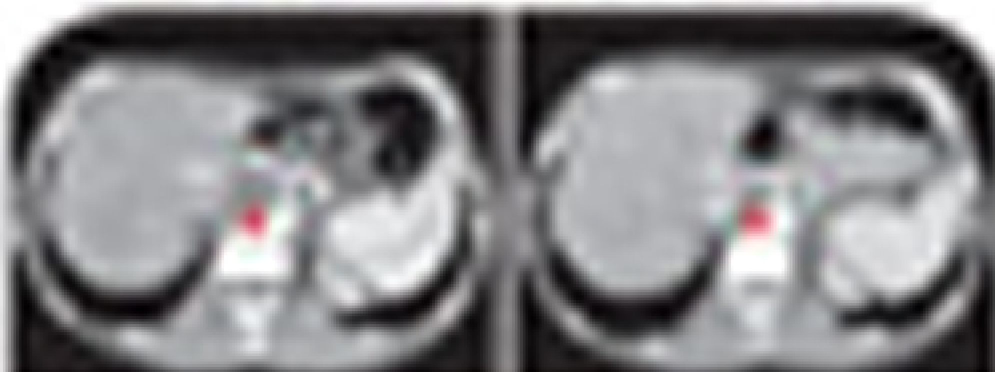
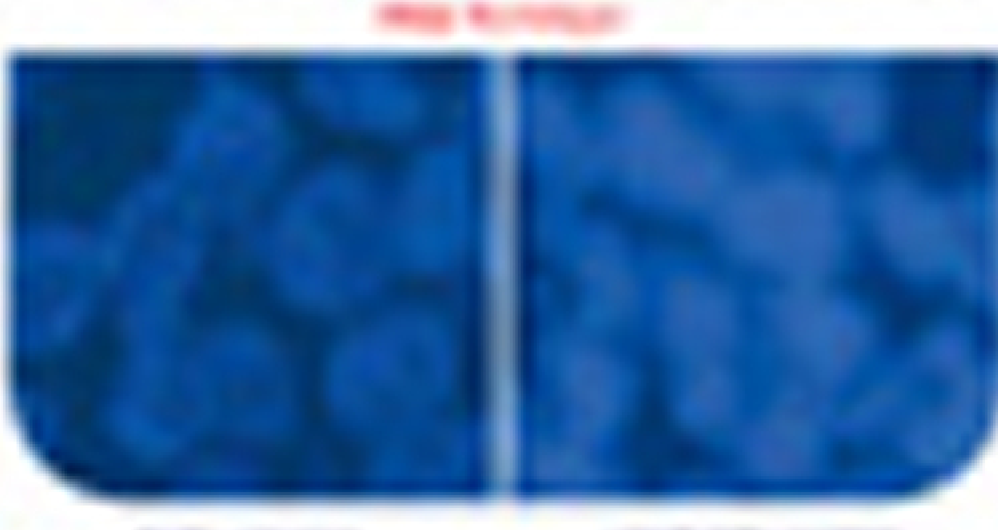
THE BANGKOK MEDICAL JOURNAL

Trastuzumab Adjuvant Therapy Effective for Advanced Gastric Carcinoma





Editorial

At Bangkok Hospital, we believe in Service from the Heart. It is thus appropriate that our 3rd edition continues to see a distinctive and varied contribution from our Cardiac Unit. We are pleased to finally see in print Dr. Gumpanart's account of how he and his capable team saved a patient's life with the first emergent primary coronary angioplasty performed in Thailand. Dr. Pradub appraises evidence-based management of Acute decompensated heart failure. Dr. Rattanapan's case study shows how conservative treatment over a longer period can be used to deal with a large thrombus where standard surgical intervention was inadequate to restore coronary perfusion. Dr. Lertlak details using MRI images to study regional wall motion of the left ventricle, to develop additional quantitative tool, with which to detect impaired myocardial regional wall motion. Dr. Poomiporn describes a rare case of Kawasaki Disease Shock Syndrome in a young child, which if untreated could lead to ischemic heart disease, myocardial infarction or sudden death.

Another rare presentation is the case study of the patient with headache onset after laughter, as related by Dr. Kiratikorn; MR imaging of the cervical spine detected a Chiari I malformation, the most likely secondary cause associated with this peculiar condition. We continue to see strength from our imaging team's close co-operation with our oncologists, using nuclear medicine for increase sensitivity and specificity in diagnosing breast cancer, using 3D software reconstructions with CT studies to improve surgery prospects in liver tumor and detection of small throat cancer by Diffusion-weighted MRI pulse sequence. Gastric cancer is still a major killer throughout the world because it is so often diagnosed at a late stage, so it is exciting to see patient prognosis improving after using adjuvant therapy with Trastuzumab being effective at reducing tumors that do not have HER2 gene amplification.

On the theme of fighting sepsis, Dr. Paithoon explains how the BMC drastically reduced catheter related blood stream infections and Dr. Panpit gives clear and up to date guidelines on how to treat urinary tract infections. Dr. Att enthuses over the new hydrosurgery tools available to debride wounds difficult to access with traditional methods. Our Spine unit describes how they are improving their accuracy of measuring surgical outcomes by incorporating Oswestry Disability Index questionnaires and the EuroQol-5D questionnaires into the pre and post operative treatment process.

We are also pleased to welcome guest authors from outside the BDMS group to this volume. Professor Douglas Kieper from the Department of Physics at the Hampton University gives further perspective on molecular breast imaging. Professor Van de Werf from Leuven University Hospital gives a cogent and useful review of Lytic therapy to treat acute myocardial infarction; after all, there are still few hospitals worldwide who provide a well staffed primary 24/7 PCI unit. Dr. Phornthip, a senior nurse researcher from Lerdsin Hospital illustrates how the concept of cognitive behavioral change is being practically enlisted into preventive public health programs to tackle the growing obesity problem in Thailand.

Finally, we'd like to announce the establishment of the Bangkok Health Research Center, which will offer up to date health information to medical professionals and the general public.

We hope our readers will enjoy and be stimulated by the diversity of this month's offerings.
Happy Valentines to you all!

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Infection control for the Reduction of Catheter Related Blood Stream Infection (CRBSI)

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Keywords:
Nosocomial infection, CRBSI, Catheter Related Blood Stream Infection

OBJECTIVE. The purpose of this research was to reduce rate of CRBSI at Bangkok Hospital by using 2002 CDC evidence-based guidelines as a preventive of CRBSI.[1]

MATERIALS AND METHODS. A target surveillance on CRBSI was conducted in all 4 adult intensive care units at the Bangkok Hospital. The findings were compared with the CDC recommendations. Then we set up a multidisciplinary patient-care project team who applied the CDC guidelines in order to work towards the reduction and eventual prevention of CRBSI's in our hospital.

RESULTS. The reduction of CRBSI incidence was observed to be sustainable after the new guidelines were implemented in October 2004. The rate of CRBSI incidence reduced gradually especially in the year of 2010. It approached to zero per 1000 catheter-day.

CONCLUSION. Nowadays, all healthcare personnel must take responsibility for preventing nosocomial infection. We has demonstrated that our multidisciplinary team can reduce the infection rates sharply.

Catheter Related Blood Stream Infection (CRBSI) is the third most common nosocomial infection. The infection results in higher antibiotic costs, prolonged hospitalization days and is even related to high morbidity and death.[2-4]

The Centers for Disease Control and Prevention (CDC) of the United States of America has provided evidence-based guidelines for catheter care to reduce Blood Stream Infections (BSI). They refer to recommendations for hand hygiene,[5] maximal sterile personnel protection equipment (PPE),[6, 7] preferred antiseptics for skin preparation,[8, 9] catheter site dressing regimens,[10] the site chosen for catheter placement,[11, 12] etc. In 2004, our Infection Control Committee set up a project aimed at reducing CRBSI at Bangkok Hospital by using the aforementioned 2002 CDC evidence-based guidelines as a preventive of CRBSI.[1]

Materials and Methods

Case Definitions for CRBSI including

1. Bacteremia/fungemia in a patient with an intravascular catheter, with at least one positive blood culture obtained from a peripheral vein and clinical manifestation of infections (such as fever, chills, and/or hypotension) but no apparent source for the BSI except for the catheter.

2. One of the following should be present:

- A positive semiquantitative (>15 Colony forming unit (CFU)/catheter segment) or quantitative (>103 CFU/catheter segment)
- Culture whereby the same organism is isolated both from the catheter segment and peripheral blood; differential period of CVC culture versus peripheral blood culture positively of > 2 hours.

Target surveillance on CRBSI was conducted in all 4 adult intensive care units at our hospital. The objective was to evaluate the incidence of CRBSI and observe how physicians performed central line insertion, their use of antiseptics, the contents in the central line insertion kit and what the daily care routine for the central line was. Then, the findings were compared with the CDC recommendations.

We set up a multidisciplinary patient-care project team working towards the reduction of CRBSI's. The team's job was in working out how to apply the CDC guidelines to prevent CRBSI in our hospital. For example, Central Supply Service Department (CSSD) was requested to provide ready to use kits for central venous catheter (CVCs) insertion, which included a sterile grown and sterile gloves, a mask, a cap, a large sized sterile drape and a bottle of 2% chlorhexidine gluconate in 70% alcohol for skin preparation, instead of 10% providone iodine solution.

The team also gave workshops on these new implementation regulations to the physicians who were privileged to perform central line insertion.

Instructions were issued to nurses on how to care for CVCs and how to use a 7 day-color-coded-sticker to ensure timely dressing and intravenous solution kits changes.

During follow up, the team also used quality improvement tools such as GAP analysis or Cause and Effect diagrams in order to improve performance in accordance with the new CDC recommendations for CRSBI prevention.

Results

The CRBSI rate is best determined by analyzing rate of infection by BSIs per 1000 catheter-day.[1] These rates can be used as benchmarks by individual hospitals to estimate how their rates compare with other institutions.

During January to August 2004, the incidence of CRBSI at the Bangkok Hospital was an average 12 per 1000 catheter-day.

Before the implementation of the new guidelines for prevention of CRBSI, more than 90% of physicians did not use all appropriate personnel protective equipment during central line catheter insertion, for example, only 20% of them used sterile gowns, usually because equipment was not readily available (Table 1). The drapes provided in the central line insertion kit were too small. The disinfectant commonly used was 10% providone-iodine solution and there was no specific system set up to remind nurses when to change dressings or intravenous solution on a timely basis.

After making new central line kits available (Figure 1) and educating physicians on the new protocol, giving nurses the new instructions for aseptic techniques for looking after CVCs and demonstrating how to use a 7 day-color-coded-color sticker (Figure 2) to ensure timely changes of specific intravenous sets and dressings, the incidence rate of CRBSI had reduced to an average 5.9 per 1000 catheter-days during September to December 2004 (Figure 3). Figure 4 shows surveillance compliance for the CVCs project. The performance improved year by year.

The reduction of CRBSI incidence was observed to be sustainable after the new guidelines were implemented in October 2004. Figure 5 shows the surveillance rate of CRBSI from 2004-2010. The rate of CRBSI incidence reduced gradually especially in 2010. It approached to zero per 1000 catheter-day.

Table 1: Summarized physician's performance during central venous catheter (CVC) insertion compared to the CDC new guidelines for CRBSI prevention.

Prevention	Amount of CVC insertion (n=38)	(%)
Maximal PPE*	3	7.9
Partial PPE*	35	92.1
sterile gown	7	
mask	12	
cap	1	
goggle	7	
Total	**38**	**100**

PPE* = Personnel Protection Equipment

Figure 1: *Guideline of the new standard of central venous insertion kit*

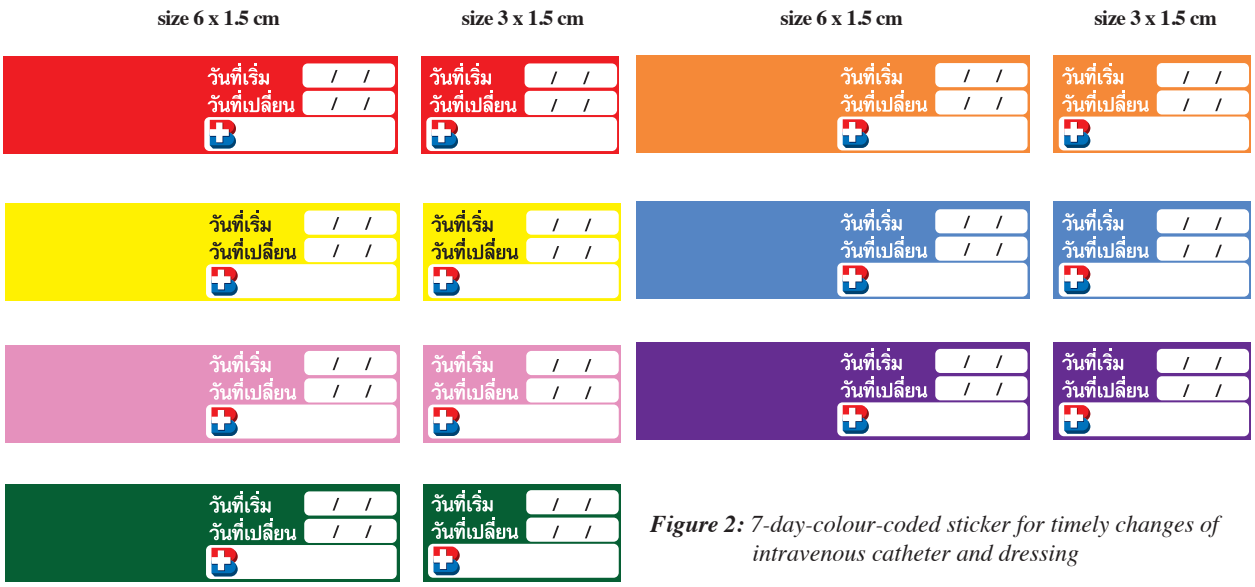

Figure 2: *7-day-colour-coded sticker for timely changes of intravenous catheter and dressing*

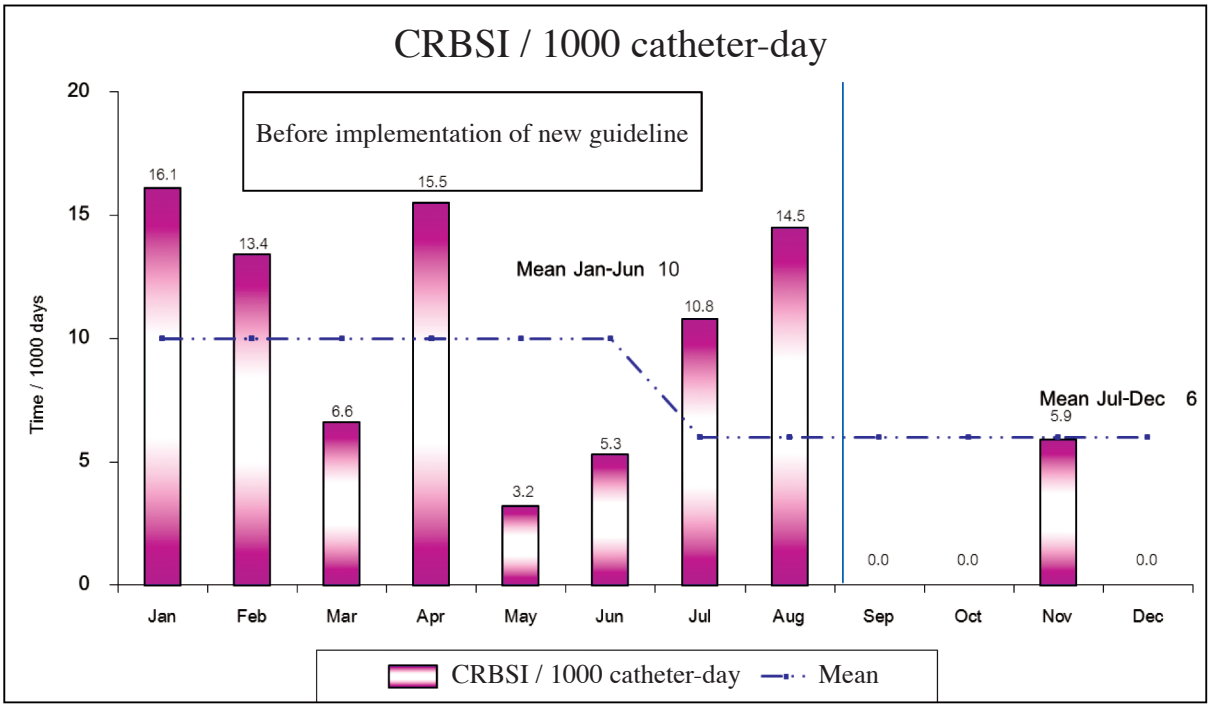

Figure 3: *Graph shows Catheter Related Blood Stream Infection Rate of Bangkok Hospital in the year of 2004.*

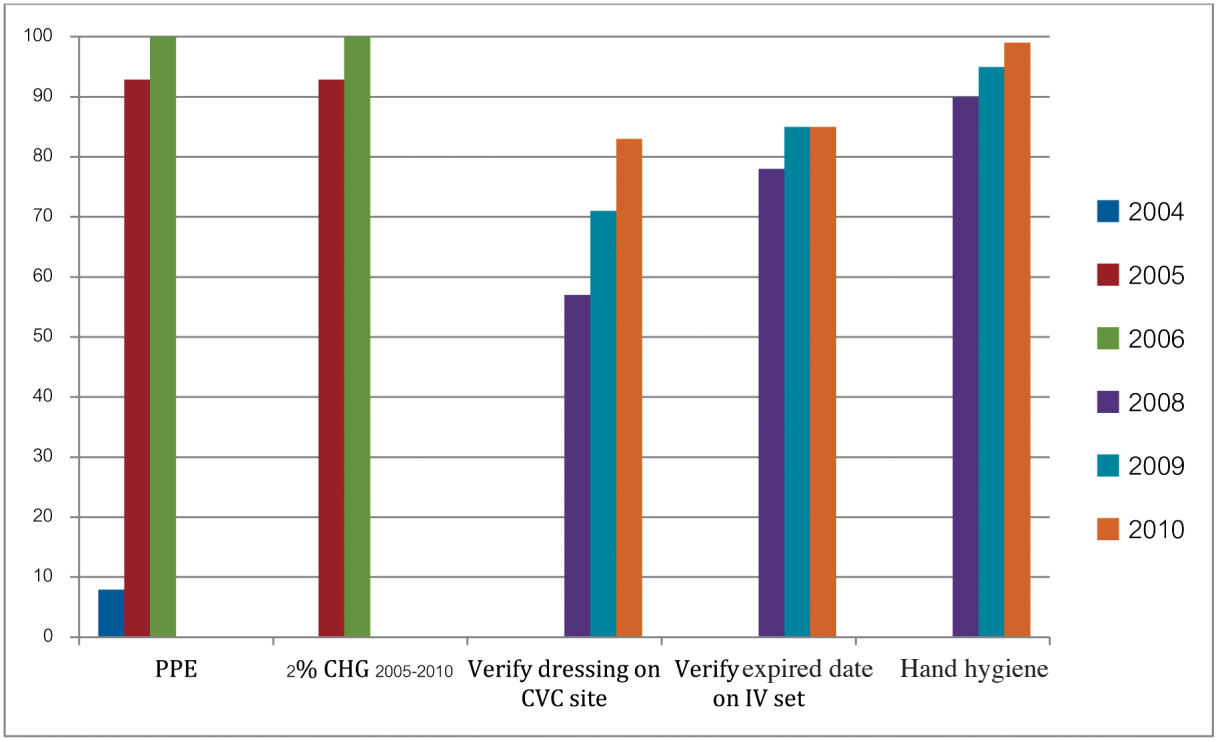

Figure 4: *Graph shows surveillance compliance for caring central venous catheter project. The performance improved yearly as can be seen.*

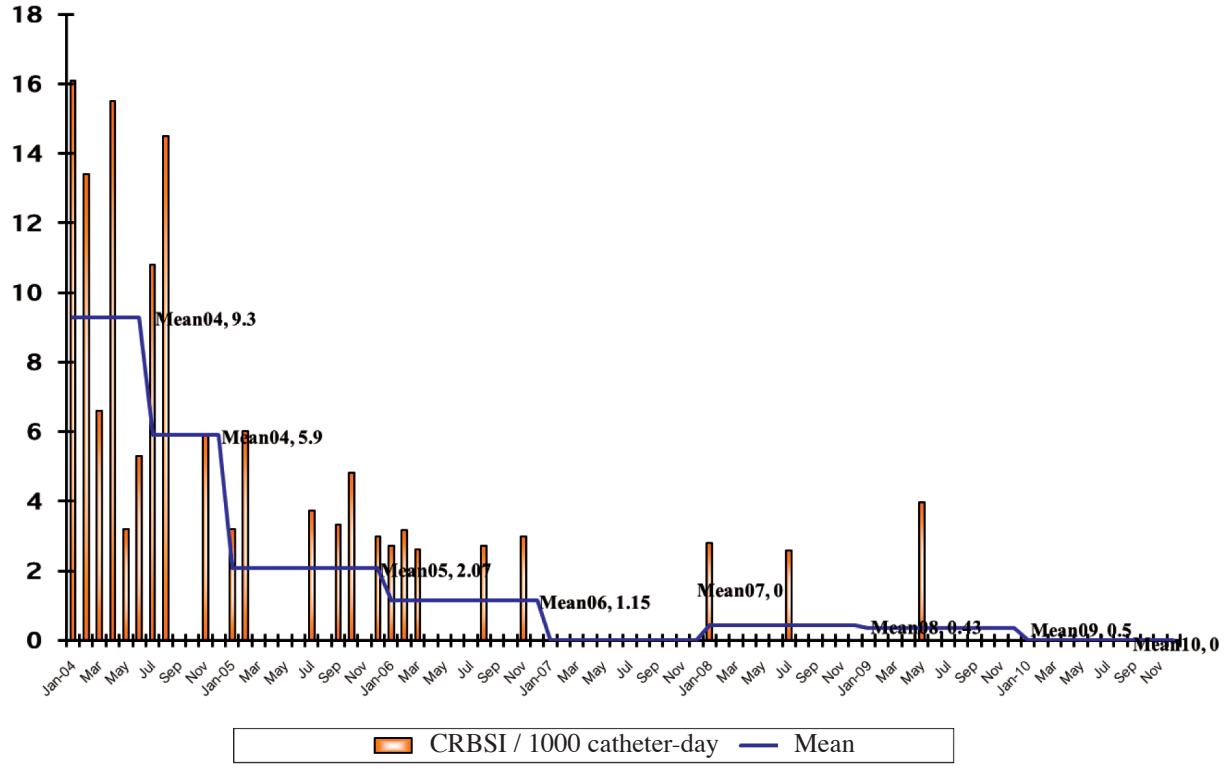

Figure 5: *Graph shows Catheter Related Blood Stream Infection/1000 catheter-day in 2004-2010.*

Discussion

Nosocomial infection associated with CRBSI is now a major concern in Modern Medicine. Due to the wide use of invasive medical devices, particularly central venous catheters, complications occurring because of infection have resulted in high mortality rates.[1-3]

In the USA, there are an estimated 250,000 cases of CRBSI annually; attributed mortality is estimated to be 12-15% for each infection, with a cost to the health-care system $25,000 cases per episode.[1]

Danchaivijitr et al[13] showed that in Thailand, about 10% of primary blood stream infections were found to be nosocomial. The CRBSI percentage was shown to be higher in university hospitals (4%) as opposed to general hospitals (0.8%) However, that study didn't analyze BSIs per 1000 catheter-day, (as per official formula for CRBSI rate) so we could not directly compare the prevalence at our medical center to other institutions in Thailand.

The key issues which are so different from previous practices of CVCs insertion and post insertion care include more stringent hand hygiene and aseptic technique during CVCs insertion, with maximal personal protective equipment (PEE), using a larger drape and skin antiseptic with 2% chlorhexidine gluconate in 70% alcohol.

Using maximal PEE and 2% chlohexidine glutconate for skin preparation prior to CVCs insertion lowered BSI rate when compared with previous standard precautions.[7-9]

The benefit of using 2% chlohexidine glutconate in 70% Alcohol instead of providone-iodine in preventing catheter-related infections is its superior and rapid skin decontamination.[8, 9]

Since our project to apply these recommendations from the CDC to reduce CRBSI reduction began in 2004, due to good cooperation from our multidisciplinary team, by 2010 we had succeeded in controlling CRBSI rate to zero rate per 1000 catheter-day.

CDC revised their guidelines yet again in 2011.[14] The major differences from their 2004 guideline are;

1) Using antiseptic/antibiotic impregnated short-term central venous catheters and chlohexidine impregnated sponge dressing.
2) An emphasis on performance improvement by implementing bundled strategies.
3) Definition of CRBSI that requires specific laboratory testing.

Since it is often problematic to establish a diagnosis, a simple definition used for surveillance purposes is

CLABSI (Central Line Associated Blood Stream Infection). A CLABSI is a primary BSI in a patient that had a central line within a 48-hour period and is not blood stream related to an infection at another site.

This year, 2012, our Infection Control Committee will revise the case definition of CRBSI to CLABSI to be in line with CDC's latest guidelines.

Conclusion

Nowadays, all healthcare personnel must take responsibility for preventing nosocomial infections. Our Team has demonstrated that a multidisciplinary team following the CDC guidelines could indeed reduce the infection. In the near future CRBSI may be the first nosocomial infection that can be eliminated from all patient-care areas.

Acknowledgement

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Comparison of Workflow Efficiency between Computed Radiography (CR) system and Wireless Flat-Panel Digital Radiography (DR) system for Checkup Chest PA examination.

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Keywords:
computed radiography, CR, digital radiography, DR, wireless flat-panel, workflow analysis, post-acquisition

OBJECTIVE. To evaluate the workflow efficiency between CR vs. wireless flat-panel DR systems for routine checkup Chest posterior-anterior (PA) erect position examinations.

MATERIALS AND METHODS. On routine checkup Chest PA view erect position. The work flow steps of CR and wireless flat-panel DR system were identified, including examination preparation, patient positioning, exposure, post-acquisition processing and total examination time were recorded. We only included post-acquisition processing time because time from exposure to appearance of imaging is relatively fixed.

RESULTS. A total of 476 patients were examined (CR, n = 244; DR, n = 232). The total time of procedure for CR system was 86.2-96.2 seconds. For the DR system it was 17.6-19.5 seconds.

CONCLUSION. Workflow efficiency of DR system is better than CR system in routine chest examination. Modern radiologic departments require a DR system.

Since the development of the technology standard digital imaging and communications in medicine (DICOM), which is now used in hospitals worldwide, many medical applications have made rapid progress. Kruger et al[1] introduced the computed radiography (CR) digital imaging system in 1980 and by 1990 the digital radiography (DR) system developed. In 2001, the efficient instrument, the flat-panel detector fluoroscopy digital subtraction angiography (DSI) made its appearance. Many articles have described the advantages of using DR in various situations in comparison with CR system. By now it is conclusive that the DR system is superior to the CR system.[3-10] We decided to show this in the BMC by studying the workflow efficiency of DR vs. CR system during routine chest PA erect position.

Materials and Methods

All patients were outpatients, requiring for their routine annual checkups, a PA Chest in erect position. The radiographic equipment was at a fixed distance between patients and x-ray tube exposure. Both the CR and DR readers were located about 6 meters from the radiographic equipment. The number of technicians who attended these 476 examinations was limited to 4 persons. The radiographic examination was performed with a cassette-based bucky in standing position. The CR system used for the study was the Kodak direct view 950 (Figure 1). The wireless flat-panel DR system used was the CXDI-70C Wireless (Cannon, Figure 2). All data was transmitted to the digital system for processing, image appearance and storage.

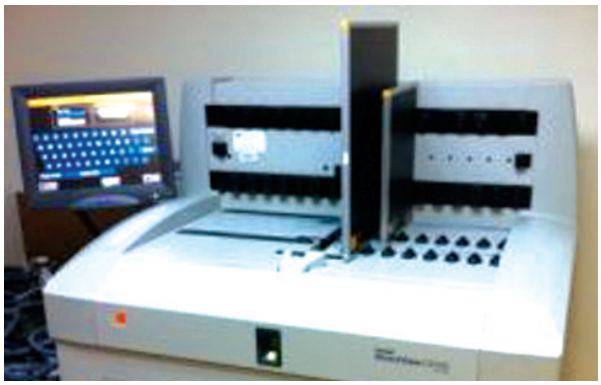

Figure 1: *Kodak direct view 950.*

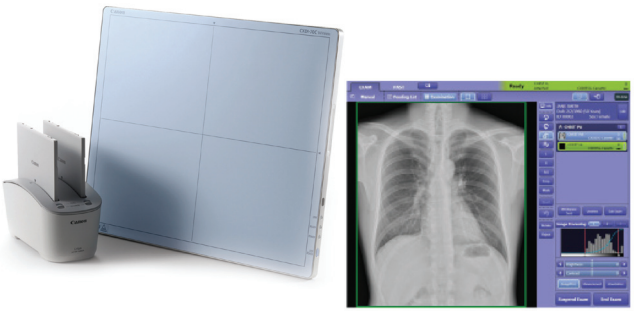

Figure 2: *The wireless flat-panel DR system-Cannon (The CXDI-70C Wireless).*

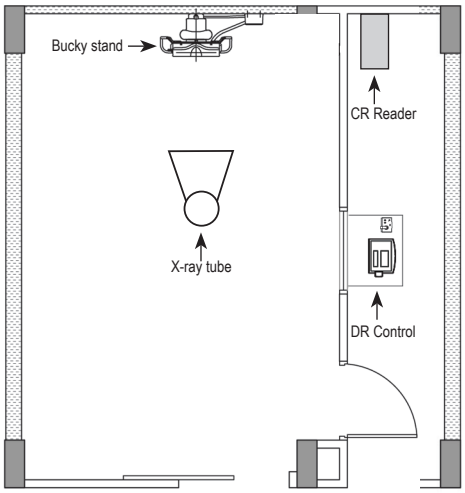

Figure 3: *Radiography unit uses bucky stand 14x17 inches for CR system digitizer cassette. For DR system; flat plate detector with wire or wireless system in bucky stand. The CR reader is installed outside the exposure room. DR with server and software connection with PACS is next to the radiographic control.*

Data collection

The workflow for each step was identified. The time was recorded for chest examination preparation, patient positioning, exposure and acquisition processing. After the positioning was done, x-ray exposure was made. Acquisition processing for CR system, included the time it took for the technician to carry the cassette from chest stand to CR reader for processing. The image manipulation time, was how long it took for technicians to review and adjust the image and then scan to the picture archiving and communication systems (PACS). Wireless flat-panel DR system time included the technician exposing the image, the data being processed until the image appeared and was then transferred to PACS.

Results and Analysis

Using statistic analysis, we found that the mean time required to evaluate x-ray examination using the CR system was 89.3 seconds. The standard variation was 24.1 and 95% confidence interval 86.2 to 96.2 seconds. For the DR system it was 18.5 seconds with a standard deviation of 7.3, and 95% confidence interval 17.6 to 19.5 seconds.

Conclusion

The acquisition time of the DR system was 68.6-76.7 seconds faster than the CR system. In a facility which regularly encounters a high patient volume, then it is sure that using a fast workflow DR system is advantageous. Our study with smaller patient numbers and focusing only on chest x-ray nonetheless confirmed Lehnert's findings in his CR/DR workflow efficiency comparative study.[11] Despite the many benefits of a DR system, it can be financially daunting to consider an entire system upgrade to digital. It should be remembered then, that hospitals can save costs by buying DR tools such as the wireless flat-panel DR system which can be retrofitted to and integrated with existing CR platforms.

Table 1: Standard variation of time examination by Computed Radiography (CR) system and wireless flat-panel Digital Radiography (DR) system.

Method	Patient (n)	Mean Time average (seconds)	Standard Variation	95% confidence interval
CR System	244	89.3	24.1	86.2 - 96.2
DR System	232	18.5	7.3	17.6 - 19.5

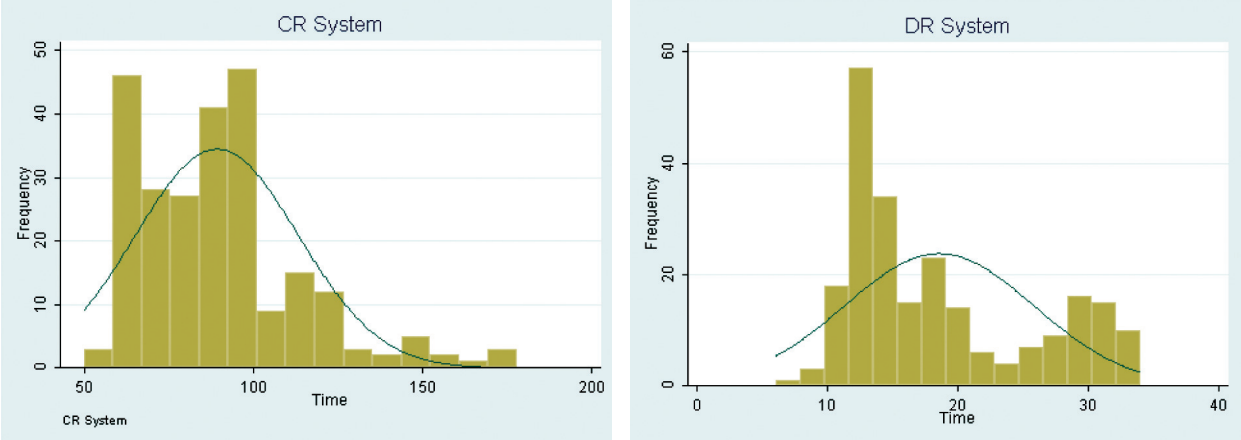

Figure 4: *Graph shows time of chest examination between CR system and DR system*

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Original Article

Early detection of endobronchial carcinoma using autofluorescence bronchoscopy

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Keywords:
endobronchial carcinoma, autofluorescence bronchoscopy

** Dr. Saenghirunvattana will present this research to the European Lung Cancer Conference in Geneva, Switzerland in April 2012*

OBJECTIVE. This study was to evaluate the benefit of using autofluorescence bronchoscopy for the detection and localization of endobronchial carcinoma.

MATERIALS AND METHODS. During January 2007 till December 2011; 350 patients, aged 35 to 90 years old, who were smokers or ex-smokers were examined by autoflorescent bronchoscopy. All cases were suspected to have lung cancer.

RESULTS. Premalignant, endobronchial cancer was found in 3 patients. Follow ups over the next four years discovered one patient developing severe dysplasia.

CONCLUSION. Autofluorescence bronchoscopy is able to enhance early detection in case of endobronchial lesion.

The majority of lung cancer patients present with symptoms at a late stage of the disease, and diagnosis occurs mostly in locally advanced or metastatic disease with poor rates of survival, of up to 5 years. Obviously, the earlier detecting of lung cancer, the better the patient's prognosis.

The new autofluorescence bronchoscopy can visualize the early change of endobronchial cancer. Autofluorescence bronchoscopy is a procedure in which a blue light rather than white light is employed for illumination and premalignant and malignant tissue is distinguished by a change in color from normal tissue without the need for fluorescence-enhancing drugs.

In 2006, Lam et al[1] demonstrated that autofluorescence bronchoscopy could increase the diagnostic yield by 8 percent, (compared with white light bronchoscopy) in patients with abnormal sputum cytology, without patients being subject to additional risk. So far only about 5 per cent of cancer treatment centers in the USA offer this diagnostic tool to their patients.[2]

This study was to evaluate the benefit of using autofluorescence bronchoscopy for the detection and localization of endobronchial carcinoma.

Materials and Methods

Between January 2007 and December 2011, autofluorescence bronchoscopy was used to examine 350 patients, aged 35 to 90 years, who were either current or ex-smokers of more than 20 cigarettes per day for up to 20 years. These patients were already suspected to have lung cancer, based on abnormal chest roentgenograms or computer tomograms of the chest, showing for example, minute lung nodules, recurrent pneumonic lesions or elevation of the carcino embryonic antigen (CEA)which is a lung tumor marker.

An autofluorescence bronchoscopy system (model BF-240 bronchoscope; Olympus; Tokyo, Japan) was used. The system was composed of a camera unit, fiber-optic bronchoscopy, excitation light source, and filing system. The white light from the xenon lamp is passed through a cut filter and then through an excitation light. Images obtained with an objective lens were transmitted via a fiber-optic image guide back to the eye piece of endoscope which specifically passed a 490-590 nm fluorescence signal.[3] Abnormal mucosa showed a cold image lack of autofluorescence. (Figure 1)

Results

There were 262 men and 88 women with a mean age of 64 years. Premalignant, endobronchial cancer was found in 3 patients; 2 patients in 2008 and 1 patient in 2011. Both patients in 2008 developed carcinoma in situ, which was destroyed by electrocautery. Annual follow ups over the next four years, by autofluorescence bronchoscopy were normal for both. The other patient in 2011 developed severe dysplasia which was ablated by electrocautery. Open lung biopsy of the left lower lobe lesion revealed broncholitis obliteran. In 2008, the patients with lung cancer in our hospital numbered 33 cases, so the aforementioned patients accounted for 6 percent. In 2011, the number of lung cancer patients we treated totaled 53, the previous two existing cases and one new case accounted for 6 percent.

Discussion

Comparison between the statistics of another hospital in Thailand in 2005, and our own in 2008, demonstrated that we were able to identify early stage of lung cancer cases (Stage 0, TNM classification 2010)[4] at a satisfactory rate of 6 percent compared with 0 percent for the other hospital[5] (Table 1).

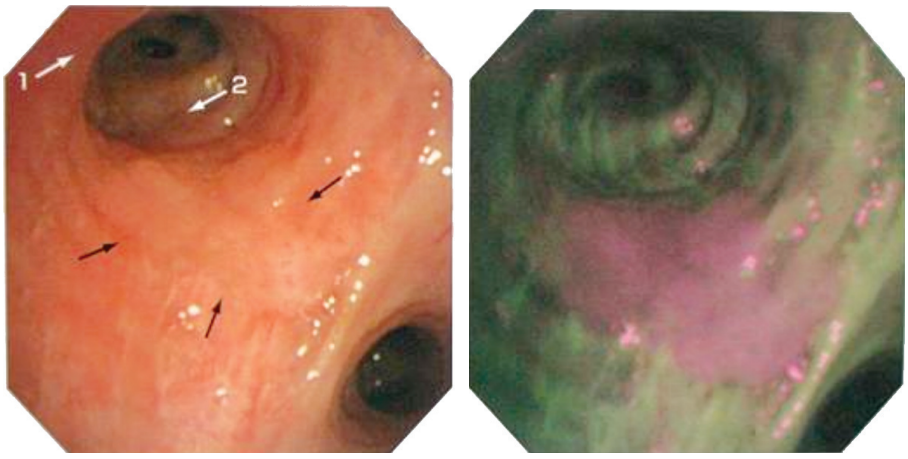

Figure 1: *Demonstrates autofluorescence bronchoscopy compared with white light bronchoscopy.*

Table 1: Comparison of staging of the lung cancer in Thailand in percentage.

Staging	Deesomchoke 2005	Samitivej Hospital 2008	Samitivej Hospital 2011
Stage 0	0	6	6
Stage I,II	9.4	25	18
Stage III,IV	90.6	69	76

Additionally, we found that in cases of ablation of invasive endobronchial carcinoma, autofluorescence bronchoscopy enabled us to obtain a more accurate assessment of the lesion size and margin.

Surgery is currently regarded as the accepted treatment of choice of carcinoma in situ and results in 80-90 percent 5 years survival rate.[6] For our patients in 2008, one was too old and his lung function test was very poor. The other one developed severe pneumonia. Both received local bronchoscopic treatment with electrocautery, a straightforward and relatively simple procedure, which did not hamper subsequent surgical resection in case of treatment failure. Both patients received annual bronchoscopic examination for 4 consecutive years of follow up and they were cancer free.

There are limitations to the present study. Our results of 2008 and 2011 were compared with the data reported in 2005 from another hospital in Thailand which had no access to autofluorescence bronchoscopy at that time.

The second limitation is that our study populations are small and come from the high income segment of the Thai population, so they may not be representative of the general Thai population who use government hospitals.

Conclusion

Autofluorescence bronchoscopy is able to enhance early detection of endobronchial cancer.

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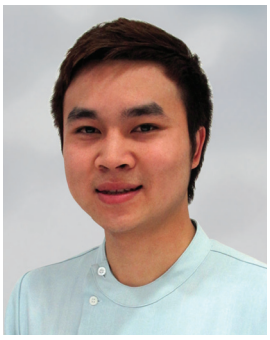
Impaired Regional Myocardial Function Detection Using the Standard Inter-Segmental Integration SINE Wave Curve On Magnetic Resonance Imaging



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Keywords:
MRI, Gradient echo CINE MRI, Standard SINE wave curve, Standard cutoff point curve (mean- 2SD)

OBJECTIVE. 1. To quantify the value of myocardial regional wall motion and to study the inter-segmental integration pattern of the circumferential regional wall motion of the left ventricle using Magnetic Resonance Imaging (MRI) in patients with normal global and regional left ventricular systolic function (LVEF ≥ 55%) and compare results to groups with impaired left ventricular systolic function (LVEF ≤ 55%).

2. To prove that the inter-segmental integration pattern of normal myocardial regional wall motion is consistent and can be used effectively as a complimentary tool with visual estimation method to detect the impaired myocardial regional wall motion.

MATERIALS AND METHODS. A total of 60 adult patients (above the age of 15 years old) who underwent cardiac MRI during January to October, 2011 were recruited. Thirty-six patients had normal ejection fraction (LVEF ≥ 55%, Mean = 64%) and normal myocardial regional wall motion, 12 patients had moderate systolic dysfunction (LVEF ≥ 35%, < 55%, Mean = 49.3%) and 12 patients had severe systolic dysfunction (LVEF < 35%, Mean = 22.8%). We retrospectively analyzed and measured the left ventricular ejection fraction and regional wall motion by computerized program in the Brilliance work station of 3 Tesla (3T) MRI. The myocardial wall was divided into 3 parts, the basal (the myocardial level above papillary muscle), the mid (the myocardial level at the papillary muscle) and the apical part (the myocardial level below the papillary muscle). Myocardial wall in each part was segmented into 6 segments for regional wall motion assessment, which was modified from the American Heart Association (AHA) recommendation. The regional wall motion in each ejection fraction group was measured in millimeters and averaged. The average value of each myocardial segment of each systolic function group was plotted in line curve from segments 1-18 (basal to apical part) to form the qualitative standard curve **(Standard inter-segmental integration curve or Standard SINE wave curve)** of normal regional wall motion. The myocardial segment specific standard deviation (SD) value of the normal cardiac function group was also calculated. We created the **standard cutoff point curve** by plotting the resulting value of the average regional wall motion value of each myocardial segment (1-18) minus the segment specific 2-SD of the average value of regional wall motion of the normal cardiac function in line curve. The standard cutoff point curve was a double functional tool because it both displayed SINE wave curve character and provided quantitative cutoff point value. We used the standard cutoff point curve in combination with the standard SINE wave curve to detect impaired myocardial regional wall motion. The impaired regional wall motion myocardial segment was considered as a distortion or deviation point from SINE wave and/or the point of curve that stood below the cutoff point value. The accuracy of these tools in

detecting impaired myocardial regional wall motion were compared to visual estimation in terms of sensitivity, specificity, positive predictive value and negative predictive value.

RESULTS. By comparison to the visual estimation method, the sensitivity, specificity, the positive predictive value and the negative predictive value of the standard SINE wave curve in impaired myocardial regional wall motion detection were of 67.8%, 74.6%, 90.5% and 32.2% respectively. By **combining the standard SINE wave curve with the standard cutoff point (mean value - < 2-SD) curve** to detect impaired myocardial regional wall motion, the sensitivity, the positive predictive value and the negative predictive value were increased to 90.9%, 90.4% and 66.7% respectively, compared to the visual estimation method.

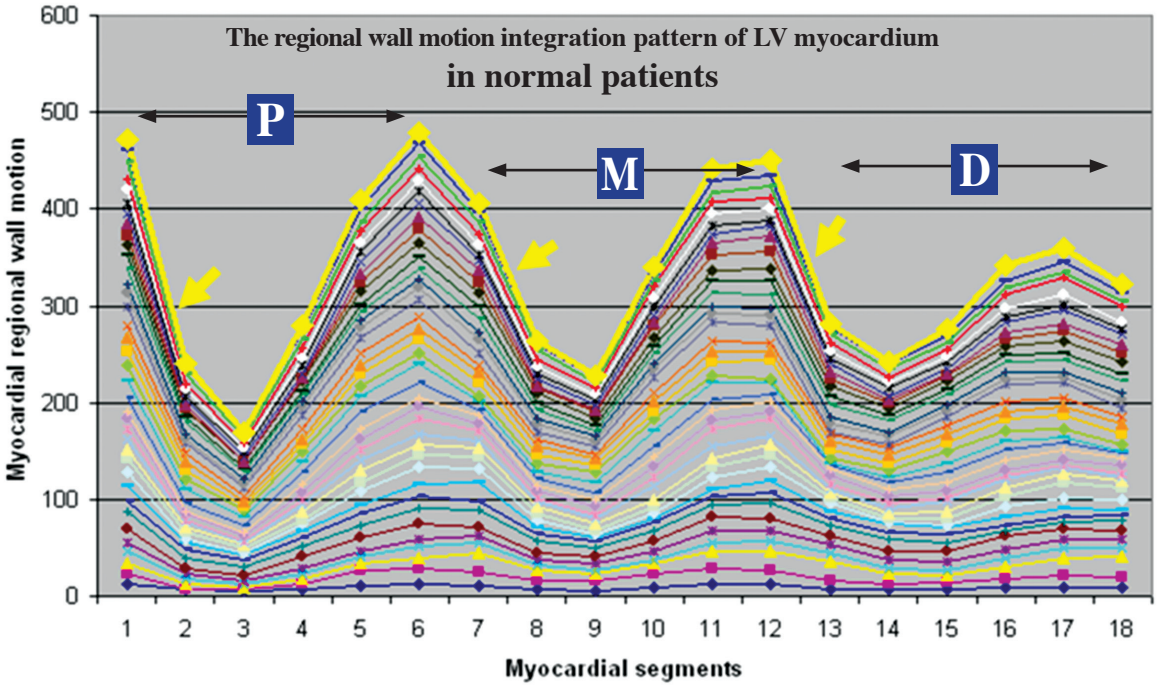
CONCLUSION. The circumferential regional wall motion integration pattern of the left ventricle in normal LVEF with normal regional wall motion patients is consistent; if characterized as a SINE wave curve, it can be used in combination with the standard cutoff point curve which displays the SINE wave character with a quantitative cutoff point, thus providing us with an additional support tool, to the visual estimation method, to detect impaired myocardial regional wall motion with acceptable high accuracy.

Magnetic resonance imaging (MRI) provides three-dimensional analysis of global cardiac function with high accuracy and reproducibility. MRI using CINE gradient technique and slice summation method is considered a gold standard tool for evaluation of the global ventricular function and is also used to evaluate regional myocardial function.[1] The left ventricular regional myocardial function is often assessed and scored by visual estimation as normal, hypokinesia (decreased wall motion), akinesia (absent wall motion), dyskinesia (wall motion in the opposite direction) and hyperkinesia (increased wall motion). However, assessment of myocardial regional wall motion by visual estimation method may be inaccurate because of inter-observer variation. The parameters which are used to express the regional myocardial function of the left ventricle are myocardial wall thickness, systolic myocardial wall thickening, circumferential and longitudinal myocardial wall motion or shortening.[2] In our study, we selected wall motion to be a qualitative and quantitative studied parameter to express the normal and impaired myocardial regional function. The aim of this study were to analyze the inter-segmental myocardial regional wall motion integration pattern and to prove that the integration pattern of normal myocardial regional wall motion can be used as a supporting tool with visual estimation method to depict the impaired regional wall motion myocardial segment.

Materials and Methods

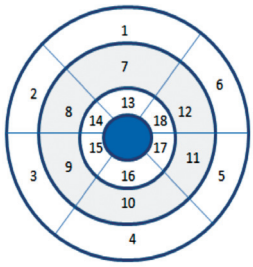
A total 60 adult patients (over the age of 15 years old) of mixed gender who came to the hospital for cardiac MRI examination during January to October in the year of 2011 were recruited. CINE gradient echo MRI with slice summation method for left ventricular function analysis was performed for every patient. Thirty-six patients were classified as having normal global and regional left ventricular systolic function (LVEF ≥ 55%), 12 patients had moderate systolic dysfunction (LVEF ≥ 35%, < 55%) and 12 patients were severe systolic dysfunction (LVEF < 35%).We analyzed the left ventricular ejection fraction and regional wall motion by computerized program in the Brilliance work station of 3T MRI scanner (Achieva, Philips company, Netherlands). The myocardial wall was divided into the basal part (above papillary muscle), the mid part (at the papillary muscle) and the apical part (below the papillary muscle). To analyze myocardial regional wall motion, myocardial wall of three levels of the left ventricle were segmented into 6 segments including the apex, which was modified from the AHA recommendation criteria.[3] Of the total 18 myocardial segments, they were referred to as anterior segments (segments 1, 7, 13), antero-septal segments (segments 2, 8, 14) , infero-septal segments (segments 3, 9, 15), inferior segments (segments 4, 10, 16), infero-lateral segments (segments 5, 11, 17), antero-lateral wall segments (segments 6, 12, 18) and the apex . Segments 1-6 were of the basal part, segments 7-12 were of the mid part and the segments 13-18 were of the apical part. The apex is the most apical segment of the left ventricle (LV). Normally, the LV apical myocardium part was divided into 5 segments by AHA recommendation, in our study however, we divided the apical myocardium into 6 segments and the apex, for more convenience in comparative analysis, as is shown in **Figure 1**.

The apex segment was excluded from the analysis process. The regional wall motion of each segment of normal left ventricular global and regional function was measured in millimeter(s) and was plotted as a line curve from the basal to the apical part respectively, in order to study inter- segmental integration pattern of the left ventricular regional wall motion. The regional wall motion of each myocardial segment in the group with normal cardiac function was averaged and was plotted as a line curve to be used as a qualitative standard SINE wave curve tool, which would depict the impaired regional wall motion myocardial segment. The 2-SD (standard deviation) value of each myocardium was calculated. The standard cutoff point curve was created by the plotting of the result value of myocardial segment specific mean-2SD. We used the standard SINE wave curve and the standard cutoff point curve in order to compare these standard curves with the curve of the regional wall motion of the case we wished to examine. The verified,



AHA recommendation for myocardial segmentation

Basal (or proximal (P)) level; Segments 1-6, **Mid** (M) level; Segments 7-12, **Apical** (or distal (D)) level; Segments 13-16, **Apex** level; Segment 17 **Segments 1,7,13** = anterior, **Segments 2,8** = antero-septal, **Segments 3,9** = infero-septal **Segments 4,10,15** = inferior, **Segments 5,11** = infero-lateral, **Segments 6,12** = antero-lateral, **Segment 14** = septal, **Segment 16** = lateral, **Segment 17** = apex



Studied design : Modified AHA recommendation map of myocardial segmentation

Basal (or proximal (P)) level; Segments 1-6, **Mid** (M) level; Segments 7-12, **Apical** (or distal (D)) level Segments 13-16, **Apex** level; Segment 17 **Segments 1,7,13** = anterior, **Segments 2,8,14** = antero-septal, **Segments 3,9,15** = infero-septal, **Segments 4,10,16** = inferior, **Segments 5,11,17** = infero-lateral, **Segments 6,12,18** = antero-lateral

Figure 1: *Demonstration of the inter-segmental integration pattern of the normal regional wall motion of the left ventricular myocardium characterized a consistent SINE wave pattern with substantial base to apex decline of the amplitude. The left ventricular myocardium was segmented into 18 segments (modified from the American Heart Association (AHA) criteria). Myocardial segments 1-6 were of basal or proximal part (P), segments 7-12 were of mid part (M), segments 13-18 were of apical or distal part (D).*

impaired myocardial segment was the segment showing distortion in comparison to the standard SINE wave curve and the segment point that stood below the standard cutoff point curve.

Statistic analysis

We compared the accuracy of using the studied tool i.e., the standard SINE wave (of normal regional wall motion) curve, the standard cutoff point curve with the visual estimation method, for detection of impaired myocardial regional wall motion in terms of sensitivity, specificity, and positive and negative predictive value.

Cardiac function assessment by MRI

Cardiac function assessment was performed on 3T MRI (Achieva, Philips, Netherlands) scanner, using Gradient echo CINE MRI technique with electrocardiogram (ECG) gating for every patient who had no contraindication for MRI examination (i.e., no metallic implants in the body, no claustrophobia etc). Short axis view of CINE image was required. The number of short axis slice was adjusted to cover the whole length of the left ventricle (from the basal through the apical part) in diastole (with no gap between each slice). The slice thickness should not be beyond 10 mm to avoid

Table 1: Value of left ventricular myocardial wall motion in normal systolic function (LVEF > 55%), moderately imapired systolic function (LVEF > 35% , < 55%) and severely impaired systolic function (LVEF < 35%)

Segment	Location	LVEF ≥ 55% Wall Motion (mm) (mean±SD)	LVEF ≥ 55% Wall Motion (mm) (mean-2SD)	LVEF ≥ 35%, < 55% Wall Motion (mm) (mean± SD)	LVEF < 35% Wall Motion (mm) (mean±SD)
1	Basal anterior	12.75±2.36	8.03	9.97+3.48	6.25+4.20
2	Basal antero-septal	6.51±2.34	1.81	3.28+3.24	2.25+2.08
3	Basal infero-septal	4.58±1.80	0.96	2.25+2.37	1.91±1.77
4	Basal inferior	7.56±2.35	2.85	5.20+3.20	4.2±2.49
5	Basal infero-lateral	11.05±2.86	5.33	9.24+3.01	5.97±3.45
6	Basal antero-lateral	12.94±1.91	9.13	12.09+2.90	6.80±3.99
7	Mid anterior	10.99±3.64	3.72	7.91+3.97	4.18±3.65
8	Mid antero-septal	7.14±2.13	2.87	3.81+2.57	3.08±1.88
9	Mid infero-septal	6.14±2.31	1.51	3.62+1.71	2.83±1.64
10	Mid inferior	9.17±3.02	3.13	6.86+2.78	3.55±2.11
11	Mid infero-lateral	11.9±3.18	5.58	9.20+2.45	4.86±2.77
12	Mid antero-lateral	12.2±3.66	4.83	9.70+4.11	4.36±3.10
13	Apical anterior	7.62±3.01	1.59	4.28+3.18	2.35±2.11
14	Apical septum	6.53±2.43	1.66	4.53+2.39	2.70±1.78
15	Apical infero-septal	7.45±3.76	2.85	5.43+2.50	2.26±2.06
16	Apical inferior	9.25±3.03	3.19	6.61+2.54	3.52±2.32
17	Apical infero-lateral	9.72±3.76	2.19	6.72+2.78	3.42±2.15
18	Apical antero lateral	8.72±3.47	1.78	5.51+3.55	2.13±1.74

the partial volume effect. MRI scanning for cardiac function assessment was done without gadolinium contrast injection. The global cardiac function (LVEF (%)), the left ventricular end diastolic volume (ml), the left ventricular end systolic volume (ml), stroke volume (ml) and cardiac output (L/min) were obtained by delineation of endocardial and epicardial contours on short axis view of CINE images. The circumferential regional wall motion of each myocardial segment was measured automatically by computerized program on the 3T Brilliance work-station after preparation by endocardial and epicardial contouring.

Results

Total 60 patients were classified into three groups according to global cardiac systolic function (left ventricular ejection fraction, LVEF). Thirty-six patients had normal cardiac systolic function, 12 patients had moderately impaired systolic function and 12 patients had severely impaired cardiac systolic function. The average ejection fraction of the normal group was of 64.8 % (55.7%-78.4%), of the moderate LV systolic dysfunction group, 49.3% (37.0%-54.8%) and of the severe LV systolic dysfunction group 19.6% (11.7%-33.6%). The regional wall motion of each myocardial segment of each cardiac function group was quantified and averaged (**Table 1**).

The average value of each myocardial segment (segments 1-18) of each cardiac function group was plotted as a line curve, in order of segment 1 to segment 18, resulting in a SINE wave form curve with amplitude declining from the basal to apical in normal global and regional cardiac function group (**Figure 1**). The average regional wall motion distance value of the anterior and of

the antero-lateral wall (segments 6, 12, 18), were at the peak of the positive amplitude and of the infero-septal wall (segment 3, 9, 15) were at the trough of the negative amplitude. For the impaired cardiac systolic function groups, the regional wall motion inter-myocardial segmental integration patterns were not consistent and were distorted from SINE wave (**Figure 2**). Therefore, the line curve with consistent patterns of circumferential regional wall motion inter-myocardial segmental integration of the normal cardiac function group was proposed to be used as a standard SINE wave curve tool, against which the impaired regional wall motion line curve, in case of interest, could be detected by comparison.

In our study, 270 myocardial segments of 15 patients with impaired cardiac systolic function and impaired regional wall motion (average LVEF = 24.84%; range 11.7-40.7%) were used to test the accuracy of the standard SINE wave curve in defining the impaired myocardial regional wall motion segment compared to the visual estimation method. The impaired myocardial segment will be shown as point of distortion from SINE wave curve as shown in **Figure 2, 3**. Two hundred and eleven of 270 myocardial segments were documented as impaired regional wall motion by visual estimation. Fifty-nine myocardial segments were normal. By using the SINE wave referent curve tool to detect impaired regional wall motion myocardial segment, 143 myocardial segments of total 211 were called impaired (143/211= 67.8%, true positive);15 segments of total 211 segments (7.1%, false positive) were considered impaired regional wall motion using standard SINE wave curve but were considered normal by visual estimation. By comparing with the visual estimation method, the sensitivity, specificity, the positive predictive value, the negative predictive value of standard SINE wave curve alone in impaired myocardial regional wall motion detection were of 67.8%, 74.6%, 90.5% and 32.2% respectively (Table 2). In addition, we can observe that the SINE wave pattern was also obtained in impaired systolic function with LV global hypokinesia. However, using only qualitative SINE wave form character of regional wall motion may not be adequate to be a single tool for detection of impaired myocardial regional wall motion. Hence we considered the quantitative cutoff point to be two standard deviation values subtracted from the average segment specific value of normal regional wall motion (**Table 1**). The average-2SD value of each myocardial segment of normal cardiac function group was plotted in line curve to form the standard cutoff point curve of normal myocardial regional wall motion. This cutoff point curve also displayed SINE wave form character that ran parallel to the standard SINE wave form curve (**Figure 4**). By using this tool combined with standard SINE wave form curve, a greater number of impaired myocardial regional wall motion

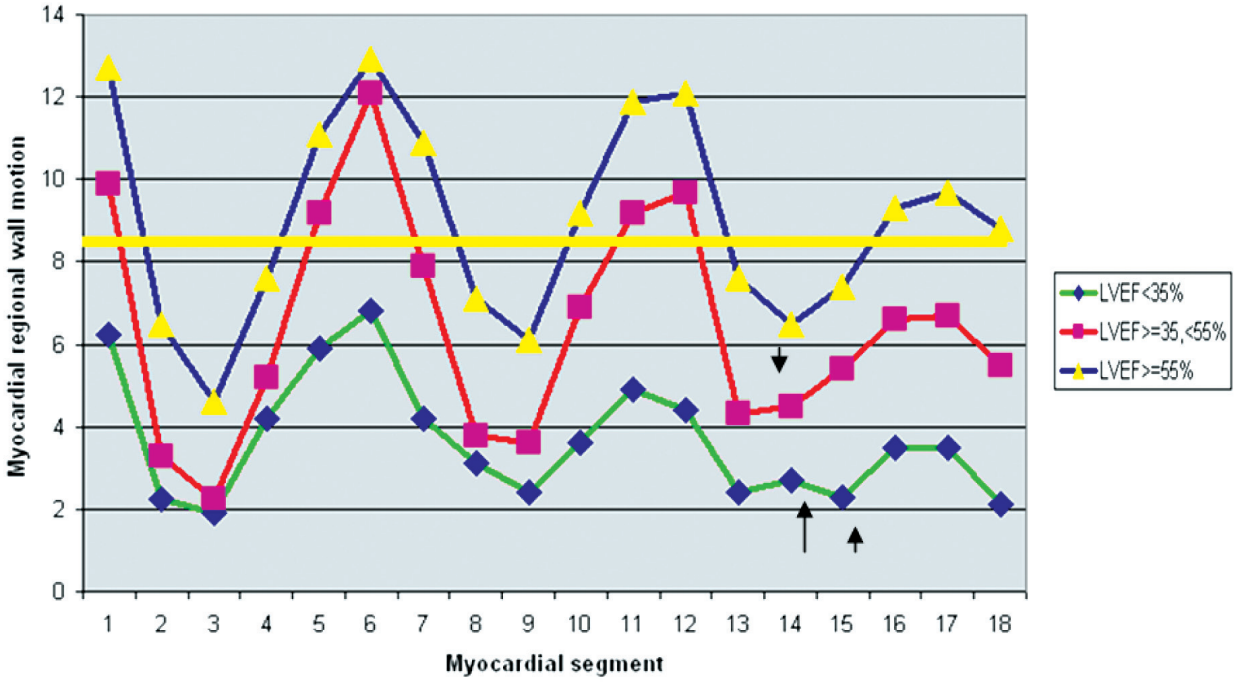


Figure 2: *Demonstration of the comparison of the inter-segmental integration pattern of the left ventricle between normal group (LVEF> 55%) and the impaired myocardial function group (Moderately impaired : LVEF >35, <55% , Severely impaired : LVEF<35%). Black arrow pointed the distortion points from SINE wave which indicated impaired myocardial regional wall motion segments.*

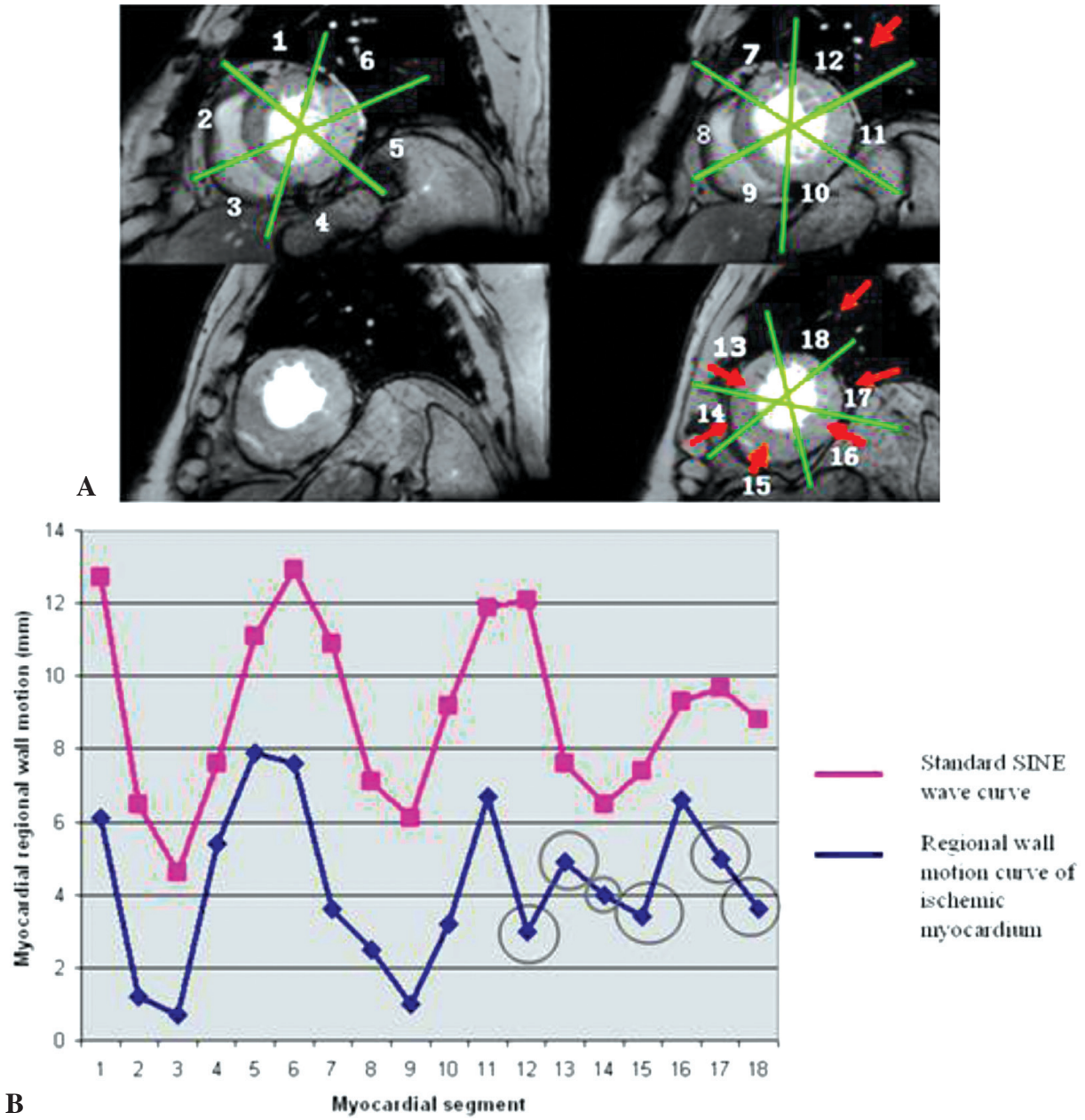


Figure 3A-B: *Demonstration of the application of the standard SINE curve as a tool for impaired regional wall motion detection by parallel comparing to the curve of regional wall motion of the interest case. The distortion point segment point from SINE wave curve was considered an impaired myocardial regional wall motion segment as shown in circle.*

Table 2: Correlative documentation of impaired myocardial segments between the visual estimation method and standard SINE wave form curve. The total studied myocardial segments were of 270 segments of 15 adult patients. The sensitivity, the specificity, the PPV and the NPV were of **60.8%** (143/211), **74.6%** (44/59), **90.5%** (143/168) and **32.2%** (44/112) respectively.

Myocardial segments	Visual estimation (+)	Visual estimation (-)
Standard SINE wave curve +	143	15
Standard SINE wave curve -	68	44

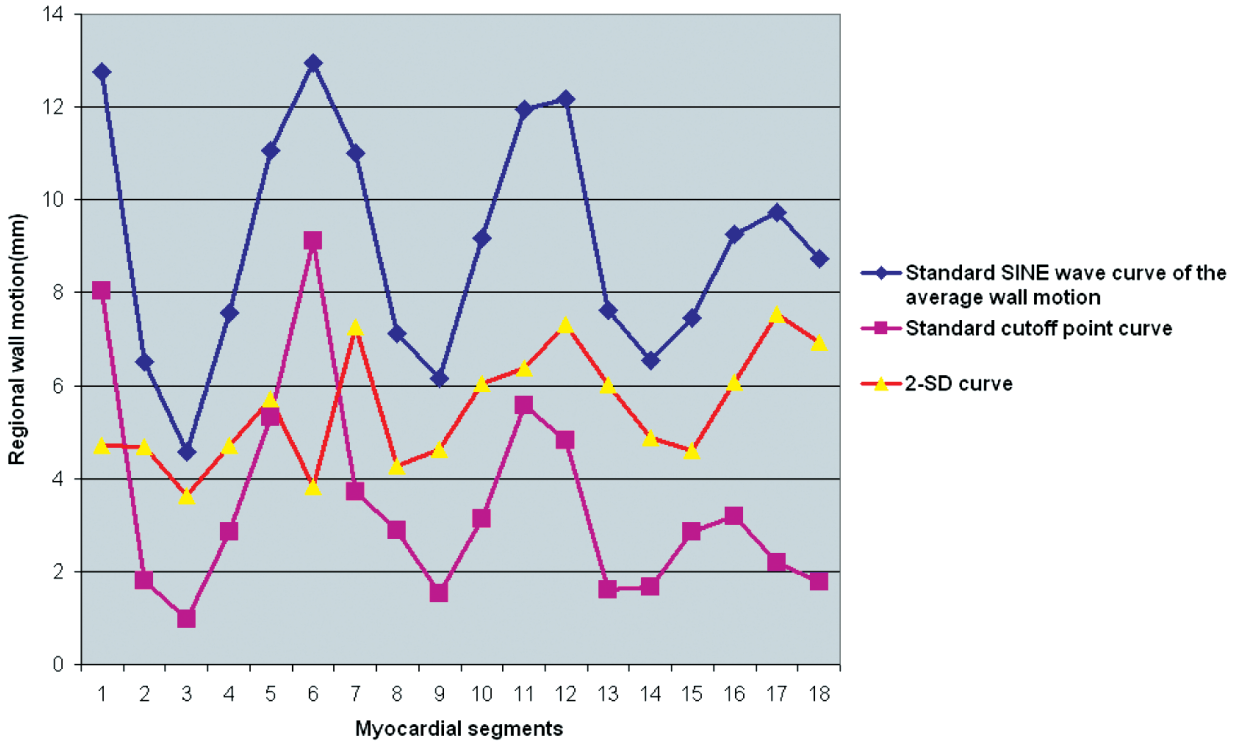


Figure 4: *Demonstration of strandard SINE wave curve, myocardial segment specific 2-SD curve and standard cutoff point curves (mean-2SD) of normal regional wall motion. Standard SINE wave curve was a qualitative tool, which was used to depict impaired myocardial regional wall motion segment by depicting the point of distortion from SINE wave. The standard cutoff point curve (segment specific mean-2SD curve) provided the segment-specific quantitative cutoff point value. Myocardial segment that has regional wall motion < segment specific mean-2SD of the average referent point is counted as for impaired regional systolic function myocardium. The standard cutoff point curve was a double function tool, which provides both qualitative and quantitative properties.*

Table 3: Correlative documentation of impaired myocardial segments between the visual estimation method and combination method (using standard SINE wave curve plus standard cutoff point curve. The sensitivity, the specificity, the PPV and the NPV were of **90.9%** (192/211), **64.4%** (38/59), **90.1%** (192/213) and **66.7%** (38/59) respectively.

Myocardial segments	Visual estimation (+)	Visual estimation (-)
Combination method +	192	21
Combination method -	19	38

segments were documented compared to using the standard SINE wave curve alone (**Figure 5**). Because the impaired regional wall motion myocardial segments were considered when they displayed a distortion from SINE wave and/or stood below the line of standard cutoff point curve. Comparing with the visual estimation method, 192 myocardial segments (90.9%, true positive) were called impaired by visual estimation and by use in combination with the standard SINE wave and standard cutoff point curve, 21 myocardial segments of 211 segments (9.9%) were detected as impaired myocardium by the combined standard curves but were specified as normal by visual estimation method. The sensitivity, specificity, the positive predictive value, the negative predictive value of the regional wall motion detection by using the combination of standard cutoff point compared to the visual estimation were **90.9%, 64.40%, 90.1%** and **66.7%** respectively (**Table 3**).

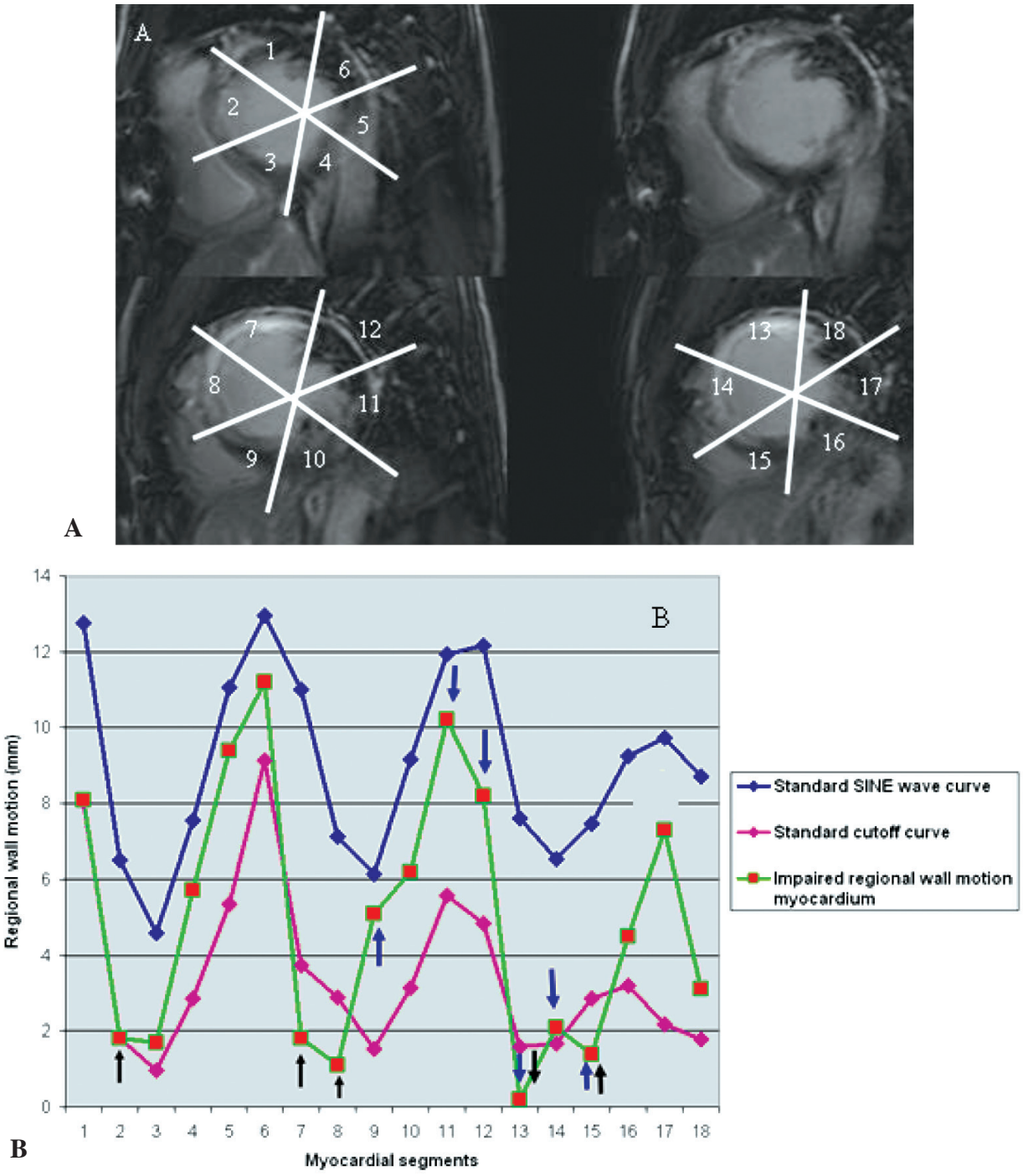


Figure 5A-B: *Demonstration of the application of the standard SINE curve tool plus the standard cutoff point curve to detect the impaired myocardial segment in validated prior myocardial infarction case. A: Delayed contrast enhancement study images showed myocardial contrast enhancement (bright signal) of myocardial infarction area corresponding to the impaired myocardial regional wall motion. B: Demonstration of using standard SINE wave curve combined with the standard cutoff point curve as tool to define impaired myocardial regional wall motion segment. Blue arrow indicated impaired myocardial regional wall motion depicted using standard SINE curve alone. The impaired myocardial regional wall motion segment was shown as a distortion point from the SINE wave. Black arrow indicates the impaired myocardial regional wall motion depicted by the standard cutoff point alone and the impaired myocardial regional wall motion segment was the point that stood below the standard cutoff point curve. The total impaired regional wall motion myocardial segments were all myocardial segments which distorted from SINE wave curve and/or the segments that stood below the stand cutoff point curve.*

Discussion

We demonstrated that the regional wall motion of normal function myocardium displayed the consistent pattern of inter-myocardial segmental integration on line curve and was characterized as a SINE wave form curve with substantial basal to apex amplitude decline. This consistent character can be used as a standard curve tool to depict the impaired myocardial regional wall motion by comparing it with the wave form of the interest case. The standard cutoff point curve is a tool which has both quantitative and qualitative properties by providing the character of SINE wave and lower limit threshold value of myocardial segment specific regional wall motion. Combined use of two standard curve methods can overcome the limitation of using standard SINE wave curve alone, in the case of global hypokinesia, which also showed a consistent SINE wave form as normal case.

In 2001, Sharir et al[4] used 2-3 SD as the cutoff point to define impaired myocardial regional wall motion on Gated myocardial perfusion Single-photon emission computed tomography (SPECT) images; this reflects the fact that detection of myocardial dysfunction is more complex in some segments. Our study used fixed 2-SD for every segment to create the standard cutoff point curve, but Sharir demonstrated that the suitable value for a better cutoff point for some myocardial segments may sometimes need more or less than 2-SD. This should be considered in future studies in order to improve the sensitivity and specificity of our studied tool.

Conclusion

Inter-myocardial segmental integration pattern of normal regional myocardial motion is characterized by a consistent SINE wave with substantial apex-to base amplitude decline. The application of standard segment-specific cutoff value curve in combination with standard SINE wave curve for defining the impaired regional wall motion myocardial segment provided reasonably accurate identification and grading of impaired regional myocardial function. It is thus suitable for use as a supportive diagnostic tool together with the visual estimation method.

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Original Article

Part I: Characteristics of Surgical Spine Patients at Bangkok Spine Academy (BSA)

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Keywords:
Back surgery, Lumbar spine surgery, Oswestry Disability Index, Euro Quality of life

OBJECTIVE. To use the Oswestry Disability Index (ODI) and Euro Quality of Life (EuroQol) as pre-screening assessment tools to improve surgery outcomes for patients with spinal disorders.

MATERIALS AND METHODS. Prior to surgical intervention, 223 (out of 311 lumbar spine) patients who were eventually treated with surgery at Bangkok Spine Academy between August 2010 and June 2011, filled out the above mentioned questionnaires pre-operatively. ODI and EuroQol were used to assess their mobility, activities, pain, anxiety etc., which could help better determine their spine disability together with their medical history and physical examination.

RESULTS. Mobility: Pre-operative 157 (92.9%) had problems, 12 (7.1%) had no problems. **Self-care**: Pre-operative 97 (57.4%) had problems, 72 (42.6%) had no problems. **Usual activities**: Pre-operative 157 (92.9%) had problems, 12 (7.1%) had no problems.**Pain/discomfort**: Pre-operative 167 (98.82%) had problems, 2 (1.18%) had no problems. **Anxiety/depression**: Pre-operative 137 (81.07%) had problems, 32 (18.93%) had no problems.

CONCLUSION. All patients who underwent surgery for the treatment of low back pain were found to be having significant disability and restrictions in their lives; using the pre-operative ODI and EuroQol measurements they could be categorized as having moderate to severe disability.

Back pain is second only to the common cold as the most frequent reason for seeing a physician. Low back pain is experienced by most individuals, with 70 to 80% of the world's population experiencing low back pain sometime during their lives.[1]

An international comparative study by Cherklin DC, et al showed the rate of back surgery in the United States was at least 40% higher than in any other country and was more than five times that of England and Scotland. Back surgery rates increased almost linearly with the per capita supply of orthopedic and neurosurgeons in the country. These findings illustrate the potentially large impact of health system differences on rates of back surgery.[2]

Surgical goals are improvements in pain, functional status and quality of life. It is well known that some patients operated on for spinal disorders will have a poor result, regardless of the apparent technical success of the operative procedure itself.[3] This has prompted the search for risk factors and the development of pre-screening tools to assist with both the patient selection procedure and the promotion of realistic expectations on behalf of the patient.[4-6] In order

to make the correct diagnosis, Bangkok Spine Academy (BSA) always focuses on the history of medical illness and a thorough physical examination of all patients. We follow the Joint Clinical Practice Guidelines from the American College of Physicians and the American Pain Society for diagnosing and treating Low Back Pain.[7]

The BSA had 2,994 low back pain patients in 2010 and 223 (7.44%) underwent surgery. BSA has begun to develop a spine registration for patients who underwent lumbar spine surgery in order to study patient's history, population, epidemic, quality of life and ability to perform daily activities. The analysis of this information will help us to improve our care and treatment of our patients.

Currently, there are several assessment tools used to measure the treatment results of patients who undergo lumbar spine surgery. Oswestry Disability Index (ODI) is an internationally accepted measure for spine disability and is used in most if not all spinal treatment result assessments. Additional measures are also used to supplement the ODI in order to fully define the patient's spine condition; commonly used questionnaires include the SF-36, SF-12 and the Euro Quality of Life (EuroQol). Therefore we decided to utilize the ODI and EuroQol[8] with our prospective surgery candidates as a pre-screening procedure and so we could also have effective tracking of the patient's improvement on follow up. The following data then shows the pre-operative state of our patients, using the abovementioned measures.

Materials and methods

Sample Size

The focus of this study is the 223 (out of 311 lumbar spine) patients treated with surgery at BSA between August 2010 and June 2011.

EuroQol

Pre-operative measurements of mobility, self-care, activities of daily life, pain, and anxiety and/or depression were determined by EuroQol using visual analogue scale (VAS) and 5 Dimensions (5D).[9]

The EuroQol Visual Analogue Scale (EQ-VAS)

The EQ-VAS is a part of the EuroQol Questionnaire. The patients rate their current health state on the line, which ranges from 0 - 100 (The worst to the best imaginable health).[10]

Oswestry Disability Index (ODI)

ODI versions with a scale ranging from 0-5 were used. Questionnaires addressing 10 common activities were administered, using both English and validated translations into other languages. Points were added up each section and plugged in to the following formula in order to calculate the patient's level of disability:

Point total / 50 x 100 = % disability (aka: 'point total' divided by '50' multiply by ' 100 = percent disability).[11,12]

In Thai patients the authenticated Thai ODI was used; in non-Thai speaking patients, the English ODI (version 0.1) was used.[13]

Thai score

In a study of the quality of life of Thai people across the country, using the EuroQol questionnaire, the formula to calculate the quality of life of Thai people was called Thai score.

Thai score = 1-0.202-(0.121*mo)-(0.121*sc)-(0.059-ua)-(0.072*pd)-(0.032*ad)-(0.190*m2)-(0.065*p2)-(0.046*a)-(0.139*N3).[14]

Table1: Interpretation of scores

Score	Description
0% to 20%	**Minimal disability:** The patient can cope with most living activities. Usually no treatment is indicated apart from advice on lifting, sitting and exercise.
21%-40%	**Moderate disability:** The patient experiences more pain and difficulty with sitting, lifting and standing. Travel and social life are more difficult and they may be disabled from work. Personal care, sexual activity and sleeping are not grossly affected and the patient can usually be managed by conservative means.
41%-60%	**Severe disability:** Pain remains the main problem in this group but activities of daily living are affected. These patients require a detailed investigation.
61%-80%	**Crippled:** Back pain impinges on all aspects of the patient's life. Positive intervention is required.
81%-100%	These patients are either bed-bound or exaggerating their symptoms.

SPSS Data Analysis

This descriptive statistic is used to analyze demographic data. EuroQol-5D is composed of five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimension has 3 levels: no problem, some problem, extreme problems.[15] The ratings in the different possible health states will be transformed into an index value. We decided to adapt this and say that each dimension has two levels of severity: No problem and problem. No problem states were those rated the health as full health (all dimensions rated as 1). The problems which were proportionally ranked from 1-3 were analyzed.

Results

Patients who filled out a questionnaire asking them to respond to questions in their native language before undergoing a surgical procedure at BSA between August 2010 and June 2011.

Patient population

Baseline parameters and patient data are presented in Table 2. The majority of patients, 169, or 75.78% were Thai. The proportion of males to female was male 129 (57.8%) female 94 (42.2%). Fifty-seven patients (25.6%) were in the age range of 51-60. Mean ± SD age of patients was 53.69 ± 15.62, minimum 20, and maximum 88. Eighty six patients (38.6%) had a body mass index range 25.1-30; Mean ± SD Body mass index was 26.28 ± 6.11, minimum 18.03, maximum 45.70. Two hundred and one (201) patients (94.6%) were non-smokers. Duration of pain for acute pain 127 (56.95%) Mean ± SD 44.60 ± 29.66, minimum 5 days, maximum 90 days and for chronic pain 96 (43.05%) Mean ± SD 733.70 ± 841.46 minimum 120 days, maximum 3,650 days. Fifteen (6.72%) of patients had previously undergone back surgery in the past. 96 patients (38.56%) had underlying diseases. Surgical procedures were categorized into five groups: Lumbar decompression with Fusion 64 (28.7%), Lumbar decompression without Fusion 76 (34.1%), Lumbar Microdiscectomy 68 (30.5%), Total Disc Replacement 1 (0.4%) and Mixed procedures 14 (6.3%) of the cases.

Mobility: Pre-operative 157 (92.9%) had problems, 12 (7.1%) had no problems. **Self-care:** Pre-operative 97 (57.4%) had problems, 72 (42.6%) had no problems. **Usual activities:** Pre-operative 157 (92.9%) had problems, 12 (7.1%) had no problems. **Pain/discomfort:** Pre-operative 167 (98.8%) had problems, 2 (1.12%) had no problems. **Anxiety/depression:** Pre-operative 137 (81.1%) had problems, 32 (18.9%) had no problems. (See Table 3 for more details)

The EQ Visual analog scale is presented in Table 4. Total patients pre-operative 223 cases, report EQ Visual analog scale Mean ± SD 50.25 ± 16.65, Median 50, 25th percentile 40, 75th percentile 60.

EQ-5D dimensions (Thai score). Thai patients pre-operative 169 cases, report EQ-5D dimensions Mean ± SD 0.488 ± 0.151, Median 0.452, 25th percentile 0.45, 75th percentile 0.57. Lumbar decompression without Fusion 0.468, Lumbar Microdiscectomy 0.483, Lumbar decompression with Fusion 0.503 and Mixed procedures 0.536 respectively presented in Figure 1.

EQ-VAS (Thai score index). Thai patients pre-operative 169 cases, report EQ-VAS Mean ± SD 50.592 ± 16.501, Median 50, 25th percentile 40, 75th percentile 60. Lumbar Microdiscectomy 46.9, Lumbar decompression without Fusion 50.741, Lumbar decompression with Fusion 50.304 and Mixed procedures 50.333 respectively presented in Figure 2.

Oswestry Disability Index Score Of the 223 pre-operative patients. Reported scores were: Mean ± SD 32.58 ± 21.60, Median 32, 25th percentile 12, 75th percentile 48. Mixed procedures 46.51, Total disc replacement 34, Lumbar Microdiscectomy 34.37, Lumbar decompression with Fusion 33.82 and Lumbar decompression without Fusion 27.34 respectively presented in Figure 3.

Discussion

Our patients'ages ranged from 20-88. Seventy-five percent (75%) were Thai and 25% were non-Thai. Both groups received pre-operation ODI and EuroQol assessment and were reevaluated at 6 months after surgery. At entry surgical patients showed a wide range of ODI values but most were in the moderately disabled range of 40-60 indicating to us a justification to consider surgical treatment.

Additional data from the EuroQol confirmed the surgical patients' disability and gave expanded detail about which aspects of the patients lives were most affected. The majority of patients experienced significant pain, with chronic pain (pain ≥ 3 months) being felt more severely than acute pain (pain ≤ 3 months). Pain/discomfort was also reported very frequently, by 98.21% of patients. Difficulty with Usual activities 92.83%, Mobility 91.93%, Anxiety/Depression 80. Seventy-two percent (72%), and Self-care 57.85% were reported respectively: see Table 3. We found the sexual dysfunction assessment not to be well defined in our patient population, which is very likely due to unspoken cultural restriction amongst Thais to fully discuss this aspect of their clinical symptoms.

Table2: Patient characterritics.

Group Categories	Thai (n=169)	Foreign (n=54)	Total (n=223)
Sex			
Male	94 (55.6)	35 (64.8)	129 (57.8)
Female	75 (44.4)	19 (35.2)	94 (42.2)
Age			
20-30	17 (10.1)	1 (1.9)	18 (8.1)
31-40	23 (13.6)	10 (18.5)	33 (14.8)
41-50	26 (15.4)	11 (20.4)	37 (16.6)
51-60	39 (23.1)	18 (33.3)	57 (25.6)
61-70	32 (18.9)	11 (20.4)	43 (19.3)
71-80	27 (16.0)	2 (3.7)	29 (13.0)
>80	5 (3.0)	1 (1.9)	6 (2.7)
Mean ± SD, (Min, Max)	**54.10 ± 16.40 (20, 88)**	**52.42 ± 12.92 (30, 87)**	**53.69 ± 15.62 (20, 88)**
BMI			
< 18.5	3 (1.8)	1 (1.9)	4 (1.8)
18.5 – 23.0	33 (19.5)	12 (22.2)	45 (20.2)
23.1 – 25.0	48 (28.4)	5 (9.3)	53 (23.8)
25.1 – 30.0	63 (37.3)	23 (42.6)	86 (38.6)
30.1 – 40.0	22 (13.0)	12 (22.2)	34 (15.2)
> 40.0	0 (0.0)	1 (1.9)	1 (0.4)
Mean ± SD, (Min, Max)	**25.79 ± 6.25 (18.03, 36.00)**	**27.92 ± 5.39 (19.03, 45.70)**	**26.28 ± 6.11 (18.03, 36.00)**
Smoking Habits			
Non smokers	158 (93.5)	43 (79.6)	201 (90.1)
Smokers	7 (4.1)	5 (9.3)	12 (5.4)
Ex smokers > 1 year	1 (0.6)	1 (1.9)	2 (0.9)
Ex smokers < 1 year	3 (1.8)	5 (9.3)	8 (3.6)
Duration of pain			
Acute pain ≤ 3 months	83 (49.11)	44 (81.48)	127 (56.95)
Mean ± SD, (Min, Max)	**43.22 ± 29.01 (7, 90)**	**51.93 ± 33.05 (5, 90)**	**44.60 ± 29.66 (5, 90)**
Chronic pain ≥ 3 months	86 (50.89)	10 (18.52)	96 (43.05)
Mean ± SD, (Min, Max)	**736.31 ± 933.32 (120, 3653)**	**727.62 ± 584.43 (120, 2190)**	**733.70 ± 841.46 (120, 3650)**
Previous back surgery			
Yes	12 (7.1)	3 (5.55)	15 (6.72)
No	157 (92.89)	51 (94.44)	208 (93.27)
Underlying diseases			
Yes	76 (44.97)	20 (37.03)	96 (38.56)
No	93 (53.02)	34 (92.96)	137 (61.43)
Group Categories	**Thai (n=169)**	**Foreign (n=54)**	**Total (n=223)**
Procedure			
Lumbar decompression with Fusion	56 (33.1)	8 (14.8)	64 (28.7)
Lumbar decompression	54 (32.0)	22 (40.7)	76 (34.1)
Lumbar Microdiscectomy	50 (29.6)	18 (33.3)	68 (30.5)
Total Disc Replacement	0 (0.0)	1 (1.9)	1 (0.4)
Mixed procedures	9 (5.3)	5 (9.3)	14 (6.3)

Table 3: EuroQol-5 Dimensions (EQ-5D)

EQ-5D dimensions		Lumbar decompression with Fusion	Lumbar decompression without Fusion	Lumbar Microdiscectomy	Total Disc Replacement	Mixed procedures	Total
		(n=64)	(n=76)	(n=68)	(n=1)	(n=14)	(n=223)
Mobility	No problems	8 (12.50)	5 (6.58)	4 (5.88)	0 (0.0)	1 (7.14)	18 (8.07)
	Problems	56 (87.50)	71 (93.42)	64 (94.12)	1 (100.0)	13 (92.86)	205 (91.93)
Self-care	No problems	36 (56.25)	20 (26.32)	29 (42.65)	1 (100.0)	8 (57.14)	94 (42.15)
	Problems	28 (43.75)	56 (73.68)	39 (57.35)	0 (0.0)	6 (42.86)	129 (57.85)
Usual activities	No problems	5 (7.81)	4 (5.26)	6 (8.82)	0 (0.0)	1 (7.14)	16 (7.17)
	Problems	59 (92.19)	72 (94.74)	62 (91.18)	1 (100.0)	13 (92.86)	207 (92.83)
Pain/ Discomfort	No problems	1 (1.56)	2 (2.63)	1 (1.47)	0 (0.0)	0 (0.0)	4 (1.79)
	Problems	63 (98.44)	74 (97.37)	67 (98.53)	1 (100.0)	14 (100.0)	219 (98.21)
Anxiety/ Depression	No problems	17 (26.56)	8 (10.53)	17 (25.00)	0 (0.0)	1 (7.14)	43 (19.28)
	Problems	47 (73.44)	68 (89.47)	51 (75.00)	1 (100.0)	13 (92.86)	180 (80.72)

Table 4: EuroQol Visual analog scale (EQ-VAS)

Visual analog scale (VAS)	Lumbar decompression with Fusion	Lumbar decompression without Fusion	Lumbar Microdiscectomy	Total Disc Replacement	Mixed procedures	Total
Mean (+/- Std. error)	54.22 ± 14.20	50.07 ± 15.57	46.18 ± 19.30	40.00 ± 0.00	53.57 ± 15.98	50.25 ± 16.65
Median	60	50	50	40	55	50
25th percentile	50	40	40	40	40	40
75th percentile	65	60	60	40	70	60
N	64	76	68	1	14	223

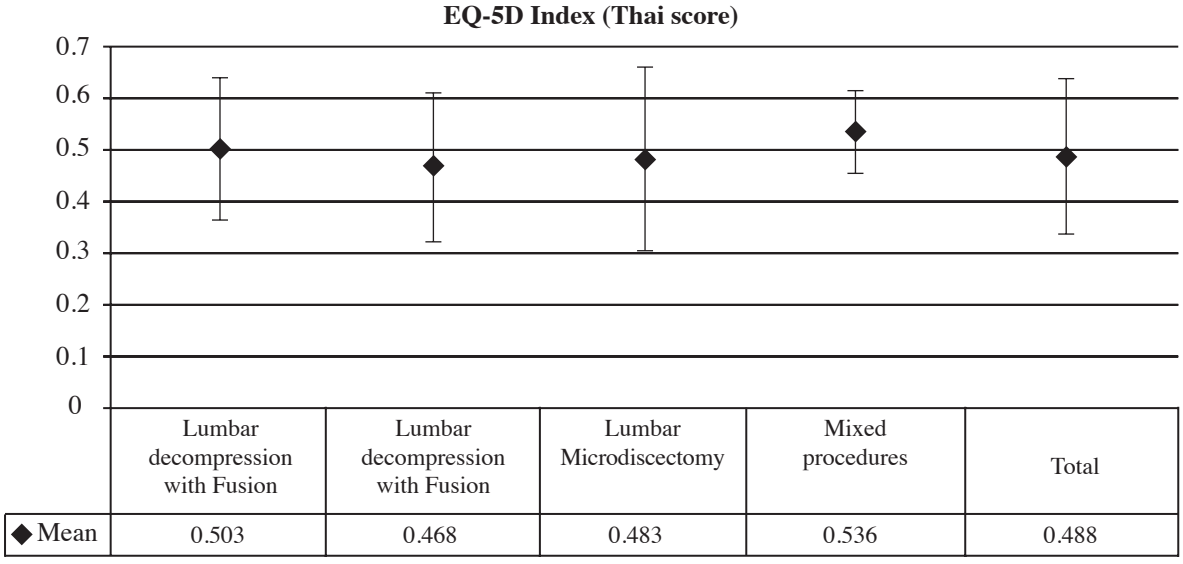
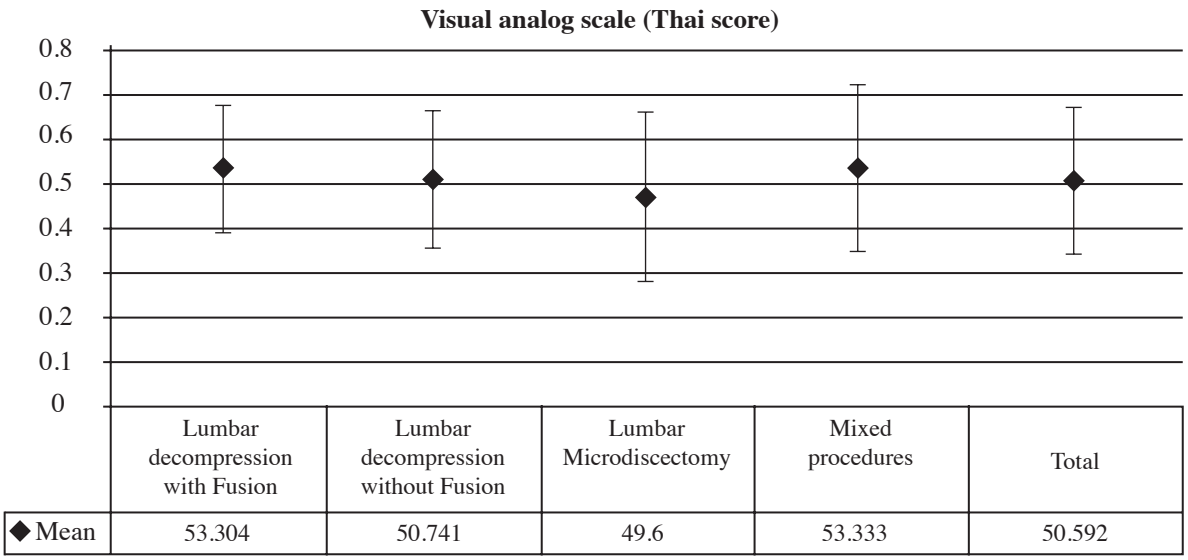
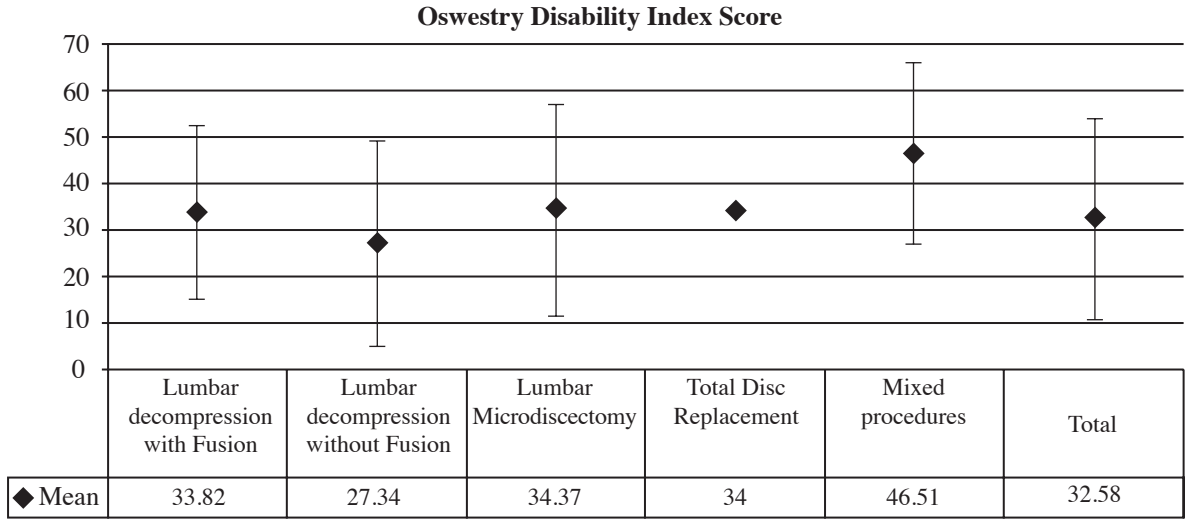


Figure 1: *Average mean EQ-5D index (Thai Score) Pre-operation in each procedure*



	Lumbar decompression with Fusion	Lumbar decompression without Fusion	Lumbar Microdiscectomy	Mixed procedures	Total
◆ Mean	53.304	50.741	49.6	53.333	50.592

Figure 2: *Average EuroQol Visual analog scale (EQ-VAS) 0-100 Pre-operation in each procedure*



	Lumbar decompression with Fusion	Lumbar decompression without Fusion	Lumbar Microdiscectomy	Total Disc Replacement	Mixed procedures	Total
◆ Mean	33.82	27.34	34.37	34	46.51	32.58

Figure 3: *Average mean Oswestry Disability Index score Pre-operation in each procedure*

Conclusion

All patients who underwent surgery for the treatment of low back pain were found to be having significant disability and restrictions in their lives; using the pre-operative ODI and EuroQol measurements, they could be categorized as having moderate to severe disability. The major problems reported were pain and mobility, there were also some problems with self-care and performance of usual activities.

Some differences were found between patients who underwent fusion and who only received laminectomies for decompression, or a herniated disc. Most patients who underwent fusion were elderly and had more co-mobility. Visual analog scale for patients with fusion was 60 and without fusion it was 50. We believe the preoperative ODI and EuroQol are both very useful in confirming the patients' disability and impaired quality of life and these same indices will be useful in reliably documenting the improvement after surgical treatment.

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Part II: Post-Operative Improvements in the Euro Quality of Life (EuroQol) and Oswestry Disability Index (ODI) Scores in Lumbar Spine Surgical Patients

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Keywords:
Post-Operative Improvements, Lumbar Spine Surgical, Euro Quality of Life,Oswestry Disability Index

OBJECTIVE. To measure the surgery outcome of patients at 6, 12 and 24 weeks using the Oswestry Disability Index and the Euro Quality of Life (EuroQol).

MATERIALS AND METHODS. Ninty-three out of a total of 311 patients who underwent spinal surgery at Bangkok Hospital between August 2010 and June 2011 and had completed their 6 months follow up.

RESULTS AND CONCLUSION. The study found that surgery did improve the functionality of patients who had back pain due to radiculopathy, lumbar spinal stenosis, and herniated nucleus pulposus. Measured by ODI and Quality of Life (QOL) methodology, the treatment outcomes showed significant improvement.

Surgery is one of the treatment alternatives for patients with spine conditions. In the United States of America, up to 4.6 million spine surgeries are performed each year.[1] Nowadays, surgical technologies and treatment options are advanced and very diverse. There have been many comparative studies in the U.S and Europe on the outcome of each treatment technique.[2] The study of Jacobs and team in 2010 compared the outcomes of surgical treatment against conservative treatment in a group of patients who were diagnosed with sciatica due to lumbar disc herniation. Comparing the efficiencies of different surgical techniques; a landmark paper by Copay AG et al,[3] measured outcomes using methods such as the Quality of Life (QOL) Questionnaire, the Oswestry Disability Index (ODI), and the Pain Scales.[4] On average, there are about 500 lumbar spine patients who undergo invasive and surgical interventions at Bangkok Spine Academy annually. This prospective study measured the outcome of patients who underwent lumbar surgery at Bangkok Spine Academy, utilizing EuroQol and ODI preoperatively and at various postoperative intervals of 6, 12 and 24 weeks.

Materials and Methods

Sample Size

A total of 311 lumbar spine surgical patients were treated at Bangkok Spine Academy between August 2010 and June 2011. Out of this group, we analyzed the available data of 93 patients who had already completed their 6 months follow up. The study is ongoing and these are therefore preliminary results.

Outcome Measures

The Euro Quality of Life (EuroQol): Pre-operative measurements of mobility, self-care, activities of daily life, pain, and anxiety and/or depression were determined pre-operation and at 6, 12, 24

weeks by EuroQol using Visual Analogue Scale (VAS) and 5 Dimensions (5D).[5]

Oswestry Disability Index (ODI): ODI versions with a scale ranking from 0-5 were used. Questionnaires addressing 10 common activities were administered, using both English and validated translations into other languages.[6,7]

The EuroQol Visual Analogue Scale (EQ-VAS): The EQ-VAS is a part of the EuroQol Questionnaire. The patients rate their current health state on the line, which ranges from 0-100 (The worst to the best imaginable health).[8]

Data Analysis

This descriptive statistic is used to analyze demographic data. EuroQol 5D is composed of five dimensions and patients can rate their perceived health status into 3 possible levels in each dimension, i.e. No problems, some problems, and severe problems. We have decided to look at the frequency of reported problems, so split the data into two levels of severity: No problem (i.e. level 1) and problems (i.e. levels 2 and 3). The paired T-Test was used for statistical analysis of ODI, and EQ-VAS both pre and post operatively. The One-way Repeated Measure ANOVA was used for comparing the data at 4 intervals.

Results

From August 2010 to June 2011, a total of 93 consecutive patients (44 males and 49 females), whose mean age was 53.12 years old (range 24-88), undergoing lumbar spine surgery were enrolled. The number of the patients who underwent lumbar decompression surgery with fusion was 33 (35.48%). Fourteen patients (27.95%) underwent the lumbar microdiscectomy surgery. Patients who underwent lumbar decompression surgery without fusion numbered 16 (17.20%). Only 1 person (1.07%) underwent total disc replacement surgery and the total number of patients who underwent mixed procedure surgery was 17 (18.27%).

The finding of ODI of 77 patients who had completed all 4 period questionnaires reported the average pre-operative score equaled 42.49, which indicated severe disability. The average score at the 6th week after surgery was 16.85. This showed that there was a significant improvement (p-value < 0.05). The average score at the 12th week and the 24th week were 11.14 and 5.36 respectively. The ODI Score after the surgery was rated at minimal disability. If compared with the baseline score, they they showed a significant improvement (p-value < 0.05), which is illustrated in Figure 1.

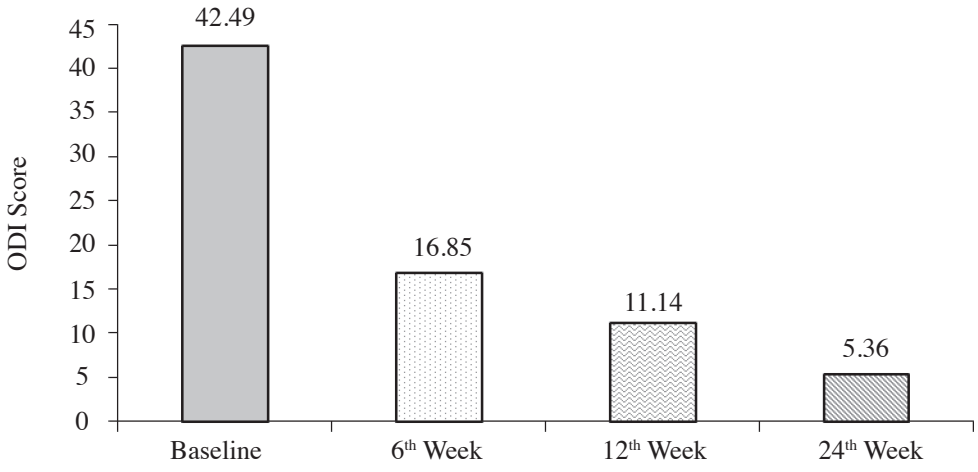

Figure 1: *The comparison of the average Oswestry Disability Index (ODI) score at pre-operation, the 6th week, the 12th week, and the 24th week.*

The finding of EuroQol VAS 0-100 showed an average pre-operative score of 50.36. The average score at the 6th week was 76.38; compared to the baseline score, there was a significant improvement (p-value < 0.05). The average score of the 12th week and the 24th week were 80.19 and 83.85 respectively. The statistically significant improvements are shown in Figure 2.

The EuroQol-5Dimensions (EQ-5D)

Using EuroQol-5D, pre-operative mobility problem was 91.96%. The mobility problems of the 6th week, the 12th week, and the 24th week post-operatively were 45.38%, 22.45% and 15.79% respectively. The self-care problem pre-operation was 58.04%. The self-care problem at the 6th week, the 12th week, and the 24th week were, 22.69%, 12.24% and 5.06% respectively. Activities of daily living pre-operation were 92.86%. At the 6th week, the 12th week, and the 24th week were 49.58%, 36.73%, and 15.79% respectively. Pain problems pre-operation were 98.21%. At the 6th week, the 12th week, and the 24th week pain was 63.03%, 31.63%, and 11.84% respectively. Anxiety and depression problems pre op were 80.8%. At the 6th week, the 12th week, and the 24th week, these had become 14.29%, 4.08%, and 2.63% respectively. The least reported health problem was self-care and the second to last was anxiety and depression. The highest proportion of problems was seen in pain and discomfort followed by usual activity. This is illustrated in Figure 3.

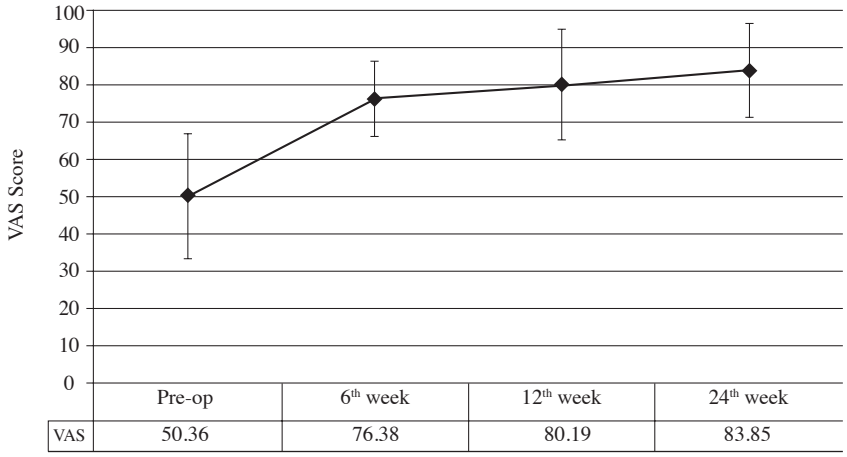

Figure 2: *The comparison of the average EuroQol VAS 0-100 at pre-operation, the 6th week, the 12th week, and the 24th week.*

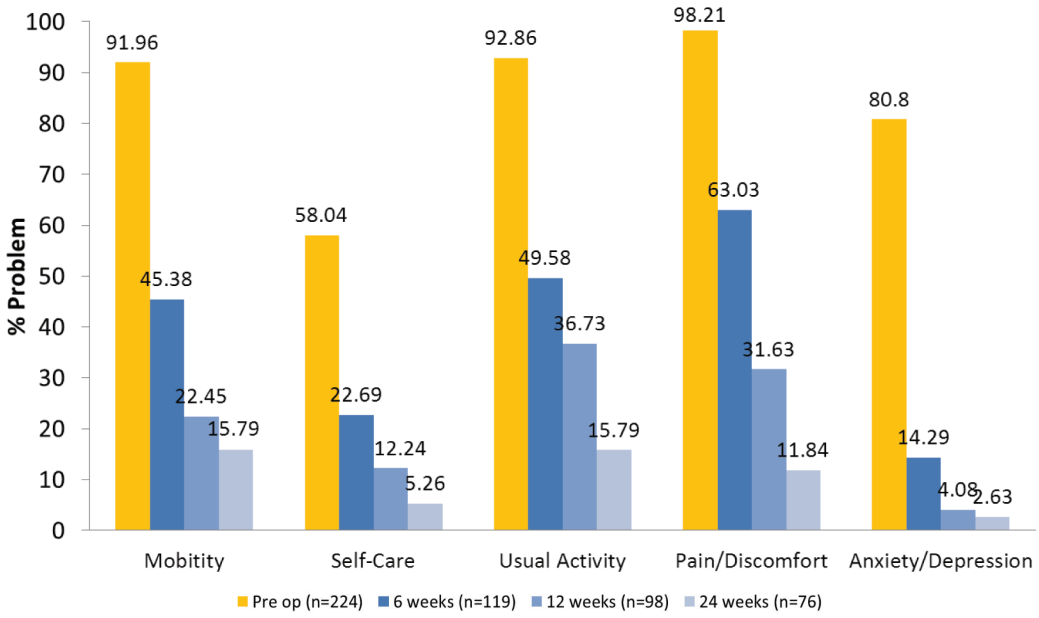

Figure 3: *The comparison of the proportion of problems EuroQol-5D at pre operation, the 6th week, the 12th week and the 24th week.*

Discussion

Results indicated that in this selective sampling of spinal surgery patients, (lumbar decompression surgery with fusion 35.48%, lumbar microdiscectomy surgery 27.95%, lumbar decompression surgery without fusion 17.2%, total disc replacement surgery 1.07% and mixed procedure 18.27%), patients' disability and quality of life all improved post operatively, as measured by ODI, EuroQol 5D and VAS.

The study found that the surgery could improve the functionality of patients who have back pain due to radiculopathy, lumbar spinal stenosis, and herniated nucleus pulposus. Measured by ODI and QOL methodology, the treatment outcomes showed significant improvement. However, the limitation of this study to date was the sample size. In the future, we will have a bigger sample size, which will enable us to do a comparative study, classifying patients by the types of surgery they underwent. In addition, the average of baseline ODI score before surgery was remarkably different from the post surgery score. The average of baseline ODI score was 42.49, and the average of 24th week post-operative score was 5.36. The data collection method at the baseline period was done by questionnaire while 80% of data collection method at the post-operative period was done by telephone interview. At any rate bias may be possible when the interview is conducted by telephone because some people are reluctant to answer phone interviews.

Based on Stephen Glassman's 2002 review of Food and Drug Administration (FDA) protocol, the excellent outcome of surgery is defined as that which can show a 15 points ODI Improvement scores over the baseline period.[9,10] Our findings showed that 79% of patients had ODI score at excellent outcome level, and 21% of them had ODI score improvement but not by as much as 15 points. The reasons that prevented this group of patients from seeing their ODI Improvement score reach 15 points were due to post-operative complication factors which included dural tear (0.3%), neurological deficit(0.3%), reoperation(1.2%), and surgical site infection rate (0.9%) at superficial levels.[11] Nevertheless, the incidence of reported complications were still relatively low when measured against with the reported international experience.[12-14]

Conclusion

The methodology of measuring the lumbar spine surgery outcome by the Oswestry Disability Index questionnaires and the EuroQol 5D questionnaires is internationally accepted; therefore, it is appropriate and practical to apply these measurements to assess our treatment outcomes. Finally, we would like to continue to apply this methodology to study spinal patients who were treated by other techniques, such as intervention treatment. We note that more consistent data collection methods should reduce or eliminate the bias seen in this set of patients.

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Original Article

Using the PROMISe Model for Health Behavior Changes of participants in Weight and Disease Reduction Programs

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Keywords:
Metabolic Disease, PROMISe Model, 3-Self Health Behavior Changes, Self-efficacy, Self-regulation, Self-care, Result-based management, Positive reinforcement, Optimism.

OBJECTIVE. 1. To study the benefits of using the PROMISe model to work towards sustainable *"3-Self"* Health behavior changes (self-efficacy, self-regulation and self-care) in a Weight and Disease Reduction program conducted at Lerdsin Hospital.

2. To study the relationship between the 6 factors of the PROMISe model (P = Positive reinforcement, R = Results based management, O = Optimism, M = Motivation, I = Individual or Client Centered and Se = Self-esteem) and the 3-Self Health Behaviors Changes in 3 areas, namely Dieting, Exercising, and Emotional control.

MATERIALS AND METHODS. This was a Cross-sectional study. The research was divided into two parts. Total of 302 people participated in the first part of this research and 173 people participated in the second part. The data used for descriptive statistical analysis came from program evaluations, health examination reports, and questionnaires completed by all participants in both phases.

RESULTS. The results showed the relationship between the 3-Self health behaviors, BMI value and satisfaction after finishing the program and 6 months later. The PROMISe model did indeed influence the sustainability of the 3-Health Behavior changes, and subsequent weight loss. The most influential factors of the PROMISe model were result-based management, positive reinforcement, and optimism.

CONCLUSION. Using the PROMISe model to design and manage activities leading to health behavior changes definitely influenced and increased the sustainability of the changes.

The National Health Security Office (NHSO) of Thailand expects public hospitals to co-operate in implementing health behavior modifications in their patients, in order to reduce or prevent health problems, with a particular focus on metabolic disease, especially obesity. Since 1991, there has been a dramatic increase in obesity in Thailand. Data from 1991, 1996 and 2004, indicates that obesity in Thai people has increased from 20% to 25% and 34% respectively. There were 13 million obese people and 12 million overweight people in 2004.[1] A survey in 2008-2009 showed the high correlation between increasing obesity and the risk factor for diabetes, high blood pressure, cardiovascular diseases and cancer in the Thai population.[1]

Programs to reduce health problems due to obesity have been set up in many hospitals with different approaches. The researcher, as a Head nurse who was in charge of the Health Promotion and Disease Prevention program of Lerd-Sin Hospital, considered that nurses play a crucial role in implementing health behavior changes at the practical level among the general public, since nurses are

responsible for educating patients about self care management.[2-6] She decided to put into effect a *"Weight and Disease reduction program"*, which would use the PROMISe model to encourage the *"3 self"* health behavior modifications (Self-efficacy, Self-regulation and Self-care) concentrated in 3 Topics, Diet, Exercise, and Emotion.

Starting in 2007, staff of the Hospital who were obese or staff who had a Body Mass Index (BMI) value greater than 25, participated in the Weight and Disease Reduction Program. The result of the program showed that 77.77 % of the participants were able to change their behaviors and reduce their weight after finishing the program. In 2009, the program expanded beyond the hospital to include the general public. In 2010, the participants of the program included overweight people or those with a BMI value greater than 23.[8] There were 302 overweight participants who completed the program activities of training and practicing food control. Five days of food prepared by the hospital dieticians was part of the program. Total daily energy intake was 1,000 kilocalories. Ninety-three percent of the participants lost weight after five days of food controlled-intake. Two to three months after the program, the percentage of participants who were still losing weight dropped to 76.8%, although the participants had a better understanding about 3-Self health behavior changes and 80.5% of the patients reported satisfaction with the program.

Findings from the previous study showed that the improvement in health behavior change score and a high reported satisfaction with the program did not explain the sustainability of the health behavior changes. There appeared to be other factors that were responsible for the sustainability of the change. Therefore, the researcher decided to conduct a study into the relationship between the factors in PROMISe model and the sustainability of the 3-Self health behavior changes, concentrating on the 3 areas which affected weight reduction of the participants in their normal daily lives. The findings from this study would improve future program activities in order to create more sustainable 3-Self health behavior changes.

The objectives of this research were threefold. To study the PROMISe model in 3-Self Health behavior change concentrating on 3 areas in Weight and Disease Reduction program. Also to identify the sustainability of the health behaviors change both after the program had ended and 6 months later using the reduction of Body Mass Index (BMI) value as an indicator. Lastly, to study the relationship between 6 factors in PROMISe model to 3-Self health behavior change in 3 areas.

Materials and Methods

Research Method

This was a cross-sectional study.

Population

The population in this study was the participants in *"Weight and Disease Reduction Program"* in 2010, members of the general public who were divided into two groups. The first group included every participant in the program, which were 302 people. The second group was made up of the participants who either attended the focus group meeting or returned the completed management survey to the Health Promotion and Disease Prevention Department. The focus group meeting and management survey was set up 6 months after participants had finished the program. The second group numbered 173 people, of which 70% had been able to lose weight and 30% had not. The weight loss ratio of the members of the second group corresponded to the ratio of all program participants, those who could and those who were unable to lose weight, at the end of the program.

Data Collection

Data used in this research was collected in 2 phases. The first phase included data collected before the program started and at the end of the Weight and Disease Reduction Program for the general public in 2010: data was collected from all 302 program participants. Tools used were the Metabolic Risk Screening Form from NHSO, and participants' self evaluation of their 3-self health behavior changes during the program, using the form developed by Ungsinun Intarakamheng.[7] Participants provided their daily calorie intake, exercise record, weight change and so on. They also had to report on the effectiveness of program activities (which had been designed to relate to the PROMISe model's 6 factors).

Developed by the researcher, tools used in the second phase were divided into 4: physical examination report, a questionnaire related to 3-Self health behavior changes in 3 areas (continuation of self evaluation as described in Phase 1) a questionnaire related to the current practice of behaviors which increase obesity risk, such as number of meals per meal, or eating between meals, (this was to see whether participants could apply the knowledge they had received during the program) and a questionnaire which asked questions designed to assess the influence of each of the 6 factors of the PROMISe model on health behavior changes. The researcher used validity and reliability assessments in order to test and improve the tools

in the second phase. Two management specialists and 5 participants from the previous program in 2008-2009 analyzed the content validity. The confidence interval of the Cronbach's alpha coefficient of the reliability test of 30 participants from the previous program in 2008-2009 was 0.89.

Data Analysis

The study used descriptive statistics such as frequency, percentage, mean, standard deviation for general data analysis. We used Chi-square and Pearson correlation coefficients to describe the relationship between 3-self health behavior changes, weight reduction, the 6 factors of PROMISe model and participants' satisfaction with the program. Finally we used t-test and paired t-test to compare the differences between the health behavior changes and changes in BMI.

Results

1. General Data Analysis showed that 83.4 % of the participants were females aged between 40 to 60 years old. Participants with an education level above or below bachelor degree were 49.3% and 50.7% respectively. About, 34.8% of the participants were housewives. Of those, 45.7% had health insurance and 44.7% had social security coverage, 13.9% of participants were civil servants or state enterprise employees. Most (67.9%) participants had immediate family members with metabolic disease. Forty-five percent of the participants were already sick or at risk of becoming being sick. Those with metabolic diseases (72.1%) which 38.1% of them suffered from high blood pressure, diabetes, gout, and brain infarction. Only 38.1% of participants who had metabolic disease took good care of themselves, or effectively controlled their disease. Participants who had a BMI value between 25 and 29.9 (61.3%) had high blood pressure and were at risk of developing metabolic disease.

2. The differences between the average 3-Self health behavior change, BMI value, and participants' satisfaction before and after finishing the program were shown in Table 1. The average of 3-Self health behavior change significantly increased in all areas (Mean > 2.5), while there was a significant average decrease in BMI values, from 29.28 to 28.39. The average of the satisfaction with the program was 3.13.

3. The sustainability of 3-Self health behavior changes (which affected both BMI value and satisfaction) at the conclusion of the program and 6 months after the program was shown in Table 2. If we compared from before the program started (Table 1), to program completion and then 6 months after, the average of 3-Self health behavior changes for 173 participants still increased in all areas. The average BMI value continued to decrease from 28.10 at program end to 27.97. The average program satisfaction increased from 3.13 to 3.28. However, the average of 3-Self health behavior changes in 3 areas, between those participants who could and those who could not lose weight at the end of the program and 6 months after the program showed a significant difference for Self-efficacy and Self-Care at 0.05 confidence level and was illustrated in Table 3.

4. The statistical relationship between the 6 factors of the PROMISe model and the sustainability of the 3-Self health behavior change in 3 areas, BMI value, and satisfaction with the program 6 months after the program, showed all 173 participants agreed that using PROMISe Model to conduct weight loss program activities affected 3-Self health behavior change in 3 areas. The average of all factors was 2.88. The average of 6 factors of the PROMISe Model, which were Positive reinforcement (P), Result based management (R), Optimism (O), Motivation (M), Individual or Client centered approach (I) and Self-esteem (Se), equaled to 2.91, 2.77, 2.92, 2.90, 2.87 and 2.93 respectively. The relationship among 6 factors of PROMISe Model to 3-Self health behavior change and program's satisfaction showed that Positive reinforcement was related to Self-regulation, Result based management was significantly related to Self-efficacy and Motivation significantly related to Self-regulation at 0.01 confidence level, as illustrated in Table 4.

The relationship between the 6 factors of PROMISe model, health behavior changes in 3 areas and weight reduction showed that Positive reinforcement, Result based management, and Optimism was significantly related to the sustainability of health behavior change in 3 areas and weight reduction at 0.05 confidence level as illustrated in Table 5 and Table 6.

5. The summary of the focus group meeting demonstrated the reasons that contributed to health behavior changes. The recommendations coming out of this session would lead to future program improvements. The purpose of the focus group meeting was to evaluate and review the effects of the health behavior changes during the program on daily life. The focus group discussions helped the participants to identify which factors led to sustainability in health behavior changes or what prevented changes. During the session, the participants shared their self control experiences in 3-Self health behavior change, answered the questionnaire about the activities management of the program using PROMISe model and then gave some suggestions of how the program could be improved in future.

5.1 The participants who either maintained the healthy behavioral changes or lost weight stated that their ability to apply their new knowledge in their daily lives,

Table 1: The differences in the averages of the 3-Self health behaviors, Body Mass Index (BMI) value and satisfaction (SAT) with the program, before and after the program. (n = 302)

Factors	Before		After		t	*p*-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.		
Self-efficacy	2.28	0.60	2.70	0.40	11.064	0.000*
Self-regulation	2.25	0.66	2.72	0.40	11.776	0.000*
Self-care	2.50	0.57	2.85	0.40	9.826	0.000*
BMI	29.28	4.17	28.39	4.26	6.963	0.000*
SAT	-	-	3.13	0.37	-	-

* *p*-value ≤ 0.01

Table 2: The differences in the averages of the 3-Self health behaviors, Body Mass Index (BMI) value and the participants' satisfaction (SAT) with the program at completion and 6 months later. (n=173)

Factors	Program Completion		6 months later		t	*p*-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.		
Self-efficacy	2.69	0.40	2.61	0.58	1.625	0.106
Self-regulation	2.69	0.41	2.71	0.60	0.519	0.604
Self-care	2.84	0.39	2.99	0.49	3.386	0.001
BMI	28.10	4.30	27.97	4.23	0.858	0.392
SAT	3.13	0.35	3.28	0.52	3.003	0.519

Table 3: The differences in averages of the 3-Self health behaviors to the ability of the participants to lose weight or not. (n=173)

3-Self behavior	Able to lose weight				Not able to lose weight			
	$\overline{X}$	S.D.	t	*p*-value	$\overline{X}$	S.D.	t	*p*-value
Self-efficacy	2.77	0.63	2.606	0.010	2.53	0.54	2.491	0.014
Self-regulation	2.83	0.66	1.902	0.059	2.65	0.56	1.814	0.072
Self-care	3.13	0.53	2.809	0.006	2.92	0.45	2.673	0.009

Table 4: The relationship between the average value of 6 factors of PROMISe model and 3-Self health behavior change and participants' satisfaction with the program 6 months after finishing program. (n=173)

PROMISe model's Factors	S- efficacy		S-regulation		S-care	
	r	*p*-value	r	*p*-value	r	*p*-value
Positive reinforcement (P)	0.142	0.063	0.081	0.017	0.121	0.114
Result based management (R)	0.196	0.010*	0.164	0.031	0.155	0.042
Optimism (O)	0.061	0.429	0.043	0.579	0.122	0.110
Motivation (M)	0.192	0.012	0.207	0.006*	0.162	0.034
Individual or Client center approach (I)	0.036	0.637	0.102	0.180	0.082	0.282
Self-esteem (Se)	0.199	0.119	0.121	0.113	0.111	0.145
Program's Satisfaction	0.401	0.000*	0.444	0.000	0.459	0.000*

* *p*-value ≤ 0.01

Table 5: The relationship between the average value of 6 factors of PROMISe model and the sustainability of health behavior change in 3 areas of the participants. (n=173)

PROMISe model's Factors	sustainable		discontinued		t	*p*-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.		
Positive reinforcement (P)	2.96	0.10	2.80	0.30	3.490	0.001*
Result based management (R)	2.83	0.26	2.64	0.43	2.916	0.005*
Optimism (O)	2.95	0.16	2.86	0.28	2.073	0.042
Motivation (M)	2.92	0.18	2.86	0.30	1.438	0.155
Individual or Client center approach (I)	2.87	0.32	2.86	0.30	0.199	0.843
Self-esteem (Se)	2.94	0.25	2.93	0.24	0.271	0.787

* *p*-value ≤ 0.01

Table 6: The relationship of the average value of 6 factors of PROMISe model and the participant's ability to lose weight. (n=173)

PROMISe model's Factors	Able to lose weight		Not able to lose weight		t	*p*-value
	$\overline{X}$	S.D.	$\overline{X}$	S.D.		
Positive reinforcement (P)	2.97	0.07	2.85	0.26	3.845	0.000*
Result based management (R)	2.85	0.26	2.68	0.38	3.293	0.001*
Optimism (O)	2.96	0.12	2.87	0.26	2.708	0.008*
Motivation (M)	2.93	0.17	2.87	0.26	1.643	0.103
Individual or Client center approach (I)	2.85	0.36	2.90	0.25	1.092	0.276
Self-esteem (Se)	2.94	0.25	2.93	0.24	0.283	0.778

* *p*-value ≤ 0.01

(for example, controlling their eating behaviors, regularly selecting food according to their individual daily energy needs or making changes during social events, improved emotional control, mind training, self control with regards to weight monitoring etc.) were what caused their health behavior changes to be sustainable.

5.2 The participants who neither maintained health behavior changes nor lost weight stated that their failure to change was due to inability to control their appetite, health problems (such as diabetes), poor time management, not having enough time for exercise, consuming food they didn't cook themselves, and attending social events.

5.3 The participants suggested that the hospital should set up a Weight and Disease Reduction Club, conduct regular meetings on Saturday or Sunday, every few months, and extend group activities training. The training material should include some games and simple formulas for calculating calories. The extended group activities should include low calorie food cooking classes, exercise classes, and the daily diet/energy intake review with an advisor. The hospital should continue selling healthy food, create a distribution channel to disseminate useful information and news to the general public, develop a mentoring program, and establish a call center or special clinic for people struggling with obesity.

Discussion

1. The results of this research showed that 3-Self health behaviors change in 3 areas had an inverse relationship to the BMI value. Using the PROMISe model to develop program activities was effective: 80.5% of participants were satisfied with the program. The aim of activities was obesity problem solving concentrated in diet, exercise, and emotional control. The principles behind activity organization came from behavioral and management sciences. The program started with Positive reinforcement (P). The specialist provided training related to the benefits of health behavior changes on reducing obesity. Result based management (R) was applied by using Appreciation-Influence-Control (AIC) management techniques (*"appreciate through listening, influence through dialogue, control through action"*) in a practical training which identified what self behaviors contributed towards obesity, set individual weight loss targets, and helped participants learn to figure out their own weight loss solutions.[9,10] Optimism (O) was used to help change participants' personal perceptions. The mentors, who were participants from the previous program, shared their observation of their personal experiences of failure in their daily lives and their perceptions of how they turned the failure into learning experiences to effect lasting health behavior changes. The researcher used Motivation (M) as the tool to cheer up the participants during the program. The research used positive language, conducted weight loss competitions similar to the U.S TV Program *"The Biggest Loser"*, and sent regular messages or program status updates to motivate the participants throughout the whole program. Individual or Client centered approach (I) was to focus on the participants' perception. Nutritionists and mentors provided advice, recommendations and suggestions to participants during group activities and food control practices. This approach was to ensure that all participants had the same understanding. The researcher used rewards and complements to build Self-esteem (Se). The certificate ceremony at the end of the program enhanced the Self-esteem of the participants. The success in either weight loss or 3-self health behavior changes after the program increased the self-confidence levels of the participants, especially those with diseases. This was all consistent with Tanphaichi's research: to solve obesity by changing the health behaviors requires an appropriate learning system about diet and exercise, especially developing awareness of weight control.[11]

2. The sustainability of the health behavior change at the end of the program and 6 months later, and the relationship between the 6 factors of PROMISe model to 3-Self health behavior change was described below.

2.1 The relationship between 3-self health behavior change in 3 areas and BMI value at the program's end was similar to the relationship 6 months later: the better the health behavior changes, the lower the BMI value. Although the average of Self-care showed a significant difference, the result was in the same direction. Satisfaction with the program 6 months later was higher than than just after the program finished. The average of 3-Self health behavior change in 3 areas between those participants who could and those who could not lose weight at the end of or 6 months after the program showed significant differences in Self-efficacy and Self-care behaviors. Participants who lost weight showed more ability to control themselves than did the participants who could not, along with the understanding of appropriate health behaviors, food control practice, success in losing weight, and the belief that appropriate health behaviors which helped them lose weight would encourage them to maintain weight control and continue to positively change their health behaviors. On the other hand, the lower average in Self-regulation of the participants who could not lose weight showed their lack of self control both during or 6 months after the program. Back in daily life, although these participants realized the benefits of appropriate health behaviors and believed in their ability to lose weight, they seemed unable to control themselves to perform continuous positive health behavior changes.

The summary of the focus group meeting indicated the reasons that the participants used as excuses for not losing weight, but gaining instead. This evidence corresponded well to statements made in the 2010 obesity report from Bureau of Policy and Strategy, Minister of Public Health[12] which mentioned that Thai people whilst able to lose weight during weight reduction treatments, were not able to maintain that loss and began to gain the weight back after stopping the program in a yo-yo effect. The stages of change theory of Prochaska & Diciemente (1983)[13] stated that people have to maintain regular healthy behavior over 6 months in order to habitualise that behavior and arrive at the *"maintenance"* stage. They need to learn how to control and manage their hunger and emotions using motivation strategies to keep on with healthy behaviors.

2.2 The results of this study confirmed that targeted behavior monitoring on weight loss, together with a motivational environment during and after the program promoted continuous changes in health behavior. All 6 factors of the PROMISe model were influential in effecting changing behaviors changes with regard to diet, exercise and emotional control and thus weight reduction. The benefits of being healthy and the results of health behavior changes such as lowering blood pressure or blood sugar levels acted as Positive reinforcement (P) for the participants. Result based management (R) enhanced the participants' ability to control their hunger and emotions as well as participating in regular exercise, in accordance with the weight reduction activities plan. Optimism (O) transformed the participants' perception of their failures into to learning lessons for their eventual better health behavior change.

Recommendations

1. The Head of the Nursing department should introduce to obese patients and encourage their participation in the Weight and Disease Reduction Program, using the PROMISE model to effect health behavior changes in 3 areas.

2. The health behavior change activities should increase interpersonal connections by using mentors, to improve communication and relationship building among the participants, to share failure and success stories, to encourage the participants during and after the program, and to help create the community for better health behavior change.

3. The health behavior change activities should focus on participants' self-practice. The patients should record and compare the results of each practice by themselves. The role of Nurses and Public health officers is only to arrange the motivational environment.

4. The management of nursing department should lead an integrated program of health promotion and disease prevention using the PROMISe model in the health care process of treating patients with metabolic diseases related to obesity.

Suggestions for future study

1. There should be a study to investigate what other factors contribute either to the success of the participants who are able to not only sustain health behavior changes and also lose weight and or failure of the participants who can neither sustain health behavior changes nor lose weight.

2. A follow up investigation into health behavior change sustainability should be conducted one to two years after participation in the program, together with continual improvements of motivational activities for the participants to practice on their own, after their return to their usual daily lives.

3. There should be a study on the effectiveness of the improvement program in health behavior change in participants who face particular challenges with the *"yo-yo effect"* using the PROMISe model, and focusing on Optimism.

4. There should be a study of knowledge management of the participants who are able to not only effect permanent changes in their health behaviors but who also achieved their targeted weight reduction.

Conclusion

Using the PROMISe model to design and manage activities leading to health behavior changes definitely influences and increases the sustainability of the changes. For the permanent sustainability of health behavior change, future program activities should concentrate on designing activities directly related to the factors which the study showed had the biggest impact, namely result based management, positive reinforcement, and optimism.

Program Participant

Before
Body weight 80 kgs.(2007)

After
Body weight 57 kgs.(2011)

Thank you Mrs. S for the permission to print your pictures.

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Case Report

Efficiency of Combining Trastuzumab with Chemotherapy in case of advanced gastric carcinoma with low level amplification HER2 (c-erb-B2 protein)

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Keywords:
HER2, Trastuzumabs, Paclitaxel, advanced gastric carcinoma, immunohistochemistry, IHC, Fluorescence in situ hybridization, FISH

Gastric cancer is the second most common cause of cancer death in the world, although its incidence is declining over the last decades. Several factors of modern medicine have improved the management of gastric cancer. There has often been a poor prognosis because once symptoms occur, gastric cancer is often advanced. However, the multidisciplinary approach of gastric cancer therapy and adjuvant therapy are a promising management treatment.[1]

Case Report

A 34-year-old known case of stomach cancer underwent distal esophageal resection. The pathological diagnosis was well differentiated intestinal type adenocarcinoma. The tumor involved the stomach and esophagus and there was serosal invasion of the entire thickness of muscular layer. The regional lymph nodes showed metastatic carcinoma. The immunohistochemical study of the tumor cell revealed no immunoreactivity with c-erb-B2 protein. The patient received complete full doses of radiation and capecitabine.

One year after the operation, the patient developed abdominal pain and the computed tomography (CT) of his abdomen showed enlargement to various sizes of para-aortic lymph nodes. The diagnosis of relapsed gastric cancer was noted. In order to to determine the new chemotherapy plan, the repeated Hematoxylin eosin (H&E) and immunohistochemical (IHC) staining of his archive tissue of gastric cancer showed negative for HER2/neu (c-erb-B2 protein). When using fluorescence in situ hybridization (FISH) technique to identify this marker, it showed a weakly positive score for HER2/neu (1.30). The patient was informed about the potential option of using target therapy, Trastuzumab, in combination with chemotherapy. After the discussion about the benefits, he was then treated by, Trastuzumab in combination with paclitaxel. Without any significant side effects, the patient responded well; and his abdominal pain resolved. The follow up CT comparison of abdominal lymph nodes showed they subsided dramatically after only 2 cycles of treatment (Table 1) and some nodes had disappeared.

Table 1: CT abdomen shows comparative size of positive lymph nodes, before and after treatment.

Position of Positive Lymph node	Before Treatment Size (mm) (September14, 2011)	After Treatment Size (mm) (December 6, 2011)
Celiac (Right)	40 x 31	25 x 13
Renal Hilum (Right)	25 x 27	12 x 13

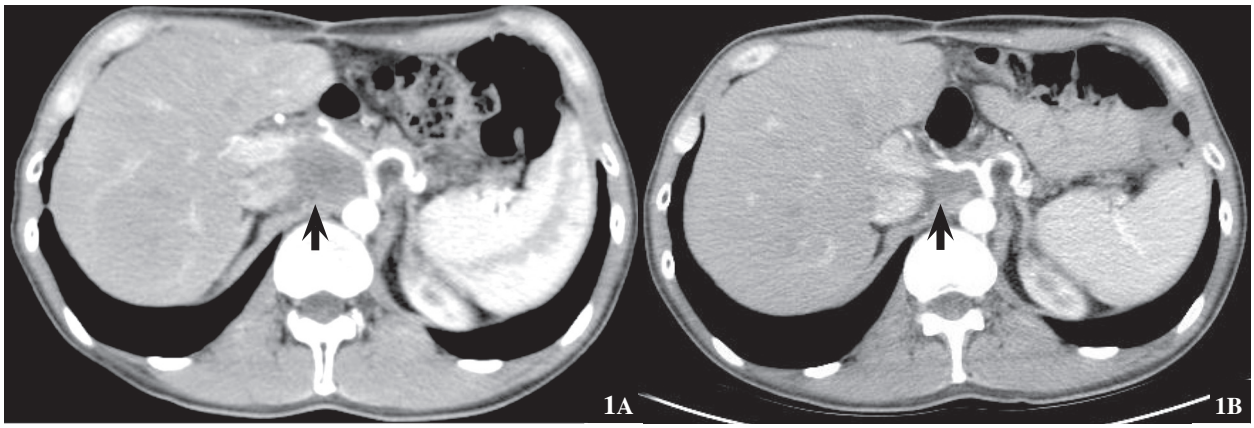

Figure 1A-B: *CT Upper abdomen at level celiac region, before treatment (1A) and after 2 courses of treatment (1B).*

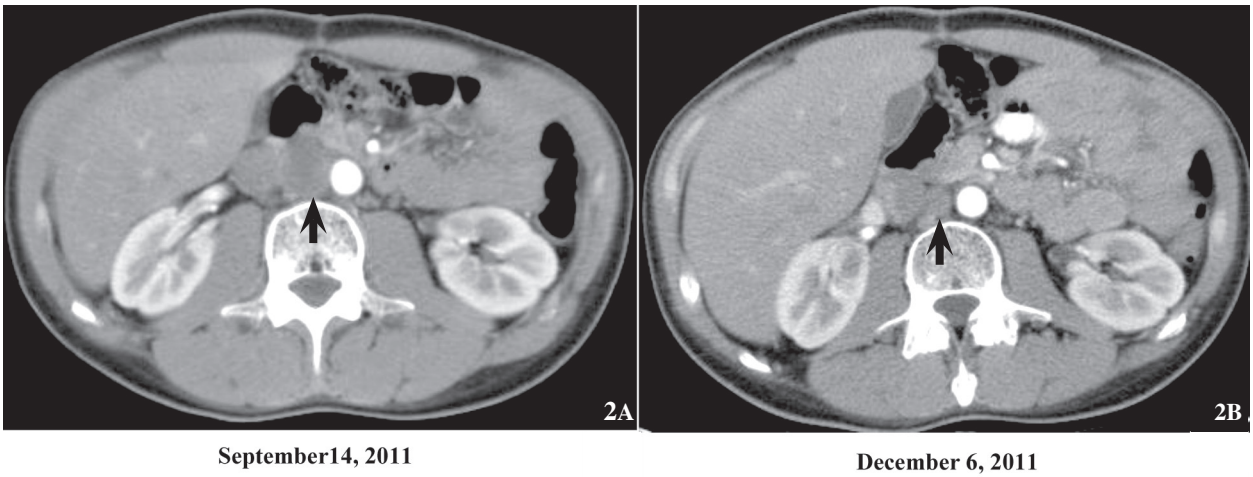

Figure 2A-B: *CT Upper abdomen at level renal hilum, before treatment (2A) and after 2 courses of treatment (2B).*

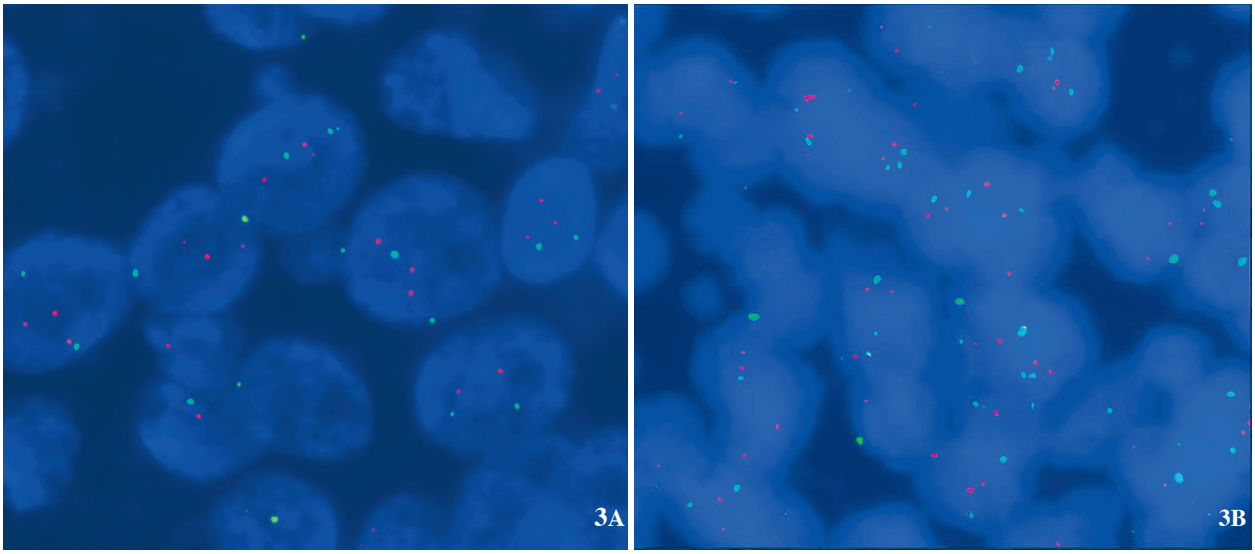

Figure 3A: *Gastric specimen FISH technique (2/11/2011); Red dots represent HER2 Score 104, Green dots represent cen -17 score 80, HER 2/CEN -17, Ratio = 1.30*

Figure 3B: *Lymph node specimen FISH technique (15/11/2011); Red dots represent HER-2 Score 73, Green dots represent cen -17 score 73, HER 2/CEN -17, Ratio = 1.00*

Discussion

In 1989, Slamon et al[2] found that there is an amplification of c-erb-B2 in the cellular membrane in cancer of the breast and ovary. C-erb-B2 protein (also called HER2 or Human Epidermal growth factor Receptor 2) is located at the long end of human chromosome 17. Overexpression of this receptor is associated with worse prognosis and higher recurrence of disease. Trastuzumab, a humanized version of a mouse monoclonal antibody that targets the receptor for therapy, was approved by the U.S. Food and Drug Administration in 1998 for treatment in combination with chemotherapy of women with HER2-overexpression metastatic breast cancer and became a popular treatment option for cancer of the breast in case of HER2/neu +ve.[3] Menard and Scholl et al also demonstrated other tumor types to also have overexpression of HER2/neu including ovary, salivary gland, lung, esophageal and gastric carcinomas.[4, 5] Tanner et al also showed HER2/neu amplification is also common in intestinal types of gastric carcinoma and might be a useful therapy target in this disease; they also commented that immunohistochemistry (IHC) staining is less accurate than FISH (fluorescence in situ hybridization) technique in defining HER2 positively as well as ascertaining which patients were most likely to respond to treatment with Trastuzumab.[6] In 2006 Menendez[7] demonstrated that Trastuzumab when combined with chemotherapy induced a receptor-enhanced chemosensitivity (REC) effect in the absence of HER2-overexpression. In 2010, Yung-Jue Bang et al[8] showed that Trastuzumab in combination with chemotherapy can be considered as a new standard option for patients with HER2-positive advanced gastric or gastro-esophageal junction cancer. In 2011, Negri et al[9] commented on one case which showed discordant HER2 results between the primary tumor and corresponding lymph node metastasis; HER2 gene was found unamplified in the primary tumor, but there was strong amplification in the lymph nodes, thus suggesting that *"HER2 positivity can be heterogeneous within the same tumor and might develop upon progression."* This suggested that HER2 status should be assumed in the metastasis, thereby making them possible candidates for Trastuzumab.

As aforementioned, target therapy and chemotherapy in cases of advanced HER2 overexpression carcinoma of stomach have now become the standard of care in this scenario. Many investigators showed an interest in the group of patients with low HER2 expression who might also be benefited by combined target therapy and chemotherapy; this may be also be applied in cases of absence of HER2 expression. We presented a case of advanced gastric carcinoma with para-aortic metastases post gastrectomy and FISH showed the tumor to have low level HER2. We successfully treated the patient with combination of anti-HER2 and chemotherapy and rapid tumor regression was observed. This supports Menendez's observation. We think therefore that FISH technique should be used to evaluate HER2 status at primary and secondary site(s) but we should consider to use trastuzumab and chemotherapy adjunctively, and effectively as a first treatment option in cases of both strong or low expression of HER2.

Conclusion

For gastric carcinoma, HER2 gene amplification by FISH technique may be different from the breast cancer. It can be heterogeneous within the same tumor, either at the primary site or at secondary lymph metastasis. HER2 may show up negative by IHC, but can be more accurately revealed using the FISH technique. Trastuzumab in combination with chemotherapy can be efficient, even if HER2 is only expressed at a low level In this patient, after the optimal course of treatment, the maintenance of systemic therapy may be warranted and this may improve the overall survival.

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Case Report

Emergent Primary Coronary Angioplasty Saved lives in Left Main Shock Syndrome:

A report of two cases with different manifestations and management

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Keywords:
Left main coronary artery occlusion, Cardiogenic shock, ST elevation acute myocardial infarction, primary (direct) angioplasty

Acute occlusion of the left main (LM) coronary artery leading to cardiogenic shock, so-called the Left Main Shock syndrome (LMSS), is an extremely dangerous life-threatening conditions.[1] Despite successful revascularization, the mortality rates of LMSS remain high, in the ranges of 33-94%.[2-4] In Thailand, the prevalence and outcome of this lethal condition is still underreported, thus we disscuss below two LMSS cases that survived emergent coronary angioplasty but who displayed different manifestation and thus altered our treatment decisions.

Case Report 1

A 78-year-old lady, had known history of hypertension, presented to out patient department in October 1995 with persistent chest discomfort since several hours. Electrocardiogram (ECG) showed sinus tachycardia with ST segment elevation (STE) in leads I, aVL,V1-5 which was suggestive of an acute ST segment elevation myocardial infarction (STEMI) involving antero-apical and lateral wall. She suddenly became hypotensive with blood pressure (BP) of 80/40 mmHg and was urgently transferred to catheterization room. It was evident that she had frank pulmonary edema, cardiogenic shock (CS) complicating acute myocardial infarction (AMI). Heparin 5,000 unit and aspirin were administered. After arriving, her BP continuously declined and became un-measurable. Intubation and intra-aortic balloon (IABP) counter-pulsation were performed along with temporary pacing for treatment of intermittent bradycardia. The echocardiogram showed severe hypokinesia of anterior-apical and lateral wall with estimated left ventricular (LV) ejection fraction (EF) of below 40%.

Subsequently she developed several episodes of ventricular fibrillation (VF) arrest, on and off, requiring intermittent cardio-version and cardiopulmonary resuscitation. The coronary angiogram performed during cardiac massage showed a subtotal stenosis of the mid left main (LM) body (Figure 1) resulting in diminished flow downstream (TIMI flow grade 2) to the left anterior descending (LAD) and circumflex (Cx) arteries. The dominant right coronary artery (RCA) was unobstructed but did not provide any significant supply to the left arteries (Figure 1B). Owing to her extremely unstable condition, we decided to perform direct balloon angioplasty of the LM.

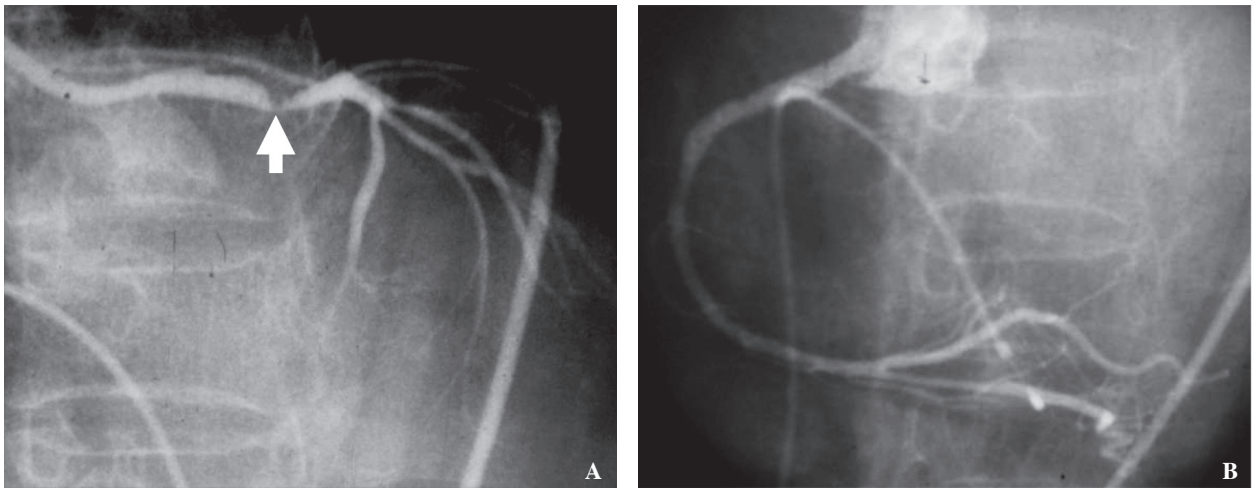

Figure 1: *Coronary angiogram showed intra-luminal thrombus in the body of the left main coronary artery (arrow) causing a subtotal luminal stenosis (A). An unobstructed right coronary is shown in B.*

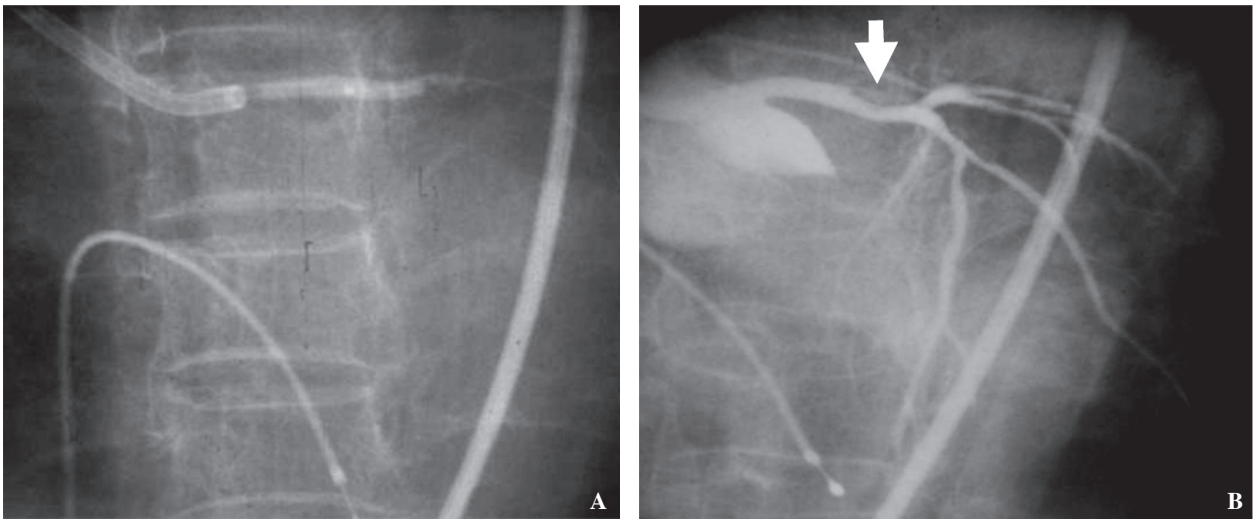

Figure 2: *Balloon dilatation (2.0/20) was performed during cardiopulmonary resuscitation (A) an resulted in re-established coronary flow with residual stenosis of less than 20% (open arrow in B).*

Balloon dilatation (2.0/20 balloon) was emergently performed during intermittent cardiac massage. After multiple short inflations and episodes of ventriculer fibrillation (VF) and bradycardia, the flow was finally re-established and she became more stable. Final angiogram (Figure 2B) showed a residual stenosis of less than 20% with no intimal dissection and the flow was normal. It should be noted that in 1995, stent were still not available so we accepted the result.

The patient slowly recovered from heart failure and pneumonia but survived. After spending weeks in coronary care unit (CCU), she was transferred to another hospital where her daughter worked as and was discharged home two months later. In 1998, she fractured a hip and was referred for pre-operative evaluation. The coronary angiogram showed a patent left main with no residual stenosis (Figure 4). There was no new lesion in the rest of her arteries. Owing to severe osteoporosis, the orthopedist decided to treat her conservatively and she is lost to follow up since then. This case represented the first primary coronary intervention for AMI in Bhumibol Adulyadej and in our country as well.

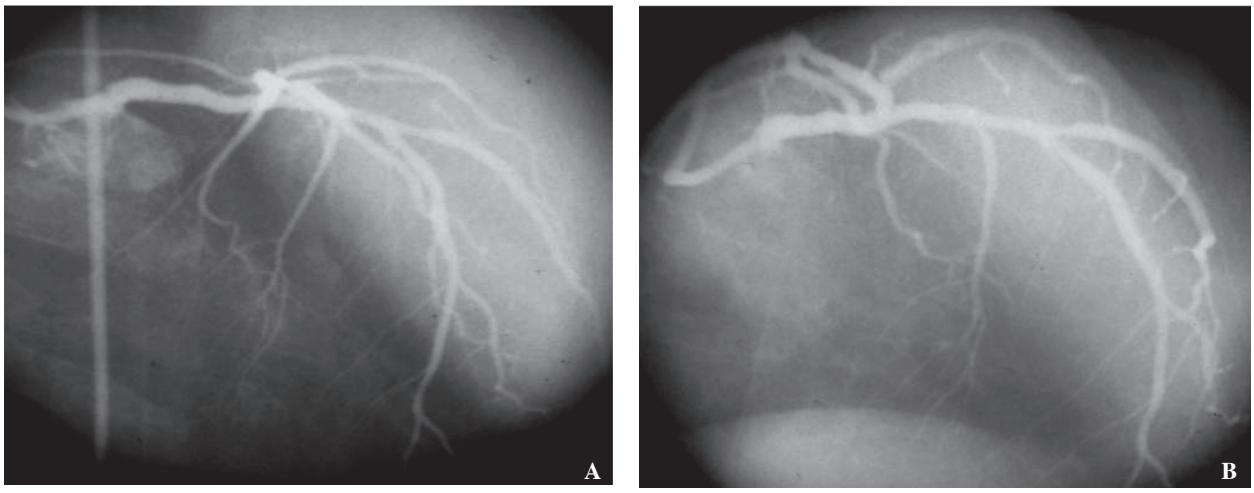

Figure 3: *Coronary angiogram performed 2.5 years later in 1998 and showed a smooth lumen of the left main trunk with no re-stenosis.*

Case Report: 2

A 60-year-old man, cigarette smoker, developed chest tightness while riding a motorcycle over the period of one hour. He presented to emergency room (ER) in July 2005 with BP of 71/43 mmHg, HR of 75 /min. The 1st ECG showed sinus rhythm with 3-5 mm ST depression (STD) in leads II, I, aVL and V2-V6 in conjunction with > 1mm STE in lead aVR and V1 (Figure 4). Echocardiogram delineated akinetic lateral wall, hypokinesia of anterior wall with the ejection fraction (EF) of less than 40%. Physical and laboratory findings were consisting with left heart failure and CS complicating the non-STEMI. Oral aspirin, clopidogrel, intravenous heparin and Tirofiban were given at ER before he was taken to the lab. On arrival, he still had 10/10 chest pain, BP was 87/54 mmHg, HR was 93/min in sinus rhythm. Right heart catheterization showed an elevated pulmonary capillary wedge pressure (PCWP) of 33 mmHg and intra-aortic balloon pump (IABP) was placed. Owing to low oxygen saturation, intubation with ventilatory support was performed.

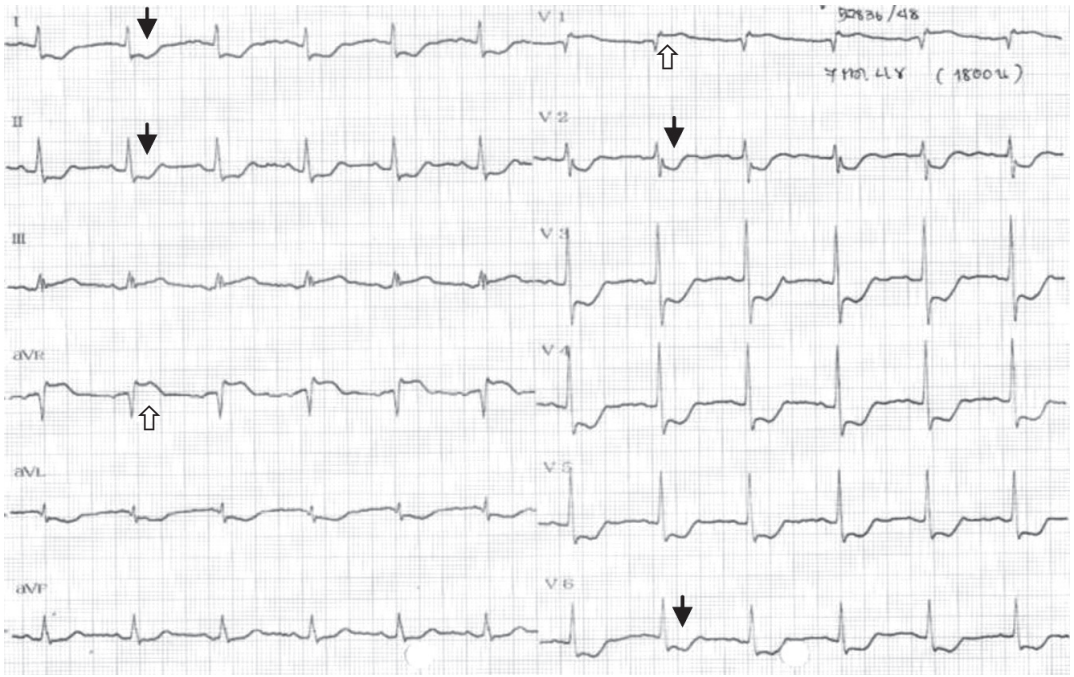

Figure 4: *The 1st ECG of case report 2 showed diffuse ST segment depression in leads I, aVL, II, V2-V6 (black arrow) and > 1mm ST elevation in leads aVR and V1 (white arrow). Early transition (tall R in V2) suggested posterior wall extension.*

Coronary angiogram revealed a totally occluded LM artery at distal bifurcation with no antegrade flow (TIMI flow grade 0). An unobstructed RCA provided major collateral supply to the left coronary arteries (Figure 5). Cardiothoracic surgery team were consulted but were not available until for the next 6 hours. Despite IABP support, he was still hypotensive and progressively deteriorating so we decided to open the occluded LM artery.

Attempts to pass the guide wire were successful only into the distal Cx but not into the LAD artery. After the 1st balloon inflation at mid-distal LM, he had PVCs and short run of ventricular tachycardia (VT), see Figure 6, but the flow to Cx artery was improved. Shortly, he became hypotensive again with systolic BP of 70 mmHg and junctional rhythm with wide QRS complex. To secure the flow in LM artery, a stent was then deployed at mid-distal LM trunk, which restored the flow and blood pressure. He was pain free and clinically stable. Post percutaneous transluminal coronary angioplasty (PTCA), ECG showed sinus rhythm with normalized ST-T changes (Figure 7).

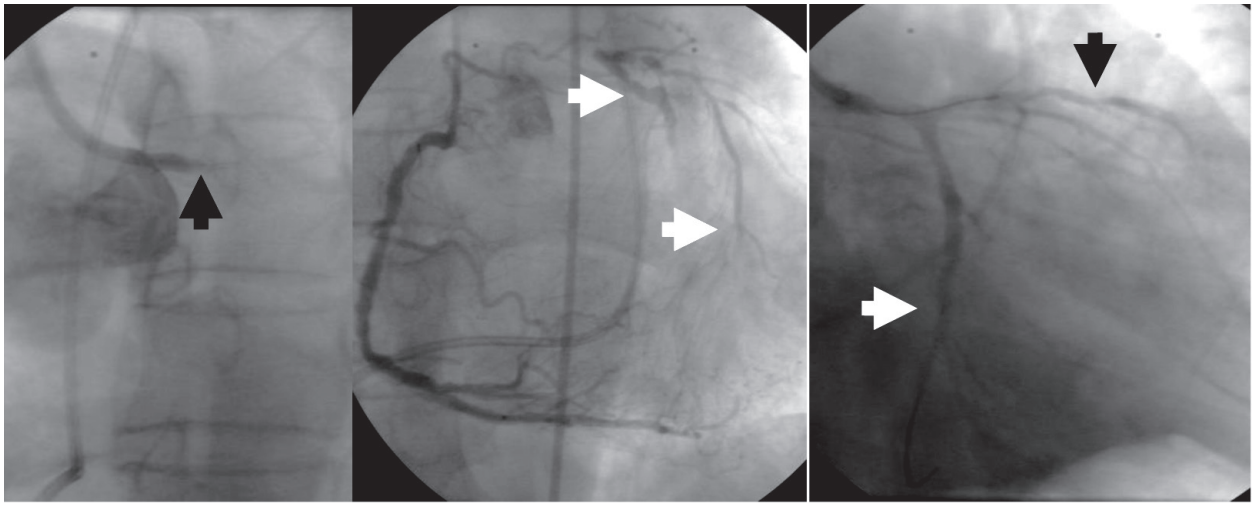

Figure 5: *Showed a totally occluded distal LM artery (black arrow, left) and unobstructed right coronary artery (middle) that provided a major collateral supply to distal part of the left coronary artery (white arrows). After balloon dilatation, the flow improved to Cx and proximal LAD/diagonal arteries (black arrow, right) but we could not pass the wire across an obstructed LAD artery.*

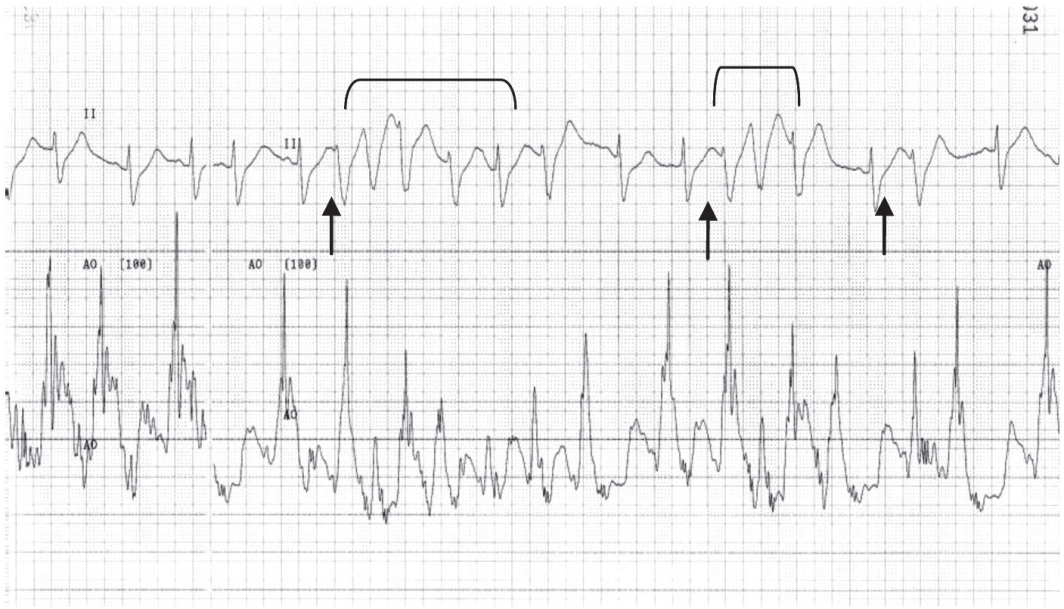

Figure 6: *Upper tracing showed frequent short coupling premapure vemtricular complexes (PVCs) (black arrow) induced non-sustained VT (in bracket) during and after balloon dilatations resulted in transient hypotension (arterial pressure 50-60 mmHg in lower tracing)*

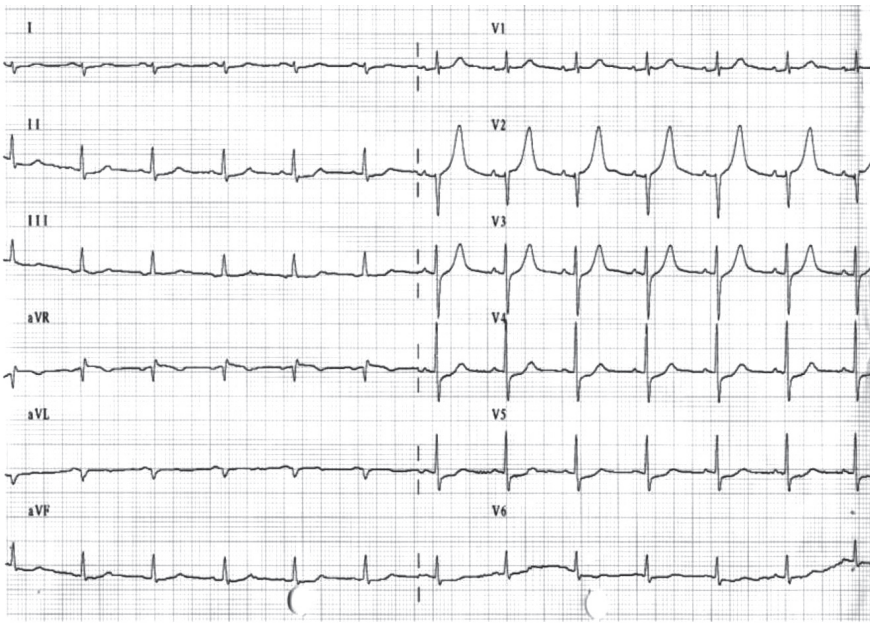

Figure 7: *ECG after PTCA showed improvement of ST depression in all leads and lesser degree of ST elevation in lead aVR. Tall R in V1, Q in V2 and tall T in V1-3 were also noted.*

For better long-term result, the CVT team was re-notified and he underwent successful coronary bypass grafting, with SVG to LAD and to Cx arteries, on the next day. After three days, IABP and endotracheal tube were removed. He was transferred to regular ward the following week and was discharged on the 22nd day. He is still alives at present.

Discussion

1. Prevalence of LMSS

Both of our cases displayed a serious AMI complication, CS (a state of systemic tissue hypo-perfusion due to pumping failure in the presence of adequate volume[5]), resulted from acute total (case report 2) and sub-total (case report 1) LM occlusion. Generally, CS is uncommon, occurred in 5-8% of AMI but the mortality is high, over 50%, in the setting of STE-MI.[6] The prevalence of AMI caused by severe (luminal narrowing >75%) stenosis of an unprotected (de novo) left main artery (AMI-LM) is even rarer, varied from 2.4-5%.[1,2] Since the LM artery mostly supplied blood to the LV, abrupt thrombotic occlusion shortly produced the states of pulmonary edema, CS and sudden death. Although the AMI-LM had been formerly reported,[7,8] the term LMSS was introduced in 1993[1] to describe a highly fatal CS that occurred in 44% of patients suffering from antero-lateral MI, like case report 1. In Quigley and colleagues' report, the mortality was very high, despite treatment, up to 94%.[1] Subsequent studies showed a reduction of LMSS mortality from 76% with combine revascularization[3] to 33% with direct coronary stenting.[4] Therefore, early detection and treatment is essential to preserve the life of patients with this condition.

2. Clinical & ECG recognition

Victims of LMSS victims tend to manifested in the same fashion, having chest pain, shortly afterwards developed pulmonary edema and later CS within few hours[2,9-11] and so did our cases. In one report, 16% of AMI-LM presented with unstable angina.[12] In a large retrospective study of 131 patients suffering from acute coronary syndrome (ACS) due to de novo LM stenosis,[13] half of them presented with STE-AMI or CS (49.6%) and the rest (51.3%) had unstable angina/non-STEMI, like case report 2. Most of the victims were men, 73-84%[2,13] and had the mean age of 67 (46-89) years.2 Our cases shared the same age range (78 and 60 years) and had occurrences of life threatening ventricular arrhythmias. Patient 1 had frequent VF before angiogram and patient 2 had non-sustained VT during coronary intervention. In 18 AMI-LM cases reported by Yip et al, 94% had pulmonary edema and 33% died from malignant ventricular arrhythmias.[4]

ECG recognition remained a primary step in diagnosing LMSS. Our first patient had diffuse ST segment elevation (STE) in anterior and lateral wall (leads I, aVL, V1-5, ECG was not available) associated with STD in inferior leads, which was found in majority of the LMSS cases.[1,9,10,13] A less common pattern, precordial STD as shown in case report 2, was found in 21.8% among 32 AMI-LM cases.[14] In addition, the aVR lead (representing the basal septal area) displayed STE

(> 0.05 mV) which was quite characteristic in AMI-LM cases.[14,15] The degree of STE in aVR, that was either equal or higher than those of V1 lead, reliably distinguished the AMI-LM from AMI secondary to proximal LAD artery occlusion, with the sensitivity, specificity and predictive value of 81, 80 and 81% respectively.[14] Recently, body surface mapping ECG had been shown superior to 12-lead ECG in detecting AMI-LM, with the sensitivity of 88% and specificity of 83%.[16]

3. Prognostic indicators

Mortality predictor are crucial in LMSS since they identified high fatality candidates. The presence of shock, as defining LMSS, by itself already carried a high mortality, from 33-76% despite treatment.[2, 3, 12, 13, 17-19] In the SALVage study of 131 AMI-LM cases, the CS/STEMI group had higher mortality than those of non-CS, NSTEMI group, 44% vs. 6%, $p < 0.001$.[13] By univariate analysis, the occurrence of VT/VF, as found in case report 1, was the most powerful mortality predictor and significantly reduced the short term survival.[3] By angiographic parameters, the pre-intervention antegrade flow (TIMI flow grade ≥ 2),[13, 19] the incomplete stenosis of LM,[2, 13, 19] the presence of collateral supply [2, 11, 17, 18] and the right dominant coronary system [2, 12, 17] had been found to be good prognostic indicators in LMSS cases. Those parameters attenuated the degree of myocardial ischemia and clearly explained the survival causes of our two cases. In case report 1, the LM artery was still patent with TIMI flow grade 2 and she had a large unobstructed RCA. In case report 2, the well developed collateral supply was obtained from a dominant RCA.

4. Choices of revascularization

Both percutaneous coronary intervention [2, 4, 12, 19, 20] and bypass surgery [3, 10, 11, 17, 18, 21] have been effectively performed but with the high mortality in comparison when those procedures are used electively. Currently, there is still no randomization study which compares between these two reperfusion strategies in AMI-LM[22] or CS from multi-vessel coronary artery disease.[23] Although CABG remains the gold standard for stable LM patients, the guideline recommendations for treating AMI-LM or CS remain unclear.[22] The recent ECC/EACTS myocardial revascularization guidelines in 2010 still recommended CABG surgery as a class IA for LM disease but spared the isolated ostium or shaft LM lesion as class IIa(B).[24] This also based on the fact that 80% of LM disease either involved distal bifurcation or there are other coronary lesions present which would benefit from CABG surgery.[24] The current ACCF/AHA/SCAI 2011 guideline for percutaneous coronary intervention (PCI) recommended the same thing, CABG for LM disease (class 1A), and class IIa(B) for PCI of LM to improve survival in unstable angina/NSTEMI patients who are not candidates for CABG and in patients with acute STEMI from LM who have distal flow < TIMI 3 under the condition that PCI can be performed more rapidly and safely than CABG.[25]

Practically, the choice of revascularization solely depends on the patient's condition (CS or stable), the site of the lesion (ostial, body or distal LM), concomitant lesions in other arteries, experience of operator, team and the availability of surgical colleagues. In the ideal situation, if the patient becomes stable after IABP placement, CABG would be a reasonable choice for long term benefit. However, typical LMSS cases are critically ill and died quickly either due to pump failure or ventricular arrhythmias, therefore PCI could be a life saving procedure as was demonstrated in our cases. The 1st patient was dying from her frequent VF and emergent PCI saved her life. The lesion at shaft of LM with no bifurcating disease or other lesions was also suitable for PCI. Without stent, this lesion healed up well after 2.5 years with no restenosis. The second case represented a bridging PCI, which was performed as the patient's condition deteriorated, in order to stabilize the patient and by the time before surgery. The bifurcating lesion was certainly not ideal for PCI and the result was still suboptimal. Fortunately he had major supply from RCA and became stable after stenting LM. He is still alive at the present time. Nowadays, a thrombus aspiration device would be suitable for removing a clot from an occluded left main artery before placing a stent. These devices have been effective in reducing infarct size, improved myocardial perfusion and 1-year clinical outcome.[26, 27]

Conclusions

We reported two LMSS cases who survived after life-saving PCI: one with direct balloon dilatation and another with bridging coronary intervention before bypass surgery. Both cases shared the common and rarer features of LMSS and the typical ECG findings. We reviewed clinical recognition and prognostic indicators along with choices for revascularization. We hoped that the details would be beneficial for emergency physicians, internist and cardiologist who may be presented with this lethal LMSS some day.

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Laughing headache

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Keywords:
Laugh-induced headache,Cough headache, Secondary headache, Arnold-Chiari malformation, Hind brain anomaly

Headache is one of the most common problems that bring patients to the neurology clinic. Several precipitants can trigger headaches such as laughing, coughing, straining, sneezing, stooping, or sexual activity.[1] Here we described an atypical presentation of headache onset after laughter in one patient.

Case report

A 50-year-old man visited the Comprehensive Headache Clinic at Bangkok Hospital Medical Center with the chief complaint of headaches occurring when he was laughing.

For the past thirty years, he had suffered from severe occipital pain provoked by laughing. He described the abrupt onset of sharp shooting pain at posterior part of upper cervical area, which radiated to bilateral occipital areas after vigorous laughing. The attacks lasted anywhere from a few seconds to a few minutes and were followed by a throbbing sensation at the same area which resolved spontaneously in less than an hour. The attacks only occured after laughing. Coughing, valsalva-like maneuver, straining when passing stool, change of position, or bending of neck could not precipitate headache or neck pain. He had no associated symptoms such as nausea, vomiting, photophobia, phonophobia, dizziness, fainting, blurring of vision, ptosis, lacrimation, conjunctival injection, or rhinorrhea during the attacks.

His past medical history was otherwise unremarkable. He denied history of head and neck injury, or chronic illness. Family history was unremarkable. No family members ever had headaches.

The neurological examination revealed normal cranial nerves function, normal motor power, no sensory loss, normal reflexes and normal gait. Neck examination showed mild restriction of range of motion both on flexion and extension, mild tenderness and spasm of upper posterior neck muscles, mild to moderate tenderness of occipital nerve area on both sides. Valsalva maneuver, coughing, and changing position (from lying to sit up and vice versa) was tried but could not provoke neck pain or headache.

Secondary cause of headache and neck pain was suspected. MRI of cervical spine including the posterior fossa was performed. MRI demonstrated Arnold-Chiari type I malformation (ACM), syringomyelia at C-3 level, and mild intervertebral disc bulging (Figure 1).

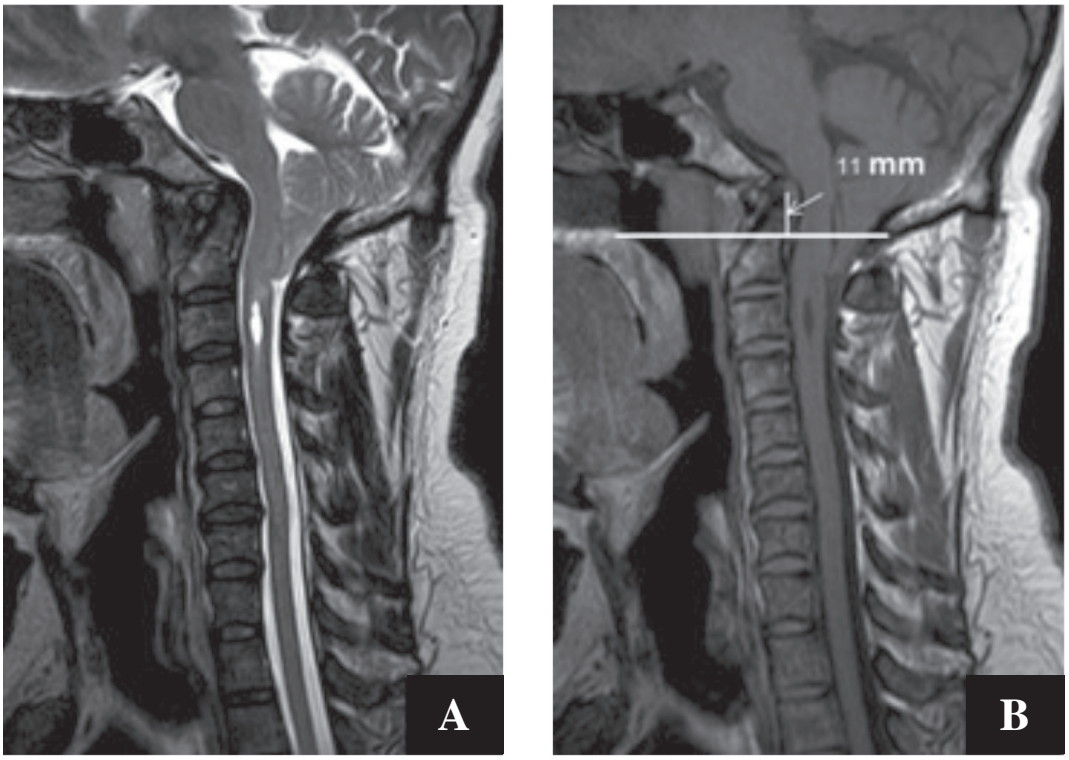

Figure 1A-B: *Sagittal T2W (A), and T1W (B) show downward displacement of the cerebellar tonsil at the posterior foramen magnum. There is high signal T2W of cavitary syrinx in cervical cord demonstrated in (A). The basilar invagination is also demonstrated as protruded dens with the tip at 11 mm. above the Chamberlain line (B).*

Neurosurgical consultation was done. Posterior fossa decompression was recommended but the patient refused the operation.

Discussion

Laughing induced headache is a rare presentation in headache clinics. To our knowledge, laughing induced headache was rarely reported in the literature.[2-4] In 1956, Sir Charles Sydmonds reported 27 patients with transient severe head pain provoked by coughing, sneezing, straining at stool, laughing or stooping.[5] International Classification of Headache Disorders (ICHD) II criteria do not include laughing headache.[6] However in the symptomatic cough headache as described in Pascual's series, head pain could also be precipitated by laughing.[7]

Cough headache can be induced by laughing, weight lifting, sudden postural change of head or body in addition to cough. Secondary cough headache has been described in hindbrain anomalies, including the Arnold-Chiari type I malformation.[7] Chiari I malformation is a congenital disorder characterized by abnormal extension of the cerebellar tonsils below the foramen magnum and is sometimes accompanied by rostral displacement or extension of the medulla. Patients with Chiari I malformation are often asymptomatic but may have associated hydrocephalus, syringomyelia, or syringobulbia.[8]

Chiari I malformation is the major cause of secondary cough headache. Occipital and suboccipital pain with frontotemporal radiation in variable duration (from seconds to bouts of several weeks) and varying in quality of pain (bursting, stabbing, dull, throbbing, or lancinating) were described. Secondary cough headache began earlier in life and each attack tended to last longer than benign cough headache.[7, 8]

Headaches are a common presentation in patients with Chiari I malformation, although different studies show the rates vary from 15% to 75%.[9] A retrospective, MRI-diagnosed Chiari I malformation case series showed fifty-nine percent of patients had or had had headaches. Fifty-two percent of Chiari I malformation patients had a headache at the time of diagnosis.[8-10] The spectrum of headaches in Chiari I malformation can present as short-lasting cough headache, exertional headache, low CSF pressure headache, long-lasting headache, or continuous headache.[10-13]

The mechanisms of headache in Chiari I malformation have not been addressed yet. It could be two different mechanisms for short-lasting and long-lasting headaches.

The mechanism of short-lasting sharp shooting headache is thought to be due to transient pressure dissociation between intracranial and intraspinal space while the patient was laughing. Differences in pressure between both compartments may cause downward displacement of the cerebellar tonsils into the foramen magnum, which causes stretching of intracranial pain sensitive structures, such as meninges, nerves, and blood vessels.[8, 10, 12, 14-15] The mechanism of long-lasting dull headache has been suggested by the theory of recurrent episodes of pain originating from the craniospinal pressure dissociation that may sensitize the pontomedullary junction and the upper cervical pain pathway to produce neurogenic headache.[12]

Treatment of laughing headache has been reported in only one literature. Divalproex sodium was reported as an effective prophylaxis agent in laughing induced headache.[4] Indomethacin was reported as a treatment in cough headache associated with Chiari I malformation.[16] Decreased cerebral blood flow and reduced intracranial pressure due to vasoconstrictor effect, and/or reduced cerebral edema have been explained as the potential mechanisms of indomethacin in cough headache.[17, 18]

For our patient, headaches started when he was a young man of 20 years, only after vigorous laughter. Other aggravating factors did not precipitate headache. The characteristic of very short sharp shooting pain followed by long lasting dull headache on occipital area with earlier onset of symptoms suggested symptomatic cause of headache. MRI of the cervical spine found Chiari type I malformation with syringomyelia. We considered the mechanisms of laughing headache in this case could see both valve-like blockage for short-lasting headaches and sensitization of pain pathway in brainstem and upper cervical for long-lasting headaches.

Conclusions

Laughing headache is a rare form of triggered headache. It is mostly associated with secondary causes such as Arnold-Chiari malformation. So, we recommend an MRI for all patients who present with laughing headaches, cough headaches, patients with posterior fossa signs, or in younger patients (under the age of fifty). Unfortunately, there are no standard treatments for this condition. Divalproate sodium, indomethacine, or surgical correction of Chiari malformation should be considered as a treatment for laughing headache patient.

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Case Study

The use of hydrosurgery debridement in penetrated wounds and deep wounds with narrow opening

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Keywords:
hydrosurgery, debridement, Versajet™, penetrated wound, deep wound

The clinical manifestation of a penetrated wound is a narrow opening with a deep sinus tract or tunnel into the body. It is difficult to perform sufficient wound debridement by traditional surgery. An encouraging advancement in surgical technology is the effective Versajet™ hydrosurgery system.[1] Its small cutting surface and fine control is especially useful for the *"difficult to access areas"*, such as on hands.[2, 3]

This innovative hydrosurgery system is a specialized powered surgical tool, which is designed to both debride biofilms and various cavities, whilst preserving adjacent viable tissue. This allows the surgeon using this instrument for soft tissue debridement considerable control and accuracy. Versajet™ utilizes a unique technology, whereby a high-velocity fluid-jet passes across the operating window and into the evacuation collector, creating a localized vacuum to hold and cut targeted tissue while aspirating debris from the site.[4] (Figure 1 & 2)

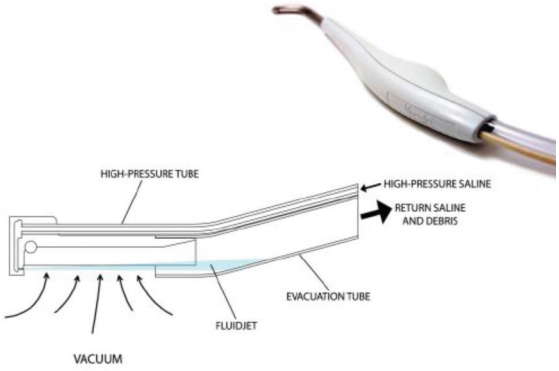


Figure 1: *The Hydrosurgery Handpiece*

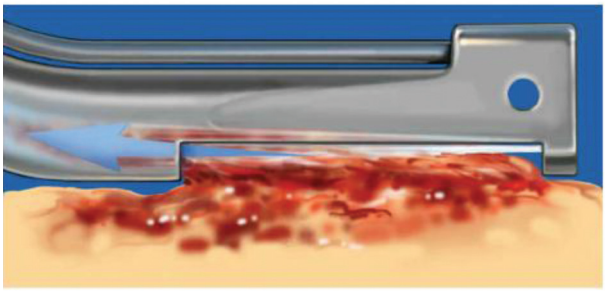


Figure 2: *Illustration of the system work*

To demonstrate the benefit of hydrosurgery system debridement in penetrated and difficult to debride wounds, the author reported the use of hydrosurgery system in 2 cases. In the 1st case, a male aged 28 was injured by a bomb and had burns, large lacerations and penetrated wounds. In the 2nd case, a non-Thai 73 year old with paraplegia had a pressure sore with a small opening but the wound bed was very deep and wide. The Versajet™ hydrosurgery system was used to debride necrotic tissue in both cases.

Case Report: 1

A 28-year-old man was injured by a bomb and had burns, large lacerations and penetrated wounds.

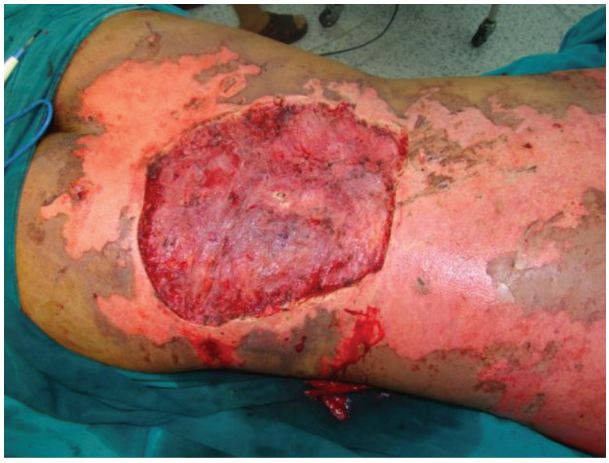


Figure 3: *Second degree burns and deep laceration along the whole posterior trunk laceration 20 x 20 cm.*

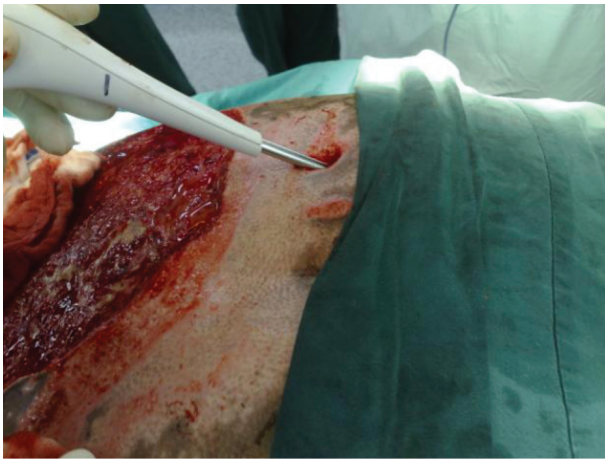
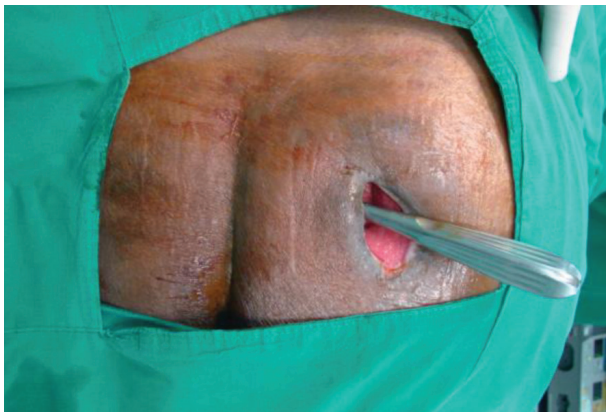


Figure 4: *Demonstrates hydrosurgery going deeper in the tunnel wound*

Case Report: 2

A 73-year-old paraplegic had a pressure sore with a small opening but deep and wide wound bed.



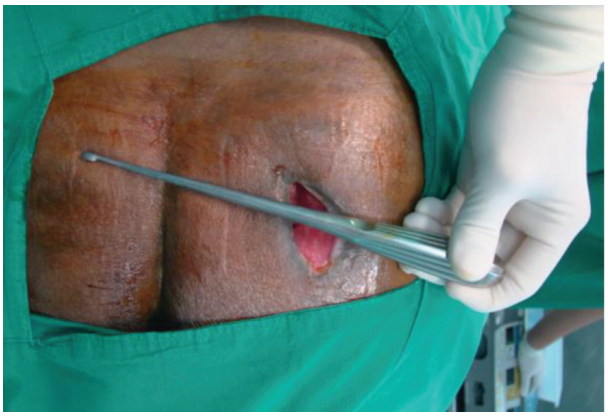


Figure 5: *Demonstrates hydrosurgery deeper in the tunnel wound*

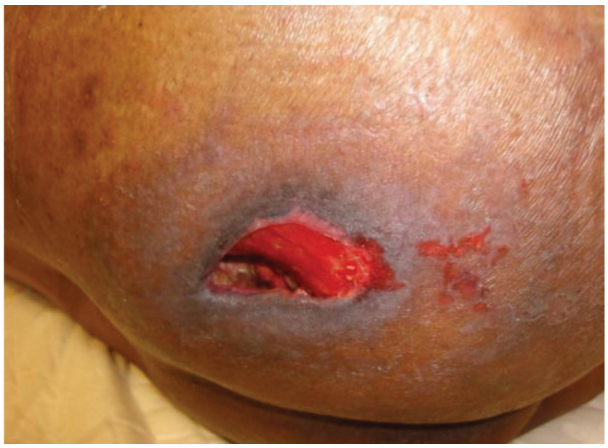


Figure 6: *Show Cavity wound*

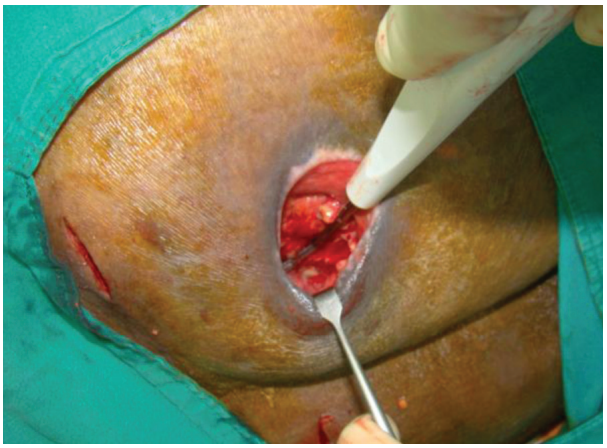


Figure 7: *Demonstrates hydrosurgery deeper in the tunnel wound*

Result

In the first case the penetrated wound was healed within 1 month. In the second case, the necrotic tissue was almost completely removed with the first application.[1] The patient was satisfied and flew back home.

Discussion

Efficient, safe and fast debridement was achieved in both patients using the hydrosurgery system. Necrotic infected tissue was easily removed. Use of this tool allowed us to target the damaged or necrotic tissue with more exactitude. There are also multiple power settings, which allowed for more restrained excision, thus delicate and viable tissues could be better preserved. We found Versajet™ more effective than traditional techniques for debriding such complex and non-uniform wounds as in our two listed cases.[2, 3]

Conclusion

Hydrosurgery system has demonstrated (in our experience) superior benefits over traditional surgical debridement to go deeper to the tunnel wounds and achieve sufficient debridement. We think this tool is likely to become a *"must"* in modern wound care.

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Kawasaki disease shock syndrome (KDSS)

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Keywords:
Kawasaki disease shock syndrome

Kawasaki disease (KD) is an acute febrile vasculitic syndrome of unknown etiology that occurs predominantly in infants and young children. The disease has also been called mucocutaneous lymph node syndrome or infantile periarteritis nodosa. Affected children present with high fever, rash, conjunctival injection, inflammation of the lips or oral cavity, cervical lymphadenitis, erythema and edema of the hands and feet. Cardiac sequelae, the most potentially life-threatening complications include coronary artery aneurysms or ectasia which can occur in up to 15-25% of untreated patients and may lead to myocardial infarction, sudden death, or ischemic heart disease.[1]

Case Report

A 2 years 8 month-old Thai boy who previously had been in a healthy state, presented with a high fever of 40 °C, red eyes, rash on both palms, both lower extremities and soles swollen. No evidence of oral mucosa change or cervical lymphadenopathy detected. He was admitted to another hospital on day 3 of fever for investigation and symptomatic treatment. Empirical antibiotics were administered and results for dengue, influenza and mycoplasma were pending. Since admission, patient remained highly febrile and did not respond to antibiotics. On day 5 of fever, he became hypotensive with a blood pressure of 70/40 mmHg, poor perfusion and was transferred to intensive care unit (ICU) to receive intravenous fluid resuscitation and inotropic drug support under clinical impression of septic shock. His transfer to Bangkok hospital was arranged by the pediatric intensivist team for further investigation and treatment.

Physical examination

Vital signs showed BP 80/50 mmHg, pulse 140/min, temperature 38.5 °C and respiratory rate 30/min. Patient appeared cranky but consolable. The body weight was 14 kilograms, body surface area 0.58 m^2. There were positive findings for bilateral nonexudative conjuntival injection, dry cracked lips, erythematous macular rash on both lower extremities and marked swollen erythema over the feet. Otherwise unremarkable.

Investigations

Complete blood count (CBC) revealed anemia and thrombocytopenia. Hb 9.2 g/dL, WBC 13,950 cell/mm^3 with 70% of neutrophil and 21% of lymphocyte, no band form, platelet 170,000 cell/mm^3. Elevation of inflammatory markers with erythrocyte sedimentation rate (ESR) 57 mm/hr and C-reactive protein (CRP) 158 mg/L. Liver function test revealed hypoalbuminemia 2.8 g/dL with normal SGOT and SGPT. Urinalysis showed evidence of pyuria

with WBC 10-20/HPF. Normal serum lactate level 1.5 mmol/L. Abnormal coagulogram showed PTT 33 second (sec), PT 14.1 sec, TT 14 sec and elevated FDP D-dimer 3,118 microgram/L FEU (Fibrinogen equipment unit). Blood and urine culture were negative, as well as tests for dengue virus, influenza virus and mycoplasma.

Electrocardiogram (Figure 1) revealed sinus tachycardia at 156/min. There was flattening of T wave in all precordial leads. No abnormal Q wave. Initial echocardiogram revealed normal coronary artery dimension with left main coronary artery (LMCA) 3 mm, left circumflex artery (LCX) 2 mm and right coronary artery (RCA) 2 mm. Left ventricular (LV) systolic function was mildly decreased with ejection fraction (EF) 50-55%. There was mild mitral regurgitation and small pericardial effusion. Small right and left pleural effusion was also noted.

Hospital course

A diagnosis of Kawasaki disease shock syndrome (KDSS) was given to this patient after the reviewing of all clinical findings and investigations. While the patient was being given dobutamine for inotropic support, intravenous immunoglobulin (IVIG) 2 grams/kilogram was commenced on day 6 of fever. Fresh frozen plasma was given due to abnormal coagulogram. Patient's hemodynamic status had improved and he finally came off dobutamine. High dose aspirin was introduced after patient started oral intake. His temperature returned to normal after finishing IVIG and remained normal for another 48 hours. On day 3 of admission, he was discharged home with a high dose aspirin. Twenty-four hours after discharge, he became febrile again with temperature of 38.7 °C. The repeated physical examination revealed bilateral non-exudative conjunctival injection. Others were unremarkable. Repeated CRP 72 mg/L, ESR 70 mm/hr. Repeated echocardiogram revealed ectasia of LMCA 3.7 mm (Figure 2) , LCX 2.2 mm and RCA 2.3 mm. LV systolic function was normal with EF 65%. There was a small pericardial effusion, which was unchanged from previous study.

A second dose of IVIG at 2 grams/kilogram was administered due to recrudescent fever > 36 hours after completion of the initial IVIG infusion. Patient had no reaction to the second dose of IVIG and was observed closely and his fever initially abated. However at 48 hours after second dose of IVIG, he had recrudescent fever at 38.7 °C. Repeated physical examinations neither revealed any evidence of occult infection nor evidence of systemic inflammatory disease. Screening tests for autoimmune disease were also negative. Due to failure of response of 2 doses of IVIG, Infliximab 70 mg was administered intravenously according to the drug protocol. There was no reaction from Infliximab and patient's temperature remained normal for the next 72 hours. Patient was again discharged home with a high dose aspirin. Repeated echocardiogram 6 months (Figure 3) after onset of disease revealed resolution of LMCA ectasia 2.5 mm with normal left ventricular systolic function.

Discussion

Kawasaki disease (KD) is now the leading cause of acquired heart disease in children both in developing and developed countries.[1] Diagnosis of KD can be straightforward if patient's clinical findings have been matched to clinical criteria or can be delayed if patient's clinical findings have not been presented accordingly (incomplete KD). The most common clinical features of KD are high, intermittent fever of at least 5 days and the presence of at least 4 of the 5 following clinical features namely;

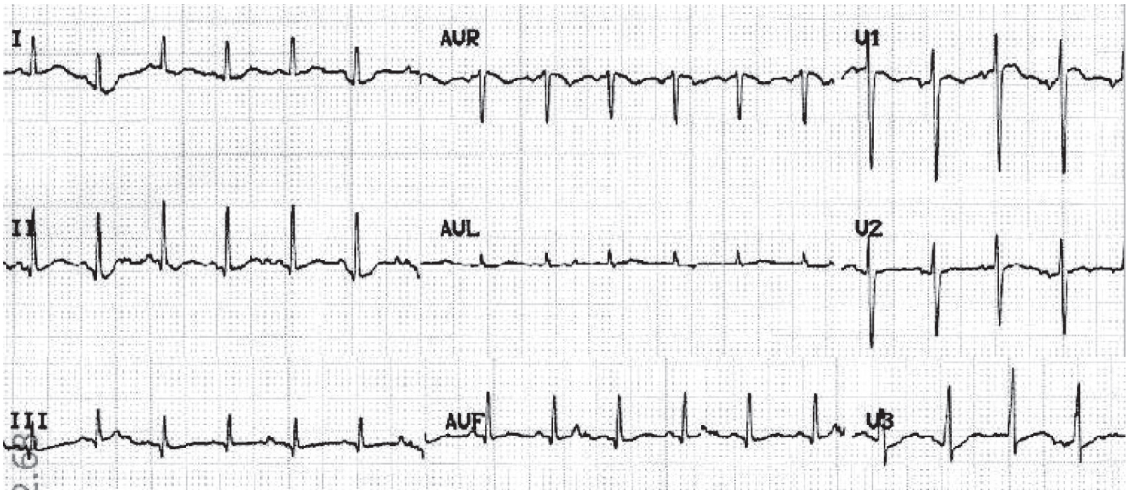

Figure 1: *Pediatric Electrocardiogram showed sinus tachycardia rate 156/min., abnormal ST-T changes and no abnormal Q wave.*

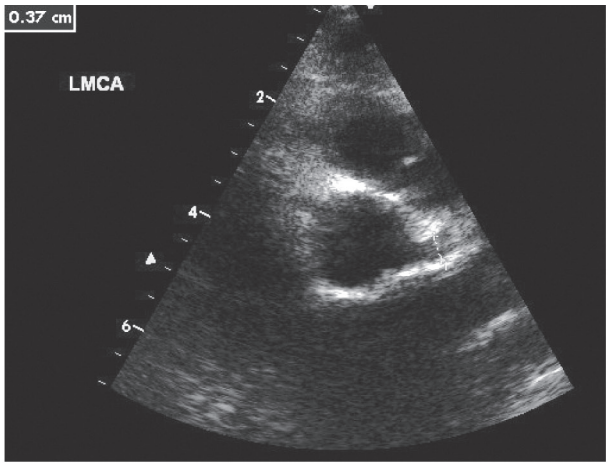

Figure 2: *Before treatment: ectasia of left main coronary artery, measured 3.7 mm in diameter*

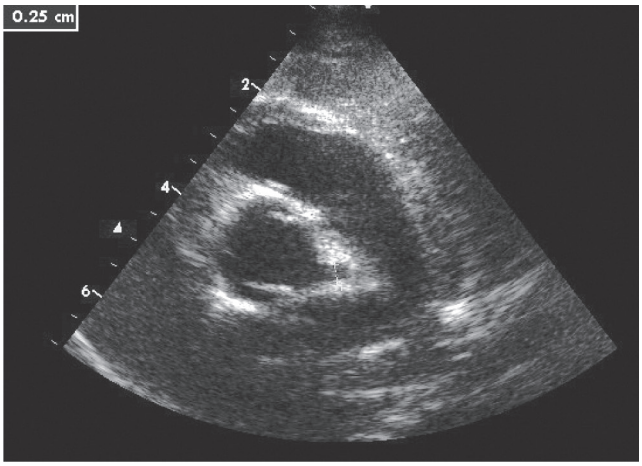

Figure 3: *Repeated echocardiogram 6 months after onset of disease revealed ectasia of left main coronary artery, measured 2.5 mm in diameter*

1. bilateral non-exudative conjunctival injection
2. mucocutaneous changes in lips and oral cavity
3. polymorphous exanthema
4. erythema and edema of the hands and feet
5. cervical lymphadenopathy (>1.5 cm diameter)

Our patient had fever for 6 days including eyes, lips, extremities changes and rash. Supporting laboratory findings included elevated ESR and CRP, anemia, hypoalbuminemia and sterile pyuria. One of the striking features presented in this patient is shock with evidence of vascular leakage. Hemodynamic instability has been reported during IVIG infusion due to allergic reaction, which did not present in our case because he had hypotension before infusion of IVIG. The occurrence of hemodynamic instability unrelated to IVIG adverse affects during the acute phase KD is uncommon unless the patient has significant cardiovascular involvement for KD, such as severe myocarditis or cardiac tamponade from rapidly developing pericardial effusion, which was also not the case for our patient.

Kanegaye et al[2] has described "Kawasaki disease shock syndrome" (KDSS) as an unrecognized complication of KD. Interestingly, 13/187 (7%) patients with diagnosis of KD developed hypotension (as defined by pediatric advanced life support guidelines) or had clinical signs of poor perfusion that required fluid resuscitation and inotropic support. Compared with KD patients without shock, patients with KDSS were more often female and had larger proportions of bands, higher CRP concentrations and lower hemoglobin concentrations and platelet counts. Evidence of consumptive coagulopathy was also common in the KDSS group. Additional findings in KDSS group are impaired left ventricular systolic function, mitral regurgitation, coronary abnormalities and IVIG resistance.

Our patient had significantly elevated CRP, thrombocytopenia, prolonged coagulogram, elevated D-dimer with supporting evidence of left ventricular systolic dysfunction, mitral regurgitation, coronary abnormalities. More important than the initial clinical and laboratory findings, our patient showed a resistance to IVIG treatment as has been reported in the Kanegaye study.

KDSS is a newly recognized complication of KD. The causes and factors contributing to the development of KDSS are still undiscovered. Some laboratory tests suggested greater underlying inflammation and more intense vasculitis in KDSS. To the best of the author's knowledge, there has to date been no report of KDSS in Thailand. This first case report emphasizes the presence of this new complication, and thus the need for pediatricians, pediatric cardiologists and pediatric intensivists to be aware of, and recognize the highly varied clinical manifestations of the most common acquired heart disease in children, namely Kawasaki disease.

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Case Report

Atherothrombotic Disease

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Keywords:
Atherothrombotic, Acute coronary syndrome

Clinical manifestations of atherothrombotic disease, cardiac arrhythmia and myocardial infarction account for the most common causes of sudden, unexpected death in all age groups.[1] A multicenter study of cardiac death in Thailand showed that of the NSTEMI 2653 cases, cardiac death were 202 cases (7.6%).[2]

Atherothrombosis is a complex, inflammatory process that begins at the site of endothelial cell injury and culminates in atherosclerotic lesion disruption with superimposed thrombus formation. Consequently it leads to acute coronary syndrome. State of the art treatments of acute coronary syndrome include balloon angioplasty with coronary artery stenting, which show evidence for reducing mortality and improving quality of remaining life in coronary artery disease patients.

However, despite advances, we still face limitations, especially in dealing with particularly large thrombus in a long segment of epicardial coronary artery thrombosis. We presented a case report, which detailed our management of this challenging situation at Bangkok Heart Hospital.

Case Report

A 69-year-old man, a Marathon runner came to Bangkok Heart Hospital early morning at 4 a.m. due to chest pain at mid-sternal chest. The chest pain radiated from mid-sternal to upper anterior chest wall with the patient reporting a feeling of more heaviness and tiredness a few hours later. At the emergency room, initial electrocardiography (ECG) showed left ventricular hypertrophy (LVH) with elevating ST-T in leads II, III, AVF. Troponin-T and CK-MB were also positive for myocardial damage.

He was sent to cardiac catheterization laboratory immediately after Acute Coronary Syndrome (ACS) pathway was activated. The coronary angiogram showed total occlusion at mid right coronary artery (RCA) (Figure A). Ad hoc Percutaneous Coronary Intervention (PCI) proceeded after the patient's relatives had been notified and given their permission.

After wiring through total occlusion RCA distally, the subsequent coronary angiogram showed a large thrombus from mid to distal RCA. The interventionist did not attempt further manipulation but preferred to administer low molecular weight heparin (Enoxaparin®) to the patient and kept the patient monitored in the coronary care unit (CCU).[3,4]

Selective Right Coronary Arteriograms

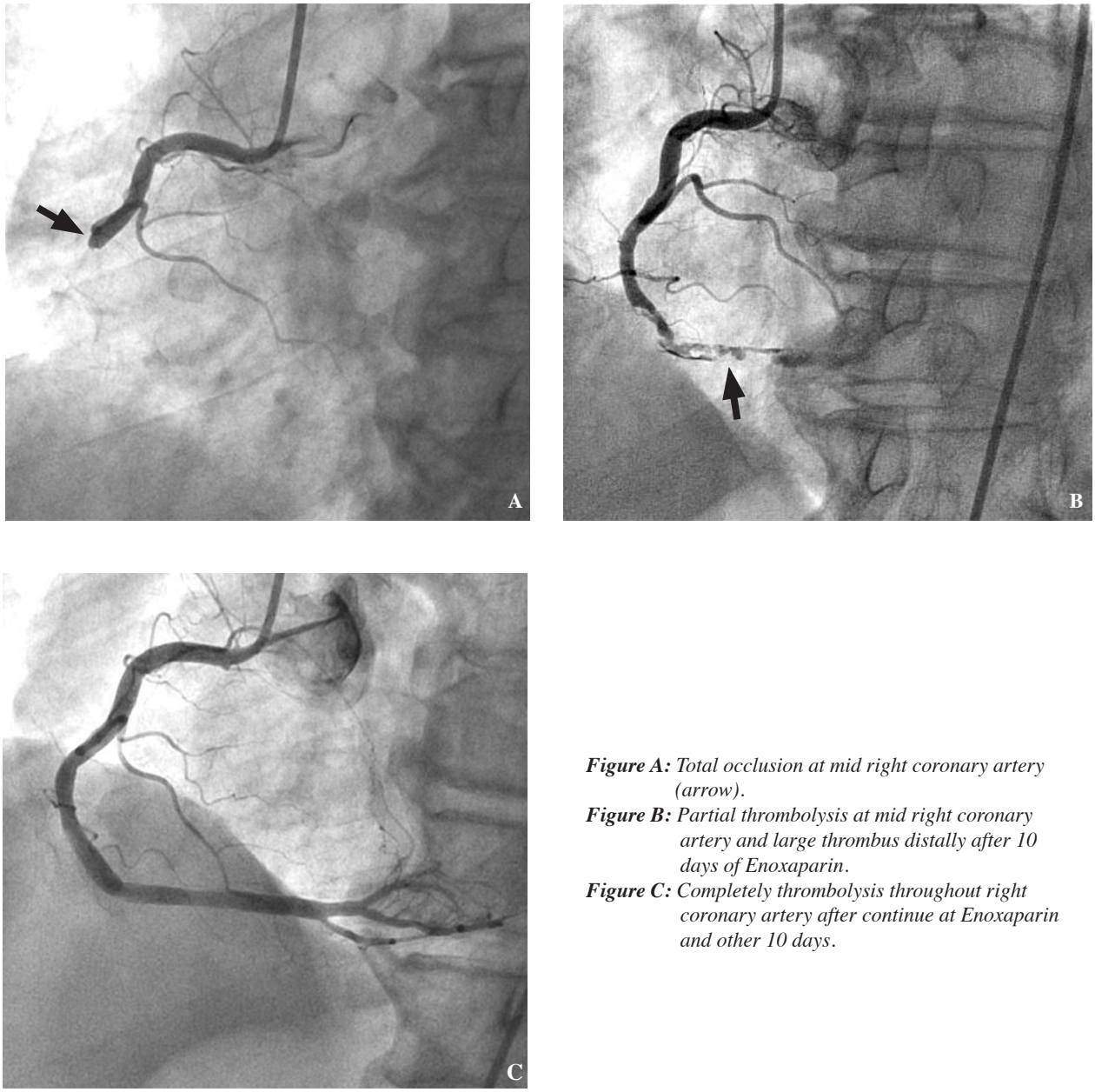

Figure A: *Total occlusion at mid right coronary artery (arrow).*
Figure B: *Partial thrombolysis at mid right coronary artery and large thrombus distally after 10 days of Enoxaparin.*
Figure C: *Completely thrombolysis throughout right coronary artery after continue at Enoxaparin and other 10 days.*

Fortunately, The patient was stable both mechanically and electrically. It was then decided to administer enoxaparin 60 mg twice daily for 10 days. The scheduled repeated coronary angiogram after 10 days of low molecular weight heparin showed partial thrombolysis at mid RCA and the large thrombus in distal RCA remained (Figure B).

With the patient in a stable condition, no longer complaining of chest pain or tiredness, we planned to continue administering the low molecular weight heparin was for a further 10 days. On the 20th day after first administration of enoxaparin, yet another coronary angiogram was done, which showed completely thrombolysis throughout RCA (Figure C).

Discussion

Currently, thrombus aspiration prior to balloon angioplasty and stenting are the standard techniques. Unfortunately, it is difficult to eliminate huge thrombus in the large artery. This kind of lesion represents a substantial risk with both short and long term complications, which can include peri-procedural myocardial infarction, distal embolization and long term re-occlusion. Many cardiac centers reported performing minimal manipulation to

restore blood flow in cases of large arterial thrombosis.[4-6] Low molecular weight heparin, one of the most preferred interventional pharmacotherapies, is frequently used to prevent and treat arterial and venous thrombosis. It works by inactivating thrombin in thrombotic process as well as stopping the formation of fibrin, a significant component of blood clots. In this case report, low molecular weight heparin was the medication of choice. Usually for general thrombolysis, enoxaparin for 7-10 days is adequate to give a good result, restoring blood flow. But for a large thrombus such as in this case study, a longer duration of enoxaparin administration to establish normal blood flow is recommended.[7]

Conclusion

Extensive coronary artery thrombosis is a difficult problem to handle. Where standard interventions were not obviously adequate to restore coronary perfusion, we report the successful use of a common drug, heparin to establish normal flow in a large long segment coronary artery thrombosis.

In summary, appropriate dosages of low molecular weight heparin and longer duration of administration (up to 3 weeks) is one of the alternatives to consider.

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Three Dimensions (3D) Reconstruction of Liver Mass

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Keywords:
3D reconstruction, Liver mass, hepatoma, cholangiocarcinoma

In cases of liver mass such as hepatoma or cholangiocarcinoma which are common in South-East Asian countries, many cases develop abdominal symptoms at the stage which is late for surgical intervention.[1, 2] Today, using the technology of computed tomography (CT) study, and 3D reconstruction of liver volume using 3D software enables us to study the boundary of tumor mass as well as visualize the major vessels. The total volume of the liver and the total volume of tumor mass can thus be calculated pre-operatively. This kind of investigation enables better surgical planning and may be a good predictor of the possibility of post operative liver failure.[3]

Case Report

A 74-year-old man presented with epigastric oppression, no nausea or vomiting. He had a physical check up, during which a liver lesion was found. The findings of the pertinent laboratory investigations, which included liver function tests were within normal limits. The immunology study revealed alpha-fetoprotein (AFP) 2.97 IU/mL. (0-7.22), CEA 2.70 ng/mL. (0-3.0). The CT of abdominal area showed an ill-defined hypodense mass with neovasculature stain at hepatic segment 3, measuring 4.5 x 3.5 x 2.9 cm. in greatest axial and coronal dimensions. The portal, right and middle hepatic veins as well as inferior vena cava (IVC) are patent. (Figure 1)

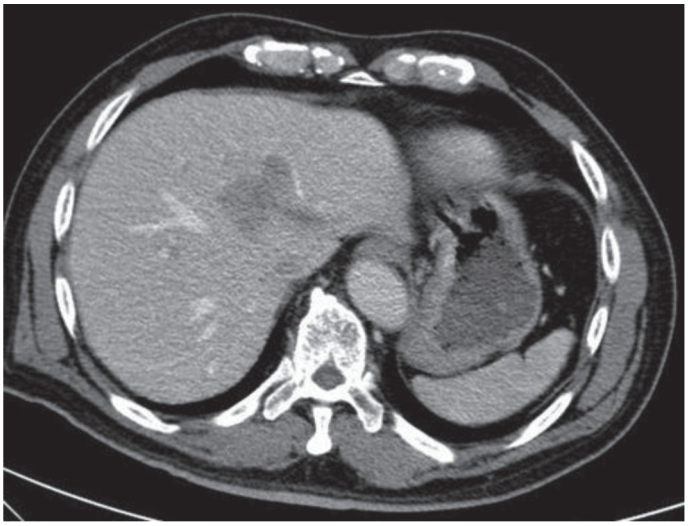

Figure 1: *The CT of abdomen showed an ill-defined hypodense mass with neovasculature stain at liver segment 3, measuring 4.5 x 3.5 x 2.9 cm.*

The 3D reconstruction of liver (Figure 2A-C) demonstrated the size of liver mass at left lobe in correlation to hepatic vein and portal vein; the total volume of liver was 1,411.50 cc., liver mass left lobe was 90 cc. Positron Emission Tomography and Computed Tomography (PET/CT) scan (Figure 3A-C) showed liver mass at segment 3 of liver with increasing metabolic activity SUV of 5.1. No ^{18}F-fluorodeoxy-glucose (^{18}FDG) avid lymph-node in the abdomen was seen. No ^{18}FDG avidity in each lung, mediastinum or hilum was observed.

The patient underwent an exploratory laparotomy and left hepatic lobectomy.

The hepatic tumor was located near the inferior vena cava, no evidence of lymph node enlargement was observed. He had an uneventful post operative course. The gross specimen of mass at left liver lobe (Figure 4A) showed a tumor which was margin free from IVC 0.1 cm. IVC was intact, right and middle hepatic and portal veins were intact. The microscopic examination (Figure 4B-C) revealed adenocarcinoma, well differentiated, compatible with infrahepatic cholangiocarcinoma, intraductal papillary neoplasm with associated invasive carcinocoma, mass forming type, nuclear grade II, tumor size 3.5 cm in greatest dimension. The follow up after surgery (see Figure 5 and 6A-C) showed complete removal of the tumor. The surgical margin was clear. IVC was intact. The 3D reconstruction of the liver showed all right lobe appearance normal, middle and right hepatic and portal veins are intact.

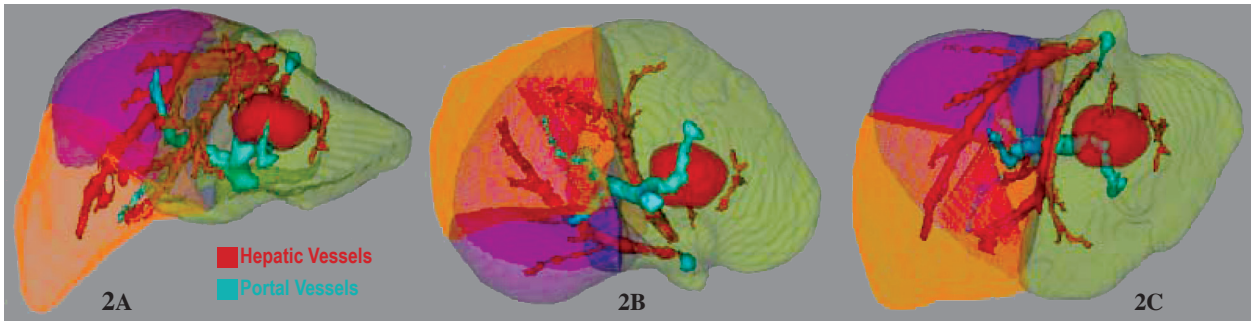

Figure 2A-C: *The 3D reconstruction of liver with demonstrated the size of liver mass at left lobe in correlation to hepatic vein (red) and portal vein (green)*

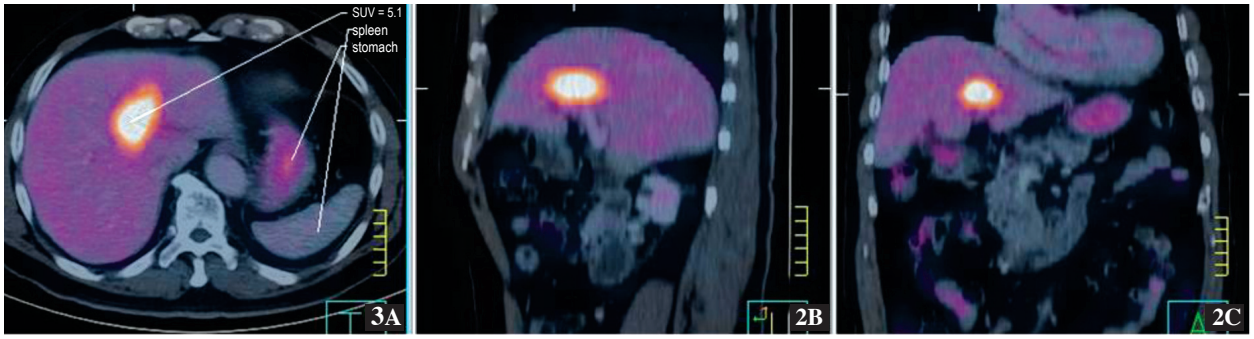

Figure 3A-C: *The PET/CT scan showed liver mass at segment 3 of liver with increasing metabolic activity SUV of 5.1.*

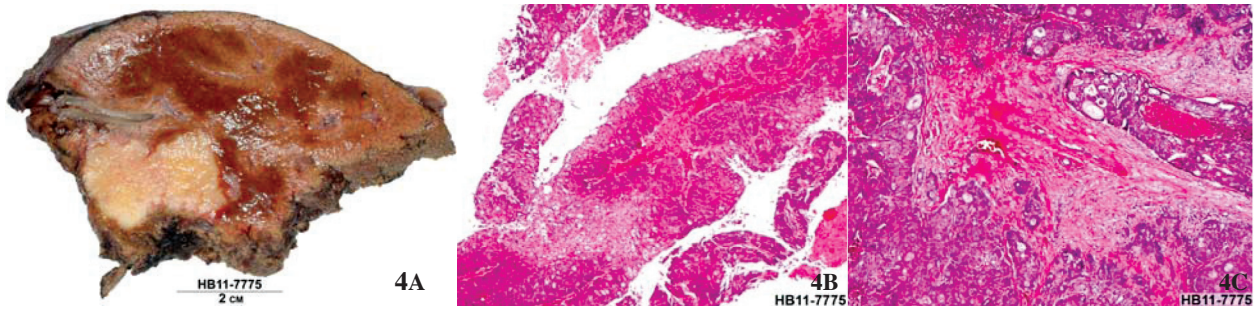

Figure 4A-C: *The specimen (4A) showed a liver mass. The microscopic examination (4D-C) revealed adenocarcinoma.*

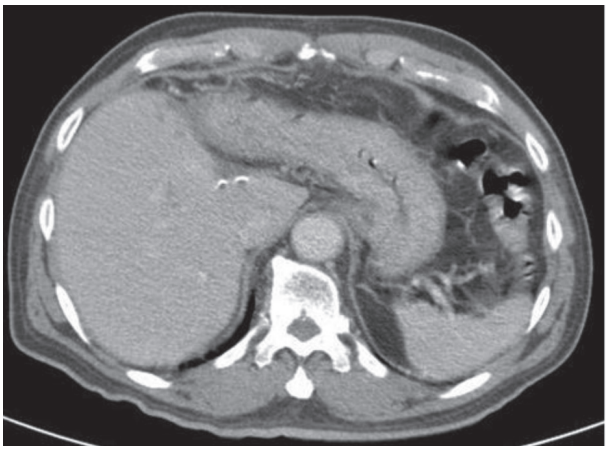

Figure 5: *The CT of abdomen with contrast enhancement revealed status post left hepatectomy, No evidence of tumor recurrence at surgical margin is observed. IVC is intact.*

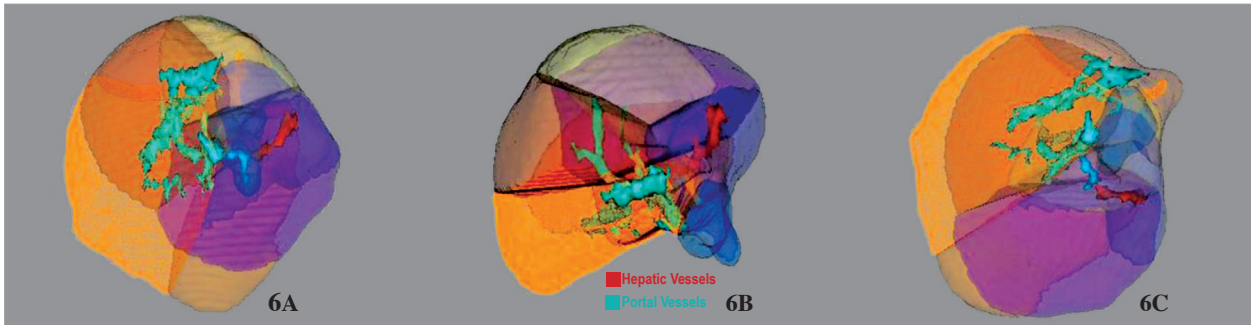

Figure 6A-C: *The 3D reconstruction of liver post left hepatectomy, patency of hepatic vein (red) and portal vein (green) are seen.*

Discussion

The 3D reconstruction of the liver has to evaluate the total volume of liver, volume of tumor mass and vascular distribution including hepatic and portal veins. These considerations are very helpful for surgeons preoperative planning. In this case the tumor invaded only the left hepatic vein. Other veins were well preserved. This indicated a good prognosis. Hence, only a left hepatectomy which sacrificed the left hepatic vein was performed.

Conclusion

The 3D reconstruction of liver mass for liver analysis to evaluate the liver segmentation, vessels, territories and lesion provides very helpful information to enable better surgical planning and is a predictor of prognosis.

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Review Article

Recommendations for an efficient and safe use of fibrinolytic agents

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Keywords:
ST elevation, myocardial infarction, Thrombolysis, Fibrinolytic agents

ST-segment myocardial infarction (STEMI) is caused by thrombotic occlusion of a major coronary artery. Rapid restoration of coronary blood flow is essential in preventing myocardial necrosis. Early reperfusion of the infarct-related artery limits infarct size and improves outcome. Achieving the shortest possible delay between symptom onset and reperfusion is therefore one of the most critical factors in the management of STEMI.

Reperfusion can be achieved mechanically, using primary percutaneous coronary intervention (PCI), or pharmacologically, using fibrinolytic agents.[1-4] Only a minority of hospitals worldwide provide a 24/7 hours primary PCI service by an experienced team. Fibrinolysis, in contrast, is universally available and does not require advanced logistics. Lytic therapy therefore is a valuable alternative, and is still used for the treatment of acute myocardial infarction in the majority of centers worldwide.

Fibrinolytic therapy & fibrinolytic agents

Clot lysis can be attained by activating the endogenous fibrinolytic system, using plasminogen-activating agents. These agents convert plasminogen to plasmin, which then degrades fibrin, a major constituent of clots (Figure 1).

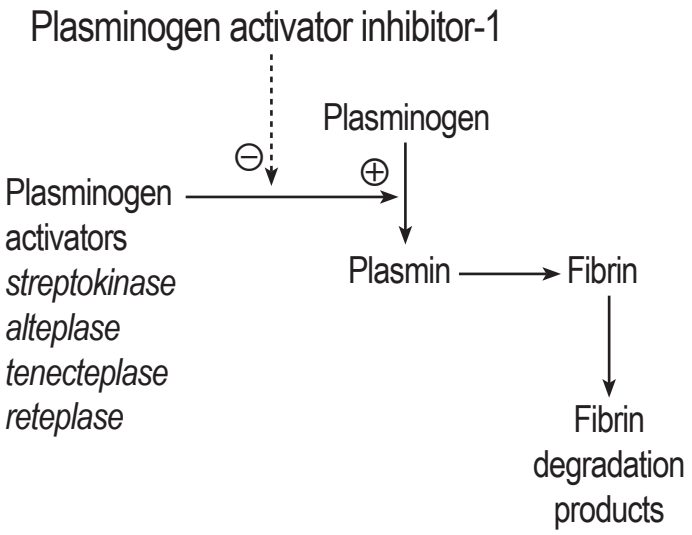

Figure 1: *Mechanisms of clot lysis.*

Fibrinolytic agents are generally divided in fibrin-specific agents and non-fibrin-specific agents. Fibrin-specific drugs, such as alteplase, tenecteplase or reteplase, are more efficient in dissolving thrombi and do not deplete systemic coagulation factors, in contrast with non-fibrin-specific agents, such as streptokinase (Table 1).

First-generation fibrinolytic regimens, including streptokinase and alteplase required continuous intravenous infusion. Contemporary fibrinolytic strategies, however, consist of intravenous bolus administration of second and third generation fibrinolytics. Using bolus fibrinolytic agents decreases the risk of dosing errors and facilitates pre-hospital initiation of reperfusion therapy.[5]

Fibrinolysis unfortunately has several limitations. Fibrinolytics need 30 to 45 minutes on average to recanalize the infarct-related artery, and complete patency is only achieved in 50 to 60 % of patients. Bleeding complications, especially intracranial hemorrhages, also continue to be a concern: up to 1% of patients experience an intracranial hemorrhage. Risk factors for developing intracranial hemorrhage include advancing age, female gender and a history of hypertension.[6]

On the other hand, reocclusion due to pro-thrombotic side effects is also common; occurring in 5 to 15% of previously recanalized arteries.[7] This results in further worsening of left ventricular function and a steep increase of in-hospital mortality. Reocclusion is mediated by the interaction of vasospasm, aggregating platelets, clot-bound thrombin, the thrombogenicity of partially lysed clot and ruptured atheroma, or the persistence of a flow-limiting stenosis in the absence of a percutaneous intervention. Fibrin-specific drugs might also promote reocclusion due to paradoxical pro-coagulant and platelet-activating side effects. As a consequence, one or more additional antithrombotic agents are required when a fibrin-specific agent is given. In addition, this alsoimplies that avoiding reocclusion whilst simultaneously minimizing the risk of bleeding complications, might be difficult.

Streptokinase

Streptokinase is a non-fibrin-specific fibrinolytic agent that indirectly activates plasminogen. Because of its lack of fibrin specificity, streptokinase depletes systemic coagulation factors, inducing a lytic state. Although newer fibrin-specific fibrinolytics have theoretical and clinical advantages, streptokinase remains widely used because of its low cost. Unfortunately, preexisting anti-streptokinase antibodies may impede reperfusion after treatment with streptokinase.[8] In addition; administration of streptokinase also invariably induces anti-streptokinase antibodies, precluding safe re-administration.

The first large trial to show a significant reduction in mortality with a fibrinolytic agent was the landmark GISSI-1 trial.[9] In this study, 11,806 patients with an acute myocardial infarction presenting within 12 hours

Table 1: Antithrombotic co-therapies with fibrin-specific fibrinolytics.

Therapy	Drug	Dosage
Antiplatelet co-therapy	Aspirin	150-325 mg orally or 250 mg IV if ingestion is not possible.
	Clopidogrel	Loading dose 300 mg (75 mg if age > 75 years)
Anticoagulant co-therapy	Unfractionated heparin	IV bolus of 60 U/kg (max 4,000 U) Infusion of 12 U/kg (max 1,000/hr) for 24 - 48 hours Target aPTT: 50-70 sec; first monitoring after 3 hours
	Enoxaparin	< 75 years • IV bolus of 30 mg • SC 1 mg/kg BID (first dose 15 min after IV bolus) until discharge • First two doses ≤ 100 mg > 75 years • No IV bolus • SC 0.75 mg/kg BID (first dose 15 min after IV bolus) until discharge • First two doses ≤ 75 mg • Creatinine clearance < 30 mL/min: same doses QD
	Fondaparinux	IV bolus of 2.5 mg. SC 2.5 mg QD until discharge

of symptom onset were randomized to either reperfusion therapy with streptokinase or standard non-fibrinolytic therapy. In-hospital mortality was 10.7% in patients treated with intravenous streptokinase versus 13.1% in controls, resulting in 23 lives saved per 1,000 patients treated. This benefit in mortality was even preserved at ten-year follow-up.[10] A second 17,187-patient landmark trial, ISIS-2, corroborated these results.[11]

Alteplase

Recombinant tissue-type plasminogen activator (rt-PA or alteplase) is a single-chain tissue-type plasminogen activator molecule. It has considerably greater fibrin-specificity than streptokinase, but induces nevertheless mild systemic fibrinogen depletion. Because of its short half-life, alteplase requires a continuous infusion.

In two large mortality trials, ISIS-3 and GISSI-2, alteplase, given as a 3-hour continuous infusion, was not found to be superior to streptokinase.[12, 13] The question which of the two fibrinolytic drugs is the most effective in terms of mortality reduction was answered in the first GUSTO trial.[14] In this large trial, a 'front-loaded' 90-min dosing regimen of alteplase was used (Table 2), which had earlier been shown to achieve higher patency rates than the previously used 3-hour scheme. 30-day mortality was significantly lower in patients receiving alteplase compared to those treated with streptokinase (6.3% vs. 7.4%). The 1% lower mortality rate at 30 days with front-loaded alteplase corresponds with a significantly higher epicardial patency rate at 90 minutes: 54% versus only 32% with streptokinase.[15]

Reteplase

Reteplase, a second-generation fibrinolytic agent, was a first attempt to improve on the shortcomings of alteplase. It is a mutant of alteplase in which the finger, the kringle-1 domain and epidermal growth factor domains are removed. This causes decreased plasma clearance, allowing double-bolus administration. The removal of the finger domain somewhat diminishes fibrin specificity, although inactivation by plasminogen activator inhibitor (PAI-1) remains similar with alteplase. Compared to alteplase, reteplase achieved higher patency rates in two pilot studies.[16, 17]

In the GUSTO-III trial, 15,059 patients were randomized to double-bolus reteplase, given 30 min apart, or front-loaded alteplase.[18] Mortality at 30 days was similar in both treatment arms (7.47% vs. 7.24%, respectively), as was the incidence of hemorrhagic stroke or other major bleeding complications. Similar mortality rates were maintained for both treatment groups at one-year follow-up.[19] In other words, higher TIMI-3 rates at 90 min with reteplase, as seen in the two pilot studies, did not translate into lower short-term or long-term mortality rates. The reason for this incongruity remains unclear, but might be explained in part by increased platelet activation and surface receptor expression with reteplase compared to alteplase.

Tenecteplase

Tenecteplase (TNK-t-PA) is also derived from alteplase, after mutations at three places (T103, N117, KHRR296-299). These changes enhance fibrin binding and specificity, plasma half-life, and resistance to PAI-1. Its slower clearance allows convenient single-bolus administration. Tenecteplase leads to faster recanalization compared to alteplase, and also has higher fibrinolytic potency on platelet-rich clots than its parent molecule. In two pilot trials (TIMI 10A and 10B), patency rates after 30 or 40 mg tenecteplase were comparable to those achieved with front-loaded alteplase.[20, 21] A 50-mg dose of tenecteplase, however, was discontinued early because of an excessive subsequent incidence of

Table 2: Characteristics and dosing regimens of fibrinolytic agents.

Characteristic	Streptokinase	Alteplase	Reteplase	Tenecteplase
Fibrin-specificity	No	++	+	+++
Half-life (min)	18 - 23	3 - 4	18	20
Antigenicity	+++	No	No	No
Administration	1-hour infusion	Bolus & 90-min infusion	Double bolus	Single bolus
Dose	1.5 MU	15-mg bolus 0.75 mg/kg i.v. (max 50) over 30 min 0.5 mg/kg over 60 min	10 U + 10 U 30 min apart	Weight-adjusted: <60 kg: 30 mg 60-69.9 kg: 35 mg 70-79.9 kg: 40 mg 80-89.9 kg: 45 mg ≥90 kg: 50 mg

intracranial hemorrhages.

In the double-blind ASSENT-2 trial, 16,949 patients were randomized to weight-adjusted single-bolus tenecteplase or standard front-loaded alteplase.[22] Specifically designed as an equivalency trial, this study showed that tenecteplase and alteplase had equivalent 30-day mortality rates (6.18% vs. 6.15%). Mortality rates remained similar at one-year follow-up.[23] Although the rates of intracranial hemorrhage were low, and similar for tenecteplase (0.93%) versus alteplase (0.94%), female patients, elderly >75 years and patients weighing less than 67 kg tended to have lower rates of intracranial hemorrhage after treatment with tenecteplase.[6] Non-cerebral bleeding complications occurred less frequently in the tenecteplase group, and as a consequence, there was also less need for blood transfusion after tenecteplase, especially in high-risk patients.

Indications and contra-indications for fibrinolytic therapy

Indications

Patients younger than 76 years with typical chest pain of up to 12 hours duration presenting with electrocardiographic ST-segment elevations or new bundle-branch block are eligible for fibrinolytic therapy.[3] The usual electrocardiographic criterion for administration of fibrinolytic therapy is at least 0.1 mV of ST-segment elevation in two or more contiguous leads. Since mortality is significantly higher in patients with complete left bundle-branch block, administration of a fibrinolytic agent is also recommended in this population.[24] Indeed, fibrinolysis in patients presenting with a new bundle-branch block, obscuring ST-segment elevation, reduces mortality by 25%.

Contraindications

Contraindications to fibrinolysis are, in essence, precautions to avoid excessive hemorrhage in patients with co-morbidities that increase the risk of bleeding complications (Table 3).

In these patients, especially those with a previous history of stroke or recent major surgery, primary PCI should be considered. Since arterial hypertension increases the risk for intracranial hemorrhage, patients presenting with persisting high blood pressure are usually also not eligible for lytic therapy, although a history of systemic hypertension in itself does not predispose to intracranial hemorrhage with lytic therapy. It is less clear whether fibrinolytic agents can be safely administered, after successful treatment of high blood pressure at initial presentation. Nevertheless, because there is a substantial mortality benefit with fibrinolytic agents, even in patients presenting with hypertension, fibrinolysis should still be considered in patients with high blood pressure on admission, after successful initiation of antihypertensive treatment, when primary PCI is not available.

Adjunctive antithrombotic therapy with lytics

Antiplatelet therapy

- Aspirin

Low-dose aspirin remains the cornerstone of antithrombotic therapy in STEMI patients. In ISIS-2, low-dose aspirin was associated with improved outcome in STEMI patients, irrespective of receiving fibrinolysis or placebo.[11] Aspirin also significantly reduced nonfatal re-infarction (1.0% vs. 2.0%) and was not associated with any significant increase in intracranial hemorrhages. In the most recent meta-analysis of the Antithrombotic Trialists' Collaboration including 19,288 patients from 15 STEMI trials, aspirin use was associated with a significant reduction in cardiovascular death (23 lives saved per 1,000 patients treated) and non-fatal reinfarction (13 events prevented per 1,000 patients treated).[25] Overall, a small increase of intracranial hemorrhages (1 to 2/1,000) was seen in patients taking low-dose to aspirin.

Two small trials suggest that the benefit of aspirin in the setting of fibrinolytic therapy might be time-dependent. Patients who received aspirin before fibrinolysis had a lower 7-day mortality than patients who

Table 3: Contraindications for fibrinolysis.

Absolute contraindications	Relative contraindications
- Previous hemorrhagic stroke or stroke of unknown origin at any time	- Surgery or trauma within past 2-4 weeks
- Non-hemorrhagic stroke in preceding 6 months	- Uncontrolled hypertension on presentation (>180/100 mmHg)
- Known bleeding diathesis	- Prolonged resuscitation
- Suspected aortic dissection	- Oral anticoagulant use with INR >2.3
- Intracranial neoplasm	- Recent (internal) bleeding
- Central nervous system trauma	- Active peptic ulcer
- Non-compressible punctures	- Previous use of streptokinase

received the first dose of aspirin after administration of the fibrinolytic agent.[26] Similarly, patients with a STEMI had a better survival rate at 30 days when they received aspirin before hospital admission compared to in-hospital initiation.[27]

• Clopidogrel

Despite systematic use of aspirin in lytic-treated patients, reocclusion and reinfarction after successful pharmacological reperfusion continues to be a problem. The CLARITY (Clopidogrel as Adjunctive Reperfusion Therapy) trial examined whether the addition of a second oral antiplatelet agent on top of aspirin, the ADP receptor inhibitor clopidogrel (300 mg bolus followed by 75 mg daily), was associated with higher rates of infarct-related artery patency in patients treated with a fibrinolytic agent.[28] At angiographic follow-up at least two days after fibrinolytic therapy, patients treated with clopidogrel had significantly lower TIMI flow grade 0 or 1 rates. Clopidogrel appeared to improve patency rates by preventing reocclusion rather than through facilitating early reperfusion.[29] No increased risk of bleeding complications with clopidogrel was observed. Since no patients over 75 years of age were included, however, it remains uncertain whether dual antiplatelet therapy is safe in the elderly treated with lytic therapy. Clopidogrel also improved outcome after PCI in CLARITY, regardless of the duration of pretreatment or whether patients received additional glycoprotein IIb/IIIa inhibitors.[30] These results suggest that starting clopidogrel at the time of fibrinolysis could obviate the need for additional glycoprotein IIb/IIIa inhibitors when a rescue PCI would be necessary.

• Glycoprotein IIb/IIIa inhibitors

The addition of glycoprotein (GP) IIb/IIIa inhibitors such as abciximab, eptifibatide or tirofiban to fibrinolytic agents reduces the risk of recurrent ischemia and reocclusion due to the prothrombotic side effects of fibrinolysis. Several trials indeed indicate that abciximab with half-dose fibrinolytic not only modestly enhances recanalization of the culprit vessel but also improves tissue reperfusion.[31] The effect of improved epicardial patency rates on outcome with combination therapy using abciximab in addition to half-dose fibrinolytic therapy, was tested in the GUSTO-V (reteplase) and ASSENT-3 (tenecteplase) trials.[32, 33] In both trials, mortality rates were similar, but half-dose fibrinolysic plus abciximab was associated with a reduction in non-fatal ischemic complications. Although intracranial hemorrhage rates were comparable between treatment arms, major bleeding complications and transfusion rates were more frequent in the half-dose fibrinolytic plus abciximab arm. Patients older than 75 years experienced significantly more bleeding complications. The combination of half-dose lytic and abciximab was also tested as a facilitation of primary PCI in the FINESSE trial.[34] In this trial, 2,452 patients planned to undergo primary PCI were randomized to half-dose reteplase plus abciximab, upfront abciximab or abciximab only just before the PCI. Although significantly more patients had early ST-segment resolution with the combination treatment, outcomes were not different between the treatment strategies. Taken together, combination therapy with half-dose fibrinolysis and abciximab results in a significant reduction in ischemic complications after acute myocardial infarction, but this benefit is offset by an increased risk of bleeding complications, particularly in the elderly.

Anticoagulant therapy

• Unfractionated heparin and low molecular weight heparin

The use of unfractionated heparin (UFH) is generally not recommended with non-fibrin-specific fibrinolytics. In contrast, UFH has been standard adjunctive antithrombotic therapy with fibrin-specific fibrinolytics since GUSTO-I, although other studies were unconvincing. Several fibrinolytic trials have studied the use of low-molecular weight heparin (LMWH), which does not require monitoring of its anticoagulant effect and can be given subcutaneously. In ASSENT-3, a significant improvement in the primary combined efficacy and safety end point was seen with tenecteplase and enoxaparin when compared to tenecteplase and UFH.[32, 35] Unfortunately, a significant increase in intracranial hemorrhages was seen in the ASSENT-3 PLUS trial, using the same combination.[36] The excess of intracranial bleeding complications was predominantly observed in elderly patients. Using an age-adjusted dose, however, enoxaparin did not increase the risk of intracranial hemorrhage after fibrinolytic therapy while still reducing the risk of ischemic complications in the ExTRACT-TIMI 25 study.[37] Another LMWH, reviparin, was tested in the CREATE study. 15,570 patients with a STEMI, of which over 70% received lytic therapy, were randomized to either placebo or reviparin.[38] Reviparin significantly reduced 30-day mortality and reinfarction, but bleeding complications were more frequent with reviparin, especially in patients receiving reperfusion therapy. Meta-analyses of trials comparing LMWH to UFH confirm that LMWH reduce the risk of death and reinfarction, but are associated with a higher risk of bleeding complications.[39, 40]

• Fondaparinux

Fondaparinux, a synthetic pentasaccharide, is a selective factor Xa inhibitor. As with LMWH, fondaparinux does not need monitoring of its anticoagulant effect. In the OASIS-6 trial, fondaparinux was compared with UFH or placebo in 12,092 patients with ST-elevation

myocardial infarction.[41] Lytic therapy was given to 45% of patients (n = 5,436), most of them receiving a non-fibrin-specific agent. In these patients, fondaparinux was associated with a significant 21% lower risk of death or myocardial infarction when compared to standard heparin or placebo.[42] Nevertheless, the risk of bleeding, including intracranial hemorrhage, was considerably lower with fondaparinux, irrespective of the type of fibrolytic agent. The latest European guidelines recommend fondaparinux as adjunctive therapy to streptokinase (class IIa B) but not to fibrin-specific agents because of paucity of +outcome data with this combination.[3]

• Bivalirudin

In contrast with UFH, which only inhibits fluid-phase thrombin, bivalirudin is a direct thrombin-specific anti-coagulant that inhibits both fibrin-bound and fluid-phase thrombin. Because inadequately inactivated thrombin at the site of thrombus is in part responsible for the proco-agulant side effect of thrombolysis, direct inhibition of thrombin might thus reduce the occurrence of ischemic complications after reperfusion.

In the HERO-2 trial, 17,073 patients were randomized to streptokinase and UFH or streptokinase and bivalirudin.[43] Mortality at 30 days was not different for both regimens, but re-infarction rate was significantly lower in the bivalirudin group (1.6% vs. 2.3% for UFH), suggesting that early and more efficient inhibition of thrombin can inhibit reocclusion. Mild to moderate bleeding complications were higher in the bivalirudin group, possibly due to higher aPTT values observed in the bivalirudin group. Bivalirudin has not been studied as an adjunctive antithrombin with fibrin-specific agents.

Fibrinolysis in the elderly

Registries have suggested an excessive mortality in fibrinolysis-treated patients over 75 years of age, possibly due to an excess of major bleeding complications.[44, 45] This excessive mortality might also be explained in part by negative selection, as fitter elderly patients might have been more likely amenable for primary PCI. Mortality rates in observational studies, however, are in contrast with findings from large randomized trials. In the unpublished SENIOR PAMI trial, primary PCI was not found to be superior to primary PCI in 481 elderly patients (≥ 70 years of age). Furthermore, data from the Fibrinolytic Therapy Trialists (FTT) group in 3,300 STEMI patients over the age of 75 showed a significant absolute mortality reduction by fibrinolytic therapy that was even greater than in younger patients (34 versus 16 patients per 1,000 randomized).[46] A larger absolute benefit of fibrinolysis in elderly patients, might in part be explained by their higher baseline risk.[47] Lower ICH rates with tenecteplase as compared to alteplase in older patients in the ASSENT-2 study indicate that the timely use of a more fibrin-specific agent might be preferable in older patients without contraindications for fibrinolytic therapy.[6]

Fibrinolysis in diabetics

Diabetic patients are less likely to be treated with fibrinolysis than non-diabetic patients.[6, 25] This probably reflects the more frequent atypical or late presentations of these patients. Because fibrinolysis is thought to be most effective in the first hours after symptom onset, late presentation in patients with diabetes may be in part responsible for the reduced use of pharmacological reperfusion. It may also be related to concerns over an increased risk of intracranial or retinal hemorrhage. These concerns, however, are unsubstantiated: patients with diabetes are not likely to experience increased retinal or major bleeding complications after fibrinolysis.[8, 26] In any case, individuals with diabetes do present later than those without diabetes. In addition, small mechanistic studies have suggested that fibrinolytic therapy may be less effective in individuals who have diabetes, irrespective of the delay between symptom onset and first medical contact. Such findings contrast with results from large clinical trials, however, which show that patients with diabetes benefit equally, if not more, than patients who do not have diabetes.[28] Thus, as in non-diabetic patients, fibrinolysis should be considered in lytic-eligible STEMI patients with diabetes and should be initiated as soon as possible if primary PCI is not an option.

Fibrinolysis and time-to-treatment

The advantages of fibrinolytic therapy are time-dependent. Although administering fibrinolytics up to 12 hours after the onset of symptoms may be beneficial in terms of outcome, every minute that reperfusion is post-poned will unavoidably result in more extensive necrosis and worse outcome. In a meta-analysis, the mortality reduction following fibrinolytic therapy was calculated to be 44% in patients treated within 2 hours versus 20% in those treated later.[48] Early in the course of STEMI, the thrombus may be smaller and easier to lyse, which might in part explain the more prominent benefit of lytics in the first hours after symptom onset.

Pre-hospital therapy

Initiation of lytic therapy at the time of first medical contact, e.g. in the pre-hospital setting, speeds up reper-fusion and might hence improve outcome. Several trials and registries have compared pre-hospital fibrinolysis with in-hospital fibrinolysis. A meta-analysis of six trials including 6,434 patients clearly demonstrates that the time gained with pre-hospital treatment resulted in a significant 17% mortality reduction compared with

fibrinolysis initiated in the emergency department.[49] In a more recent cohort study, time to fibrinolysis was almost 1 hours shorter with pre-hospital diagnosis and lytics administered by trained paramedics in the ambulances, when compared with regular in-hospital lytic therapy.[50] The significant amount of time gained by administrating fibrinolytics in the pre-hospital setting resulted in a reduction of adjusted 1-year mortality by almost 30%. In the French USIC registry, the risk of death at one year was even more than 50% lower after pre-hospital fibrinolysis, compared to other treatment strategies.[51] In patients treated prehospitally within 3.5 hours of symptom onset, 1-year survival was close to 99% in this study.

Studies comparing on-site fibrinolysis with transport for primary PCI in low-risk patients suggest that, even with transport-related time delays up to 90 minutes, primary PCI is superior to fibrinolysis. Nevertheless, time gained with pre-hospital administration might challenge this difference in outcome. In the CAPTIM trial, patients were randomized to either pre-hospital fibrinolysis with accelerated alteplase or primary PCI after transport to a center with interventional facilities.[52] In essence, CAPTIM compared two reperfusion strategies, because more than 30% of patient in the pre-hospital lytic arm underwent urgent (rescue) angiography. Results from CAPTIM suggest that outcome after pre-hospital fibrinolysis is at least comparable to that with primary PCI, especially in patients presenting very early after symptom onset.[52, 53]

Fibrinolysis or referral for primary PCI?

In hospitals without interventional facilities, patients presenting with STEMI can either be treated with fibrinolysis on-site or referred to another hospital for primary PCI. Current guidelines explicitly recommend primary PCI in patients presenting with STEMI.[54, 55] On aggregate, they require that an experienced team starts the intervention within 90-120 minutes after initial presentation. In non-interventional hospitals, patients need to be transported to the nearest PCI center, requiring established communication and transportation routines between the referring and receiving hospitals. In a real-world setting, however, door-to-balloon times are unfortunately often much longer than 90 minutes, with only a minority of patients effectively treated within these targets.[4, 56] Uncertainties about delays associated with communicating with the receiving catheterization laboratory, arranging patient transfer and mobilizing an interventional team within a 90-to-120-min interval often confuse physicians who refer patients for primary PCI. Results from studies comparing on-site fibrinolysis to primary PCI have even raised the impression that the superiority of primary PCI justifies long treatment delays caused by transportation. Different meta-analyses pooling these studies, however, suggest that the mortality benefit of primary PCI over fibrinolysis disappears with PCI-related delays exceeding one to two hours.[57, 58] An analysis of the NRMI databases sheds more light on how to triage patients to fibrinolysis or transport for primary PCI [59] (Figure 2).

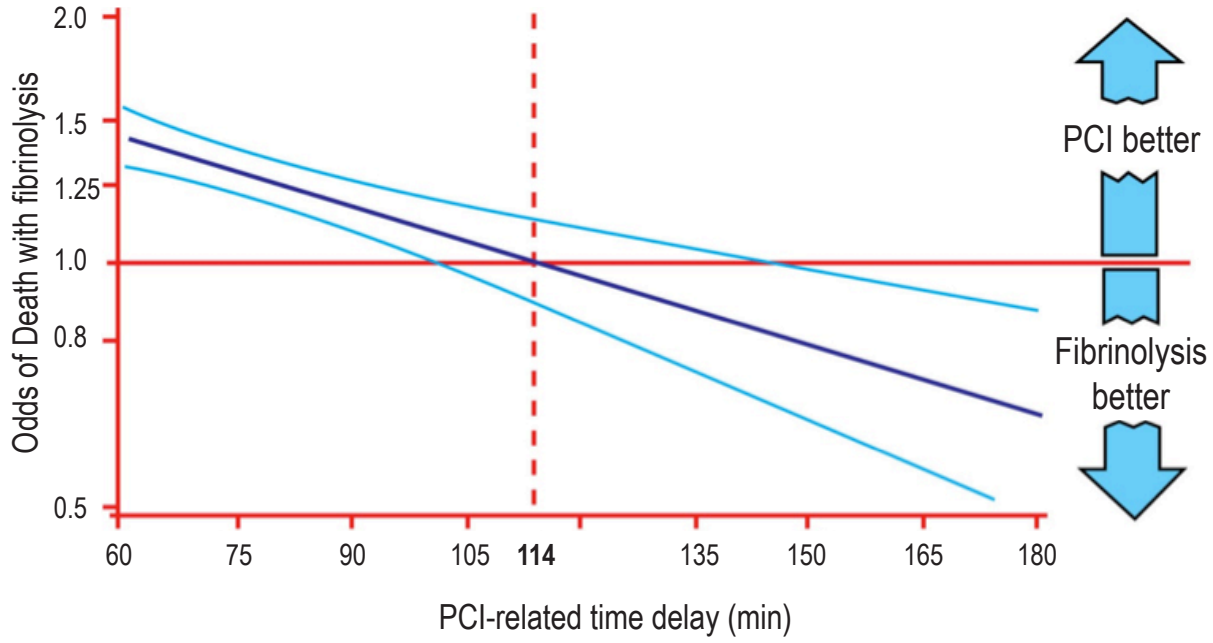

Figure 2: *Decision in selecting reperfusion strategies, based on NRMI databases analysis.(License No:2800051106031)*[59]

Increasing delays between door-to-needle times, versus door-to-balloon time was found to impair outcome: a 10% increased risk of in-hospital mortality for every 30 minutes delay that is lost with transferring the patient versus on-site fibrinolysis. When the PCI-related delay reaches 114 minutes, the benefit of primary PCI over fibrinolysis disappears in the overall population. The advantage of primary PCI over fibrinolysis in terms of outcome is lost even at much shorter PCI-related delays in younger patients (< 65 years) presenting with an anterior infarction within 2 hours of symptom onset. The benefit of lytic therapy might indeed be more pronounced in fresh occlusive clots jeopardizing a large myocardial area at risk, while younger patients are less at risk for bleeding complications. On aggregate, when primary PCI is not available within 90 (AHA/ACC) to 120 (ESC) minutes or when in doubt about transportation delays, STEMI patients should receive lytic therapy in the absence of contra-indications.[3, 54] In the latest ESC guidelines, the anticipated PCI-related treatment delay should even be shorter in patients presenting within 3 hours of symptom onset and with a large amount of ischemic myocardium at risk.[3] Likewise, current AHA/ACC guidelines indeed imply that there is no strong preference of PCI over fibrinolysis in patients presenting within three hours of symptom onset.[54]

Angiography and PCI after fibrinolysis

Unsuccessful or suboptimal epicardial reperfusion of the infarct-related artery occurs in 20 to 40% of fibrinolytic-treated patients, and is associated with poor functional recovery of the left ventricle and increased mortality. Failure of fibrinolysis to recanalize the occluded artery is generally suspected when chest pain or ST-segment elevation persists at 60 to 90 minutes after treatment initiation. Results from the recent REACT study clearly indicate that immediate rescue PCI is preferred over repeated fibrinolysis or a conservative approach when fibrinolysis is unsuccessful.[60] In contrast with earlier studies that failed to show a benefit with rescue PCI, almost half of rescue PCI patients received additional abciximab, indicating that additional antiplatelet therapy might be necessary to prevent early (re)thrombosis.

It is less clear whether a systematic approach of early planned PCI after fibrinolysis, often referred to as *'facilitated PCI'*, is beneficial. Earlier small studies showed that this strategy was both effective and safe.[61, 62] Results from the large ASSENT-4 PCI outcome trial, however, suggest that a planned PCI within the first two hours after fibrinolysis might even be harmful. In this trial, STEMI patients were randomized to full-dose tenecteplase followed by early planned PCI or primary PCI alone.[63] Unfortunately, the study was halted prematurely because of excess mortality and early reinfarction in the facilitated arm. This might have been caused by a lytic-induced prothrombotic state, unopposed by potent antiplatelet agents early after PCI, as neither up-front clopidogrel nor abcixmab were given to lytic-treated patients. In any case, the combination of reduced-dose reteplase with the glycoprotein IIb/IIIa inhibitor abciximab also failed to improve outcome compared to primary PCI plus abciximab alone in the FINESSE trial.[34]

A meta-analysis of studies comparing PCI within 24 hours after fibrinolysis versus a more conservative approach, suggests that routine early stenting might improve outcome.[64] In these studies however, rescue PCI was only rarely used in the conservative arm. Moreover, PCI was only performed very late after fibrinolysis, precluding potential myocardial salvage. The question as to whether lytic-treated patients should be immediately transferred to an interventional facility versus being transferred only when rescue PCI is indicated was directly addressed in the recent CARESS study. In this study, 600 high-risk STEMI patients in non-interventional hospitals were treated with half-dose reteplase plus abciximab and randomized to either immediate transfer to a PCI facility or local care with transfer only in case of persistent ST-segment elevation or clinical deterioration.[65] Median time between fibrinolysis and PCI was only 135 minutes in the routine referral group. Immediate transfer was found to be clearly associated with a lower risk of death, reinfarction or refractory ischemia at 30 days. The recent TRANSFER-MI and NORDISTEMI studies confirm a benefit of an invasive treatment after lytic therapy.[66, 67] All these results suggest that all high-risk STEMI patients who are treated with fibrinolysis should be systematically and if possible immediately transferred to a PCI-capable center. However, to avoid reocclusion during early PCI, due to prothrombotic side effects of the lytic agent and spontaneous reocclusion later, the ESC guidelines recommend performing a diagnostic angiography and PCI within 3 to 24 hours after successful fibrinolysis, in order to decide on the final treatment (PCI, CABG or medical management).[3]

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Acute decompensated heart failure. What are we missing?

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Terminology

1. Acute decompensated heart failure
2. Acute heart failure syndrome
3. Acute heart failure
4. Hospitalized heart failure

Differences of acute heart failure and chronic heart failure

The treatment of chronic heart failure, particularly when due to systolic dysfunction, is built around therapies that have been shown to reduce long-term mortality and improve symptoms such as: angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta blockers and aldosterone antagonists. More recent evidence-based management includes device therapy such as Cardiac Resynchronization Therapy (CRT), Implantable Cardiovertor Defibrillator (ICD) or the Ventricular Assist Device (VAD).

In contrast, the goals of the initial management of acute decompensated heart failure (ADHF) are hemodynamic stabilization, correction of the intravascular volume abnormalities, and symptom relief. The main therapy goal for these abnormalities is to lower the ventricular filling (diastolic) pressures by diuretics and vasodilators. The aggressiveness of each treatment depends on the patient's hemodynamic and volume status.[1, 2] Some of the cornerstones of chronic heart failure therapy such as prescribing ACE inhibitors, angiotensin receptors or beta blockers, should either not be used at all, or only used with caution in ADHF, particularly during the period of initial stabilization. Such therapies may be initiated or titrated upward later in a patient's course (except those patients that already have been on these medications prior to admission).

Management of Acute Heart Failure Symdrome (AHFS) is challenging due to the heterogeneity of the patient population, absence of a universally accepted definition, incomplete understanding of its pathophysiology, and lack of good evidence-based guidelines.

Pulmonary and systemic congestion due to elevated ventricular filling pressures with or without a decrease in cardiac output is a nearly universal finding in AHFS.[1, 2] Occasionally, severe pulmonary congestion develops abruptly when precipitated by a rapid increase in systemic blood pressure, particularly in patients with diastolic dysfunction, or ischemia causing sudden rise of left ventricular filling (diastolic) pressure. Pulmonary congestion in this set up is due to fluid redistribution rather than fluid accumulation.

Acute heart failure may be a new case (15-20%) or an exacerbation of chronic disease (80%), with gradually or rapidly worseningheart failure (HF) signs and symptoms requiring urgent therapy orhospitalization. Currently there are only few evidence-based guidelines for acute heart failure and they largely reflect a relative lackof robust data. Clinical practice guidelines for the management ofAHFS have only recently been addressed and many recommendations are from expert consensus. ADHF guidelines have beenpublished by the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) - 2009, the European Society of Cardiology (ESC) - 2005, 2008, and the Heart Failure Society of America (HFSA) - 2010.[3-6]

Definition

For Chronic heart failure (and Acute heart failure)

The definition of heart failure proposed by ACC/AHA 2005 Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult [7,8] is as follows:

Heart failure is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.

The cardinal manifestations of heart failure are dyspnea and fatigue, which may limit exercise tolerance, and fluid retention, which may lead to pulmonary congestion and peripheral edema.

For acute decompensated heart failure

AHFS is defined as gradual or rapid change in heart failure signs and symptoms resulting in a need for urgent therapy. These symptoms are primarily the result of severe pulmonary congestion due to elevated left ventricular filling pressures (with or without low cardiac output). AHFS can occur in patients with preserved or reduced ejection fraction (EF).[1]

Characteristics of patient admitted with acute decompensated heart failure

Table 1 reveals that acute heart failure syndrome (ADHF) patients have significant concomitant diseases. They have a ratio of left ventricular systolic and preserved systolic function of about 50 / 50.

Table 2 reveals that almost all ADHF patients have symptoms or findings of congestion, high left ventricular filling pressure (PCWP = pulmonary capillary wedge pressure) and adequate cardiac output. Most of them have normal or elevated systemic blood pressure. Very few of them actually have blood pressure lower than 90 mmHg.

It is increasingly recognized that many patients with this syndrome have relatively preserved ejection fraction, as many as those patients with depressed systolic function, which indicates that left ventricular ejection fraction is not the only or major factor inducing ADHF. The diastolic (filling pressures) component appears to be the

Table 1. Demographics and concomitant diseases of acute decompensated heart failure.[9-11]

Characteristics	ADHERE (N=107,920)	EHFS (N=11,327)	OPTIMIZE-HF (N=34,059)
Mean age (yr)	75	71	73
Women (%)	52	47	52
Prior HF (%)	75	65	87
LVEF < 0.40 (n)	59	46	52
CAD (%)	57	68	50
Hypertension (%)	72	53	71
Diabetes (%)	44	27	42
Atrial fibrillation (%)	31	43	31
Renal insufficiency (%)	30	18	NA

ADHERE = Acute Decompensated Heart Failure National Registry
EHFS = EuroHeart Failure Survey
OPTIMIZE-HF = Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure Registry
CAD = coronary artery disease
HF= heart failure
LVEF = left ventricular ejection fraction
NA = not available.

Table 2: Clinical Presentation of Patients Hospitalized with Heart Failure.[12]

Clinical presevtation	%
Any dyspnea	89
Dyspnea at rest	34
Fatigue	32
Rales	68
Peripheral edema	66
CXR congestion	75
SBP >140 mmHg	50
SBP 90-140 mm Hg	48
SBP <90 mmHg	2
Mean heart rate (bpm)	90
PCWP (mm Hg)	25-30
Cardiac index	Usually preserved

CXR = Chest x-ray
SBP = Systolic blood pressure
PCWP = Pulmonary capillary wedge pressure

Table 3: Diagnostic value of clinical markers of congestion.[13, 14]

Signs or symptoms	Sensitivity	Specificity
Dyspnea on exertion	66	52
Orthopnoea	66	47
Edema	46	73
Resting JVD	70	79
S3	73	42
Chest X-ray		
Cardiomegaly	97	10
Redistribution	60	68
Interstitial oedema	60	73
Pleural effusion	43	79

JVD = jugular venous distension
S3 = third heart sound.
All numbers are expressed as percentages.
Note : that Chest x-ray findings are only about two thirds sensitivity and specificity

Table 4: The most useful symptoms and signs[15]

Symptoms and Signs	Sensitive	Specific	Identifying ADHF
Dyspnea on exertion	Most		
Paroxysmal nocturnal dyspnea		Most	
Jugular venous pressure elevation			Most

dominant factor and in fact managing ADHF by trying to improve ejection fraction or cardiac output with the available inotropes (dobutamine, milrinone, dopamine) has deleterious effects in most cases (See inotrope section).

Pulmonary and systemic congestion due to elevated ventricular filling pressures with or without a decrease in cardiac output is a nearly universal finding in ADHF. The degree of fluid retention in each patient is varied. A variety of pathophysiologic mechanisms may play a role in this disorder, many of which remain poorly understood.

Dyspnea on exertion is the most sensitive clinical marker. Paroxysmal nocturnal dyspnea is the most specific, and elevated jugular venous pressure is the best indicator for identifying acute decompensated heart failure, although measurement of jugular venous pressure (JVC) will be inaccurate if it is not performed correctly (Table 4).

Pathophysiology

It is believed that ventricular abnormalities, systolic or diastolic, activate several neurohormonal systems. The principle neurohormone systems are the renin-angiotensin-aldosterone system, and sympathetic nervous system. Others include antidiuretic hormone, arginine vasopressin, vasoconstrictor endothelin, cytokine and vasodilator natriuretic peptide.[16, 17] These neurohormone levels are consistently elevated in heart failure patients. Initially these neurohormones will secrete in response to compensatory mechanisms which are initially beneficial. However sustained neurohormone elevation has many deleterious cardiovascular and renal effects. These unfavorable effects include vasoconstriction, tachycardia, myocyte toxicity, cellular structural and molecular change, increasing fibrosis and remoldeling. The compensatory renal sodium and water retention induced by these maladaptations, together with elevated left ventricular

filling pressure from various reasons ultimately results in pulmonary congestion and pulmonary edema. Occasionally, severe pulmonary congestion develops abruptly when precipitated by a rapid increase in BP, particularly in patients with diastolic dysfunction or sudden rise of left ventricular diastolic pressure from ischemia. Pulmonary congestion in this set up is due to fluid redistribution rather than fluid accumulation.

To further validate the significant involvement of neurphormones, several pharmacologic interventions have resulted in improving both mortality and morbidity.[18-24]

Congestion

High left ventricular and right ventricular diastolic pressure resulting in pulmonary and systemic congestion with or without low cardiac output is the main reason for the majority of acute heart failure admissions. An oversimplified explanation of the development of cardiac congestion at the pulmonary or systemic capillary sites is that it is due to the capillary pressure (hydrostatic pressure) exceeding oncotic pressure of that system, originating from the left and right ventricular filling pressures.

Pulmonary congestion may be defined as pulmonary venous hypertension (increased pulmonary capillary wedge pressure (PCWP), often resulting in pulmonary interstitial and alveolar edema. The PCWP should be equal to the left ventricular filling pressure. Systemic congestion manifests clinically by jugular venous distention. Jugular venous pressure should be equal to the right ventricular filling pressure. The degree of peripheral edema and increased body weight can vary.

Occasionally, severe pulmonary congestion develops abruptly when precipitated by a rapid increase in systemic blood pressure (afterload effect), particularly in patients with diastolic dysfunction. Renal impairment, severe neurohormonal or endothelial abnormalities, dietary indiscretion, and certain medications such as non-steroidal anti-inflammatory drugs, glitazones, and first generation calcium-channel blockers, may also contribute to fluid overload.

In the ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial, PCWP and not cardiac output was a significant predictor of subsequent survival.[25]

Neck vein examination

Despite several reports and guidelines which indicate the high sensitivity and specificity of jugular venous pressure examination for assessing fluid volume, this method has been significantly underutilized, particularly the semi-quantitative method. The technique is useful for both acute heart failure and chronic heart failure. When combined with other parameters (symptoms, edema, chest rales, tender liver enlargement, etc.), it helps the diagnosis of heart failure. Jugular venous pressure (JVP) examination also assists with both follow up diuresis and estimation of the patient euvolemic (dry) weight. Results from ESCAPE trial showed that if jugular venous pressure is 11 cmH_2O, PCWP should be 22 mmHg or higher.[25]

However the semi-quantitative method of jugular venous pressure examination is technically demanding in many cases. The examiner needs training under supervision from an experienced person. There will be cases where this method of measurement is not feasible.

The semi-quantitative method of jugular venous pressure assessment:

1.Equipment
   a. Preferably an adjustable upper body angulation examining bed. (Figure 1)
   b. Bright light such as Halogen or LCD with adequately wide beam.(Figure 2)

2.Adjusting upper body height (angulation) for best identification of the highest level of jugular venous pulsation. The patient's upper body inclining angle varies from patient to patient and in the same patient at different times.

3.Shine the light from different points (directly on the side of the patient's neck, from the front, from behind, using lighting shadow).

4.Determine the highest point of internal jugular pulsation from both right and left side. The right side may be easier to examine.

5.Measure the height of the internal jugular pulsation by drawing an imaginary parallel line to intersect the straight up line from sternal angle. Measure the height of that straight up line then add 5 cm (approximate distance from sternal angle to right atrial level). The result will be recorded in centimeters of water (cmH_2O). (Figure 3)

These flashlights are of various shapes and sizes (usually about one third or half the length and double the body size of a pencil). They require different kinds of battery and are usually inexpensive.

Decongestion versus improving ejection fraction/ cardiac output (EF/CO) during acute decompensated heart failure treatment

The last 2 decades have seen the successful development of a number of therapies for chronic systolic dysfunction. Angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers, β-blockers,

Figure 1: *Example of an examination bed*

Figure 2: *Examples of examination light source*

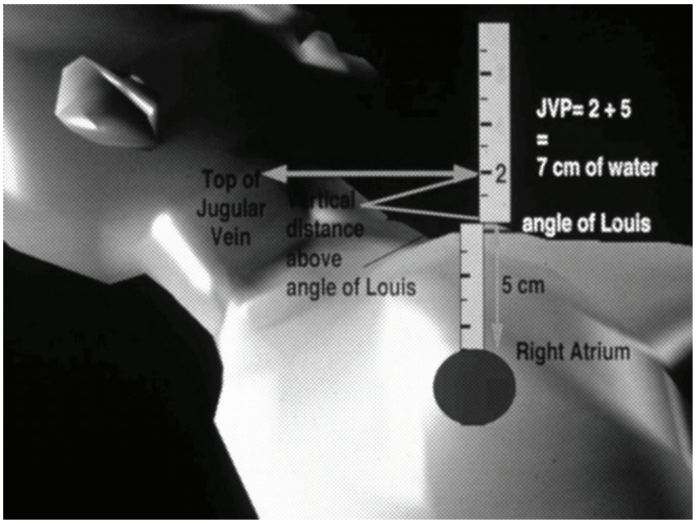

Figure 3: *Measurement of jugular venous pressure.*

aldosterone antagonists, implantable cardioverter defibrillators and cardiac resynchronization therapy have all been shown in large, prospective, randomized controlled trials to reduce morbidity and mortality among patients with stable congestive heart failure and reduced left ventricular ejection fraction.

Unfortunately, the same success has not been seen in the treatment of acute decompensated heart failure. Consequently, therapy for ADHF has not changed significantly over the past 30 years. There have been comparisons made between treatment of decreasing PCWP (= decongestion) and treatment of patients with cardiac output at different levels. It appears that achieving a lower PCWP leads to better immediate long-term mortality results. (Figure 4)

It appears that attempts to diuresis heart failure patients with evidence of fluid retention (after careful assessment of the patient with all appropriate parameters) should not only improve the symptoms (making the patient feel better) but also keep them alive longer.

Diuretics - The good and the bad

Intravenous therapy with a loop diuretic currently forms the foundation of care for patients with acute decompensated heart failure who have volume overload, but even furosemide use in acute decompensated heart failure is controversial.

Patients with acute decompensated heart failure who present primarily with low cardiac output and renal dysfunction pose a more difficult clinical challenge. Inotropes have traditionally been used in such cases but have consistently failed to show benefit in clinical trials.

Issues that should be kept in mind when using diuretics. (This paper will only cover outline without detail)

- Pharmacokinetic of loop diuretics such as wide range of absorption for furosamide (Lasix), 20-80%. Initial treatment should use IV route. Practitioners should know how to use both bolus or continuous drip with proper loading dose.

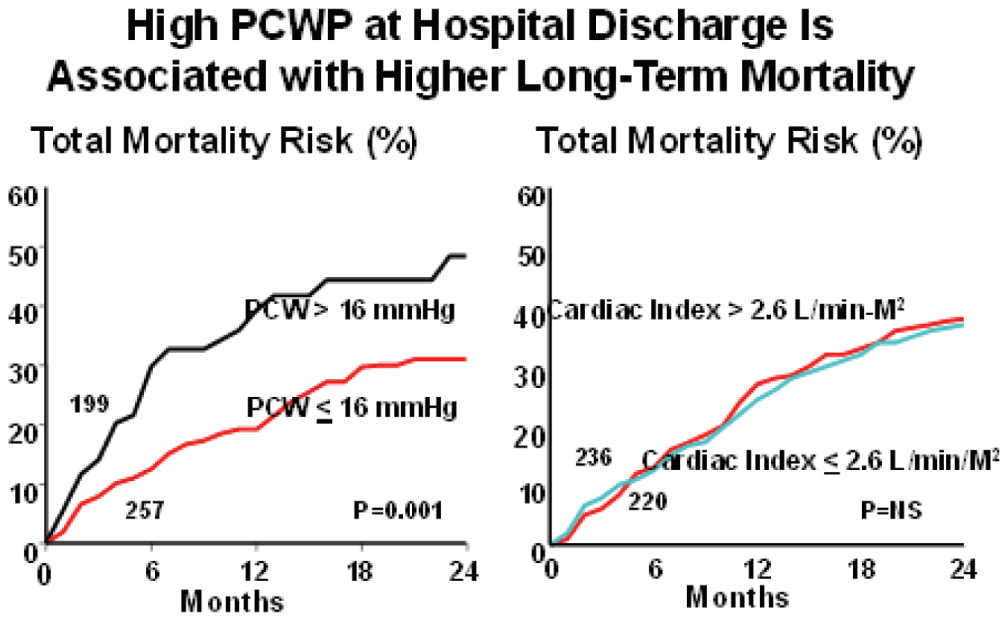

Figure 4: *A study by Fonarow[26] which demonstrated that if PCWP waslower than 16 mm Hg at discharge, the mortality at 24 months was better than for those whose PCWP was higher than 16 mm Hg. There is no mortality difference between the 2 groups that have cardiac index higher or lower than 2.6 L/min/M2*

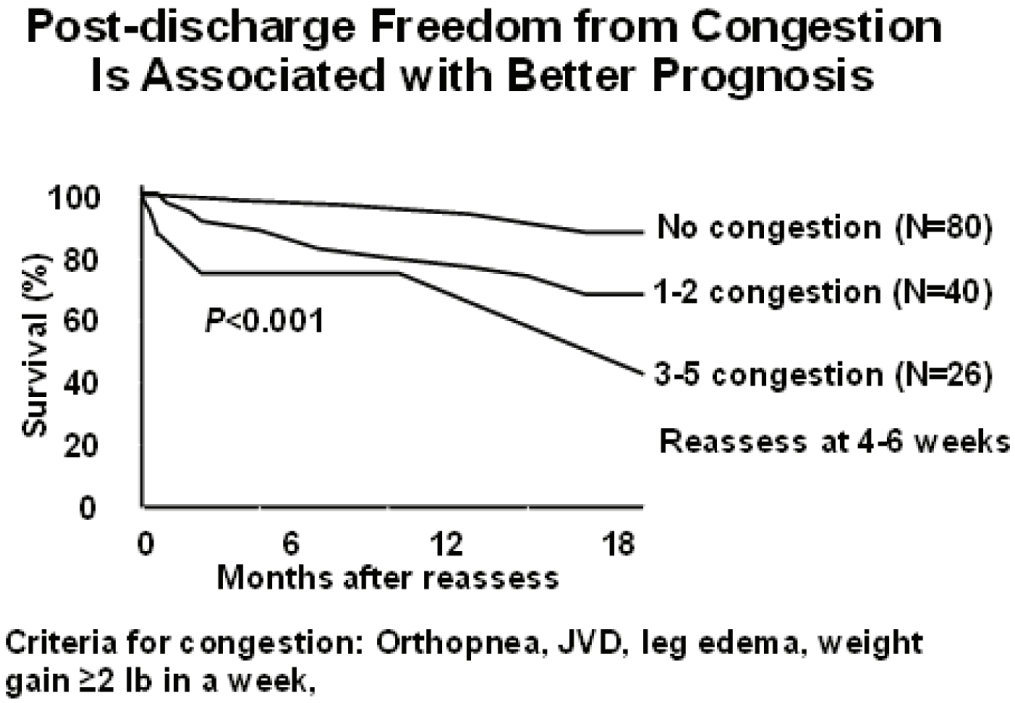

Figure 5: *A study by Lucas C, et al.[27] which shows the linear relationship between the degree of congestion and survival rate at 18 months: the less congestion, the better survival rate.*

- Furosamide (Lasix) has a short half-life. It should be used more than once a day during the diuresing phase. This practice will help prevent post diuretic sodium reabsorption (rebound).
- With more diuretic resistance, practitioners should use the proper dose and proper route. Then add the next diuretic that works at a different nephron site. This technique is called sequential blocking.
- Plan each day how much fluid retention the patient has and how much diuresis should be done. May have to check the response more than once a day for dose adjustment.
- Monitor electrolytes, BUN, Creatinine, BP and any symptoms or signs of over diurese.
- There are many down sides of diuretics:
    - o Increased neurohormonal activation
    - o Electrolyte disturbances and/or arrhythmias
    - o Worsened renal function
    - o Metabolic alkalosis, hyperuricemia

Finally it is essential to search for patients' euvolemic (dry) weight, using the below guidelines:

- Patient should be symptom free of *"congestion"*.
- Peripheral edema or *dependent* edema should have been eliminated.
- *Neck veins should be less than 5-7 cm of water* (Excepting patients with severe TR). The author uses this examination rather extensively.
- Abdominojugular reflux should be negative.
- Monitor creatinine, while diuresing patient (creatinine should not increase more than 30%).
- Ongoing volume overload is poorly tolerated and a frequent cause of hospital admission in patients with heart failure

Reminder

- Aggressive diuresis can be associated with worsening renal function, especially in the presence of ACE inhibitors
- High diuretic doses have been associated with increased mortality rates

Inotropes - The bad

The old concept that heart failure is only due to poor left ventricular systolic function (low ejection) is no longer valid. It is now clear that ADHF occurs in patients with either systolic dysfunction, preserved systolic function or both. The diastolic (filling pressures) component appears to be the dominant factor in ADHF patients. Furthermore, attempts to improve systolic function or increase cardiac output by various inotropes have failed in several trials over the past 20 years. (Table. 5)

Patients with acute decompensated heart failure who present primarily with low cardiac output and renal dysfunction pose a more difficult clinical challenge. Inotropes have traditionally been used in such cases but have

Table 5: List of inotrope studies over the past 20 years[28-44]

(A) Increase mortality	(C) Aggravation and induction of arrhythmias
• Milrinone	• Milrinone
• Enoximone	• Dobutamine
• Imazodan	• Dopamine
• Vesnarinone	(D) Tachycardia
• Dobutamine	(E) Tachyphylaxis (dobutamine)
• Xamoterol	(F) Neurohormone activation of lack of suppression
• Ibopamine	(G) Physiologic effects antagonized by beta blockade
(B) Increased risk of hospitalization	(dobutamine, dopamine)

Table 6: Data of inotrope utilization frequency continue to be high

	US ADHERE* 2006-2008	Europe ADHERE* 2006-2008	Asian Pacific ADHERE* 2006-2008	Thailand ADHERE** 2006-2007
Dobutamine	4	10.2	11.1	22
Dopamine	4	11.3	8.7	16
Milrinone	3			

*2nd Interim ADHERE International Report 2006-2008
**Thai ADHERE Registry Report 2006-2007

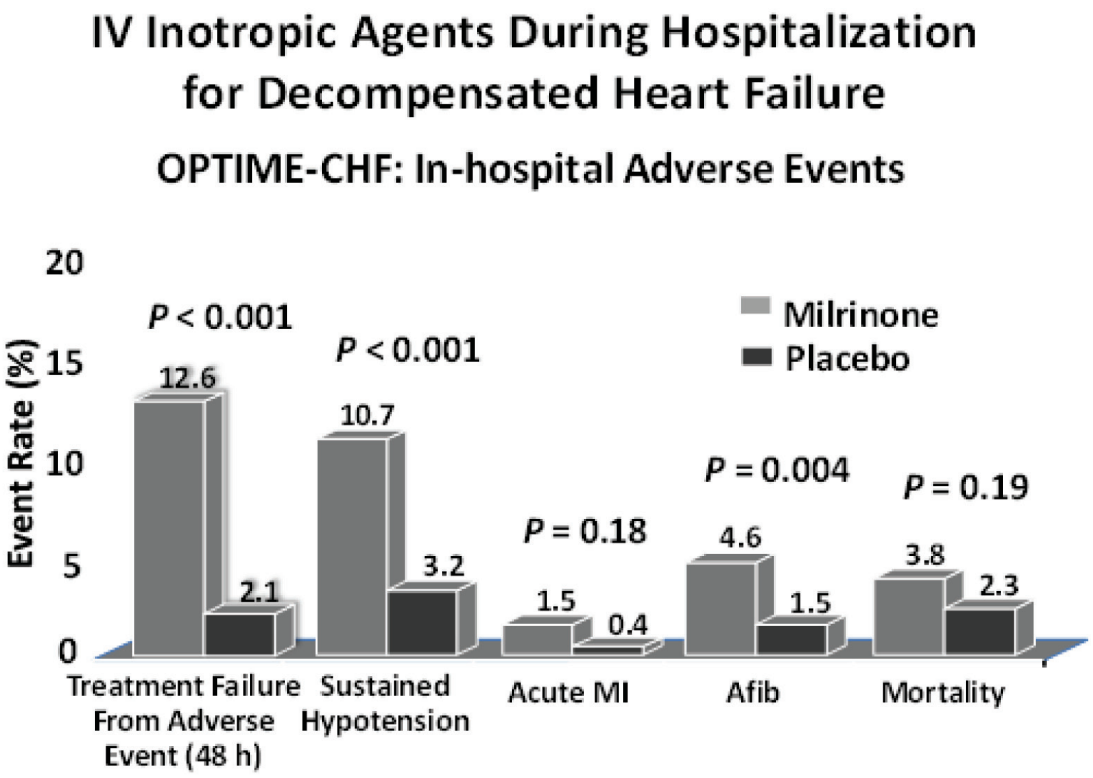

Figure 6: *Results of the most recent randomized control trial for milrinone, a phospho-diesterest inhibitor inotrope in ADHF. All the end points in this figure showed deleterious effects from milrinone when compared with a placebo. These end points included treatment failure from adverse events, sustained hypotension, acute myocardial infarction, atrial fibrillation and mortality; 4 out of 6 had statistic significance.*[30]

consistently failed to show benefit in clinical trials. Data of inotrope utilization frequency continue to be high, suggesting that we are hanging onto the old concept of ejection fraction and cardiac output as the major cause of ADHF whereby it is postulated that the condition can be improved by using inotropes (Table 6).

Indication for inotropes has been summarized as follow:[45]

1. The routine use of inotropes for heart failure therapy is not indicated in either the short or long term setting.

2. The use of inotropes is potentially appropriate in:
   - Cardiogenic shock
   - Diuretic/ACE inhibitor-refractory heart failure decompensations
   - A short-term bridge to definitive treatment, such as revascularization or cardiac transplantation

3. Inotropes may be appropriate as a palliative measure in patients with truly end-stage heart failure as part of hospice care.

Conclusion

- Evidence-based management of acute decompensated heart failure lags behind that of chronic heart failure.
- Pulmonary and systemic congestion due to elevated ventricular filling (diastolic) pressures with or without a decrease in cardiac output is a nearly universal finding in ADHF. Pathophysiology is not clearly understood.
- Symptoms and findings reflect pulmonary congestion, systemic congestion and fluid retention to varying degrees among ADHF patients.
- Jugular venous pressure (distension) is one of the most helpful examinations but also one of the most challenging. It should be considered an essential part of physical examination for heart failure patients. It needs to be conducted and reported with correct technique.
- Decongestion, to lower the left and right ventricular filling (diastolic) pressure is the goal of therapy for ADHF, best done by intravenous loop diuretics and, in some cases, with additional vasodilators.
- Know how to use diuretics properly. Diuretics also have downsides.
- Limit use of inotropes.
- The benefit of using neurohormone antagonists have been validated only in heart failure management

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Review Article

Molecular Breast Imaging Using Tc99m-Sestamibi and Breast Optimized Detector Systems

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Keywords:
Breast-specific Gamma Imaging, BSGI, molecular breast imaging, MBI,

Mammography and ultrasound are common anatomical imaging procedures used to detect breast cancer. While screening mammography, especially when combined with ultrasound, has demonstrated the ability to detect non-palpable breast cancer, these modalities still suffer from some significant limitations. According to the results of the American College of Radiology Imaging Network (ARCIN) 6666 clinical trial, the combination of mammography and ultrasound resulted in a positive predictive value of only 11.2% and a missed breast cancer in 8 of the 40 (sensitivity 80%) participants with malignant lesions.[1] In recent years, molecular imaging technologies have been developed to address these limitations.

Breast-specific Gamma Imaging (BSGI), also referred to as molecular breast imaging (MBI), scintimammography or mammoscintigraphy, is a nuclear medicine breast imaging technique which has been significantly improved within recent years with the invention of breast optimized gamma camera designs. Prior to this development, such studies were generally conducted with standard, large field-of-view (LFOV) gamma cameras. Nearly 100 peer-reviewed papers dating back more than 15 years have documented the experience of this imaging technique using Tc^{99m} methoxyisobutylisonitrile, (Sestamibi) and several studies comparing standard and optimized camera designs have provided evidence that the breast-optimized designs improve the clinical accuracy of this procedure, especially in sensitivity for sub-centimeter lesions.[2-5] Clinical evidence proving the increased lesion sensitivity of Breast-Specific Gamma Imaging (BSGI) over scintimammography is now available.[6-8] In addition, there have been several publications indicating that the sensitivity and specificity for BSGI are both around 89 - 96% and 65 - 90% respectively.[9, 10] Although alternate pharmaceuticals are available and others are under investigation, Sestamibi is currently the only US FDA (Food and Drug Administration) approved single-gamma emission isotope approved for breast imaging.[11, 12]

Indications

According to the Society of Nuclear Medicine Guideline for Breast Scintigraphy with Breast-Specific Gamma Cameras released in 2010, There are several potential indications for the use of this imaging technology.[13]

Patients with recently detected breast malignancy:

1. Evaluating the extent of disease (initial staging)
2. Detecting multicentric, multi-focal, or bilateral disease
3. Assessing response to neoadjuvant chemotherapy

Patients at high risk for breast malignancy

1. Suspected recurrence
2. Limited mammogram or previous malignancy was occult on mammogram

Patients with indeterminate breast abnormalities and remaining diagnostic concerns

1. Nipple discharge with abnormal mammogram and/or sonographic abnormality with or without contrast ductography.
2. Bloody nipple discharge with normal mammogram and/or ductogram
3. Significant nipple discharge with unsuccessful ductogram
4. Evaluation of lesions when patient reassurance is warranted (BIRADS 3)
5. Evaluation of lesions identified by other breast imaging techniques, palpable or non-palpable
6. Evaluation of palpable abnormalities not demonstrated by mammography or ultra-sound
7. Evaluation of multiple masses demonstrated on breast imaging
8. To aid in biopsy targeting
9. Evaluation of diffuse or multiple clusters of microcalcifications
10. Evaluation of breasts for occult disease in cases of axillary lymph node metastases with unknown primary
11. Unexplained architectural distortion
12. Evaluation of suspicious mammographic finding seen on one view only
13. Evaluation of enhancing areas seen on MRI to increase specificity

Patients with technically difficult breast imaging

1. Radiodense breast tissue
2. Implants, free silicone, or paraffin injections compromising the mammogram

Patients for whom Breast MRI would be indicated

1. MRI is diagnostically indicated, but not possible
   a. implanted pacemakers or pumps
   b. ferromagnetic surgical implants
   c. risk of nephrogenic systemic fibrosis response to gadolinium.
   d. body habitus exceeding the inside of the MRI bore
   e. patients with breasts too large to be evaluated within the breast coil
   f. patients with acute claustrophobia
   g. other factors limiting compliance with a prescribed MRI study.
2. As an alternative for patients who meet MRI screening criteria: BRCA1, BRCA2 mutations; parent, sibling, or child BRCA+; Lifetime risk of 20-25% established; chest radiation between ages 10 and 30

Monitor neoadjuvant tumor response in patients undergoing preoperative chemotherapy

1. Determine the impact of therapy
2. Surgical planning for residual disease

MIBI

^{99m}Tc-hexakis-2-methoxyisobutylisonitrile, also known as Sestamibi or MIBI, was cleared by the US FDA in 1991 for cardiac perfusion studies. In 1996, breast imaging was added as an indication to the drug package insert following a clinical trial conducted with standard gamma cameras equipped with high-resolution collimators. According to the Dosage and Administration section of the drug package insert, breast imaging is to be conducted using a dose of 740 - 1110 MBq (20-30 mCi). This dose was determined largely by the low photon sensitivity of the imaging systems when equipped with high-resolution collimators. Since that time, several breast optimized gamma camera systems have been developed with three times higher photon sensitivity.

^{99m}Tc-Sestamibi is a 140 KeV gamma ray emitting isotope in a lipophilic cation molecule. It is injected intravenously and is retained in cells by electronegative cellular and mitochondrial membrane potentials.[14-16] Studies show that its accumulation is roughly proportional to blood flow, desmoplastic activity and cellular proliferation and therefore it accumulates preferentially in breast cancers compared with surrounding tissues.[17-19] It is a lipophilic substrate for the P-glycoprotein (Pgp), a cellular efflux pump for various compounds.[20-22] Therefore, Sestamibi exhibits rapid tumor wash-in (within about 2 minutes) followed by a slow tumor washout (over the course of several hours).[23, 24] Based on these factors, imaging can begin within minutes after injection and can continue for up to about 90 minutes post injection, providing ample time for all required views to be conducted before the washout cycle negatively impacts lesion-to-background tracer concentration ratio.

Breast-Optimized Detectors

According to the MIBI drug insert package and to the Society of Nuclear Medicine Breast Scintigraphy Guidelines released in 2004, a high-resolution collimator should be used for imaging with the standard gamma camera systems. This recommendation is due to the relatively large distances between the detector and the breast

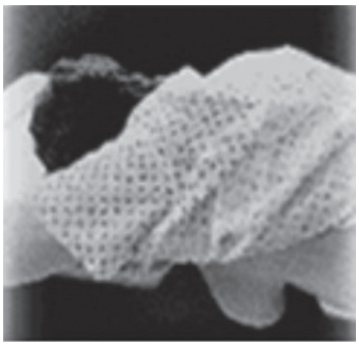

Figure 1: *A patient positioned for breast imaging on a standard gamma camera system.*

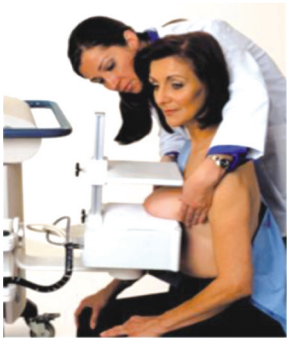

Figure 2: *A patient positioned for imaging on a breast-optimized imaging system.*

Table 1: System sensitivity (counts . min^{-1} kBq^{-1}) comparison using the appropiate collimator and energy window for each system

System	Collimator	Energy window	Sensitivity	Relative sensitivity*
CZt	GE LEHR	20%	3.56	34.2%
Csl SS	DIGIRAD LEHR	20%	3.27	27.2%
Nal PSPMT	Dilon LEHS	-5%/+15%	8.07	100%
Anger camera	Elscint LEUHR	20%	2.89	20.4%

when the patient is in the prone, breast pendent position (Figure 1). The newer, breast optimized imaging systems allow the breast to be compressed directly against the detector system (Figure 2). This close imaging geometry maximizes spatial resolution and allows high-sensitivity collimators to be used.

The Mayo Clinic conducted an analysis of detector performance for a number of commercially available breast-optimized detector systems. These results are shown in Table 1.[25]

Based on these results, the dedicated breast imaging systems provide a photon sensitivity up to 2.79 times greater than the standard gamma camera.

According to more recent publications, the Mayo clinic has continued to improve the design of the CZT detector system and according to data released in 2008,[26] the photon sensitivity of this system is now approximately equal to that of the Dilon 6800. Thus both detector technologies should able to conduct breast imaging using approximately 35% of the usual dose or roughly 259-370 MBq (7-10 mCi).

Dose Reduction Trial

In 2010, Böhm-Vélez et al initiated a prospective, IRB approved, clinical trial to examine breast tissue uptake as a function of injected dose.[27] In their study, patients scheduled for breast scintigraphy as deemed clinically necessary by a referring physician had imaging conducted using a Dilon 6800 Gamma Camera, following the new Society of Nuclear Medicine Practice Guidelines for Breast Scintigraphy With Breast-Specific Gamma Cameras,[28] but with one modification, each patient had a 740 MBq (20 mCi) dose separated into 2 syringes containing either two 370 MBq (10 mCi) doses or a 185 MBq (5 mCi) dose and a 555 MBq (15 mCi) dose. 43 subjects were randomized into receiving a fractional dose of 185 (n=14), 370 (n=14) or 555 (n=15) MBq followed by bilateral cranio-caudal (CC) acquisitions, (Figure 2). Then the remaining fraction of the 740 MBq dose was delivered and a normal 4-view imaging procedure was conducted, including an additional pair of CC images.

A region-of-interest (ROI) encompassing the breast was drawn for each of the CC images obtained from the low-dose and normal dose acquisitions and the mean number of counts per pixel (MCP) was calculated. Following correction of the MCP values for radioisotope decay and biological washout, the MCP of the first (low dose) image was expressed as a percentage of the MCP of the 740 Mbq image for each breast. The left and right breast percentages were averaged and compared to the activity of the first injected dose expressed as a percentage of the total injected dose.

Due to the time delay between first and second injections, corrections for radioactive decay and tissue redistribution, based on the model proposed by Del Vecchio et al[29]

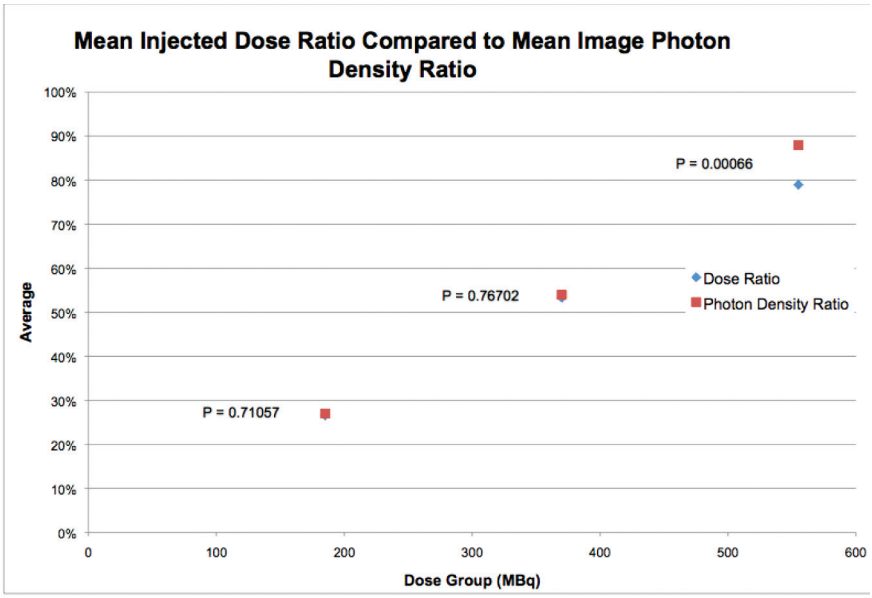

Figure 3: *Graph plotted injected dose ratio compared to uptake ratio*

were applied to the activity of the first dose when calculating the total activity at the time of the second injection.

As illustrated in Figure 3, for the first injected doses of 185 MBq, 370 MBq, and 555 MBq, the difference between the injected dose ratio and the measured uptake ratio was 0.4%, 0.6%, and 8.9%, respectively. Given the null hypothesis of equal uptake, the two-tailed t-test p values for these differences were 0.71, 0.76, and 0.0007, respectively.

These results suggest the uptake of Sestamibi in breast tissue may not be proportional to the injected dose, with decreased proportionality for higher injected doses. From this analysis of breast tissue uptake and image characteristics, it seems that the 555 MBq (15 mCi) dose provides nearly equivalent imaging to that obtained at 740 MBq (20 mCi). In addition, the breast tissue uptake at the lower doses of 370 and 185 MBq (10 and 5 mCi) appears to be more linear relative to the injected dose implying there is no obvious physiologic limitation to using these lower doses. It should be noted however that here is a broad variation in breast tissue uptake of +/- 30% of mean uptake value.

Dose Considerations

From the available data, it appears that these new detector technologies may reduce the dose required to conduct breast imaging with Tc99m-MIBI or dramatically improve image quality compared to those from the standard gamma camera systems using the same 740 MBq dose. Reducing the dose from 740-1110 MBq (20-30 mCI) to 259 -370 MBq (7 – 10 mCi) can reduce patient radiation exposure by nearly a factor of 3; however, as with all radiologic procedures, lower doses increase image noise which will make the visualization of small, low contrast lesions more difficult. The radiation exposure from a 259 MBq (7mCi) injection of MIBI is approximately 2 millisieverts (mSv) and is approximately equivalent to the radiation dose patients receive from the combination of screening and diagnostic mammograms. [30, 31]

It is important to note that while several manufacturers of breast gamma cameras are promoting the use of doses as low as 74 - 148 MBq (2 - 4 mCi) there is no peer-reviewed published clinical data to validate the sensitivity of low dose BSGI/MBI. Of the articles published on BSGI/MBI imaging more than 100 have been conducted using a dose of 740 MBq or more. Table 2 provides a comparison of the radiation dose patients receive from BSGI/MBI and other medical imaging procedures.

Risk

There are several references available to help understand the potential health risks of radiation exposure. The first, according to a statement from the Health Physics Society *"There is substantial and convincing scientific evidence for health risks following high-dose exposures. However, below 5 -10 rem (per year), risks of health effects are either too small to be observed or are nonexistent."*[32] Using a dose of 740 MBq, this equates to approximately 8 BSGI/MBI studies in a single year or 16 in a lifetime. The United States National Institutes of Health's radiation dose risk model estimates the likelihood of a radiation induced cancer from the 740 MBq dose of MIBI to be 24 cancers per 1,000,000 examinations or 0.024%.[33]

Table 2: The radiation dose from BSGI/MBI compared to other diagnostic imaging techniques.

Examination	Administered Dose	Energy window	Sensitivity
Screening MMG 4 view only	n/a	0.44 - 0.7	0.4 - 0.7
Diagnostic MMG	n/a	0.4 - 1.3	0.4 - 1.3
BSGI/MBI	259 - 740 MBq	2.1 - 5.9	0.07 - 0.2
CT chest	n/a	7.8	2.4
Coronary CT (Women)	n/a	10.2	3.5
PET (F-^{18} FDG)	370 MBq	7.2	0.3
CT abdomen and pelvis	n/a	14.7	0.08
PET/CT	185 - 370 MBq	10.0 - 23.0	2.7

Protocol Development

Determining the optimal imaging dose is an important part of establishing an institutional protocol and several factors must be considered. The primary consideration should be a risk vs. benefit analysis based on specific indications. For the typical diagnostic patient, the primary concern should be image quality while for the asymptomatic screening patient; the radiation dose should be minimized. Secondly, one must consider how to address the relatively broad variation of breast tissue uptake. As aforementioned in the dose reduction section, there is a 60% (+/- 30%) variation in breast tissue uptake for any given dose delivered. Therefore the clinician must either choose a dose high enough to ensure good image quality for all patients or be willing to increase imaging time for patients on the low end of the uptake range.

The clinical impact of molecular breast imaging in patient management, a comparison of BSGI and Sono-graphy for patients with negative or indeterminate mammograms.

Objectives

Breast-Specific Gamma Imaging (BSGI) is a diagnostic breast imaging procedure becoming more common in clinical practice. The goal of this work is to quantify the clinical performance of BSGI against that of ultrasound in the management of patients who have a negative or indeterminate mammogram but require additional imaging.

Methods

A multi-center patient registry was maintained for all patients sent to BSGI as part of their diagnostic work up. From the registry data, patients who had a BIRADS 0, 1, 2 or 3 mammogram followed by ultrasound and BSGI were selected for evaluation. The BIRADS rating schematic was used for sonography and a similar, 5-category system was used for the BSGI images. For each modality, the reports were classified as negative BIRADS 0-3, or positive BIRADS 4, 5. Needle biopsy was conducted as deemed clinically necessary and lesions were classified as benign, malignant and high-risk (non-malignant pathologies requiring excisional biopsy). Pathology or a minimum of 6 months of follow up imaging was used as the gold standard.

Results

A total of 190 lesions were evaluated in 188 patients; 155 benign, 27 malignant, and 8 high-risk. BSGI was positive in 24 malignant and 8 high-risk lesions and ultrasound was positive in 17 malignant and 4 high-risk lesions. The overall sensitivity for BSGI and ultrasound was 92% and 60% respectively while the specificity was 80% and 72% respectively. BSGI also performed better than ultrasound in terms of negative and positive value (52% vs. 32%) and (98% vs. 89%) respectively.

Case Report

A 48-year-old with a previous negative biopsy of the right breast noted a dimpling near the nipple of her right breast during breast self-examination. The patient was seen for a mammogram (Figure 4) to evaluate the area of concern. No significant change from mammogram 2 years prior. No mass or spiculated lesion noted at the sight of the subtle dimpling and stable calcifications are noted in the medial aspect. Ultrasound shows a small cyst and a hypoechoic area likely representing scarring from the previous procedure. BIRADS 3. Patient was asked to return for additional imaging in 6 months.

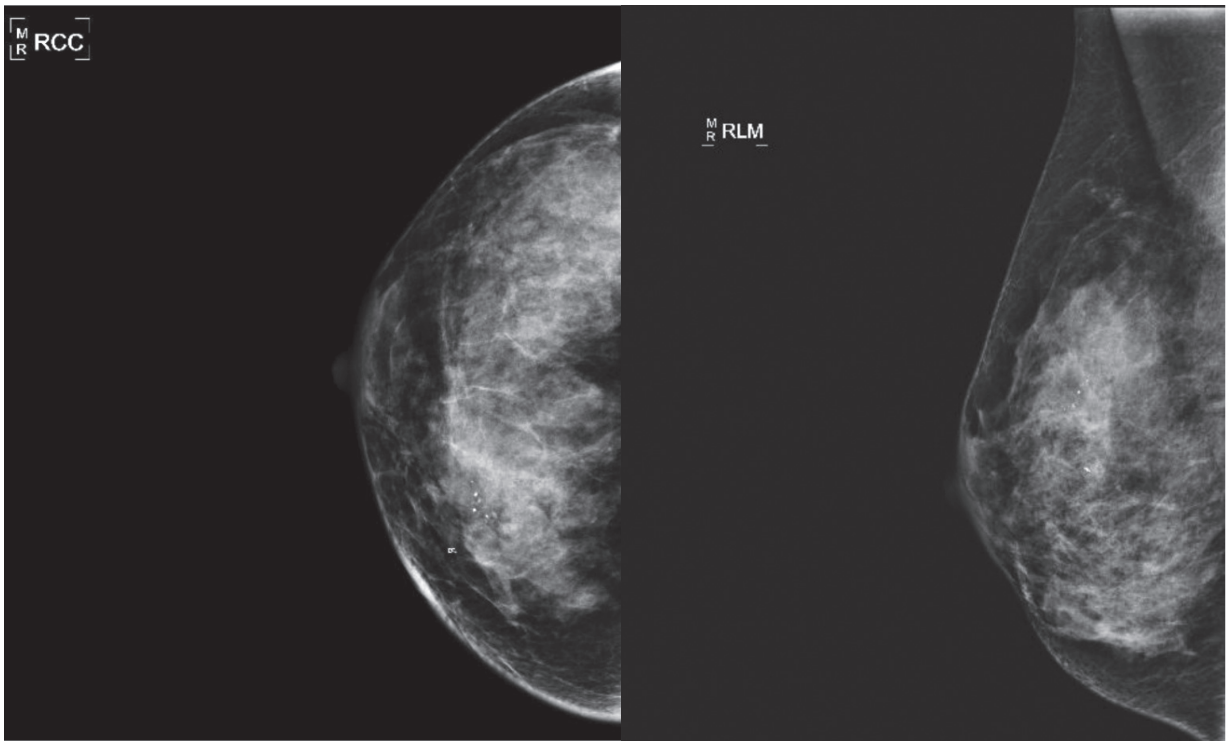

Figure 4: *Mammograms revealed no mass or spiculated lesion noted at the sight of the subtle dimpling and stable calcifications.*

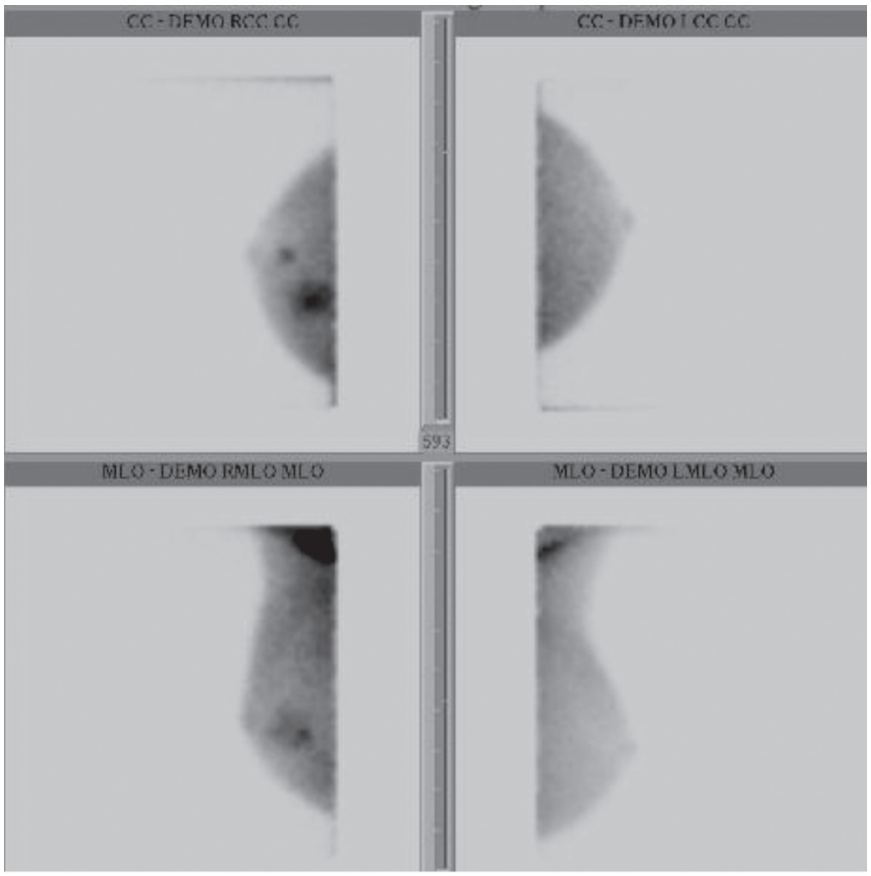

Figure 5: *BSGI showed a large area of increase uptake in the upper inner quadrant and other small intense focus at retroareolar region of the right breast.*

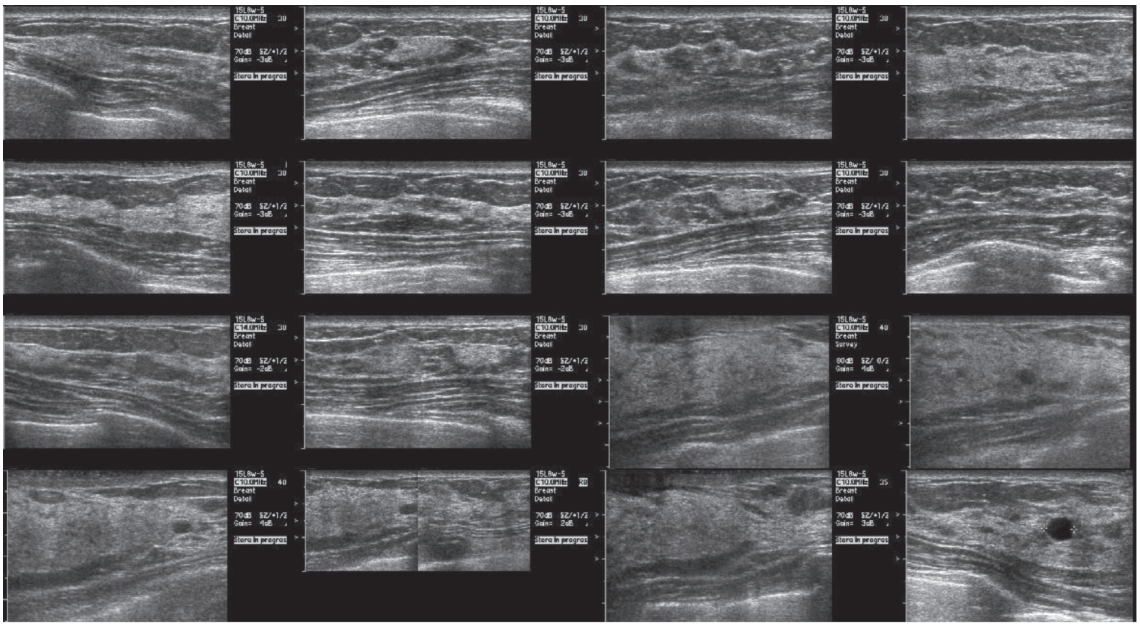

Figure 6: *Second look ultrasound showed irregular hypoechoic mass at 6 o'clock position*

8 weeks later the patient returned reporting an increase in dimpling. Clinical examination and sonographic evaluation of this area were negative leading to the suggestion of a BSGI for additional evaluation.

BSGI was utilized for this patient due to complex dense breast tissue, history of a benign right breast biopsy (upper inner quadrant), and a current complaint of dimpling in her right breast. The area of the palpable mass is stable on mammography and negative in clinical and ultrasonic examinations.

BSGI (Figure 5) of the left breast has normal, uniform distribution. The right breast has a large area of increased uptake in the upper-inner quadrant, measuring approximately 2 cm. A second, smaller and more intense focus is located retroareolar, measuring about 1 cm at the 6 o'clock position. In addition, there are areas of increased activity in the right axilla.

Second look ultrasound (Figure 6) was performed using the BSGI images as a reference and an irregular hypoechoic mass was noted in the 6 o'clock position consistent with the focal intensity noted in BSGI. Biopsy of this area was conducted resulting in a ductal carcinoma dignosis. In the area of the larger medial focal uptake on BSGI, ultrasound demonstrated fibroglandular tissue with complex cysts, but no mass or other distortion.

The large focal intensity noted in the upper inner quadrant of the right breast on BSGI was negative in ultrasound and corresponded to a cluster of stable microcalcifications visualized in the mammogram however, this uptake was still of concern to the surgeon who decided to place a localization wire marking the site of the microcalcifications under mammographic guidance prior to surgery in order to obtain tissue from this site at the time of the lumpectomy procedure for the retroareolar cancer. Pathology of this region revealed a 2 cm ductal carcinoma in-situ.

Conclusion

Patients who have a negative or indeterminate mammogram, but require additional imaging represent a difficult to manage group. This is especially true for patients with radiodense breast tissue which can easily obscure malignancies. Many times additional imaging is requested due to difficulty in interpretation of the mammogram, a lack of confidence in the technical sufficiency of the mammogram or difficulty in correlating radiographic results with clinical signs and symptoms. For this group of patients, BSGI can Figure 5: Second look ultrasound provide better sensitivity for the detection of breast malignancies than ultrasound while maintaining an equivalent specificity. Perhaps most importantly, the high negative predictive value of BSGI (98%) provides the clinician reasonable assurance that malignancy is not present in these difficult cases. Of the 190 patients imaged, 32 (17%) had a malignant or high-risk lesion requiring surgery but not detected by mammography. The theoretical risk for radiation-induced malignancy due to a BSGI study is 0.025% therefore the benefit (17%) substantially outweighs the risk (0.025%) by a factor of 680:1 for this patient population.

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Breast Specific Gamma Imaging (BSGI)/ Molecular Breast Imaging (MBI)

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Keywords:
Breast Specific Gamma Imaging, BSGI, Molecular Breast Imaging, MBI

Breast cancer is one of the most frightening cancers for women because of its high incidence: it is the most common cancer in Thai females. Genetic and environment are both important causative factors, especially the latter. Changing life styles, and increased use of drugs and food supplements have contributed towards the increasing incidence of breast cancer. Early detection of cancer may lead to successful treatment and a longer life span. Teaching women how to examine their own breasts is recommended worldwide to detect abnormal breast mass and cancer. However, the size of the lump, different examination techniques and density of the breast also play a role in detectability.

Mammography currently plays a major role in in breast cancer screening. The sensitivity of screening mammograms in breast cancer detection is 85% or less; 68%, in denser breasts.[1] Nuclear medicine offers additional investigative options which may improve the accuracy of cancer detection. Techniques include breast scintimammography and most recently, Positron Emission Mammograhy (PEM). We have used the Technetium-99m 2-methoxyisobutylisonitrile (Tc-99m MIBI) breast scintimammo graphy for many years with sensitivity ranging from 62%-95.8 % and specificity of 69%-100%.[2-5] Dense fibroglandular breast tissue dose not decrease the sensitivity. However, small lesions, especially where the size is less than 1cm can directly reduce the sensitivity by 35% - 64%. This decreased sensitivity is directly affected by the properties of the collimator. The design of both general purpose and high sensitivity collimators do not generally allow for optimal breast imaging and prohibit the acquisition of standard mammographic views. The development of a high resolution, small field of view, breast-specific, gamma camera improves the sensitivity because this new machine can increase intrinsic spatial resolution and accessibility to the posterior and medial aspect of the breast and can decrease the high scatter radiation from nearby organs such as heart, liver and gall bladder. We can gently press this small gamma camera to the breast to minimize the distance between the breast and detector to improve the resolution.

Tumor imaging with Tc-99m MIBI was first reported in 1987.[6] It is a molecular imaging tool for breast cancer detection, which takes advantage of the functional differences between normal and cancerous tissue. Although the exact mechanism of Tc-99m MIBI cellular uptake is not really known, *"it has been suggested that it may be related to factors such as passive diffusion, plasma membrane electrical potentials, mitochondrial index, and the lipophilic nature of MIBI."*[7] So Tc-99m MIBI imaging has been used to detect various cancers such as lung cancer, osteosarcoma, brain tumors and some benign tumors such as parathyroid adenoma. Before the year 2000, diagnosis of breast cancer and recurrent

brain and lung tumor by using Tc-99m MIBI and Tl-201 chloride were extensively studied. However, in the early 21st century, more pilot studies on high-resolution scintimammography were reported. Brem RF[8] found that BSGI provided better resolution and detectability of lesions than the conventional Single-photon emission computed tomography (SPECT).

The following indications are based on the guidelines for breast scintigraphy with Breast-Specific Gamma Camera 1.0 created by the Society of Nuclear Medicine (SMN) in 2010.

Indications

For patients with recently detected breast malignancy:

1. Evaluation of tumor extension in Staging. Some axillary node metastasis can be demonstrated with scintigraphy.

2. Detecting multicentric, multi-focal, or bilateral disease. (Brem et al[9] reported that BSGI can detect additional suspicious lesions occult to mammography and physical exam in 29% of patients. In another study, 16.7% of patients have multifocal disease. Brem was able to detect an additional 7.2% of occult cancers, which were not seen at the mammographic study.[10]

3. Assess patient response to neoadjuvant chemotherapy.

4. Patients at high risk for breast malignancy.

4.1 Suspected recurrence such as differentiated recurrence of disease from scar.
4.2 Limited mammogram or previous malignancy was occult on mammogram.

5. Patients with indeterminate nature of lesion in breast and malignant is still suspicious.

5.1 Nipple discharge with abnormal mammogram and/or sonographic abnormality.
5.2 Bloody nipple discharge with normal mammogram.
5.3 Significant nipple discharge with unsuccessful ductogram.
5.4 Evaluation of lesions when patient reassurance is warranted (BIRADS 3).
5.5 Evaluation of lesions identified by other breast imaging techniques included palpable and non-palpable lesion.
5.6 Evaluation of palpable abnormalities not demonstrated by mammography or ultra-sound.
5.7 Evaluation of multiple masses demonstrated on breast imaging.
5.8 To aid in biopsy targeting.
5.9 Evaluation of diffuse or multiple clusters of microcalcifications.
5.10 Evaluation of breasts for occult disease in cases of axillary lymph node metastases with unknown primary.
5.11 Unexplained architectural distortion.
5.12 Evaluation of suspicious mammographic finding seen on one view only.
5.13 Evaluation of enhancing areas seen on magnatic resonance imaging (MRI) to increase specificity.

Breast Specific Gamma Imaging (BSGI) can also detect invasive lobular carcinoma, which is the second most common breast malignancy, accounting for about 10% of breast cancers and may be difficult to be detected by mammography. BSGI has the highest sensitivity for detection of invasive lobular carcinoma with sensitivity of 93%, whereas mammography, sonography and MRI showed sensitivity of 79%, 68% and 83% respectively.[8]

In cases of carcinoma in situ, BSGI is a powerful complimentary imaging for the detection of ductal carcinoma in situ (DCIS) with an overall sensitivity of 89.5 percent. In a retrospective study, 55 women with 57 biopsy-proven DCIS lesions were included. All patients had baseline BSGI then image findings were compared to the tissue study from biopsy or excision. The sensitivity for the detection of DCIS were calculated and correlated with size of the DCIS. Of the 38 cases of biopsy-proven DCIS in 34 women, 89.5 percent were detected with BSGI. The findings indicated that the pathologic tumor size of the DCIS ranged from 0.1-3.1 centimeters in 33 cases. BSGI had sensitivity for 1 centimeter or smaller DCIS of 90.5 percent and could detect DCIS as small as 1 millimeter. The sensitivity of BSGI detection of DCIS is comparable to that reported for MRI detection of DCIS (87.9 percent and 92 percent).[10]

6. Patients with technically difficult breast imaging:

6.1 Radiodense breast tissue.
6.2 Implants, free silicone, or paraffin injections compromising the mammogram.
6.3 Post surgical breast.

Dense breast tissue can reduce the sensitivity of cancer detection by mammography because of its high attenuation. The scintimammography has better detection rates because the gamma rays from Tc-99m MIBI can penetrate the dense breast very well. This causes higher sensitivity of cancer detection.

7. Patients for whom Breast MRI would be indicated:

MRI is diagnostically indicated, but not possible
a. implanted pacemakers or pumps
b. ferromagnetic surgical implants
c. risk of nephrotoxicity from gadolinium
d. patients with breasts too large to be evaluated in a breast coil

e. patients with claustrophobia
f. other factors limiting compliance with a prescribed MRI study.

Lanzkowsky et al[11] reported the comparative study of indeterminate lesions detected on the breast by MRI whereby BSGI was able to correctly rule out the need for biopsy or follow up for 35% of cases, correctly identified necessary intervention in 12%, of cases, resulted in no change in management for 29% and accounted for unnecessary biopsy for 24% of cases.

A retrospective review published in 2010 by Brem et al showed BSGI detected additional suspicious lesions occult to mammography and physical exam in 29% of women (46 of 159) with one suspicious or cancerous lesion detected on mammography and/or physical exam. Breast biopsy or surgery demonstrated occult cancer in 35% of women who underwent biopsy because of findings on BSGI, which constituted 9% of all women.[12] Considering the advantages of BSGI over MRI, including cost, ease of study for patients, time of interpretation for radiologists, and the ability to image all women, BSGI is an effective imaging modality in the identification of occult breast cancer.

BSGI is more cost-effective than MRI and can be performed in all patients regardless of claustrophobia, renal insufficiency, metal/cardiac implants or patient weight.

8. Monitoring neoadjuvant tumor response in patients undergoing preoperative chemotherapy.

8.1 Determine the impact of therapy
8.2 Surgical planning for residual disease

Patient precautions

1. No special preparation for the test is needed.

2. Patient should be informed about BSGI process.

3. Known hypersensitivity to 99mTc-sestamibi is a contraindication, extremely rare.

4. Pregnancy is a contraindication

5. The date of last menses or pregnancy and lactation status of the patient should be determined.
   a. BSGI should be performed between day 2 and day 12 of the patient's cycle if possible.
   b. If pregnancy is possible, study should be delayed until onset of menses.

6. Ideally, BSGI should be performed prior to interventional procedures. Breast scintigraphy (BSGI) is commonly used in pre-surgical planning and can effectively evaluate the remainder of the breast tissue in such cases. If performed within 2 weeks after a cyst aspiration/fine needle aspiration, or 3 to 4 weeks after a core or excisional biopsy, it can produce false positive results at the interventional site. This effect is less likely if imaging is conducted within the first 72 hours after needle procedures.

7. There was no significant difference in the likelihood of detection of occult cancer as a function of menopausal status, personal or family history of breast cancer, mammographic parenchymal density, index cancer pathology, or size.

Radiopharmaceuticals

1. 20 mCi of the radiopharmaceutical (Tc-99m MIBI) will be injected via venous catheter or butterfly needle followed by 10 ml of saline to flush the vein.

2. When possible, tracer should be administered via upper extremity vein on the opposite side of the breast with the suspected abnormality or via the peripheral vein of leg.

Protocol/Image Acquisition

1. Patient Position
   a. The patient is seated for the entire scan. Image positions should duplicate standard mammo graphic views according to the most recent mammogram.

2. Imaging
   a. Imaging begins 5-10 minutes after administration of the radiopharmaceutical.
   b. Planar images are acquired for 10 minutes each or 175K, (7 minutes minimum)
   c. Planar images should be acquired for each breast beginning with the side of the suspected.
   d. Four standard views included right and left craniocaudal (CC), right and left mediolateral oblique (MLO)
   e. Additional views which may be asked for by the interpreting physician include 90 degree lateral (LM and ML), axillary tail (AT), cleavage view (CV), exaggerated craniocaudal (XCC), implant displacement (ID), Right Antero-posterior View (axilla), Left Antero-posterior View (axilla).

As for the radiation dose, American people receive an average radiation dose of about 3 millisieverts (mSv) per year from the environment. (13) The average effective dose from two-view screen-film (0.56 mSv) or digital mammography (0.44 mSv) is equivalent to approximately two months of the natural background radiation, while the effective dose from BSGI and Computed Tomography (CT) scan of pelvis and abdomen are 6.2 and 10.0 mSv

respectively. In the recent RSNA meeting in 2011, Breast-specific gamma imaging was presented as having higher sensitivity and comparable specificity when compared with mammography and ultrasound in the diagnosis of breast cancer and can serve as an adjunctive test when the two other methods do not yield a clear diagnosis.

Currently, no one is advocating using the BSGI as a screening method to replace mammography. These exams are typically performed on women with suspicious breast lesions and in women with dense breasts who are difficult to examine with other techniques.

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Current Management of Urinary Tract Infections

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Urinary tract Infections, acute pyelonephritis, cystitis, asymptomatic bacteriuria antibiotics

Urinary Tract Infections (UTIs) are among the most common infections in both the out and inpatient settings. Increasing antimicrobial resistance of urinary pathogens has highlighted the need for reevaluation of the treatment options.[1-3] Since management of UTIs widely varies, these guidelines may help physicians choose cost-effective options. [4-10]

Diagnosing a UTIs often requires examination of a urine sample in addition to clinical signs or symptoms (Table 1). However, many guidelines indicate that a urine culture is not needed in most cases of uncomplicated lower UTI or cystitis.[11, 12] Escherichia coli remains the most common etiologic agent of community-acquired, uncomplicated UTIs, particularly in women under 50 years of age, with Staphylococcus saprophyticus the second commonest. For this reason, in treating uncomplicated cystitis, the first-line empiric antibiotic recommendations are those which are narrow-spectrum and used predominantly only for this indication.

Risk factors in UTIs

Factors of functional and anatomical alterations play the important role in the pathogenesis of UTIs. In women, the shortness of urethra, with its close proximity to the anus, makes it easy for bacteria to ascend the genito-urinary tract. Therefore, fecal-perineal-urethral contamination is the most common cause of UTIs.

Altered vaginal flora (AVF) also plays a similar role in the pathogenesis of UTI in women. Lactobacilli is the dominant bacteria found in the vagina, possessing antimicrobial properties that regulate the local vaginal host defenses, by maintaining an acidic pH and producing hydrogen peroxide. The use of lactobacillus-containing probiotics has been studied as a potential prophylactic for recurrent UTIs. However, the efficacy of this result of UTI prophylaxis remains as yet inconclusive. Alteration in vaginal flora can also be observed in UTIs occurring in postmenopausal women, because estrogen stimulates the proliferation of lactobacilli and reduces local pH.[13-14]

Pregnancy and UTIs.

Bacteriuria is the most common finding in pregnant women. Many studies have shown that upper UTI or acute pyelonephritis is more common in the second or third trimester of pregnant women with asymptomatic bacteriuria. For this reason asymptomatic bacteriuria in pregnant women has to be treated.[15, 16]

Table 1: Definition of terms[20]

Term	Standard definition	Application to management of urinary tract infection (UTI) in elderly patients
Significant bacteriuria	Presence of a specified number (usually > 105 CFU/mL) of a single species of bacteria in freshly voided, midstream specimen of urine.	This level of bacteriuria is significant because it is unlikely that it can be explained by contamination of the urine sample with perineal flora. It DOES NOT indicate clinically significant bacteriuria. "Significant" bacteriuria is often asymptomatic and does not necessarily require treatment. Lower levels may sometimes be significant.
Uncomplicated urinary tract infection	Lower urinary tract infection in an adult woman who is not pregnant and has no underlying abnormality of the urinary tract or indwelling urinary device.	The evidence about effectiveness of short (3 day) courses of treatment for UTI only applies to uncomplicated UTIs. All UTIs in males, all UTIs associated with urinary catheters, and all UTIs with systemic symptoms are complicated UTIs.
Lower urinary tract infection	Infection confined to the tissue of the bladder or urethra. The presence of symptoms or signs of systemic infection indicates upper urinary tract infection.	Both nitrofurantoin and fosfomycin only achieve effective concentrations in the lower urinary tract infection. These antibiotics should not be used to treat patients with systemic symptoms or signs.

Diabetes and UTIs

The risk of developing symptomatic UTI is increased in diabetes.[17] Asymptomatic bacteriuria is also increased in patients with diabetes over a longer duration. However studies showed only a weak correlation between increased risk of symptomatic UTIs and poor control of diabetes and microalbuminuria or macrovascular complications, also, antibiotic treatment did not decrease incidence of symptomatic UTI.[18, 19]

Antibiotic treatment of UTIs [4, 21-23]

An appropriate antibiotic varies according to the following information or criteria:

1. Patient's individual risk
2. Patient's previous antibiotic treatment
3. Pathogen spectrum and susceptibility
4. Pathogen resistance prevalence
5. Drug effects including adverse reactions

Antibiotic of choice for acute uncomplicated cystitis

1. Trimethoprim-Sulfamethoxazole for 3 days is an appropriate choice of therapy in USA, if local resistance rate of uropathogens causing cystitis do not exceed 20% (A-I)

2. Fluoroquinolones : Oflocaxin, Ciprofloxacin and Levofloxacin are highly effective in 3 days regimens (A-I)

In many countries, where the uropathogen resistance to Trimetoprim-Sulfamethoxazole and Fluoroquinolone is high, those agents may no longer be recommended for empiric treatment of UTI.

3. Fosfomycin trometamal, 3 gm sachet, in a single dose is an alternative for those with drug-resistant UTIs, but it appears to be less efficacious when compared with the standard 3-5 days regimen of other antibiotics according to data published. [23, 24]

4. ß-lactam antibiotics, including Cephalosporin (2^{nd} or 3^{rd} generation), and betalactam-betalactamase inhibitors, such as amoxicillin-clavulanate/ampicillin-sulbactam, in 3-7 days regimens are appropriate choices when other agents cannot be used. (B-III)

Antibiotic treatment for acute pyelonephritis

From a clinical point of view, acute pyelonephritis should be considered as tissue infection of the whole urinary tract; whereas an exact anatomical distinction on clinical grounds can often not be made. Blood and urine cultures should always be performed, and initial empirical intravenous antibiotic should be started as fast as possible, due to the somewhat higher incidence of bacteria in adult pyelonephritis. (A-III)

Most patients with acute pyelonephritis require hospitalization and initially intravenously administered empiric antibiotics, such as cephalosporin, fluoroquinolone, aminoglycoside or carbapenem; the choice between these agents should be based on local resistance data. Later, the antibiotic regimen should be tailored on the basis of susceptibility results.

Table 2: Strength of recommendations and Quality of Evidence

Category/grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for or against use
B	Moderate evidence to support a recommendation for or against use
C	Poor evidence to support a recommendation
Quality of evidence	
I	Evidence from ≥ 1 properly randomized, controlled trial
II	Evidence from ≥ 1 Well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from > 1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

NOTE. Data is from periodic health examination. Canadian Task Force on the Periodic Health Examination. Health Canada, 1979.
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The appropriacy of the initial or empirical antibiotic for acute pyelonephritis also depends on the severity of illness at presentation as well as local resistance and comorbidity of patients, and host factors.

For some areas of the world, including Thailand, the prevalence of Fluoroquinolone resistance exceeds 10%; therefore the generally recommended initial antibiotic is a parenteral 3rd generation long-acting cephalosporin, normally ceftriaxone.

Duration of antibiotic therapy for lower UTI

A 3-day course of highly effective antibiotics or tissue-directed antibiotic such as Trimethoprim-Sulfame thoxazole and Fluoroquinolone, is recommended for women and a 7-day course for men.[25] If ß-lactam is used, the duration recommended is 5 days for women, of all ages.

Duration of antibiotic therapy for upper UTI- (acute pyelonephritis)

Most published guidelines recommend a 14 days regimen (A-I),[4, 26-30] however a 7-10 days regimen is also recommended if a highly active agent, such as Fluoroquinolone, is used.

Recently, the Infectious Diseases Society of America in collaboration with the European Society for Microbiology and Infectious Diseases (ESCMID) have systematically updated ISDA clinical practice guidelines for treating acute uncomplicated cystitis and pyelonephritis in women. (Table 2) [4, 32]

Management of asymptomatic bacteriuria

Definition of asymptomatic bacteriuria [33, 34]

1. Asymptomatic women, defined as 2 consecutive voided urine culture with isolation of the same bacteria, counts ≥ 10^5 CFU/ml (B-II)
2. A single, clean-catch voided urine of ≥ 10^5 CFU/ml (B-II)
3. A single catheterized urine of ≥ 10^5 CFU/ml in women or men (A-II)

Asymptomatic bacteriuria is common in many groups of patients with indwelling catheters, where there is a very high prevalence of asymptomatic bacteriuria; such as in patients with spinal cord injury, where the prevalence ranges between 23-89.[35]

Studies have shown that it is worth treating asymptomatic bacteriuria only in pregnant women and patients in whom a urinary tract intervention is intended that may be expected to damage the mucosa.

Conclusion

Urinary tract infections are responsible for a large proportion of antibiotic administrations; bacterial resistance is increasing. For this reason, in treating UTIs, treatment recommendation should take into account to the efficacy of the antibiotics and also, especially factors relating to their sustainability. Asymptomatic bacteriuria should only be treated in a few exceptional cases, such as during pregnancy or before genitourinary tract interventions.

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Questions of Urinary Tract Infections

Q1. Which of the following duration of antibiotics for treatment of uncomplicated cystitis is not correct?

a. 3 days of Fluoroquinolone is adequate
b. 5 days of oral Cephalosporin is adequate
c. Single dose of Fosfomycin trometamol is effective
d. Single dose of Parenteral Ceftrioxane is effective
e. 5 days of Amoxycillin-Clavulanate is effective

Q2. What is the most appropriate and cost-effective parenteral antibiotic for acute pyelonephritis?

a. Cefuroxime
b. Ceftazidime
c. Ceftotaxime
d. Ceftriaxone
e. Ampicillin-Sulbactam

Q3. In which of the following patients does asymptomatic bacteriuria need to be treated with antibiotic?
a. Diabetes Mellitus
b. The elderly
c. Pregnant women
d. Hypertension
e. Spinal cord injury

Q4. Regarding duration of antibiotic in acute pyelonephritis, which of the following is not correct?

a. Based on current evidence, 14 days is recommended for most antibiotics
b. If Fluoroquinolone is used, 7-10 days is probably adequate
c. If 3rd generation Cephalosporin is used, 7-10 days is adequate
d. If Amoxycillin-Clavulanic is used, 14 days is recommended
e. In bacteremic patient, duration should be more than 14 days.

Q5. Duration of antibiotic therapy for UTI could be shorter if using tissue-directed antibiotic(s) such as…?

a. Ciprofloxacin
b. Cefdinir
c. Cefditoren
d. Levofloxacin
e. Amoxicillin-clavulanate

Answers of Urinary Tract Infections

Answer 1: d. Duration of treatment of uncomplicated cystitis with any ß-lactam recommended by most authors is 3-5 days.

Answer 2: d. Ceftriaxone is the most cost-effective parenteral antibiotic, due to good PK-PD against uropathogens.

Answer 3: c. From many published studies, antibiotic treatment is only beneficial in pregnant women with asymptomatic bacteriuria.

Answer 4: e. From many published studies, duration of antibiotic in bacteremic adult pyelonephritis did not differ from non bacteremic patients.

Answer 5: a and d. Fluoroquinolones are tissue-directed antibiotics with high tissue and urine concentration, so called good PK/PD, bactericidal: for this reason duration could be shorter than ß-lactam.

Mass at Vocal Cord

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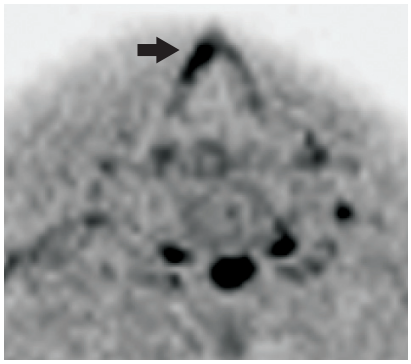
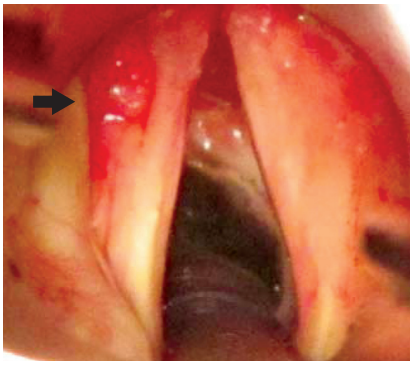


A



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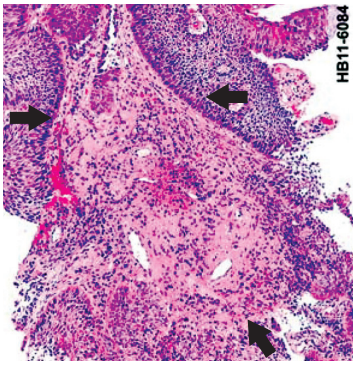

C

A 79-year-old man man presented with hoarseness since 3 months, he was a heavy smoker for many years. Indirect laryngoscopy was unable to demonstrate the lesion. MRI-Diffusion Weighted pulse sequence at vocal cord (Figure A) revealed localized hyper intensity (reversed image) at anterior one third of left vocal cord.[1] The patient underwent general anesthesia. Then a direct laryngoscopy revealed the tumor. Exoplytic mass at anterior haft of left vocal cord is shown in Figure B. Anterior commissure appears intact. The microscopic examination (Figure C) revealed neoplastic proliferation of squamous epithelium of larynx with atypia. There was evidence of early invasion into subepithelial tissue.

This example illustrates the usefulness of DW pulse sequences, which can make abnormalities in certain pathologies more obvious,especially for identifying small tumors at the vocal cord, as in our case.

Reference

1. Mass CL, Mukherjee P. Diffusion MRT. Apply Radiology 2005;45-60.

Book Review

Neuroradiology Companion

Methods, Guidelines, and Imaging Fundamentals, 4th Edition 2012

Mauricio Castillo, MD: The University of North Carolina School of Medicine, Chapel Hill, North Carolina

Publisher: Lippincott Williams & Wikins, a Wolters Kluwer Health business

Reviewer: Chirotchana Suchato, MD[1] and Rergchai Varatorn, MD[1]

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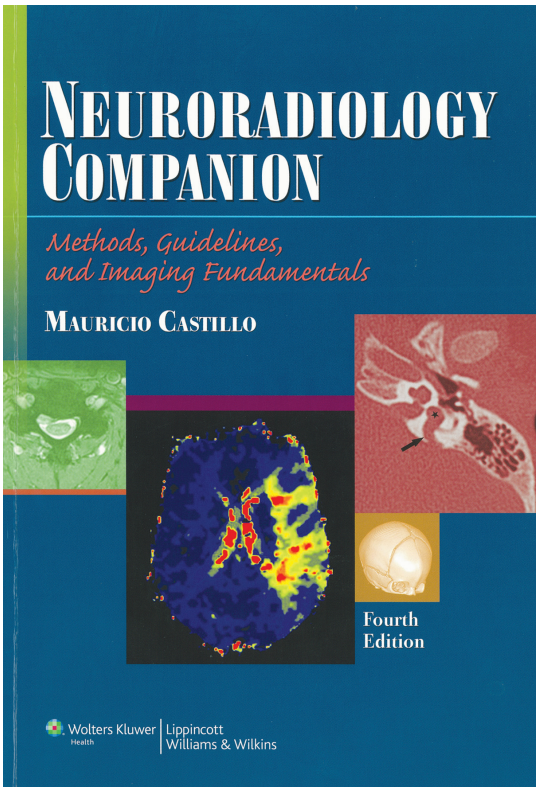

In 1995, Dr. Castillo wrote the first edition of this unique book, which provides a basic overview of all areas of neuroradiology. Now in 2012, we are pleased to see an expanded and updated 4th edition. This paperback is of 2.4 cm thickness, with 605 pages covering key facts and useful information in bullet form for each disorder. The first part is entitled *"Imaging protocols and guidelines"* and covers CT, MRI, myeolography, digital subtraction angiography (DSA), sedation and anxiolysis protocols, medications in neuroradiology and sample dictations. This section is very valuable as a reference aid in daily practice. Sedation and anxiolysis protocols are also described as well as medications and management of contrast media reactions. The sample dictations of normal findings in MR, CT, can indeed serve as a template, which can be adjusted to the particular institution's protocol, so this section will be particularly useful for trainees.

Part two of the book deals with *"Imaging fundamentals"* of the brain, spine and head & neck. As for the descriptions of congenital malformations, the examples of each condition are easy to understand but because of brevity, may lack some details. The interpretation for CT or MR perfusion for management of each patient should be clarified more clearly. There is no description of technique with relation of CT to MR perfusion or MR spectroscopy, and few examples are given of using MR perfusion to assess cerebral infraction or tumors. The chapter on brachial plexus has excellent and clear illustrations. We can nevertheless imagine that this section would be a good companion for emergency physicians with little imaging experience, helping them to distinguish between conditions in the absence of an available consultant, such as on night shift.

Overall, we highly recommend this book as a very good reference for trainees in neuroradiology, and indeed imaging radiologists and technicians in general. We give part one 9 out of 10 for its brief and clear summary points. Most of the illustrations are new, and there are more images per entry than in the 3rd edition. Other reviewers were critical but we appreciate that there is plenty of space left for the reader to add notes and salute Dr. Castillo who is an excellent teacher for all of us.

Bangkok Health Research Center (BHR Center)

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Interesting News

Feb 10, 2012

1. **The Global Task Force on Expanded Access to Cancer Care and Control** in Developing Countries published a report which details a comprehensive action plan on expanded access to cancer treatment with practical suggestions that will have advantages beyond cancer care alone. Parallel to other recommendations, the report highlights a number of interventions in six areas of the cancer management and control and outlines key concepts, including innovative delivery of care, improvement of access to affordable medicines and vaccines. From **The Lancet**

Source: *The Lancet, **Volume 378, Issue 9803**, Page 1605, 5 November 2011*

2. **The European Centre for Disease Prevention and Control** (ECDC) has reported the data on antibiotic resistance. The report details a significant increase in the percentage of carbapenem-resistant Klebsiella pneumonia. In addition, EU member states have found that 15%-50% of K pneumonia from bloodstream infections are resistant to carbapenems. From **CIDRAP,** also **The Telegraph (UK)**

Source: *http://www.cidrap.umn.edu/cidrap/content/other/news/nov1711antibiotic.html http://www.telegraph.co.uk/health/healthnews/8896015/Superbugs-are-becoming-untreatable-doctors-warn.html*

3. USA Today reported that researchers are supposed to have established that the change in the levels of specific components of the cerebrospinal fluid (CSF) in the brain and spinal cord antedate the onset of Alzheimer's Disease (AD) by five to ten years. The results from the study on patients diagnosed with mild cognitive impairment, showed that about 54% of the patients went on to develop AD, whereas 16% were diagnosed with different forms of dementia. From **USA Today (US)**

Source: *http://yourlife.usatoday.com/health/story/2012-01-03/Changes-in-cerebrospinal-fluid-may-signal-early-Alzheimers/52354378/1*

4. Researchers from France found that absence of a key protein, FKBP52, and the accumulation of amyloid plaques outside neurons, may be used as an initial signal for Alzheimer's Disease (AD) and other Tau Diseases. In addition, the study reported that, researchers were able to stall the disease progression by boosting the FKBP52 protein. One suggests that FKBP52 is the best drug target reception that has been identified so far against AD. From **Google News**

Source: *http://www.google.com/hostednews/afp/article/ALeqM5iXH-OUin3LrrWy26r7f2bVt8ce7Q?docId=CNG.0239284d58d24d0a964e617e235750cd.411*

5. **The US Centers for Disease Control and Prevention's** Advisory Committee on Immunization Practices has published the 2012 recommendations about the 'routine' Human Papilloma Virus (HPV) vaccination for all boys aged 11-12 years and a 'scale-up' vaccination for

males aged 13-21 years. From **CBS News (US)**

Source: *http://www.cbsnews.com/8301-504763_162-57371255-10391704/hpv-vaccine-now-recommended-for-all-boys-cdc-says/*

6. Macmillan Cancer Support has reported that in UK, all types of cancer have improved the mean survival from one year to six year in 1970s and 2007, respectively. However, this information also had a highly variation between the natural history for different types of cancer, with impressive improvements highlighted in bowel and breast cancers and almost no improvement found from lung, brain and pancreatic cancer. From **Daily Mail (UK)**

Source: *http://www.dailymail.co.uk/health/article-2064659/Cancer-sufferers-surviving-times-longer-1971.html?ito=feeds-newsxml*

7. Mefloquine is the anti-malarial drug, has banned by the US Army because of its adverse effects related to psychiatric and physical, after it invented for four decades. **In addition**, it was found that over the past three years, the US Army **decreased** the amount of mefloquine it **prescribes** by **75%**, with **spending** on the drug **dropping** from USD 1.8 million in 2009 to around **USD 50,000** this year. From **USA Today (US)**

Source: *http://www.usatoday.com/news/military/story/2011-11-19/military-malaria-drug/51311040/1*

In Memorial - Professor Dr. Somchart Lochaya

Professor Dr. Somchart Lochaya, M.D., FACC, FRCP (C) can be best described as a good person who dedicated himself to creating benefits and happiness for his beloved family, friends, patients and homeland. He was a positive role model for many medical staff because he was successful in his work and also enjoyed a rich domestic life: sadly, many successful doctors rarely achieve both well being in family life and career triumphs.

He was born on 25th December, 1934 in Chiang Mai, Thailand. His surname was bestowed upon the family by His Majesty King Phra Mongkut Klao Chao Yuhua (King Rama VI). *"Lochaya"* was a combination of his grandfather's name *"Loch"* and his grandmother's name *"Aya"*. His father, Phra Chuang Kashetra Silprakan (Mr. Chuang Lochaya), was known as *"The Father of Maejo Agriculture"* at the Maejo University in Chiang Mai. His mother was Khunying Sam-ang Chuang Kashetra Silprakan.

Prof. Dr. Somchart Lochaya began to study medicine at Siriraj Medical School in 1955 and graduated in 1959. During this period, his father had been appointed as Cultural Ambassador and was working in the Office of Educational Affairs at the Royal Thai Embassy in Washington D.C. For this reason, Prof. Dr. Somchart decided to do his internship and medical residency at the Providence Hospital in Washington. In 1961, he moved to the Lemuel Shattuck Hospital, Boston continuing his residency for another 2 years. Prof. Dr. Somchart actually longed to be a surgeon but this was impossible due to his unfortunate allergy to the pre-operative hand cleanser used at that time. He decided instead to specialize in cardiology and internal medicine.

Between 1963 and 1965, he joined the fellowship program in Cardiology at Chicago's Michael Reese Hospital. In 1965, he was appointed as the Head of Clinical Hemodynamic Laboratory, Department of Medicine, Ottawa Civic Hospital, Ontario, Canada. In 1967, he achieved Diplomate of the American Board of Internal Medicine and the year later, Diplomate of the American Board of Cardiovascular Disease; he also became a fellow of the Canadian Royal College of Physicians and Surgeons.

In 1969, after a total of seven years in the United States and three years in Canada, he decided to come back to Thailand, because his father needed to undergo a cholecystectomy. Upon his return, he entered the Thai government service at the Faculty of Medicine Ramathibodi Hospital, Mahidol University in Bangkok. He also established a private clinic in Ladya Road, close to his home, naming it the *"Dr. Somchart Clinic"*. Many local newspapers wrote about him extensively because he was the first Thai physician at that time to have achieved an American Diplomate in both Internal Medicine and Cardiovascular Disease. His reputation grew, spreading dramatically by word of mouth.

After having taught Thai medical students for 16 years, he was a natural candidate to be an editor of the first cardiovascular textbooks that were composed and published in Thai language. The two textbooks became very famous because the details were clearly explained and thus easy to understand. They were offered to His Majesty King Bhumipol Adulyadej. His Majesty graciously distributed these textbooks to every district hospital in Thailand for public usage and medical reference.

In 1982, Prof. Dr. Somchart Lochaya had a chance to provide medical assistance to His Majesty King Bhumibol Adulyadej. Thereafter, he also followed His Majesty to remote areas and provided medical services to patients there. He held the King in the utmost esteem and was willing to endure any sacrifice to assist with the multifarious duties of His Majesty.

After 18 years working in a government hospital, Prof. Dr. Somchart understood well that the development of an excellent heart clinic in a competent private hospital could afford relief to patients from heart disease, and would reduce the risks they were exposed to when they travelled abroad for treatment. Therefore, in 1987 Prof. Dr. Somchart decided to join Bangkok Hospital. Bangkok Hospital made huge investments in both people and state of the art technology in order to develop its Heart Clinic into a one-stop service Heart Center. This was one of the turning points in Bangkok Hospital's history, as it became more clearly differentiated from other private hospitals and its reputation increased accordingly. The grand opening of Bangkok Heart Center (BHC) was held on 26th January, 1989 and the then Prime Minister Chuan Leakpai served as the honorary Chair of ceremonies.

Over 10 years, Prof. Dr. Somchart and other team physicians at the BHC provided seamless medical treatment to more than 10,000 heart disease patients. The Professor took many responsible positions both in Bangkok Hospital and network hospitals, and various local organizations in Thailand. Prof. Dr. Somchart was well known for his competent medical skill, but was also loved for his generous personality. He was very friendly and never short of a sincere smile for the people surrounding him. His laugh was unique and easily recognizable. Although he worked very hard he never exhibited signs of weariness or discouragement. This was probably because he was lucky to have found a good balance between work and his beloved family.

Prof. Dr. Somchart passed away peacefully at the age of 66, on Monday 10th April, 2000 at Ramathibodi Hospital, Bangkok, Thailand after being diagnosed with acute leukemia. He was survived by his widow, M.R. Sasijuthapa Worrawan and 3 sons, Mr. Swechuk Lochaya, Mr. Khumsap Lochaya, and Mr. Jomsap Lochaya.

Bangkok Hospital members remember Professor Dr. Somchart Lochaya's untiring efforts and endeavors with heartfelt gratitude and sincere appreciation.