75.
45. Ha YC, Kim SY, Kim HJ, et al. Ceramic liner fracture after cementless alumina-onalumina total hip arthroplasty. *Clin Orthop Relat Res* 2007;458:106-11
46. Park YS, Hwang SK, Choy WS, et al. Ceramic failure after total hip arthroplasty with an alumina-on-alumina bearing. *J Bone Joint Surg Am* 2006;88:780-7
47. Toni A, Traina F, Stea S, et al. Early diagnosis of ceramic liner fracture. guidelines based on a twelveyear clinical experience. *J Bone Joint Surg Am* 2006;88:55-63.
48. Hasegawa M, Sudo A, Hirata H, et al. Ceramic acetabular liner fracture in total hip arthroplasty with a ceramic sandwich cup. *J Arthroplasty* 2003;18:658-61.
49. Elkins JM, Pedersen DR, Callaghan JJ, et al. Fracture Propagation Propensity of Ceramic Liners During Impingement-Subluxation. *J Arthroplasty* 2012;18:520-6.

Syncope in Children

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Keywords:
syncope, fainting, neurally mediated syncope, cardiac syncope, children

Syncope is a relatively common condition in children and adolescents. Most children with syncope do not have serious diseases and their prognosis is generally benign. However, in certain patients, syncope may be the first presentation of a serious cardiac pathology. Therefore, the understanding of its pathophysiology, causes and investigative work ups are important for general pediatricians dealing with this entity.

Definition

Syncope is a transient loss of cerebral function due to lack of energy substrate (low blood pressure, decreased oxygen tension or low blood glucose). The results are loss of consciousness and postural tone.

Causes of syncope

Normal brain function requires adequate blood pressure, oxygen supply and energy substrate (glucose). Inadequacy of any one of these factors (due to, for example, hypotension, hypoxia or hypoglycemia) can lead to syncope. Other conditions that mimic syncope include abnormal brain discharge (seizure), vestibulocerebellar migraine, hyperventilation syndrome and pseudo-syncope (psychogenic syncope).

Syncope in children most commonly occurs from a reflex transmitted via the autonomic nervous system (Bezold-Jarisch reflex) that causes peripheral vasodilation or bradycardia, or both (the so called *"vasovagal"* or *"neurocardiogenic"* syncope). In a small number of patients, hypotension and syncope may result from cardiac pathology (cardiac syncope). The distinction between these 2 etiologies is important and is the main subject discussed in this article.

Prevalence

It is uncertain how frequently children have syncope, partly because most children with a single episode of syncope do not come to medical attention. One study showed the incidence of children and adolescents with syncope that came to medical attention to be 126/100,000.[1] It was estimated that up to 15% of normal children would experience at least one syncope before the age of 18.[1] Most of these children had neurocardiogenic (vasovagal) syncope and were otherwise healthy. The peak incidence of syncope in children occurs at around the age of 15-19 years with a higher prevalence in females.[2]

Neurocardiogenic syncope (vasovagal syncope or the common faint)

The usual form of neurocardiogenic syncope is caused by stimulation of the intramyocardial mechanoreceptor (stretch receptor or C fiber) as a result of forceful myocardial contraction from various etiologies such as decreased cardiac preload from prolonged standing. A neural impulse from the myocardium is sent to the brainstem, causing a reflex that leads to a withdrawal of sympathetic stimulation and/or an increase in vagal tone, resulting in paradoxical bradycardia and/or vasodilation. This is called *"Bezold-Jarisch reflex"*. This mechanism explains syncope occurring in children while standing in line at school in hot weather or while standing in a church. It also serves as the basis for treatment of neurocardiogenic syncope with medications that decrease cardiac contraction such as beta adrenergic blockers or medications with vagolytic property such as disopyramide.

Apart from prolonged standing (especially in hot or crowded places), there are also other afferent pathways that may trigger neurocardiogenic syncope. For example:

1. From the cerebral cortex: after emotional circumstances such as the sight of blood and/or pain such as venipuncture or immunization.
2. From receptors in the respiratory, genitoureteral or gastrointestinal systems: for instance, cough syncope, micturition syncope or defecation syncope.
3. From other stimulations, such as hair grooming syncope.[3]

Diagnosis

Because neurocardiogenic syncope is common in children and adolescents, most often the diagnosis is made from a clinical ground. The usual descriptions of children who experience neurocardiogenic syncope are as follows:

1. Pubertal girls and boys.[2, 4] The age at presentation is relatively older than other etiologies of syncope in children with the possible exception of psychiatric disorders causing syncope-like conditions.[4] In general, neurocardiogenic syncope is rare in small children, with the exception of the pallid-type of breath holding spell (pallid infantile syncope) which is a related condition and is considered a type of neurally mediated syncope.[1]

2. Syncope occurs when the patient is in an upright posture without activity (standing) or with light activity; it rarely occurs during exercise or sleep.

3. There may be triggering events such as prolonged standing, sight of blood, prolonged fasting, recovering from illness or any conditions which have led to dehydration.

4. There may be prodromal symptoms that signify vagal nerve stimulation, such as nausea or vomiting. The patient may feel tired, weak, or lightheaded. The patient may feel hot, cold, or sweaty.[1, 4] Some people report repeated yawning or hyperventilation before syncope onset.

5. The cardiovascular response (if recorded) can be divided into 3 types
   a. Cardioinhibitory: bradycardia is pronounced.
   b. Vasodepressor: hypotension without bradycardia, as a result of peripheral vasodilation.
   c. Mixed type: both bradycardia and peripheral vasodilation.

6. The patient may lose consciousness (syncope) or may not (pre-syncope), and have loss of postural tone. The episode is generally brief, does not result in bodily injury (or only minor injury) and generally is not associated with tonic or clonic posturing and/or loss of bladder or bowel control. The patient often appears pale (pallor) but usually does not stop breathing or develop cyanosis. After regaining consciousness, the patient may continue to feel weak but should be lucid almost immediately.[5]

Cardiac syncope

Heart diseases that cause syncope in children are generally severe structural defects, coronary anomaly or aneurysm, or are arrhythmia syndromes that cause ventricular tachyarrhythmia. All of these etiologies can lead to sudden cardiac death. Examples of these conditions are left or right-sided heart outflow obstruction, severe pulmonary hypertension, coronary obstruction causing myocardial ischemia, cyanotic spell, sick sinus syndrome, heart block, long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, Wolff-Parkinson-White (WPW) syndrome and Brugada syndrome.

Etiology and diagnosis of cardiac syncope

1. Left or right heart outflow obstruction. These patients generally have a loud heart murmur.
   a. Aortic stenosis (severe)
   b. Pulmonary stenosis (severe)
   c. Hypertrophic cardiomyopathy with obstruction

2. Severe pulmonary hypertension. Syncope is caused by acute and severely increased pulmonary arterial pressure (pulmonary hypertensive crisis). Careful physical examination usually reveals right ventricular heave and/or accentuated second heart sound ± systolic murmur from tricuspid valve regurgitation.

3. Coronary ischemia
   a. Coronary anomaly, such as presence of a left main coronary artery (LMCA) arising from right sinus of valsalva. The LMCA in this condition

may take a course in-between the aortic root and the main pulmonary artery. It is believed that expansion of both great arteries with exercise can compress the LMCA (the one that gives rise to anterior descending artery and circumflex artery) and cause cardiac ischemia.

b. Coronary obstruction post Kawasaki disease.
c. Other rare causes of myocardial ischemia such as myocardial bridging, coronary spasm and coronary-cameral fistula.
d. Coronary atherosclerotic disease is rare in children unless there is familial hypercholesterolemia or diseases with premature aging such as progeria.

Unlike left or right heart outflow obstruction, physical examination in patients with coronary anomaly or stenosis is often normal. Resting EKG may also be normal. Diagnosis is usually made by further investigation such as exercise stress testing, echocardiogram or coronary angiography/CT scan.

4. Cyanotic spell

Severe cyanosis from congenital heart disease can result in loss of consciousness and postural tone similar to other causes of syncope but the diagnosis is generally straightforward. The patient usually has visible cyanosis and examination reveals abnormal heart sounds.

5. Cardiac arrhythmia

a. Arrhythmia syndromes that cause ventricular tachyarrhythmia (ventricular tachycardia or ventricular fibrillation.
- Long QT syndrome (Figure 1). The diagnosis is usually made by prolongation of corrected QT interval (QTc) on the 12-lead EKG. The diagnosis may be difficult in certain patients whose QT interval may fall within *"borderline"* or normal range. Expert referral is needed for the diagnosis of a patient who is suspected to have long QT syndrome when the 12-lead EKG is not diagnostic.
- Wolff-Parkinson-White (WPW) syndrome (Figure 2). Although rare, syncope and sudden death can occur in patients exhibiting WPW syndrome with atrial fibrillation and rapid ventricular conduction (Figure 3). The diagnosis of WPW syndrome is made by 12-lead EKG showing shorten PR interval with delta wave.
- Catecholaminergic polymorphic ventricular tachycardia (CPVT). Children with this disease develop polymorphic ventricular tachycardia (VT) (Figure 4) upon sympathetic stimulation such as exercise. The disease must be distinguished from long QT syndrome. Resting EKG in these children demonstrates no or only minor abnormality with normal QT interval. Diagnosis is made by presence of polymorphic VT and/or bidirectional VT during exercise.
- Brugada syndrome (Figure 5) is a more common etiology of syncope and sudden death in adults rather than children. The diagnosis is made by presence of RSR' and ST elevation in right chest lead (V1-V2). Abnormal EKG may not be seen all the time, hence in patients suspected to have this disease with normal EKG, expert referral is recommended.

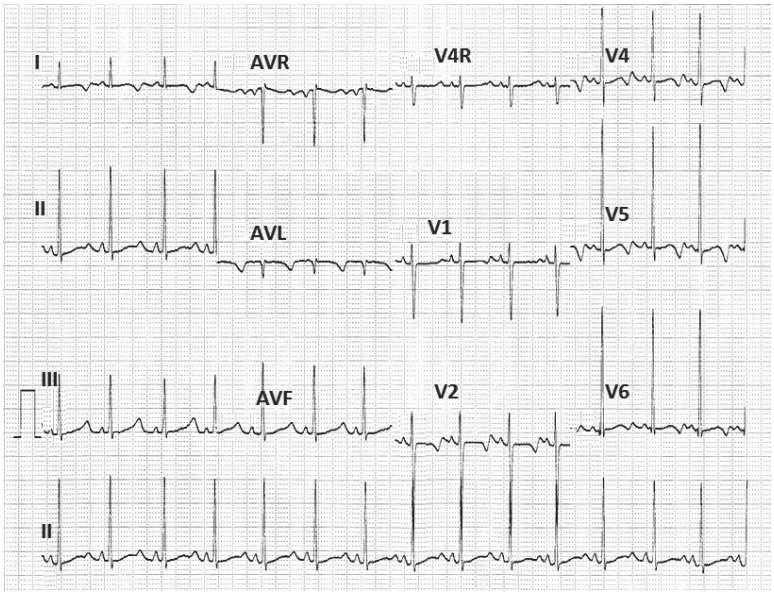


Figure 1: *Long QT syndrome. This child has a family history of long QT syndrome and neurosensory deafness.*

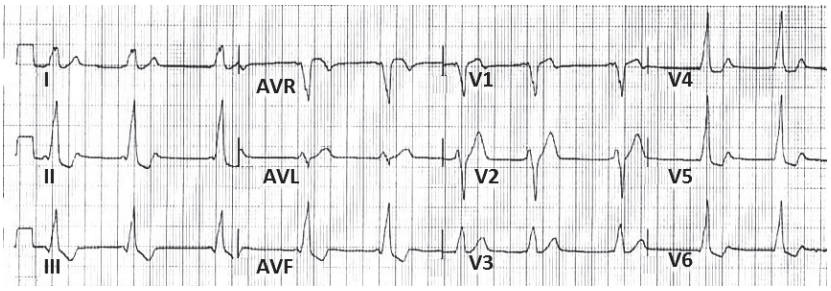


Figure 2: *Wolff-Parkinson-White syndrome. There are delta waves (slurring of R wave) and short PR interval.*

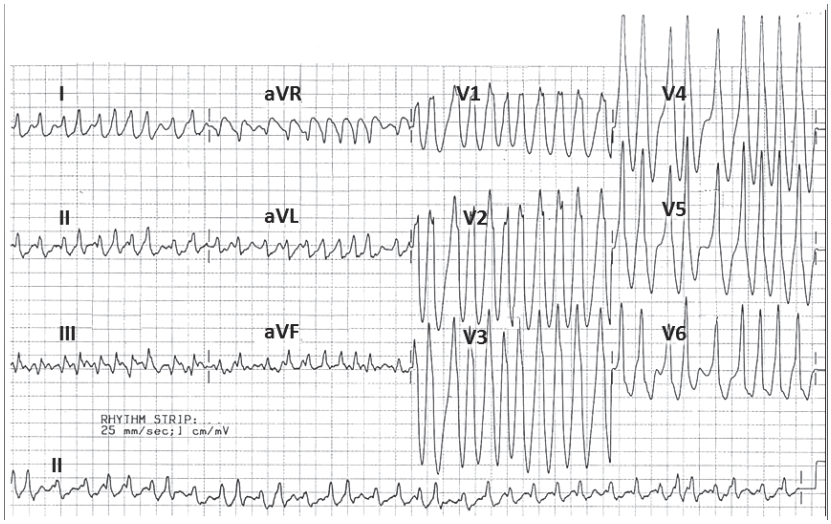
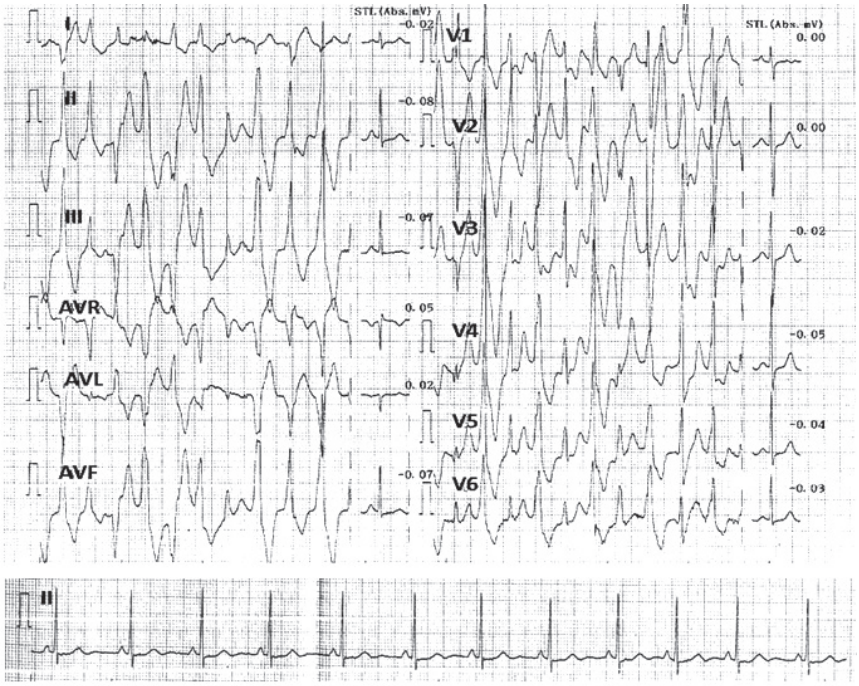


Figure 3: *Atrial fibrillation with rapid ventricular conduction via the Kent's pathway which makes the 12-lead EKG look like ventricular tachycardia. Rapid ventricular conduction and fast ventricular rate may lead to ventricular fibrillation, syncope or sudden death. (Courtesy of Dr. Somchai Prichawat, MD)*



Top

Bottom

Figure 4: *Catecholaminergic polymorphic VT during exercise in a child who presented with recurrent exertional syncope (Top). The resting EKG was normal (Bottom). Physical examination was normal.*

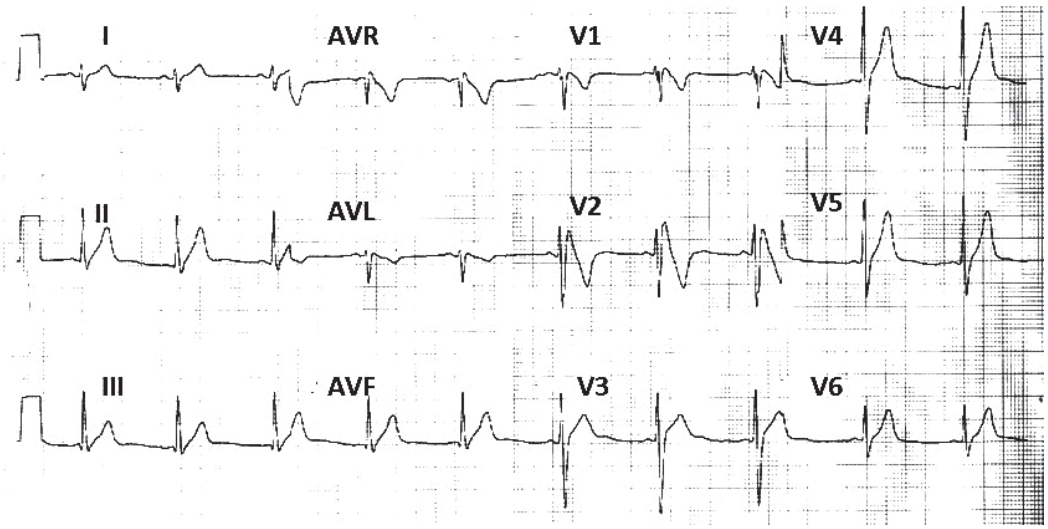


Figure 5: *Presence of right bundle branch block pattern with ST elevation in right chest leads (V1 and V2), suggestive of Brugada syndrome.*

- Arrhythmogenic right ventricular dysplasia.
- Short QT syndrome (QTc < 300 ms).

b. Heart block. Presence of syncope with complete heart block is ominous. Patients with heart block can have syncope from prolonged asystole or bradycardia-induced VT.
c. Sick sinus syndrome

6. Other rare causes of cardiac syncope include mitral valve prolapse, left or right heart inflow obstruction.

Approach to children and adolescents with syncope

Most previously healthy children with a typical history of neurocardiogenic or vasovagal syncope can be diagnosed by careful history and physical examination. Twelve-lead EKG is recommended by many experts as a routine investigation in children and adolescents who present with syncope to rule out the possibility of heart disease.[1,2,6] Apart from EKG, other investigative work ups such as EEG, Holter monitoring, echocardiogram, exercise stress testing or other specialized testings are done selectively, as dictated by the clinical setting of the patient.

In general, investigative work up for syncope is indicated in children with syncope and one or more of the following features.[1,2,5]

1. Presence of previous heart diseases, neurologic abnormalities, metabolic diseases (such as diabetes mellitus) or other chronic diseases.
2. Syncope during exercise
3. Syncope when not in upright posture.
4. Syncope preceded by palpitation, dyspnea and/or chest pain.
5. History of convulsion or abnormal posturing/ movement of body and/or extremities or neurologic deficits. History of loss of bowel or bladder control. History of appearing dazed or having a blank look before fainting (suggestive of seizure disorder).
6. History of Kawasaki disease or coronary heart disease/ coronary anomaly.
7. History of taking medication(s) that may cause syncope or arrhythmia such as antihypertensive medications, medications that may cause prolong QT interval (diuretics, cisapride, tricyclic antidepressant, etc.)
8. Family history of sudden death or inherited heart disease (congenital long QT syndrome, Brugada syndrome (aka Lai-tai in Thailand), catecholaminergic polymorphic VT, hypertrophic cardiomyopathy, etc.) or family history of recurrent syncope or seizure that is suggestive of inherited arrhythmia syndrome. Family history of deafness (can be associated with long QT syndrome).
9. Abnormal physical examination including cardiovacular and/or neurologic examination. However, it must be kept in mind that normal physical examination does not preclude serious heart disease, since many of the heart diseases that case ventricular arrhythmia or coronary ischemia, typically show a normal physical examination.
10. Syncope that requires cardiopulmonary resuscitation (CPR), results in apnea or is associated with cyanosis.

The choice of further investigation(s) depends on the differential diagnosis. EEG and neurologic referral is indicated in a patient who is suspected to have seizure. The initial evaluation in children suspected to have cardiac syncope with normal physical examination begins with 12-lead EKG to look for evidence of ventricular hypertrophy/dilation, ST-T abnormality suggestive of myocardial ischemia, cardiac conduction defects or presence of arrhythmia syndrome such as long QT, WPW and Brugada

syndrome. The diagnosis of coronary ischemia usually requires further investigation such as exercise stress test, echocardiogram or coronary angiogram. Resting 12-lead EKG is usually normal or shows only minor abnormality in patients with polymorphic catecholaminergic VT but the diagnosis can be made on exercise stress testing (exercise testing in patients with exercise-induced syncope can be dangerous so it should be done by an expert). Holter monitoring and event recorder (loop recorder) is useful if cardiac arrhythmia is suspected. Cardiac MRI is useful to diagnose arrhythmogenic right ventricular dysplasia or other types of silent cardiomyopathy. Finally, an invasive cardiac catheterization, angiography and electrophysiologic study may be needed in the rare cases whereby other non-invasive testing is not diagnostic.

Tilt table testing is a provocative test for neurocardiogenic or vasovagal syncope. The test is done by tilting the patient upright for prolonged period of time, with or without administration of a medication that increases cardiac contraction (to stimulate myocardial mechanoreceptor) such as isoproterenol infusion or a medication that decreases cardiac preload, such as sublingual nitroglycerine. Because the specificity and sensitivity of tilt table testing for the diagnosis of neurocardiogenic syncope are not very high[6,7], the test is usually done when the diagnosis of neurocardiogenic syncope is questionable, such as in patients with unusual symptoms or unusual triggering events, or in patients with recurrent syncope of unclear etiology. It must be kept in mind that tilt table testing can be positive in patients with other etiologies of syncope as well, hence the interpretation of the test must be made in light of the pretest probability (i.e. the patient's history, physical examination and the results of other investigations). Infusion of isoproterenol or sublingual administration of nitroglycerine usually increases the sensitivity but may decrease the specificity of tilt table testing.[8,9]

Treatments

Treatments of syncope in children largely depend on the etiology. Children with (or suspected to have) cardiac syncope need to be seen and treated by a pediatric cardiologist. Neurologic or psychiatric referrals are recommended for children suspected to have seizure or neuro-psychiatric disorders such as hyperventilation syndrome or pseudo-seizure. Children with the diagnosis of neurocardiogenic or vasovagal syncope can be treated and followed by a pediatrician, unless there is uncertainty about the diagnosis or if there is frequent recurrence of the symptom.

There is no single treatment that is most effective for children with neurocardiogenic syncope. It should be explained to the parents and patient that the disease is not life-threatening although it may recur in the future and may cause injury from falling. The child should be taught to avoid the conditions that may precipitate syncope, such as prolonged standing in a crowded or hot environment, dehydration, missing a meal or lack of sleep. Drinking more water or consuming more sodium (eating salty food) may help to prevent syncope occurrence. If the child experiences a prodromal symptom, such as lightheadedness, nausea or vomiting, he/she should sit or lie down immediately (with or without the feet raised above the chest) to avoid the total loss of conscious which may cause a fall or bodily injury.There are additional maneuvers that the patient can do to abort the syncope, such as crossing and squeezing the arms and legs or squatting down to increase systemic blood pressure.[1]

Medication is usually reserved for children with neurocardiogenic syncope who experience frequent recurrence or those who have severe symptoms. There is no medication that has been shown to be most effective in this disease. Many drugs have been used with variable success or in some studies, even showed no benefit.[10,11] These medications include beta adrenergic blockers (to decrease cardiac contraction and stimulation of myocardial stretch receptors), disopyramide (used for its negative inotropic and anticholinergic properties), fludrocortisones (to make the kidney retain salt and water), midodrine (to increase venous return by stimulating adrenergic α-receptor) and pseudoephedrine (for vasoconstrictive effect). Physicians must help patients and their parents to understand that no medication is universally effective and despite taking medication, the child is still at risk for recurrent syncope and all other measures described in the previous paragraph should still be adhered to.

Children with neurocardiogenic syncope generally have excellent prognosis. Spontaneous remission as the child gets older is common.[7] The most important thing when evaluating children suspected to have neurocardiogenic syncope is to rule out other etiologies of syncope and to advise the patients and their parents on how to live with this usually benign condition.

References

1. Martin K, Bates G, Whitehouse WP. Transient loss of consciousness and syncope in children and young people: what you need to know. *Arch Dis Child Edu Pract Ed* 2010;95:66-72.
2. Driscoll DJ, Jacobsen SJ, Porter CJ, et al. Syncope in children and adolescents. *J Am Coll Cardiol* 1997;29: 1039-45.
3. Evans WN, Acherman R, Kip K, et al. Hair-grooming syncope in children. *Clin Pediatr* 2009;48:834-6.

4. Chen L, Zhang Q, Ingrid S, et al. Aetiologic and clinical characteristics of syncope in Chinese children. *Acta Paediatr* 2007;96:1505-10.
5. Kanter R. Syncope and sudden death. In: SR N, editor The science and practice of pediatric cardiology. Baltmore: William & Wilkins, 1998:2169-99.
6. Steinberg LA, Knilans TK. Syncope in children: diag nostic tests have a high cost and low yield. *J Pediatr* 2005;146:355-8.
7. Levine MM. Neurally mediated syncope in children: results of tilt testing, treatment, and long-term follow-up. *Pediatr Cardiol* 1999;20:331-5.
8. Foglia-Manzillo G, Giada F, Fteita N, et al. Tilt testing potentiated with sublingual nitroglycerin in children with unexplained syncope. *Eur Heart J* 2007;28: 2605-9.
9. Alehan D, Lenk M, Ozme S, et al. Comparison of sensitivity and specificity of tilt protocols with and without isoproterenol in children with unexplained syncope. *Pacing Clin Electrophysiology : PACE* 1997;20: 1769-76.
10. Salim MA, Di Sessa TG. Effectiveness of fludrocortisone and salt in preventing syncope recurrence in children: a double-blind, placebo-controlled, randomized trial. *J Am Coll Cardiol* 2005;45:484-8.
11. Zhang Q, Jin H, Wang L, et al. Randomized comparison of metoprolol versus conventional treatment in preventing recurrence of vasovagal syncope in children and adolescents. *Med Sci Monit* 2008;14:199-203.

Questions of Syncope in Children

Q1. Investigative work-up (other than history taking and physical examination) is most indicated for which of the following patients who present with syncope?

a. A 7-year old girl developed syncope while standing in line at school
b. A 10-year old girl developed syncope during venipuncture procedure
c. A 13-year old boy had syncope while standing after urination
d. A 15-year old boy had syncope while playing basketball
e. Investigative work up is not indicated in any of the above patients

Q2. Which is the following is LEAST frequently seen in a child with neurocardiogenic (vasovagal) syncope?

a. Pallor
b. Cyanosis
c. Nausea, vomiting
d. Blurring of vision
e. Feeling hot and sweaty

Q3. Syncope is one of the typical presentations in which of the following heart diseases?

a. Atrial septal defect
b. Ventricular septal defect
c. Aortic valve stenosis
d. Patent ductus arteriosus
e. All of the above

Q4. A 3 year-old boy has a history of recurrent syncope (4-5 times in the past year) while feeling frightened or hearing loud noises. The last episode occurred yesterday after swimming, with the patient having tonic posturing of the extremities before gaining consciousness. Physical examination revealed no abnormality. There is a family history of unexplained death in a young cousin of the boy's father. Which of the following investigation is most likely to yield the diagnosis?

a. 12-lead EKG
b. Electroencephalogram (EEG)
c. Echocardiography
d. Coronary CT scan
e. Intracardiac electrophysiologic study

Q5. Which of the following is LEAST likely to be effective in preventing neurocardiogenic syncope?

a. Avoid standing for a long time
b. Consuming more salty food
c. Taking more water before school
d. Taking medication with beta blockade property
e. Taking medication with vasodilatory property

Answers of Syncope in Children

Answer 1: **e.** Most children with syncope have the diagnosis of vasovagal or neurocardiogenic syncope with good prognosis. However, there are certain children with significant heart diseases that cause syncope. Physical examination in these children may be abnormal in cases of right or left heart outflow obstruction but could also be normal in patients with cardiac arrhythmia or coronary anomaly or obstruction. Thus, careful history taking is important for evaluation of a child presenting with syncope. The history in items A to C could be consistent with vasovagal syncope. On the other hand, a history of syncope during exertion is more consistent with cardiac syncope and requires further investigation.

Answer 2: b. Children with vasovagal syncope may have prodromal symptoms and/or signs of low blood pressure such as feeling dizzy, having blurring of vision or looking pale prior to fainting. Additionally, he/she may feel hot and sweaty, report excessive yawning nausea or hyperventilation prior to syncope. History of cyanosis is rare.

Answer 3: c. Severe left or right heart outflow obstruction can cause syncope, especially during exertion due to inability to further increase cardiac output or because of ischemia and/or cardiac arrhythmia. Left-to-right shunt such as an ASD, VSD or PDA, however, rarely causes syncope.

Answer 4: a. One of the most common causes of cardiac syncope for children with no past history of heart disease and who have normal physical examination is cardiac arrhythmia, especially ventricular arrhythmia (ventricular tachycardia and ventricular fibrillation). Many of these children have inherited diseases, causing abnormal function of ion transport across the cardiac cells or within the cells. The description of this patient is typical for a long QT syndrome, which usually causes syncope during exertion or during an emotional event such as being frightened or hearing a loud noise. During an episode of ventricular arrhythmia and cerebral ischemia, tonic posturing of the whole body may be seen which could be mistaken for seizure disorder. Twelve-lead EKG usually confirms the diagnosis, however, the fact that QT interval is normal neither excludes long QT syndrome nor other arrhythmic syndromes such as catecholaminergic polymorphic ventricular tachycardia.

Answer 5: e. Patients with vasovagal syncope should avoid any situation that may cause syncope such as prolonged standing, especially in a hot or crowded place. He/she should avoid being dehydrated and taking more water and salty food may help preventing syncope. Most patients with vasovagal syncope do not need pharmacologic intervention but if required, medications with beta blockade or vasoconstrictive effects have been used with variable success. Other medications that had been used are fludrocortisone (to cause sodium and fluid retention) and medications with vagolytic effect.

Demonstration of coronary venous stenosis via intraventricular wall injection in case of left ventricle to coronary venous fistula.

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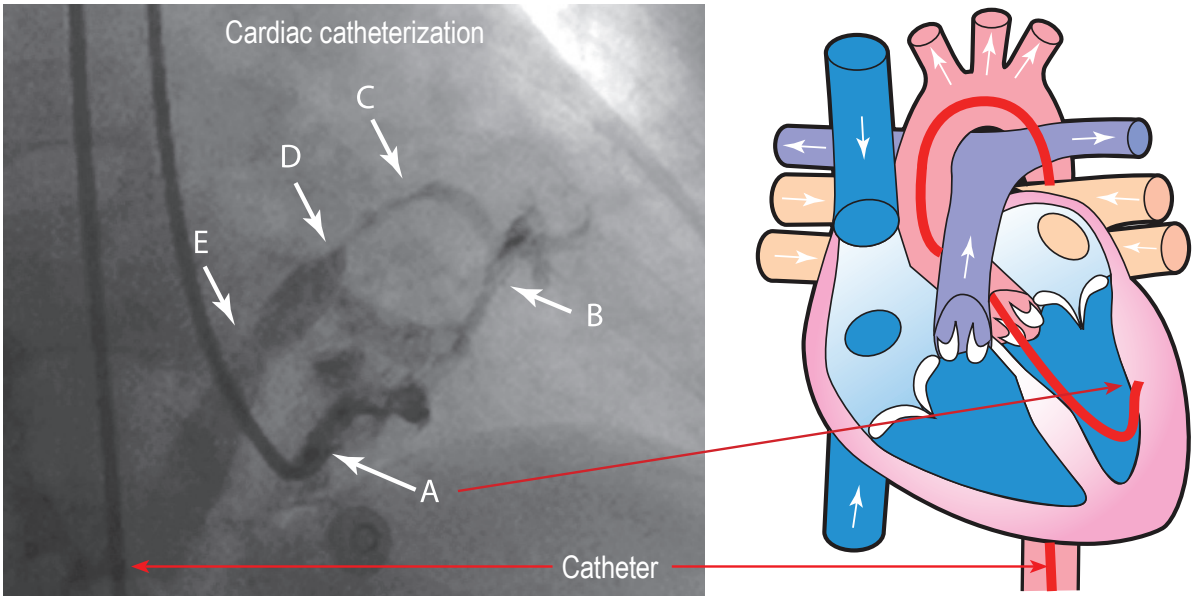


A: Represent catheter tip ***B: Represent anomalous of great cardiac vein***

C, D: Represent coronary venous stenosis ***E: Coronary sinus***

A 77-year-old-woman, a known case of coronary artery disease (CAD), diabetes mellitus (DM) and hypertension developed dyspnea and oppression. She had a history of congestive heart failure, and hyponatemia. This responded well to conservative management. The coronary angiogram showed normal left main coronary artery left anterior descending (LAD) and showed the patent stent at mid LAD. The left circumflex artery (LCX) was normal. The right coronary artery showed proximal focal 30% stenosis. The left ventriculography (LVG) showed Left ventricular hypertrophy (LVH) with good contractility and function ejection fraction (EF) 75%. The tip of the catheter embedded in the left ventricular wall (A) which is proved by injection the opaque media. It filled the cardiac venules, the great cardiac veins (B) and segment of coronary sinus vein stenosis (C, D). The coronary sinus (E) is seen.

Coronary sinus stenosis usually occurs due to iatrogenesis, for instance closure of a secundum atrial septal defect[1], late complication of catheter ablation in Wolff-Parkinson-White syndrome or complications of resynchronization therapy.[2,3] Reviewing the literature, only one case reported by Rao et al.[4] demonstrated absence of the coronary venous sinus without associated structural abnormalities. This is a case of coronary sinus stenosis which is congenital and is associated with anomalous coronary venous fistula.

References

1. Ulma G, Stevenson JG, Lupinetti FM, et al. Transesophageal Echocardiographic diagnosis of iatrogenic coronary sinus stenosis -a case report. *J Thorac Cardiovasc Surg* 1997;114:493-5.
2. Wang SY, Yeh SJ, Lin FC. Coronary sinus stenosis as a late complication of catheter ablasion in Wolff-Parkinson-White syndrome. *Cathet cardiovasc diagn* 1997;42:70-2.
3. De Voogt GW, Ruiter HJ. Occlusion of the coronary sinus. A complication of resynchronization therapy for severe heart failure. *Europace* 2006;8:456-8.
4. Rao CV, Raghu K, Sharada K, et al. Absent Coronary Venous Sinus: A Rare Anomaly. *Indian Heart J* 2001;53:353-3.

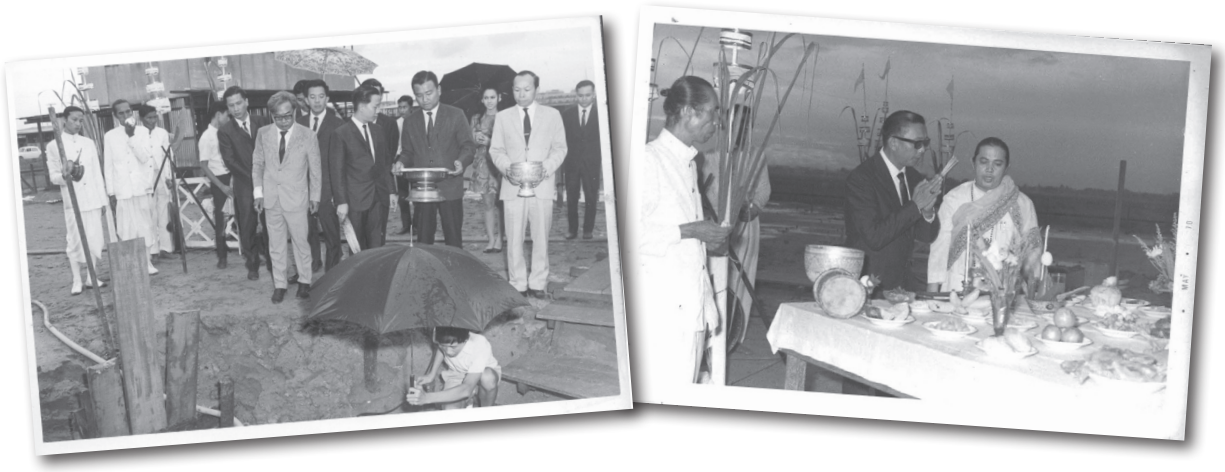
A Difficult Gestation and Painful Labor The Birth of Bangkok Hospital

Here is a brief history of Bangkok Hospital, told from the perspective of someone who was involved with it for most of his life. I recall the days of its initial conception, all the way through its establishment, beginning of operations, and progressive expansion up to the present day.

Bangkok Hospital commenced due to the aspirations of three groups of physicians who wished to establish a state-of-art private hospital in Thailand, which would be able to provide topflight medical standards and nursing care to suffering people. The first shareholder meeting was called on 24th August, 1969 and it was agreed to name the hospital as *"Bangkok Hospital"*. The mission of Bangkok Hospital was later defined as follows:

1. Bangkok Hospital should be a modern private hospital with advanced medical techniques, and state-of-the-art medical equipment.
2. Bangkok Hospital should lighten the burden of government hospitals which was continually growing heavier from the increase of patients.
3. Bangkok Hospital should be a place that would attract physicians that had graduated from or were practicing overseas to come back to Thailand.
4. Bangkok Hospital should promote advances in medicine and nursing care and disseminate medical knowledge to the public.
5. Bangkok Hospital should collaborate with international medical institutes.

On 30th October, 1969, the company was registered at the Department of Economics, Thailand, as *"Bangkok Dusit Medical Services Company Limited"*. The registered capital was 10 million Baht. At that time, it was an immense sum and raising the funds was challenging. The stock was divided into 10,000 shares, priced at 1,000 baht each. The founding team primarily desired to sell stocks to people in the medical field because it was thought appropriate to have them as owners. The team approached many physicians, dentists, pharmacists, and nurses to invest but most people underestimated the possibilities of success. Some laughed; some were standoffish; some disregarded the invitation and others said evasively *"no money"*. Some people (in the interests of a quiet life) were persuaded to buy *"one share"*.



A lot of stock remained unsold. In order to attract more investors, the team agreed to extend the invitation to people outside of medical circles and also offered the preliminary down payment of one third, with the balance to be paid later. When ten thousand shares were finally sold, the team was exhausted. By offering a preliminary payment at one third of stock price, it was expected that the first installment of approximately 3 million Baht would be enough to cover the first month's expenses. However, by the due date of the second installment, some stockholders still owed the first installment.

In the meantime, the location for establishing a hospital was explored. Subsequently, 8,000 square meters of land at Soi Soonvijai, New Petchburi Rd., Bangkapi District, Bangkok, nearby the Thai Medical Association was purchased. In those days the land was quite far from the entrance to the *"Soi Soonvijai"* and might be likened to an island in the sea. The public road leading to the hospital, surrounded by fields and unoccupied area, was rough and muddy when it rained. The streetlights of New Petchburi Road were not as bright as present and there were no public lights along the road to hospital so it was really dark at night. When the land contract was made and the deposit paid, the balance payment was scheduled for three months later. The cost of the land alone was already over a third of our invested capital.

The construction company experienced challenges dealing with us. We had to delay payments to them many times due to inadequate cash flow. Outstanding stock payment receivables still had not been successfully collected. I felt very guilty towards the owner of the construction company. Once he came to see me at my office and cried because our cheque was unredeemable. It took hours to console him by promising that this problem would be solved soon. I knew that the loss of liquidity was due to uncollected stock payments and that eventually we would have adequate cash to pay for the construction.

Then the payment of land became due. The landowner requested the outstanding payment. We asked her to extend the credit but our negotiations were unsuccessful. The owner insisted on terminating the contract and seizing the deposit. We felt really discouraged, depressed, and exhausted. We decided to approach the owner's husband in the hope of mediation and explain our intentions to enhance Thai public health by establishing a first rate hospital and we fully disclosed our financial situation. Luckily, the landowner's husband well understood our crisis and provided us the necessary financial support by extending the period of payment. I have never stopped appreciating the understanding and kindness he offered us: without his support, Bangkok Hospital could not have been completed.

However, our problems were not over. The construction was stopped because there was no more money. Every Board Director exerted effort to try to solve the financial crisis. Finally the President of the Thai Military Bank agreed to support our business by investing in one million stocks and granting a loan. Thereafter, the construction of Bangkok Hospital was finally completed and could start providing service.

We were struggling financially for 3 years from the date that we decided to set up the hospital, to the grand opening day on 26th February, 1972. On that day, we were honored that the illustrious monk, His Eminence Somdej Phra Wanrat was active in the ceremony. A merit making ritual was performed around the hospital. We held this day as the hospital's birthday. At the entrance to the hospital, there was a big sign with shiny brass letters reading "Bangkok Hospital". As His Eminence Somdej Phra Wanrat anointed the signage, it was a very impressive moment for all of us. However, early next morning, there

was tumult amongst the staff because all of the brass letters had disappeared. No one ever discovered who had stolen our letters.

As aforementioned, the hospital location was not the well inhabited residential area it is today but used to be surrounded by vacant land. If we looked out at the view from the second or third floor, we would feel lonely. At night, looking towards the hospital from the Medical Association, we could see the brightness from our hospital illuminating the surrounding darkness. There was only the sound of frogs and insects. The municipality informed us that the dark unlit road to hospital did not belong to the government but that the landowner could not be found therefore the municipality could not install public lights in that area. The hospital decided to install public lights along the road. In the early days our nurses had the additional job of cleaning up the dead insects attracted to the hospital lights at night, of which there were many, because we were surrounded by fields.

The road to the hospital created continual problems. We had to pay a lot of for its upkeep. Whenever there was heavy rain, it flooded. Transportation was hindered because of mud. The flood crisis in Thailand of 1983 cost us millions of baht for maintenance. Eventually, a tarmac road was successfully constructed. After the road surface was improved, the access to the hospital was still not convenient enough for people because there was no public transport. It thus became necessary for the hospital to provide a shuttle bus service between New Petchburi Road and the hospital for patients. We were also pleased to offer some benefits to the general public by offering our shuttle bus service for their use as well as for our patients and staff. Now we have many shuttle buses serving a variety of destinations all over Bangkok.

That was the early days and I have only mentioned some of the difficulties. Much has changed since. We've continued building and established many specialized clinics. Bangkok Hospital Group is now the kingdom's largest hospital operator with 28 network locations throughout Thailand. We continue to fulfill our mission and we have lots of plans for future developments. I write as ex-Chairman of the Board of Directors, and when I think of the developments from the past until now, I feel delighted and proud to have been part of this. Now I am elderly, inevitably I have also become a patient in our hospital, and been treated by our neurology, cardiac, kidney and rehabilitation specialists. I have then experienced in a different way, the respect, friendliness, and sincere support of our competent and knowledgeable staff and I can truly say from my own experience that we continue to realize our dream:

The origins of the AO Foundation

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Keywords:
AO foundation, AO founders, Mucoluskeletal trauma, osteosynthesis, mission and vision of AO

In 1958, a group of Swiss general and orthopedic surgeons established the AO (Arbeitsgemeinschaft für Osteosynthesefragen). Their mission was to transform fracture treatment in Switzerland, which at that point in time included prolonged bed rest in traction and subsequent application of a cast or splint, often resulting in poor functional results and lifelong disability. The *"core group"* of founders consisted of Maurice E. Müller, Hans Willenegger, Martin Allgöwer, and two other early members, Robert Schneider and Walter Bandi. Today, the AO Foundation (which was officially established in 1984) is a medically guided, global network with over 10,000 surgeons, in more than 100 countries. It is the world's leading educational and research organization for trauma and musculoskeletal treatment and reflects a global knowledge network and interdisciplinary teamwork. The AO Foundation is founded on the four principles of documentation, teaching, research, and instrumentation. The AO Foundation's vision is excellence in the surgical management of trauma and disorders of the musculoskeletal system. Its mission is to foster and expand a network of healthcare professionals in education, research, development and clinical investigation to achieve more effective patient care worldwide.

Founded in Biel-Benne, Switzerland
November 6, 1958

Developing early fracture fixation techniques

In the 1950s, when the core group of five Swiss surgeons Maurice E. Müller, Hans Willenegger, Martin Allgöwer, Robert Schneider and Walter Bandi came together, they set out to extensively examine treatment goals. They then decided to develop a system of implants, instruments, and surgical techniques that would allow the reliable treatment of fractures. During this early period, the AO developed a new method involving application of a compression plate and the concept of the lag screw to achieve their goal of rigid internal fixation of fractures. The AO pioneers also realized that immobilization resulted in atrophy of the soft tissues, osteoporosis, thinning of articular cartilage, severe joint stiffness, and, at times, causalgic pain. To prevent these complications and improve the results of fracture treatment, they introduced *"functional after-treatment."* This concept was based on the observation that when stable fixation of a fracture was achieved surgically, most of the pain was effectively eliminated, which made immediate and full mobilization of the extremity possible. Thus the much-quoted and timeless expression among the AO Foundation members *"Life is movement, movement is life"* was born. The demands on this type of operative treatment were great. The reduction had to be anatomic, and the fixation had to be sufficiently strong, stable, and lasting to allow functional use without the risks of hardware failure, delayed union, nonunion, or deformity. Soft-tissue handling was also of paramount importance since infection should not mar the outcome. In close collaboration with two Swiss manufacturing firms, the AO began an intensive period of development to produce comprehensive new sets of instruments and implants for fracture treatment.

Today, continued development along with clinical testing of new instruments and implants and the creation of educational materials for these products are handled within the AO Foundation by a system of medical-technical committees: the TK-System. It consists of several specialty Expert Groups and the core Technical Commission (AOTK). Research is one of the pillars on which the success of the AO is based and the network of AO surgeons and scientists actively pursue clinical and laboratory investigations.

A brief history of the Davos Courses

The first ever Davos Course took place on December 10, 1960. Prof Hermann Kraus (1899-1972) from Freiburg, Germany, the first senior surgeon from outside Switzerland to support the AO, was the guest of honor. The first four-day course was led by Maurice Müller and was held at the AO laboratory in Davos with 69 attendees. In 1961, the second AO Course in Davos registered 102 participants. In 1963, the third AO Course was held in German. English and French were introduced at the fourth AO Course in December 1963. The AO Course was extended from four to five days in 1964. From 1966 onwards, the AO Courses were hosted at the newly built Congress Centre in Davos (where they are still held to this day). The first ever Advances Course was also held the same year. Being practicing surgeons themselves, the AO members understood that a large part of the success of their treatment method would be dictated by good cooperation with operating room personnel (ORP). Hence, in 1967, at the Davos Courses, a teaching program for ORP was developed. The AO Foundation Davos Courses are now an annual flagship educational event that attracts 1,700 participants and more than 400 faculties from around the world.

How the Asia Pacific region was formed

The concept of regionalization was born when Prof Marvin Tile was the President of the AO Foundation

(from 1992 to 1994). In November 1994, AO East Asia (AOEA) was founded under the leadership of Dr Suthorn Bavonratanavech, who also became the first chairman of AOEA. At the time of its inception the region included Hong Kong, Indonesia, Malaysia, Philippines, Singapore, South Korea, Taiwan and Thailand. Prof S P Chow, the second chairman, spearheaded the growth of scientific activities within AOEA and the third chairman, Dr G On Tong united the region of AO Asia-Pacific (AOAP). In 2003 Japan joined AOAP and in November 2006, the AO trustees of the People's Republic of China also became members. Additional momentum built up at the AO courses in 2006 in Davos when Trustees from Australia and New Zealand agreed to join the Asian Trauma Group. At that time, the chairman of AOAP, Dr G On Tong, decided to rename this new body AO Trauma Asia-Pacific (AOTAP). At the Tips for Trainers event in New Delhi in February 2007, the Trustees from India accepted an invitation to join AOTAP. In less than six months, AOTAP became a reality, representing one of the major regions of the AO Foundation.

In the past, Asian surgeons learnt about AO principles and techniques by attending courses in Davos and through visits from AO guest lecturers. Over the past few years, the number of AO courses in Asia has increased significantly because of the availability of Practical Workshop Sets (PWS). Other milestones in the development of the Asia Pacific region include:

- The first issue of the AOAP newsletter in 2000, the launch of the AOAP website in 2001, the formation of study groups in 2003, the first AOAA-Asian Chapter Symposium in Chiang Mai, Thailand, the formation of the ORP group in 2004, and the first combined regional AO courses in Chiang Mai, Thailand in 2006.
- The minimal invasive study group in AOAP published its first book on the subject of minimally invasive plate osteosynthesis (MIPO) in 2006. This marked the first publication of an AO book not originating in Europe and North America.

A history of the AO in Thailand

On 22-24 June 1985, the first AO Basic Course was held in Thailand at Pramongkutklao Royal Thai Army Hospital, followed by another in August of the same year. We encountered lots of problems organizing the course and they should be recorded for the awareness of the younger generation.

Starting from the course name, it was initially prohibited to use the word *"AO"*, which was deemed to be an advertisement, so the course had to be named *"Operative Treatment of Fracture"*. When the AO concept and principles became more accepted, then the course name was changed to *"AO Principles of Operative Fracture Management"* as it is known nowadays. Each training institute wished to have their senior surgeons taking most involvement in the lecture session. In order to reduce conflicts, we attempted to meet their requirements. Problems also occurred with the evaluation as the participants were asked to fill in a form to evaluate each lecturer. Some surgeons complained that we had no right to evaluate them. Nevertheless, the lecturers and their presentation have improved gradually since then.

The greatest difficulty in the course arrangement related to the practical exercises, as there was only one set of instruments for each procedure. So the participants could not simultaneously practice the same exercise. When arranging the course program, we had to set the lectures on Thursday and Friday whereas Saturday and Sunday were for practical exercises. The residents travelling from upcountry would perform the exercises first so that they could travel back for work on Monday. The residents in Bangkok would be allocated to do the exercises on the following Saturdays and Sundays. As a result, the complete arrangement took 4 weeks. Each workshop could only take 18 persons i.e. 2 persons per exercise doing 9 exercises.

In 1994 the AO East Asia (AOEA) was founded and it united a group of orthopedic surgeons from several countries in East Asia with the aim of collaboration for education, teaching, research, etc. The most significant change was the formation of Permanent Workshop (PWS) for the AOEA group. There is now availability of the instruments for teaching activities among the member countries without the need to wait for the instruments from Switzerland. This allows flexibility for each country to set the timing of courses, resulting in more convenience and greater benefits. However, in Thailand, the workshop rotation system still has to be utilized as it helps to reduce the costs of instrument procurement. We need only 10 sets of instruments for 20 participants. In the case of 60 participants performing the same exercise in concurrence, there is the need for 30 sets for each of 9 exercise instrument sets. Thus, to let participants rotate to perform 3 exercises at the same time is an economical solution, saving costs by one-third.

The cost of workshop instruments sets of CHF 6 million was the combined investment of Mathys and AO International. I would like to express my gratitude to Prof. Peter Matter who was the President of AO international at that time to take a courageous decision to set up the PWS in East Asia. Since 1995, the arrangement of practical exercises has been the pattern as today's practice and we are very pleased that that this year more instruments have been supplemented. The theory session has been designed to follow the module of Education Commission of AO International to guarantee the teaching is up to worldwide standards. We are

proud to have fought against and overcome problems and obstacles until the AO principles and knowledge of operation for fracture treatment could be widely imparted among instructors, senior surgeons and junior surgeons, resulting in direct benefits to the patients.

Initiation of ORP Course

Accurate and fast surgery in the operating room relies on the capability of several staff members working closely with the surgeons, such as scrub nurses, or nurses who prepare the instruments required during the surgery. Initially, when orthopedic surgeons were not well acquainted with AO instruments; surgeons sometimes said, *"Give me that stuff,"* as they could not correctly name those instruments. Quite often, they asked for the instruments which had strange names such as lizard-mouth forceps, weight device, etc. If the nurses were not aware of the required instruments, they then sent the whole tray of instruments to the surgeons for selection. The lack of knowledge of the function of each instrument and the failure to understand the surgical steps caused tremendous problems in the surgery. Consequently, both surgeons and nurses got upset and frustrated, resulting in negative results for the patients. These problems would not have arisen if they had mutual understanding and had worked as a team.

This is what led me to decide to teach a few nurses in the OR of Maha Vajiralongkorn Building by looking at the pictures in books and some available slides. I explained about the structure of screws, the application of various sizes of drills, the use of lag screw, types of plates and other existing instruments. Having acquired more understanding, the nurses then were able to prepare everything correctly before the operation and accurately send the instruments during the surgery, which eased the operating work a lot. Besides, once senior nurses acquired more profound understanding, they then naturally imparted this knowledge to their juniors. When the nurses at Maha Vajiralongkorn Building became more confident, I knew it was time to disseminate information and knowledge to nurses in other hospitals too.

The Orthopaedic Department of Pramongkutklao Hospital then organized the first AO Course for ORP in May 1985. The OR nursing lecturers were very excited as it was new for them to speak in front of an audience. They rehearsed the lectures several times beforehand to ensure accurate content, nice pictures, and an interesting presentation. I had to observe their rehearsals and listen to the lecture both to support them and to guarantee that the lecture content was correct. The biggest difficulty for the nurses was to overcome their fearful tension before giving their first talk. Early on there was just the instrument presentation and demonstration. Later when there was increasing number of instruments, the nurses had the opportunity to perform practical exercises just like the surgeons, resulting in better understanding of instrument usage.

I would like to express my sincere appreciation to Ms. Rigmor Texhammar, Director of ORP education in Thailand, who gave us full support and her successor, the late Ms. Anne Murphy who came to our course many times, and was convinced that Thailand's ORP education became a model for Asia. Ms.Susanne Baeuerle who is the present Director of ORP Education attended the ORP course in 2003 and had the same impression as Anne. Recently, nurses from other hospitals who share a passion for teaching have joined the team as lecturers and table instructors. In addition, the demand for attending the ORP Course has increased every year which led us to conducting 2 courses a year.

Nevertheless, we still haven't been able to satisfy the increasing demand. There are around 300 hospitals of which the operating rooms are equipped with AO instruments. If each hospital sends only one nurse to attend the course, the number of nurses attending per year would reach 300. However, we can accept only 60 participants at a time, and 120 in total every year. No matter where the course is organized, the strong intention still remains unchanged. Now is the time when the younger generation of surgeons needs to step forward and take on the responsibility of continuing to run the ORP courses. Assisting the nurses by continuing to help with their education will ensure that surgeons and nurses can work efficiently as a team for the sake of the best patient outcomes.

In summary AO Foundation is a medically oriented nonprofit organization with international research and educational activities, led by specialized surgeons. Its mission is to promote medical advances and further improve patient care in the fields of trauma surgery, orthopedics and diseases of the musculoskeletal system. The AO mission is to foster and expand our network of healthcare professionals in education, research, development and clinical investigation to achieve more effective patient care worldwide. Education remains one of the pillars since the first course in 1960, 352,067 surgeons from 124 countries and 146,929 operating room personnel from 73 countries have participated in an AO Course. There are more than 10,000 AO surgeons worldwide in different regions who work voluntarily to propagate the AO philosophy which is to continuosly improve the care given to our patiens.

Practical exercise was organized during the week end.

References

1. http://www.aofoundation.org/the-ao-foundation/about/Pages/history.aspx
2. Communications & Publicity Committee. (2008). History of AO in the Asia Pasific Region. AO Asia Pasific.
3. Schlich, T. (2002) Surgery, Science and Industry A Revolution in Fracture Care, 1950s-1990s, Great Britain, Antony Rowe Ltd, Palgrave Macmillan
4. Heim, Urs F.A. (2001) The AO phenomenon: Foundation and early years of the Association for the Study of International Fixation (ASIF) , Toronto, Huber

Book Review

Sabiston Textbook of Surgery

The Biological Basis of Modern Surgical Practice 19th Edition 2012

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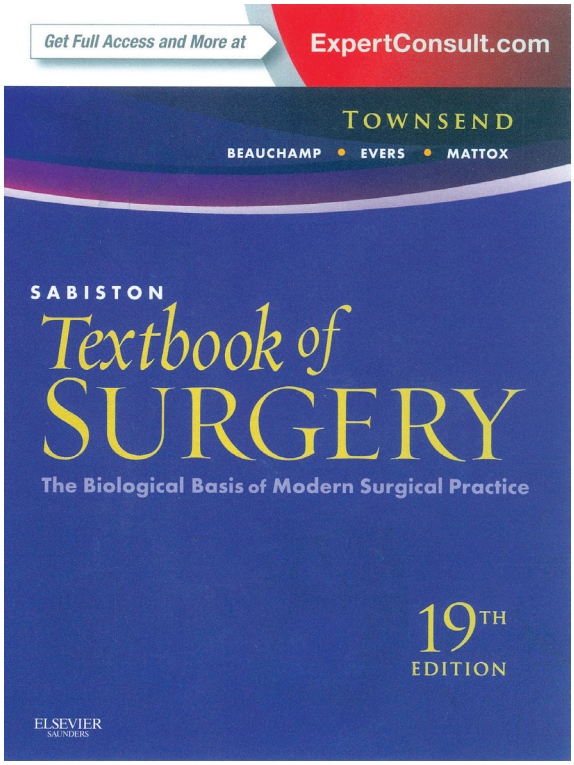

The 19th edition of the Sabiston Textbook of Surgery includes fundamental medical knowledge which is tremendous useful to all. It begins, as is traditional, with a history of surgery and ethics, and then gives an overview of molecular and cellular biology before moving on to customary surgical tenets such as metabolic support and wound healing. Subsequent sections deal with perioperative management, trauma and transplantation and oncology, breast, endocrine, and abdominal procedures before dividing into surgery subspecialties such as head and neck, thoracic, vascular, urology and neurosurgery.

Additional to this edition are the latest developments in rapidly evolving areas such as minimally invasive surgery or tumor immunology and immunotherapy. New chapters also reflect the current emphasis on surgical safety, new technologies, and unconventional civilian disasters. In general this surgical text book is complete and thorough. The diagrams are brilliant demonstrations. The color photographs are usually superb although some black and white x-ray pictures are not sharp as they should be. Other criticisms include the amount of information that has not been retained from the 17th and 18th editions.

However, we still judge the overall presentation as excellent. Furthermore, in this digital age, the tremendous value of this edition of the Sabiston is that it includes access to the e-book which can be read on a Kindle (conveniently portable in your lab coat) and is even easier to navigate and view using an iPad.