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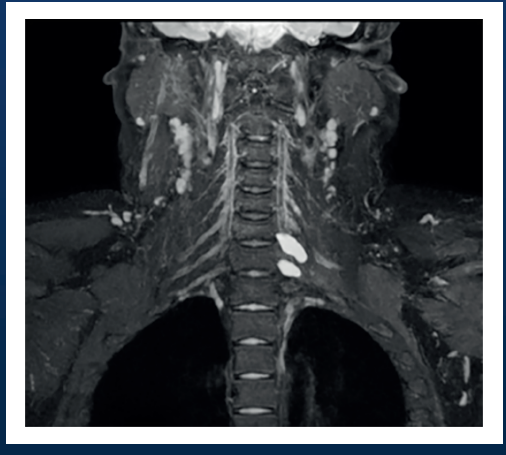
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Agreement between Emergency Physicians and a Cardiologist on Cardiac Function Evaluation after Short Training

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ABSTRACT

Objective: Delayed diagnosis and treatment of shock patients may lead to multiorgan dysfunction syndrome and death. Volume status assessment in shock patients is crucial for guiding early management. Focused echocardiography has become an important tool for assessing volume status because it is non-invasive and easy to perform. We aimed to ascertain the degree of agreement between emergency medicine (EM) residents and a cardiologist on cardiac function evaluations using echocardiography. We also assessed the extent of agreement on pericardial effusion diagnoses.

Methods: A cross sectional study was conducted at the Emergency Department, Siriraj Hospital. The EM residents who had limited experience in ultrasound examination underwent a 3-hour echocardiography training course consisting of a lecture and a workshop before starting the study. Patients with shock or suspected hypervolemia were included. Echocardiography was performed by EM residents to evaluate ventricular function of each patients. With visual estimation, they classified the left ventricular function (LVF) into 3 categories: good, moderate and poor. The video files were recorded and re-evaluated by a cardiologist offline. The correlation of left ventricular function estimation and the diagnosis of pericardial effusion between the two operators were determined.

Results: Ninety-two patients were enrolled between October and December 2014. The overall agreement of ventricular function assessment between the EM residents and the cardiologist was 79.4% (weighted kappa = 0.73). The degree of agreements of LVF classified as poor, moderate and good LVF were 87.5%, 37.5% and 95% respectively. Moreover, the residents diagnosed the pericardial effusion with 100% accuracy, compared to the cardiologist.

Conclusion: Following a short educational training, the EM residents efficiently assessed the left ventricular function with a high level of agreement with a cardiologist.

Keywords: Cardiac function evaluation; limited echocardiography; volume assessment (Siriraj Med J 2019; 71: 253-260)

INTRODUCTION

Delayed diagnosis and treatment of shock can lead to multi-organ dysfunction syndrome and possibly death. In general, shock can be classified into four categories[1]: hypovolemic, distributive, cardiogenic, and obstructive. The different types of shock need different approaches to the management of volume resuscitation. Most types of shock improve with fluid bolus except cardiogenic shock, for which fluid bolus may be harmful. Therefore, a left ventricular function (LVF) assessment is one of the important

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initial steps in deciding whether to give fluid. Cardiogenic shock should be considered if the LVF is poor, but fluid should not be given for that condition. Furthermore, performing an accurate volume status assessment is one of the critical steps in effectively and safely managing shock, and it results in a decrease in mortality.[2,3] However, volume assessment using only a physical examination has some limitations, for example, in overweight patients or when it is performed by inexperienced physicians.[4] Moreover, a physical examination alone is inadequate for differentiating hypovolemic from cardiogenic shock.[5] A chest radiograph is another measure used to evaluate volume status; however, it might not be feasible for use with some overweight patients or those who cannot inspire deeply. Even when interpreted by a radiologist, the sensitivity of chest radiographs has been found to be only 53%, with an accuracy of only 68% for diagnosing acute congestive heart failure.[6]

Nowadays, point-of-care ultrasound (PoCUS) has become an important tool for assessing the LVF and volume status because it is non-invasive, is easy to perform, and can be used to perform a dynamic assessment of fluid responsiveness in critically-ill patients.[7] Moreover, the combination of PoCUS applications, which are inferior vena cava variation, lung ultrasound, and focused echocardiography, may enable physicians to give more accurate fluid therapy.[8] Many studies have shown that echocardiography is comparable to other invasive methods, such as central venous catheterizations and pulmonary artery catheters, in terms of cardiac function assessment and fluid treatment guidance.[9,10] Furthermore, focused echocardiography performed within 15 minutes of Emergency Department (ED) arrival significantly reduces errors in diagnosing shock patients.[11]

Previous studies have shown that emergency physicians (EPs) have been able to assess the LVF by visual estimation with a high degree of agreement with cardiologists (> 80%).[12,13] However, the investigators in those studies were experienced EPs or emergency medicine (EM) residents who had used PoCUS for at least 150 cases each. At our institution, which is the largest tertiary hospital in Thailand, EM is still a relatively new department, having been established for less than 10 years. Although the usage of ultrasound in the ED is becoming more common, the number of experienced operators is limited.

This study aimed to evaluate the ability of EM residents with limited experience to evaluate the LVF using echocardiography. To this end, we aimed to ascertain the level of agreement between the EM residents and a cardiologist on cardiac function estimations. Furthermore, we assessed their agreement on pericardial effusion diagnoses as well as evaluated the appropriateness of the echocardiographic views and the time taken for the residents to complete the scans.

MATERIALS AND METHODS

A cross sectional study was conducted between October and December 2014 at the Emergency Department, Siriraj Hospital. The hospital, located in Bangkok, is the largest tertiary care university hospital in Thailand. We enrolled patients aged over 18 years who needed a volume status assessment. The conditions with which the patients would require an assessment of the LV function were 1) shock (systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg); and 2) suspected heart failure, defined as having at least 1 of the Framingham criteria.[14] Patients were excluded if they were uncooperative or had an ST-segment elevation myocardial infarction. Intubated patients were excluded because of the difficulty of placing the patients in an appropriate position for scanning. Patients for whom focused echocardiography might delay their standard treatment were also excluded. This study was approved by Siriraj Institutional Review Board (Si 546/2014) and complied with the Code of Ethics of the World Medical Association.

The study investigators who performed the ultrasounds in this study were second- and third-year EM residents. The residents had been working in the ED for less than 3 years. They had not participated in any formal ultrasound training courses because emergency ultrasound was not part of the EM curriculum.

We arranged our study into two phases: training and data collection. In the training phase, we provided a focused echocardiography course for the residents. This course consisted of a 2-hour lecture and a 1-hour hands-on workshop conducted by a cardiologist. After the course, each participant had to practice on at least two patients in the ED. All recorded images and video files of the practice were subsequently sent to the cardiologist to assess the residents' ability to perform focused echocardiography. The cardiologist had to approve each participant's performance before he or she was permitted to proceed to the next phase.

During the data collection phase, the attending EP staff assessed the eligibility of patients. If the patients met the inclusion criteria, written, informed consent was obtained. They then notified a study investigator (i.e., one of the 2nd or 3rd year EM residents who had attended the training course) who was not the primary treating physician of the patients to perform focused

echocardiography. The patients were scanned in the supine position for as long as they could tolerate. A Philips HD15 PureWave ultrasound machine was used in this study. The LVF was assessed using parasternal long axis, parasternal short axis, apical 4-chamber, and apical 5-chamber views with an S5-2 phased array transducer (5-1 MHz). The LVF was categorized into three groups, based on the left ventricular ejection fraction (LVEF): normal/good (LVEF > 55%), moderate (LVEF 30%-55%) and poor (LVEF < 30%). Pericardial effusion was also assessed using the subxiphoid view with a C 5-1 convex array transducer (5-1 MHz). The patients' baseline characteristics and details of the medications or inotropic agents administered to the patients in the ED were also recorded. All images and video files of the focused echocardiographic findings were sent to the cardiologist to assess the LVF and appropriateness of the echocardiographic views. The cardiologist was blinded to the patients' clinical information, the identity of the study investigators, and their results.

Sample size calculation

From a previous study by Randazzo[13], the kappa statistic of agreement between EPs and cardiologists on cardiac function evaluation was 0.71. With a confidence interval of 95% and a margin of error of 5%, a sample size of 88 patients was required (nQuery Advisor). After adding 10% to adjust for potential missing data, the final total sample size was 97.

Statistical analysis

We used SPSS Statistics for Windows, version 18.0 (SPSS Inc., Chicago, Ill., USA) to analyze the data. Frequency and percentage were used to describe the categorical data. Mean and standard deviation were used to describe continuous data with normal distribution. Median and interquartile range were used to describe data with non-normal distribution. The kappa statistic and 95% confidence interval were used to assess the degree of agreement between the EPs and the cardiologist on the LVF evaluations. Fisher's exact test was used to find the factors that affected the correlation.

RESULTS

A total of 101 patients were assessed for eligibility between October and December 2014. Of those, 9 (8.9%) were excluded due to incomplete data, leaving 92 patients. Forty-one patients (44.6%) presented with hypotension, and the remaining 51 patients (55.4%) were suspected to have hypervolemia based on the Framingham criteria. The patients' mean age was 67 years, and the mean systolic blood pressure was 108 mmHg. The baseline characteristics are shown in Table 1. The focused echocardiography was performed by four second-year and three third-year EM residents.

The residents classified the patients' LVF as "good contraction" in 60 patients (65.2%), "moderate contraction" in 24 (26.1%), and "poor contraction" in 8 (8.7%). The cardiologist classified the patients as having good, moderate, and poor contraction in 69 (75%), 12 (13%), and 11 (12%) patients, respectively (Table 2). The overall agreement on the LVF assessments by the EM residents and the cardiologist was 79.4%, with a weighted kappa of 0.73 (95% CI 0.58-0.89). The patients with a moderate contraction represented the majority in the disagreement category (Fig 1). No factors affected the correlation of the cardiac function evaluations. The studied factors included a BMI of more than 23 kg/m^2 and inotropic drug use. The agreement between the EM residents and the cardiologist on the pericardial effusion diagnoses was 100%.

The most appropriately performed views were the subxiphoid and inferior vena cava views (94.6%). The least properly performed view was the apical 5-chamber (Fig 2). The EM residents were able to achieve all appropriate views in 47 patients (51.1%; Fig 3). None of the following factors had an effect on the appropriateness of the echocardiographic views: being overweight, the operators, and patients having congestive heart failure.

The final diagnoses are detailed in Table 3. The most common cause of shock was sepsis or septic shock (92.6%). The lowest level of agreement on LVF evaluation was found in patients with pneumonia (42.9%); however, there was no statistically significant difference from other diagnoses. The mean time taken for the residents to perform the focused echocardiographies was 19.8+7.1 minutes.

DISCUSSION

In our study, EM residents with limited experience in focused echocardiography were able to assess the LVF by visual estimation alone with a high level of agreement with a cardiologist (weighted kappa = 0.73) and after only a short training course. This result is similar to the findings of previous studies, which also reported a high level of agreement between experienced and inexperienced scanners.[9,12]

We categorized the LVFs into three groups using visual estimation because this method was easy and not time-consuming. Moreover, previous studies have shown no clinical difference between LVF assessments by visual estimation and other complex methods.[15,16]

TABLE 1. Baseline characteristics.

Baseline characteristics	N = 92 (%)
Age (mean ± SD; years)	68 ± 14
Sex (males)	39 (42.4)
BMI† ≥ 23 kg/m^2	36 (39.1)
Comorbidities	
Hypertension	50 (54.3)
Diabetes mellitus	34 (37.0)
Heart disease	26 (28.3)
Others	9 (9.8)
SBP‡ (mean ± SD; mmHg)	108 ± 30 (50–190)
HR‡ (mean ± SD; bpm)	90 ± 21 (49–153)
Inotropic drugs	
Dopamine	2 (2.2)
Norepinephrine	6 (6.5)
Indication	
Hypotension	41 (44.6)
Suspected hypervolemia	51 (55.4)
Performer	
Resident 2	27 (29.3)
Resident 3	65 (70.7)

†BMI: Body Mass Index; BMI ≥ 23 kg/m^2 represents being overweight[15]
‡while performing focused echocardiography

TABLE 2. LVF categorizations by EM residents and cardiologist.

	Cardiologist		
Emergency Physicians	**Good contraction no. (%)**	**Moderate contraction no. (%)**	**Poor contraction no. (%)**
Good contraction no. (%)	57 (95.0)	3 (5.0)	0 (0)
Moderate contraction no. (%)	11 (45.8)	9 (37.5)	4 (16.7)
Poor contraction no. (%)	1 (12.5)	0 (0)	7 (87.5)

TABLE 3. Final diagnoses and correlations for LVF evaluations.

Final Diagnosis	Correlation (%)	No correlation (%)
Hypotension (n = 45)		
Severe sepsis/septic shock	26 (92.9)	2 (7.1)
Hypovolemic shock	5 (62.5)	3 (37.5)
Cardiogenic shock	2 (100.0)	0
Unknown	7 (100.0)	0
Suspected hypervolemia (n = 47)		
Congestive heart failure	28 (77.8)	8 (28.6)
Pneumonia	3 (42.9)	4 (57.1)
Others	3 (75.0)	1 (25.0)

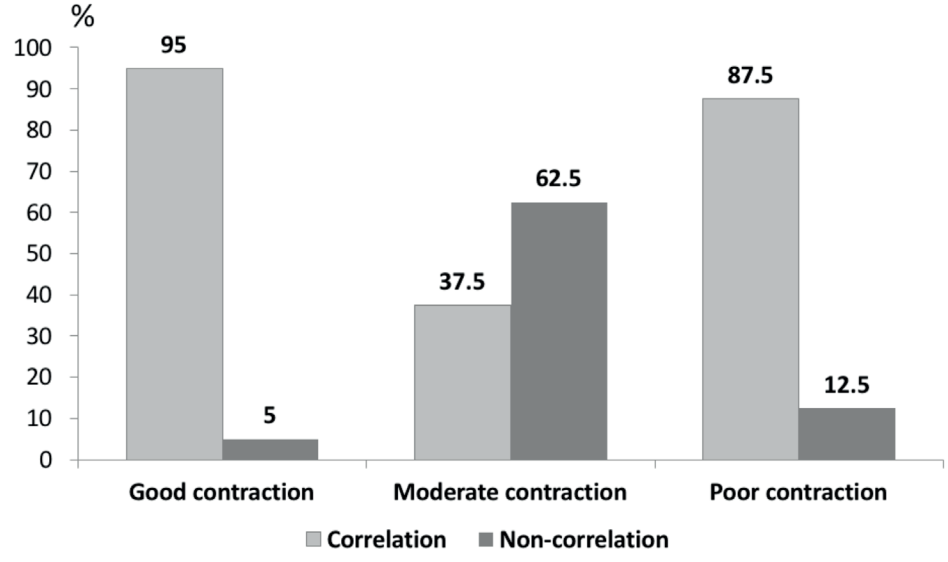


Fig 1. Percentage of correlation between EM residents and cardiologist in LVF assessment.

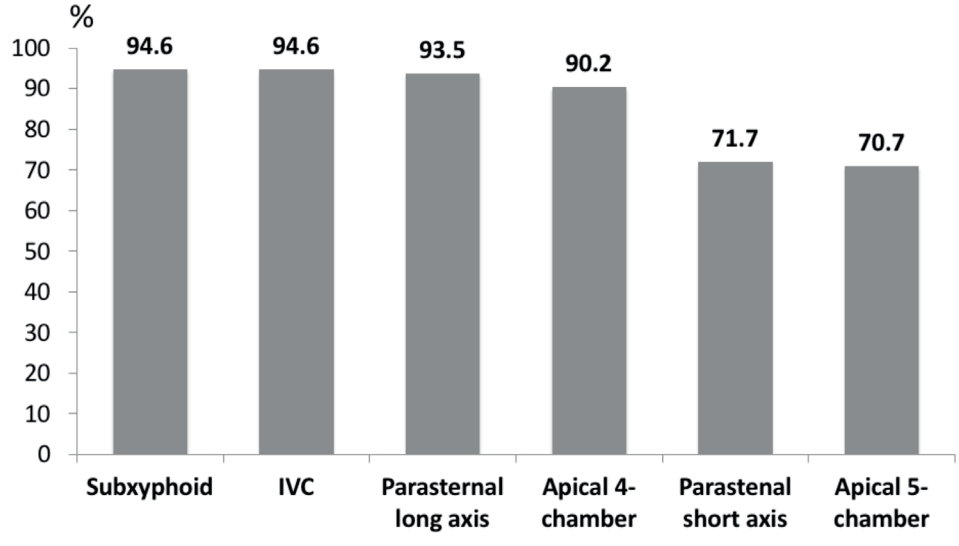


Fig 2. Appropriateness of each echocardiographic view.

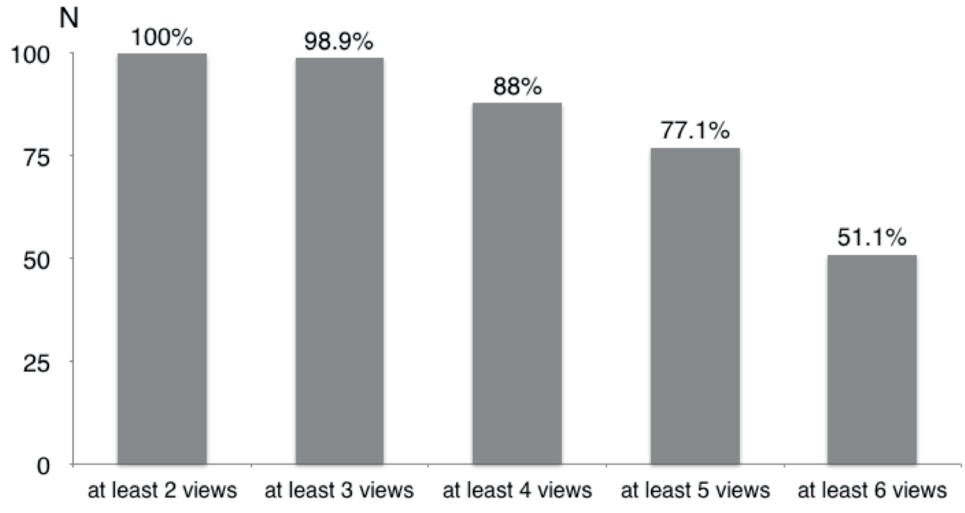


Fig 3. Percentage of appropriateness of echocardiographic views.

The credentials for performing PoCUS differ from country to country. In the United States, the American College of Emergency Physicians requires a physician to perform PoCUS in at least 25 cases in order to be qualified.[17] In contrast, the British Society of Echocardiography requires at least 250 scans and a written examination to be passed for emergency physicians who want to perform echocardiography.[18] In Australia, the Australasian College for Emergency Medicine requires 50 examinations of bedside echocardiography and a pass in a practical bedside examination.[19] In Thailand, the Emergency Medicine Residency training program was established in 2004; to date, however, no specific requirement regarding PoCUS training has been included in the curriculum. As a result, the EM residents in our study had various levels of experience in focused echocardiography. Accordingly, our results might indicate that after proper training, even performers with limited experience in PoCUS are able to assess the LVF with comparable accuracy to a cardiologist.

The duration of the didactic sessions and practice has varied from study to study, ranging from web-based learning to 12-hour, didactic lectures.[12,13,20,21] Similarly, the practice session duration has ranged from 5 scans of real patients to a 10-hour observation and practice.[12,13,20,21] In our study, the training session comprised only 2 hours of lecture and 1 hour of practice. Therefore, our findings suggest that a short training session could also enable physicians with limited PoCUS skills to achieve a high level of agreement with an expert. However, it might have been because the EM residents in our study were not blinded to the patients' clinical presentations; the general appearance of the patients might therefore have biased the residents' echocardiographic findings.

The best correlation for the LVF evaluations was seen in the good contraction group. This finding was also similar to those of previous studies, which demonstrated that the strongest correlation was found in the good and poor contraction groups.[12,13] However, the EPs in the current study could not evaluate the LVF as accurately in patients with a moderate contraction. This was also concordant with previous studies and might have been due to the less apparent findings. Nonetheless, echocardiography might help EPs to identify the cause of shock more rapidly, which could lead to a faster provision of appropriate treatment.

Furthermore, the accuracy of the pericardial effusion diagnoses was 100%, which was as high as that found by a previous study.[22] This might have been because our study investigators were familiar with the FAST (Focused Assessment with Sonography in Trauma) exam, which uses the subxiphoid view to evaluate pericardial effusion. The subxiphoid view was thus the most properly performed view by the EPs in this study. However, this finding was discordant with some previous studies,[20,23] which reported that the parasternal short and long axes were the most properly performed views. This might have been because those studies included performers who had some experience in focused echocardiography, making it easy for them to acquire the proper parasternal short and long axis views. In comparison, the subxiphoid view might be the easiest view to achieve in the case of inexperienced performers. Furthermore, the apical 5-chamber view was the least properly performed view in the present study, which might have been due to the need both cooperation from the patient and a skillful operator. Nevertheless, as the apical 5-chamber view is employed to evaluate cardiac output, we should improve providers' skill performing it.

The mean time taken to perform the focused echocardiographies was 19 minutes, which was comparable to the times reported by previous studies, which had mean durations ranging from 5 to 25 minutes.[9,11,12,24] Many factors can affect the scan time. The first influential factor is the performers' experience. If the investigators in the present study had performed many scans, they would have had more experience and would therefore have been able to complete the scans faster than the more inexperienced scanners.[9] In addition, the apical 5-chamber view, which is difficult to achieve, might have caused an increase in the scan time. Other factors that might have affected the scan time in the current study were machine familiarity, the cooperation of the patients, and the patients' habitus; however, those data were not collected.

Our study had some limitations. Firstly, the cardiologist did not perform the echoes on real patients but instead conducted a review of recorded pictures or video. This might have led to some misinterpretations of the LVFs due to inappropriate views. Moreover, no inter-rater reliability between experts was obtained because there was only one participating cardiologist. As well, we included some patients who could not tolerate a supine position for a long duration for various reasons. This could have made their focused echocardiographies more difficult and might have affected the appropriateness of their echocardiographic views. Fourthly, some conclusions could not be made due to the small number of patients in the subgroups, such as patients with diagnoses other than sepsis and patients with inotropic use. Finally, the number of supervised cases was very small. Therefore, further studies with increased supervised practice and real time feedback should be conducted in order to achieve a higher correlation.

From this study, we conclude that emergency physicians with only short training in focused echocardiography can assess the LVF by visual estimation, and they are able to achieve a high level of agreement with a cardiologist. This might help emergency physicians to more quickly and accurately identify the causes of shock, which in turn should lead to the more rapid and appropriate management of emergency patients.

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Incidence and Risk Factors of Necrotizing Enterocolitis Following Gastroschisis Repair in Correlation with Modes of Abdominal Wall Closure and Umbilical Management at Siriraj Hospital: an 11-Year Retrospective Review

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ABSTRACT

Objective: We investigated the correlation between umbilical management and NEC in infants with gastroschisis as well as the incidence and potential risk factors of NEC in patients with gastroschisis at Siriraj Hospital from 2005 to 2016.

Methods: A retrospective chart review was conducted of patients with gastroschisis who were surgically repaired at Siriraj Hospital from January 2005 to January 2016. The baseline characteristics, umbilical management, and short-term outcomes were analyzed in relation to NEC complications to determine the associated correlations and potential risk factors.

Results: Overall, 106 patients were enrolled. The incidence of NEC following gastroschisis repair was 16% (17/106). Umbilical preservation was a significant potential risk factor for NEC ($p = 0.009$; hazard ratio = 5.14; 95% CI = 1.51-17.42). There were no significant differences between the NEC and non-NEC group for gender, median Apgar scores, gestational ages, and birth weight. The short-term outcomes were significantly higher for the NEC than the non-NEC group, with a time to first oral feeding of 15 vs. 9 days ($p = 0.006$), duration of total parenteral nutrition, 22 vs. 12 days ($p < 0.001$), and length of stay, 32 vs. 23 days ($p = 0.01$) respectively.

Conclusion: Umbilical preservation following gastroschisis repair was associated with a higher incidence of NEC, even in term infants. Thus, NEC should be carefully monitored after abdominal fascial closure with umbilical preservation.

Keywords: NEC; gastroschisis; umbilical preservation (Siriraj Med J 2019; 71: 261-267)

INTRODUCTION

Gastroschisis is a congenital, abdominal-wall defect with eviscerated abdominal content. Usually, the defect is less than 4 cm in width and is located on the right of the umbilicus. The incidence varies from 2-4.9 per 10,000 live births.[1–3] Necrotizing enterocolitis (NEC) is a well-recognized and serious complication, particularly after gastroschisis repair, and is responsible for increased morbidity and occasional mortality.[4–6] The incidence of NEC has ranged from 4%–18.5% in infants with gastroschisis following abdominal wall closure.[4–7]

Previous studies have reported the association of NEC in infants with gastroschisis with a lower birth weight[5,8] and prematurity[5], although the association is

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unclear following the initiation of enteral feedings.[4–5] The predisposing factors for NEC in normal term infants have been speculated to be the combination of reduced mesenteric perfusion and feeding with artificial formula.[9] The risk factors for NEC in infants with gastroschisis have rarely been documented.

The current definitive surgical management of gastroschisis is by early return of the eviscerated abdominal content into the abdomen through the primary abdominal fascia and skin closure.[3,4] If primary abdominal closure is impossible due to visceral-abdominal disproportion or increased intraabdominal hypertension, an artificial pouch or silo is placed with a subsequent serial reduction of the extra-abdominal content[3,4] and a succeeding definitive closure.

The difference in umbilical cord management during and after abdominal closure depends on individual surgeons' preferences. Several previous studies have demonstrated the advantages of umbilical preservation in cosmetic outcomes, and most did not report any major complications such as cellulitis or omphalitis.[10–12] Conversely, research by Komuro et al. revealed a possible association between umbilical preservation and wound infection.[13]

Concerns about periumbilical necrotizing fasciitis led to umbilical cord and urachal remnant excision, as reported by Kosloske and Bartow.[14] The infection was speculated to spread along the umbilical arteries and vein as well as the urachal remnant. However, the association between umbilical preservation and NEC has not yet been defined.

Objectives

The purpose of this study was to determine the association between umbilical cord preservation and NEC in infants with gastroschisis. The incidence and risk factors of NEC in infants with gastroschisis were also evaluated.

Keywords and variables in the study

Preterm refers to a baby born before 37 weeks of pregnancy have been completed. Preterm infants experience a greater risk of morbidity and mortality than term infants due to immaturity-related complications.[15]

Low Apgar score is defined as a score of less than 7 at 1 minute.[16]

Low birth weight is defined as a birth weight of less than 1,500 grams.

Modes of surgical treatment for gastroschisis were classified into:

- ***Primary fascial closure with umbilical preservation***: closure of the abdominal fascial wall, either immediately or in the first operation, with preservation of the umbilical cord.
- ***Primary fascial closure with umbilical cord removal***: closure of the abdominal fascial wall, either immediately or in the first operation, with an umbilical cord excision followed by an umbilicoplasty.
- ***Staged abdominal wall closure***: a salvage technique providing temporary intestinal coverage, which allows for the gradual reduction of the contents, followed by a definitive closure and an umbilical cord excision.

Umbilical cord excision: the excision of the umbilical cord from a newborn by cutting the umbilical arteries, umbilical vein, and urachal remnant at the level of the peritoneum.

NEC Staging: classified according to the modified Bell's clinical staging criteria.[17]

MATERIALS AND METHODS

A retrospective clinical-chart review was conducted of patients with gastroschisis who had been surgically repaired at Siriraj Hospital January 1, 2005-January 31, 2016. The inclusion criterion was neonates with gastroschisis operated at Siriraj Hospital during the 11-year study period. Excluded were patients who had undergone a definitive operation at another hospital or who had incomplete medical records.

In all, 110 patients with gastroschisis were identified as having been treated at Siriraj Hospital from 2005 to 2016. Complete medical records of 108 of the patients were available and formed the basis of the retrospective review. However, as two of those patients were subsequently found to have undergone definitive surgical repair at other hospitals, they were excluded. The patients' demographic and clinical data that were collected comprised gender, gestational age, birth weight, Apgar score, type of delivery, mode of surgical treatment, comorbidities, operative findings, and umbilical management. The variables of the NEC and non-NEC groups were compared. The significant variables were reanalyzed to find the potential risk factors for NEC. The short-term outcomes (time to first oral feeding, duration of total parenteral nutrition [TPN], and length of stay) were reviewed with respect to overall complications, sepsis, wound infections, necrotizing enterocolitis, morbidities, and mortalities.

The statistical analyses were performed using SPSS Statistics for Windows, version 17 (SPSS Inc., Chicago, Ill., USA). The data were presented as mean, median, mode, min, max, and standard deviation. Student's t-test was used for normally distributed data, and the Mann–Whitney U test was employed for deviated distribution or non-parametric tests in comparative quantitative data analysis. The qualitative data were compared using the Chi-square test, and if the sample size was deemed too small, a two-tailed Fisher's exact test was used. Statistical significance was determined by a p-value of less than 0.05. The significant factors from the univariate analysis were reanalyzed in a stepwise selection of variable and logistic regression processes.

Ethics approval

The institute's ethics review board approved the review of the medical records undertaken by the present research (Si 341/2015).

RESULTS

A total of 106 infants with gastroschisis were studied. There were 50 male and 56 female patients (47% vs. 53%), as summarized in Table 1. Sixty five percent of the cases were preterm infants, mainly weighing more than 1,500 grams (92.5%) and mostly with good Apgar scores (73.6%). The most common associated anomaly was bowel atresia with or without volvulus, with an incidence of 12.3% of the study population. In this study, 70 out of 106 patients (66.1%) underwent primary fascial closure, which included 17% of the cases with umbilical preservation and 49% with umbilical cord excision. Thirty six out of 106 patients underwent staged fascial closure, accounting for 34% of the cases with delayed umbilical cord removal. The incidence of NEC in this study was 16% (17/106), and the mortality rate was 7.5% (8/106). All mortalities were not related to NEC (1 abdominal compartment syndrome, 2 bowel atresia with complications, 1 midgut volvulus, 2 sepsis, 1 pneumothorax, and 1 congenital heart disease and associated hydranencephaly).

There were 13 complicated patients with gastroschisis with associated bowel atresia or midgut volvulus. Twelve patients had associated intestinal atresia, of which 9 underwent fascial closure with constructed ostomy and 3 underwent fascial closure with primary anastomosis. There were two mortalities from the ostomy group. One died from very short bowel syndrome, with a jejunal length of 12 cm. Another died of complicated anastomotic dysfunction after operative ileostomy closure.

A univariate analysis to identify the potential risk factors of NEC in infants with gastroschisis is presented in Table 2.1. There were no significant differences between some of the parameters of the NEC and non-NEC groups (gender, median gestational age, Apgar score, and birth weight). However, the univariate analysis showed that umbilical management (including umbilical preservation), umbilical excision, and delayed umbilical resection during staged abdominal wall closure were significantly different between the NEC and non-NEC groups, with a p-value of 0.001. The significant variables were reanalyzed in a stepwise logistic regression, as detailed in Table 2.2. Umbilical preservation was identified as a potential risk factor for NEC in infants with gastroschisis, with a p-value of 0.009 (hazard ratio = 5.13; 95% CI = 1.512-17.42), and staged closure showed a tendency towards a preventive effect of NEC, but with no statistical significance (adjusted odds ratio = 0.378; 95% CI = 0.078-1.937).

Excluding 8 mortalities, the short-term outcomes were compared between the NEC and non-NEC groups. Table 3 details the comparison of the outcomes (the median time to first oral feeding, duration of TPN, and length of stay), all of which were significantly higher in the NEC than the non-NEC group (p-values = 0.006, 0.000, and 0.01, respectively).

The overall postoperative complications were intestinal obstruction, respiratory complications, and NEC (Table 4). There were no significant differences between the groups with different umbilical management in terms of the overall complication rate, sepsis, and wound complications. The infants with gastroschisis who underwent a staged abdominal wall closure with delayed umbilical resection had the highest overall complication rate (58.3%). This incidence was similar to the figure of 55.6% for a primary fascial closure with a preserved umbilicus group. The primary fascial closure with umbilical removal group had the lowest overall complications (36.5%) and wound complication rate (9.6%). The incidence of sepsis was highest in the staged closure with a delayed umbilical resection group (27.8%).

The incidence of NEC was analyzed based on umbilical management, which was classified according to the modified Bell's clinical staging criteria. The analysis found significant differences between the 3 umbilical management groups, with a p-value of 0.01 (Table 5). The primary fascial closure with preserved umbilicus group had the highest NEC incidence of 44.4%. The umbilical removal approaches (primary fascial closure or staged closure) had significantly lower incidences of NEC (13.5% and 5.6%, respectively).

TABLE 1. Demographic data of 106 neonates with gastroschisis treated 2005–2016 (n = 106).

Parameter	Category		Incidence	%
Gender	Male/Female		50/56	47.1/52.8
Mean GA (weeks)	< 37/≥ 37		69/37	65/34.9
Birth weight (g)	≤ 1,500/> 1,500		8/98	7.5/92.5
Apgar	< 7/≥ 7		28/78	26.4/73.6
Comorbidities	Bowel atresia/volvulus		13	12.3
Umbilical management	Primary closure	Preserve umbilicus	18	17
		Remove umbilicus	52	49
	Staged closure (remove umbilicus)		36	34
NEC			17	16
Mortality			8	7.5

TABLE 2.1. Univariate analysis of potential risk factors for NEC in infants with gastroschisis (n = 106).

Variable	NEC (n = 17)	Non-NEC (n = 89)	P-value
Gender (M:F)	7:10	43:46	0.59
Median GA (weeks; range)	37 (34–39)	36 (30–44)	0.71
Median Apgar score (range)	9 (7–10)	10 (5–10)	0.97
Median birth weight (g; range)	2,340 (1,730–3,647)	2,060 (1,200–3,700)	0.08

TABLE 2.2. Logistic regression analysis of potential risk factors for NEC in infants with gastroschisis (n = 106).

Variable	NEC (n = 17)	Non-NEC (n=89)	P-value	Adjusted odds ratio (95% CI)	Hazard ratio (95% CI)
Umbilical management			0.001		
Preserve umbilicus	8 (47.7%)	10 (11.2%)	0.009		5.143 (1.512–17.42)
Remove umbilicus	7 (41.2%)	45 (50.6%)			1
Staged closure (remove umbilicus)	2 (11.8%)	34 (38.2%)	0.24	0.378 (0.078–1.937)	

TABLE 3. Comparison of short-term outcomes of NEC and non-NEC groups (excluding 8 mortality cases; n = 98).

Variable		NEC (n = 17)	Non-NEC (n = 81)	P-value
Time to feeding	Median (min-max)	15 (6–45)	9 (4–73)	0.006
TPN duration	Median (min-max)	22 (12–45)	12 (0–100)	0.000
LOS	Median (min-max)	32 (19–67)	23 (9–365)	0.01

Abbreviations: TPN = total parenteral nutrition, LOS = length of stay, P-value of < 0.05 considered statistically significant

TABLE 4. The complication rates of each mode of treatment and umbilical management (n = 106).

	Primary closure		Staged closure (n = 36)	P-value
	Preserve umbilicus (n = 18)	Remove umbilicus (n = 52)		
Complications	10 (55.6%)	19 (36.5%)	21 (58.3%)	0.97
Sepsis	3 (16.7%)	9 (17.3%)	10 (27.8%)	0.44
Wound complications	4 (22.2%)	5 (9.6%)	8 (22.2%)	0.21

P-value of < 0.05 considered statistically significant

TABLE 5. The incidence of NEC for each mode of treatment, classified according to the modified Bell's clinical staging criteria[17] (n = 106).

	Primary closure		Staged closure (n = 36)	P-value
	Preserve umbilicus (n = 18)	Remove umbilicus (n = 52)		
NEC stage	8 (44.4%)	7 (13.5%)	2 (5.6%)	0.011
IA	4	3	1	
IB	3	4	1	
IIB	1	0	0	

P-value of < 0.05 considered statistically significant

DISCUSSION

Necrotizing enterocolitis occurring in infants after gastroschisis repair is not uncommon. It tends to occur later in the clinical course, although it can often be successfully managed nonoperatively.[4] In this study, the incidence of NEC was 16%, which is similar to the findings of previous studies that reported incidences ranging from 4%-18.5%.[4–7] Most cases were diagnosed early in stages I-II, and they were successfully treated nonoperatively by fasting and intravenous empirical antibiotics. Comprehensive studies by Snyder[7] and Eggink et al.[18] reported lower NEC incidences of 4% and 9%, respectively, which illustrates the reduction is a consequence of more advanced stage inclusion criteria.

NEC in infants with gastroschisis is a distinctive condition in that no significant relationship has been established with any known predisposing conditions, such as prematurity, low birth weight, or low Apgar score.[4,18] Conforming to previous reports, our study found no significant association between NEC and gestational age, birth weight, or Apgar score. However, substantial studies by Oldham et al.[4] and Suttiwongsing et al.[8] acknowledged the combination of low birth weight, compromised intestinal vascular perfusion, and associated gastrointestinal anomalies as predisposing factors for NEC after gastroschisis repair.

A study by Komuro et al.[13] reported the disadvantages of umbilical preservation as a possible cause of wound infections, omphalitis, cellulitis, and the development of ventral hernia. This corresponds to earlier reports by Kosloske and Bartow,[14] which emphasized the importance of umbilical cord and urachal excision in complicated periumbilical necrotizing fasciitis infants where there were concerns of an infection spreading along the umbilical vessels and urachal remnant. Based on those reports, it can be speculated that the concept of infection spreading along the umbilical vessels and urachal remnant may be related to the development of NEC in infants with gastroschisis. The hypothesis is that umbilical preservation results in bacterial colonization in the area of the umbilical insertion; consequently, spread through the fascial defect, together with operative fascial closure procedures, may lead to impaired tissue perfusion, reduced mucosal blood flow, and cellular hypoxia. Therefore, intestinal mucosal injury and break-down precipitates the development of NEC. Our study showed that umbilical preservation was highly correlated to the development of NEC in infants with gastroschisis, accounting for 47% of the NEC cases. Accordingly, the incidence of NEC in the 18 patients who underwent primary fascial closure with umbilical preservation was as high as 44.4%, which is the highest compared to both primary and staged umbilical resection, with 13.5% and 5.6% respectively. As a result, umbilical preservation was identified as a predisposing factor for NEC in infants with gastroschisis after surgical repair (p-value = 0.009; hazard ratio = 5.13; 95% CI = 1.512-17.42). Further additional pathophysiological studies may be required.

Alternatively, various studies[10,11] have advocated umbilical preservation as it offers better cosmetic results. Nagaya et al.[11] reported the approach in later gastroschisis cases, following complaints about the subsequent absence of the umbilicus in earlier cases. In the 5 patients who underwent fascial closure with umbilical preservation, the procedure provided excellent cosmetic results with no complicated omphalitis or cellulitis. Those studies[10,11] did not identify the incidence of NEC or its correlation to umbilical preservation; in addition, they had fairly small sample sizes. Our study found no difference in the incidences of overall complications, including sepsis and wound complications, in the different umbilical management groups. Nevertheless, the highest overall complication rate of 58.3% in the staged fascial closure group may be a consequence of a more critical population group, for which a primary closure is impractical. Furthermore, wound infections are common and likely to occur with a staged fascial closure. As to the research by Fonkalsrud,[19] it found a much smaller percentage of patients (31%) undergoing a primary fascial closure (compared to 66% in the current study) and cited a higher incidence of complications in those with a staged silo repaired. It was postulated by Fonkalsrud that the significant visceral-abdominal disproportion precluded a primary closure.

With respect to the incidence of sepsis, aside from the higher risk of wound infections in staged fascial closure wounds, a delay in the time to the first oral feeding results in the prolonged use of a central venous catheter, which in turn can ultimately predispose the patient to septicemia more than any other reason.[20] In the present study, the significantly longer time to first oral feeding, prolonged duration of TPN, and length of hospital stay of the NEC group were due to the early detection and treatment of the condition. When NEC was suspected, the patient would be fasted and promptly provided empirical intravenous antibiotics as well as parenteral nutrition. Not only was NEC diagnosed early (no later than stage IIB), all cases were successfully managed nonoperatively. Only one severe case developed pneumatosis intestinalis, and it was in the umbilical preservation group.

Several earlier studies[4,7] included either only definite NEC cases or cases from stages IIA upwards. This contrasts with the current study, in which the majority of cases

were in stages IA and IB, with only 1 case in stage IIB. As to the diagnosis of stage I, some of the cases of NEC may actually have been a delayed gut function, which is common in patients with gastroschisis; however, this is one of the limitations of conducting a retrospective review. Despite the fact that most studies[4,7,8] reported higher incidences (18%-18.5%) of NEC in infants with gastroschisis, including only definite NEC cases, the declining rate of NEC[8] over the past 2 decades has presumably been the result of early detection and the availability of more efficient antimicrobial agents. The lower incidence of NEC in the staged fascial closure group in the present study (5.6%) was consistent with the conclusion of Schlatter et al.[21] that the improved outcome was attributable to lower intraabdominal pressure following the initial preformed silo coverage, allowing sufficient intestinal perfusion.

The current study identified only one significant predisposing factor for NEC in infants with gastroschisis, which is the preservation of the umbilicus. The patients in the primary fascial closure with preserved umbilicus group had 5 times the risk of developing NEC than those in the umbilical removal groups over the study period. A staged fascial closure conveyed the lowest incidence of NEC, despite having the highest incidence of wound infections, sepsis, and overall complications. Nevertheless, the decision to perform any method of fascial closure depends on a patient's condition rather than the prevention of wound complications. Therefore, NEC should be closely monitored when preserving the umbilicus for a patient.

CONCLUSION

Umbilical preservation following gastroschisis repair was strongly associated with the development of NEC, with no correlation to gestational age. Thus, NEC should be carefully monitored after abdominal fascial closure with umbilical preservation. NEC may lead to a prolonged time to the first oral feeding, an extended duration of TPN, and a lengthened hospital stay. Staged fascial closure showed a tendency towards a preventive effect of NEC, but with no statistical significance.

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The limitations of this study were those of a retrospective analysis, a single center, and a relatively small sample size. In addition, the study provided only short-term outcomes of patients with gastroschisis; a long-term study period may provide a more extensive illustration of the outcomes and complications.

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The Relationship among a Palliative Care Service, Patient's Factors, and Quality of Life of Post Treatment Cervical Cancer Patients: a Causal Model Approach

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ABSTRACT

Objective: To test a causal pathway of palliative care (PC) service delivery system on quality of life (QOL) of patients with post-treatment stage II-III cervical cancer (PT2-3CC-PTs).

Methods: The cross-sectional design with two-staged sampling was implemented to recruit 447 PT2-3CC-PTs and 16 healthcare providers from 12 cancer center hospitals. Standardized tools and procedures were used, followed by the structural equation model (SEM) analysis to measure variables of interest.

Results: The average age was 54.07 (SD 11.72) years, most of the patients (90.2%) received radiotherapy and chemotherapy, and more than two-thirds (68.7%) had comorbidities. The results showed that the patients had problems with the physical, role, emotional, and social functioning due to urinary and vaginal symptoms which made them anxious about sexual health. SEM analysis also revealed that the PC service delivery system did not improve the patients' QOL significantly. Finally, it was found that healthcare providers had low competencies in PC, and their caring did not respond to the patients' needs concerning a woman's specific role and responsibility.

Conclusion: The PC service delivery system in Thailand mainly provides physical care without encouraging family to collaborate in care of the patients. PC training to increase competency of providers to care for PT2-3CC-PTs should take the patients' age, severity of comorbidities, treatment differences, and a woman's role, especially sexual health into account. Thus, to enhance QOL (general and sexual health) in PT2-3CC-PTs, healthcare providers should focus on patients' self-management and provider support.

Keywords: Quality of life; post-treatment cervical cancer; palliative care delivery service; sexual health; self-management; social support (Siriraj Med J 2019; 71: 268-277)

INTRODUCTION

Quality of life (QOL) is one of the measurements used to evaluate outcome of the patients' cervical cancer (CC) care, self-management (SM), and CC health-related palliative care (PC). Patient care is found to be associated with patients' QOL[1] and impacted by functioning problems including physical functioning[2], role functioning[3], social functioning[4,5], emotional functioning[6], cognitive functioning[7],

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sexual functioning[7], and symptoms experience affecting daily lives.[8-11] Patients with CC need PC for symptom and psychosocial management so as to maintain all dimensional functioning. Healthcare providers are responsible for providing information and practical care so they should acknowledge patients' competency knowledge on disease and treatment, and they should possess effective communication skills and understanding of women with CC.[9,11,12] Previous studies have reported that QOL was lower in ACC-PT post-treatment compared to that of other women.[2-4,13] PC is one of health delivery services that support symptom management, symptom control, and QOL of post-treatment cervical cancer patients (PTCC-PT).[14-16] PC could be applied early on in the course of illness or in conjunction with other therapies intended to prolong life.[17] However, several studies of PC have been undertaken only with the advance stage cervical cancer patients (ACC-PT) or stage 4. There was a few studies on PC during post-treatment stages 2-3 cervical cancer patients (PT2-3CC-PTs).[2,11,13,24] In fact, the study of PC among PT2-3CC-PTs is needed due to the highest prevalence of this disease among the female population. It was anticipated that the results of the present study could be utilized to provide knowledge of PC for PT2-3CC-PTs.

This study aimed to promote QOL for the PTCC-PT depending on multidimensional factors, including patients' dimensional factors and PC dimensional factors that enhance patients' self-management behaviors to reduce physical, mental, and social health problems. Patients' dimensional factors investigated in this study included demographic factors (age of the patients[9,18], social support[4,5,19], and patients' self-management)[7,12,15,20], as well as medical factors (the stage of disease[13], radiation therapy/combination of radiation therapy and chemotherapy (RT/CCRT)[9,21], and comorbidities[3]). PC dimensional factors included model of care[22,23], provider competence[7], and provider support.[7,24] In addition, the relationship between the patients' dimensional factors and the PC dimensional factors and QOL of PT2-3CC-PTs[14,15] has rarely been studied in the country. Therefore, this study also examined the association of the patients' dimensional factors and the PC dimensional factors on QOL of PT2-3CC-PTs.

Research Questions

1. What factors in the patients' dimensional factors (age, stage of disease, RT/CCRT, comorbidity, social support, self-management, and symptom experience) have a direct effect on QOL of Thai PT2-3CC-PTs?

2. What factors in the PC dimensional factors (model of care, provider competence, and provider support) have an effect on QOL of Thai PT2-3CC-PTs?

3. What factors between the patients' dimensional factors (age, stage of disease, RT/CCRT, comorbidity, social support, self-management, and symptom experience) and the PC dimensional factors (model of care, provider competence, and provider support) have an effect on QOL of Thai PT2-3CC-PTs in tertiary care cancer centers in four regional service areas in Thailand?

MATERIALS AND METHODS

Design

A cross-sectional study design was conducted from May 2016 to April 2017. The data were presented focusing on the results regarding the relationships between patients' dimensional factors and PC dimensional factors on QOL of Thai PT2-3CC-PTs.

Sample and Recruitment Methods

The two-stage sampling was used to select service areas and recruit participants of this study. Field data collection comprised four regional service areas in Thailand categorized by health service networks from the guideline of the Ministry of Public Health. Finally, the four areas were selected including the fourth, fifth, sixth, and 13th service areas. These four areas had the highest registry number, 61.1% of 3,771 new CC patients in the year 2013 (1,844 of whom were PT2-3CC-PTs).

The research was implemented in 16 follow-up clinics including five obstetric-gynecological clinics and 11 radiological clinics of 12 tertiary HC centers. The power analysis was implemented to calculate the sample size for SEM, the sample size required in this study was 480.[25] Then, the distribution of patient participants in each hospital setting was calculated based on the probability proportional to size sampling[26] that was appropriate for an unequal number of CC population in each clinic. There were 16 provider participants (one provider participant per clinic) in the study.

The participants of this study were divided into two groups including patients and HC providers. The first group was patients with 2-3CC-PT who underwent RT/CRT for three to 12 months as prescribed by the physician to ensure completeness of response for cancer treatment. Then, the patients received care provided at the onco-gynecological clinic, radiotherapy clinic, and obstetric-gynecological clinic in the out-patient department of cancer centers. Next, the patients age was 18 years and over, and they understood or could read or

write in Thai. Patients who had recurrence or metastasis, had been diagnosed with cognitive impairment, or were unable to communicate were excluded from this study.

The second group was HC providers including physicians, radio-oncologists, gynecological-oncologists, and registered nurses (oncology nurse specialists and registered nurses in the radiotherapy clinic, onco-gynecological clinic, or obstetric-gynecological clinic in the out-patient department of the cancer centers). The HC providers were selected based on the settings where the patients received care. Temporary HC providers in the clinics were excluded.

Ethics

Ethical approval for the study was obtained from the Ethics Committee of the Faculty of Medicine, Siriraj Hospital, Mahidol University (Si 281/2016) and Human Research Ethics Committee of each 11 cancer center hospitals.

Measures

The participants' self-reported questionnaires were used to collect data including dimensional factors, PC dimensional factors, and QOL.

Patient's dimensional factors were measured using the Patients Demographic and Medical Information Questionnaire (PDMIQ) to collect the demographic data and medical information of the PT2-3CC-PTs. Next, the Cervical Cancer Patient Self-management Questionnaire (CCSMQ) was used to assess the patients' ability to use available resources, information, decision making, and SM skill by sharing decision making and utilizing coping strategies. The reliability of the tool was determined using internal consistency, with Cronbach's alpha equal to 0.92. Then, the Medical Outcome Study-Social Support Survey (MOS-SSS) was employed to measure perceptions of the availability of support or the support from partners, family, and peers including its adequacy.[27] As for reliability of the instrument, internal consistency was calculated and Cronbach's alpha was 0.90. Lastly, data regarding comorbidity, which was defined as one or more additional diseases or disorders co-occurring with a primary disease or disorder that the patients had before cancer diagnosis, were retrieved from the patients' health record based on the Charlson Comorbidity Index (CCI).[28] Each comorbidity was reassigned into the number weighting by the severity of diseases.

Furthermore, data regarding PC dimensional factors were collected by means of the Structure of Palliative Care Delivery Service Questionnaire (SPCDQ) and the Palliative Care Delivery Service Questionnaire (PCDQ) which were developed by the researchers. Firstly, the SPCDQ consisted of the palliative care delivery structure questionnaire (PCDSQ) and the provider information questionnaire (PIQ). The PCDSQ questionnaire was used to collect data regarding the type of care, number of providers in the clinic, and number of patients who received care per day, etc. The provider information questionnaire (PIQ) was used to gather provider information including gender, age, educational background, work experience, duration of work experience, specialist certification, and role in the clinic. Secondly, the PCDQ consisted of the provider competence questionnaire (PCQ) and the provider support questionnaire (PSQ). The PCQ assessed HC provider competence. The competency included symptom monitoring and management, use of simple language with the patients, capability to enhance good relationships with patients and other providers, being an effective advocate for the patient, and referral to the specialist. The reliability of the tool was determined in terms of internal consistency, with Cronbach's alpha equal to 0.95. Also, the provider support questionnaire (PSQ) was used to measure four behaviors of care provided for patients including coaching, training, goal setting, and performance feedback. The reliability of the tool was determined using internal consistency, and Cronbach's alpha was 0.97.

The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QOQ-C30) was a 30-item core cancer specific questionnaire measuring QOL in cancer patients. The instrument was provided by the EORTC Quality of Life Group.[29] The reliability of the tool using internal consistency by means of Cronbach's alpha was 0.78. Finally, the EORTC QOQ CX 24 was a 24-item questionnaire to assess patients' perception of symptoms related to CC.[30] The reliability of the tool was determined using internal consistency, with Cronbach's alpha equal to 0.78.

Data Collection Procedures

The study protocol was submitted to and approved by Human Research Protection Unit, Faculty of Medicine Siriraj Hospital, Mahidol University, and Human Research Ethics Committee of each 11 cancer center hospitals. In addition, formal permission from the cancer center administrators was sought after. Then, the researchers approached prospective participants who met the inclusion criteria and agreed to participate in the study. After the participants signed the informed consent form to indicate their willingness to take part in the study, data collection commenced. The researchers collected data from the PT2-3CC-PTs and retrieved the patients' medical

history and CCI from existing medical records. The EORTC QOQ-C30 and the EORTC QOQ-CX24 were administered to explore patients' QOL. Then, the PDMIQ, CCSMQ, and MOS-SSS were administered to collect data regarding patient dimensional factors. The time required to complete all questionnaires was approximately 30-45 minutes. If the participants had visual problems, their caregiver or the researchers helped them complete the questionnaires by giving them verbal assistance.

The researcher collected data from HC providers who were key informants and agreed to participate in the study after the informed consent form was signed. The SPCDQ and the PCDQ were administered. The time to complete the questionnaires was approximately 30-45 minutes. All providers completed the questionnaires by themselves.

Data analysis

SEM statistics were conducted to identify the causal pathway of the PC dimensional factors and the patient dimensional factors that affected QOL of PT2-3CC-PTs.

RESULTS

The study sample comprised 450 patients, three of whom subsequently dropped out. One had a severe pain problem, another went back to work and were unable to participate in the study, and the last one was too tired to join due to her old age. Finally, the total number of participants was 447 PT2-3CC-PTs and 16 HC providers.

Patient Dimensional Factors on QOL

The mean age of PT2-3CC-PTs was 54.07 years old (SD 11.72). More than a half (51.1%) were classified as stage 2, and almost all (90.2%) received radiotherapy with chemotherapy. Moreover, more than a half (60%) had mild severity of comorbidity before cancer diagnosis (Table 1). The patients received less SS and performed good self-management. For instance, the results showed that most of the patients did not receive overall dimension of SS as they needed. Furthermore, the patients had low ability to use HC resources and HC provider information to perform SM and collaborate in decision making with the HC provider (Table 2).

PC Dimensional Factors on QOL

The results regarding PC delivery structure in this study are shown in Table 3. There were a limited number of PC nurses. As regards provider characteristics, nurses were found to be the professionals providing overall PC for CC-PTs. The age of nurses was older than 45 years, and a few of the providers had experience in PC.

The PC delivery service was composed of two essential structures, including provider competence and provider support, as shown in Table 3. In this study, it was found that the providers had less competence in disease and treatment knowledge. Providers also had a variety of forms of symptom and complications which impacted patient communication. In multidisciplinary care, the providers had the highest competence in PC. Providers used simple language, had effective symptom and complication impact communication, had effective patient support, and referred the patients to the specialist when needed. Comparing with providers in the multidisciplinary team, the providers in the specialist care team had the lowest competence in PC. The majority of the providers in this study provided training, goal setting, and performance feedback; however, they had limited ability to perform coaching. Such results indicated that providers in the PC delivery service system perceived themselves as having low competence in PC, resulting in the ineffectiveness of PC services provided to patients.

Relationship between Patient Dimensional Factors and PC Dimensional Factors and QOL

Structural equation model was performed to examine the effects of the PC dimensional factors and the patient dimensional factors on QOL of PT2-3CC-PTs by using the program AMOS version 23. Table 5 presents the hypothesized model (theoretical model) which did not fit the empirical data due to high inter-correlation, the poor goodness of fit coefficient, and misspecification parameters. Thus, the hypothesized model (Fig 1) was modified to achieve a better fit. In this step, the modifications were maintained until acceptable fit indices were achieved. Error covariance of self-management, provider support, model of care, and quality of life were set free. One variable, stage of disease, one path from the model of care to QOL, and eight covariances were deleted. On the contrary, two paths, one from CCI score to model of care and one from the model of care to patient self-management, were added. In the end, the modification model improved the model of fit better than the hypothesized model (Table 5).

The results regarding SEM of QOL in PT2-3CC-PTs showed that the theoretical model explained less than the modified model (Table 5). The modified model (Fig 2) shows the factors that directly affected differences in QOL of PT2-3CC-PTs like age difference ($\beta = -0.161$, $p < 0.001$), patients' SM difference ($\beta = -0.265$, $p < 0.001$), and palliative care delivery service difference ($\beta = 0.114$, $p < 0.01$), as well as factors that indirectly affected QOL through patients' SM like treatment difference ($\beta = -0.031$, $p < 0.01$), severity of comorbidity prior to cancer

TABLE 1. Demographic and Medical Characteristics of PT2-3CC-PTs (N = 447).

Characteristics	Number	Percent
Age (years) Mean = 54.07, SD = 11.72, Range = 24 - 86		
≤ 45	107	23.9
> 45	340	76.1
Marital status		
Single	21	4.7
Marriage	282	63.1
Widowed	87	19.5
Separated	57	12.8
Education		
No formal education	36	8.1
Primary school	251	56.2
Lower than Bachelor's degree	114	25.5
Undergraduate and graduate degree	46	10.3
Living with		
Other family/ No one	21	4.7
Couple	109	24.4
2-generation family	136	30.4
≥ 3 generation (extended) family	181	40.5
Monthly Income (Baht)		
no income	201	45.0
1-5,000	70	15.7
5,001-10,000	88	19.7
10,001 baht or more	88	19.7
Medical Payment Method		
Universal healthcare coverage	265	59.3
Social insurance scheme	111	24.8
Government reimbursement	64	14.3
Others (self-payment, insurance, company benefit, Private Education Commission: OPEC)	7	1.6
Stage (FIGO)		
2A	51	11.4
2B	222	49.7
3A	14	3.1
3B	160	35.8
Treatment		
Radiotherapy	44	9.8
Radiotherapy & chemotherapy	403	90.2
Number of comorbidities		
No comorbidity	140	31.3
1 comorbidity	185	41.4
2 comorbidities	88	19.7
≥ 3 comorbidities	34	7.6
CCI severity scores		
0	140	31.30
1-2 (mild severity)	196	43.80
3-4 (moderate severity)	76	17.00
≥ 5 (high severity)	35	7.80

TABLE 2. Social Support and Self-management of PT2-3CC-PTs (N = 447).

Variables	Possible range	Actual range	Median	Mean	SD
Social Support	**16-75**	**26-83**	**68.00**	**65.92**	**11.01**
Number of close friends		0-30	2.00	3.89	14.63
Number of close cousins		0-40	4.00	4.72	5.09
Material support	5-20	5-20	18.00	16.92	3.36
Emotional/informational support	6-30	6-30	23.00	22.75	5.18
Social relation support	3-15	3-15	12.00	11.79	2.61
Affective support	2-10	3-10	10.00	9.00	1.39
Self-management	**19-76**	**26-76**	**56.00**	**56.69**	**9.01**
Healthcare resources used	4-16	4-16	11.00	10.82	2.95
Ability caused by healthcare information	4-16	4-16	12.00	11.51	2.41
Collaborative care with healthcare providers	5-20	7-20	15.00	15.55	2.50
Shared decision making	3-12	3-12	9.00	8.84	1.77
Behavioral changes	3-12	4-12	10.00	9.97	1.55

TABLE 3. Characteristics of palliative care delivery service system.

Characteristics	Total score	Median	IQR (Q1,Q3)
Palliative care delivery structure			
Number of physicians		4.0	6.0 (4.0,10.0)
Number of onco-gynecologists		0.9	2.8 (0,2.8)
Number of onco-radiologists		4.1	2.3 (3.2,5.5)
Number of gynecologists		0.7	4.4 (0,4.4)
Number of registered nurses		5.9	5.9 (3.7,8.6)
Number of onco-nurses		1.8	2.8 (0.8,3.6)
Number of PC nurses		0.4	1.8 (0,1.8)
Work experience in clinic (yrs.)		9.8	9.2 (5.4,14.6)
Work experience in profession (yrs.)		22	16.1 (12.7,28.8)
Work experience in onco-specialization (yrs.)		2.4	14.7 (0.2,14.9)
Work experience in palliative care (yrs.)		1.8	7.3 (0,7.3)
Total service time/ one patient(min/patient)		132.8	111.5 (57.1,168.6)
Nurse service time/one patient(min/patient)		79.5	56.9 (29.8,86.7)
Screening time		3.8	3.4 (2.6,6.0)
Need/symptom assessment time		9.5	9.6 (4.5,14.1)
Need/symptom management time		13.4	15.6 (3.3,18.9)
SM resource information time		9.4	11.7 (4.5,16.2)
SM consultancy/coaching/skill training time		19.4	22.0 (6.9,28.9)
Referral to unit/service appropriate for patient need time		9.1	7.5 (5.4,12.9)
Physician service time/one patient (min/patient) (Monitor recurrence time)		54.2	56.3 (21.0,77.3)
Palliative care delivery service			
Provider competence	100	88	15 (81-96)
Knowledge of disease	32	18	4 (15,19)
Use of simple language	12	12	3 (9,12)
Effective symptom and complication management			
Effective communication	24	21	5 (18,23)
Patient relation building	12	11	3 (9,12)
Effective patient support	12	10	3 (9,12)
Referral to specialists	20	15	4 (15,19)
Provider support	80	71	12(60-72)
Coaching	40	36	8 (30,38)
Training	20	17	3 (15,18)
Goal setting	12	9	2 (9,11)
Performance feedback	8	7	1 (6,7)

TABLE 4. Quality of life scale scores* in PT2-3CC-PTs (N = 447).

Quality of life	Possible range	Actual range	Median	Mean	SD
EORTC QLQ C30 scale score					
General quality of life	2-14	2-14	11.00	11.20	2.06
Physical functioning	5-20	5-20	7.00	7.29	2.73
Role functioning	2-8	2-8	2.00	2.46	0.99
Emotional functioning	4-16	4-16	6.00	6.11	2.24
Cognitive functioning	2-8	2-8	3.00	2.90	0.90
Social functioning	2-8	2-8	2.00	2.55	1.01
EORCT C 30 symptoms					
Fatigue	3-12	3-12	5.00	5.49	1.77
Nausea and vomiting	2-8	2-6	2.00	2.35	0.76
Pain	2-8	2-8	3.00	3.30	1.34
Dyspnea/Shortness of breath	1-4	1-4	1.00	1.38	0.58
Sleep disturbance	1-4	1-4	2.00	1.72	0.82
Lack of appetite	1-4	1-4	1.00	1.59	0.77
Constipation	1-4	1-4	1.00	1.52	0.68
Diarrhea	1-4	1-4	1.00	1.33	0.55
Financial problems	1-4	1-4	1.00	1.73	0.90
EORCT CX 24 symptoms					
Sexual vaginal functioning** (n = 293)	4-16	4-16	5.00	4.73	4.12
Symptom experience	11-44	11-34	14.00	15.28	3.29
Body image	3-12	3-12	4.00	4.65	1.90
Neuropathy	1-4	1-4	2.00	1.76	0.79
Menopausal symptom	1-4	1-4	1.00	1.51	0.72
Sexual pleasure** (n = 293)	1-4	1-4	4.00	3.70	0.70
Sexual functioning**	1-4	1-4	4.00	3.73	0.61
Sexual anxiety	1-4	1-4	1.00	1.27	0.61
Lymphedema	1-4	1-4	1.00	1.17	0.45

* higher score = more symptoms/problems, ** higher score = less symptoms/problems

TABLE 5. Statistical fitted index values of hypothesized model and modified model (N = 447).

Fitted Index	χ^2	χ^2/df	GFI	CFI	RMSEA	Largest Standardized Residual
Hypothesized model	37.362 (df = 18,	2.076 p= 0.005)	0.984	0.986	0.049	3.469
Modification model	20.220 (df=24,	0.843 p = 0.684)	0.990	1.000	0.000	1.804

Abbreviations: df = degree of freedom GFI = Goodness of fit index (≥0.95), CFI = Comparative fit index =[d(Null model)- d (purposed model)]/d (Null model) (≥0.95), RMSEA = Root mean square error of approximation= $\sqrt{(\chi 2 - df)} / \sqrt{[df(N - 1)]}$ (≤ 0.05) Standardized residual (≤ 2.58)

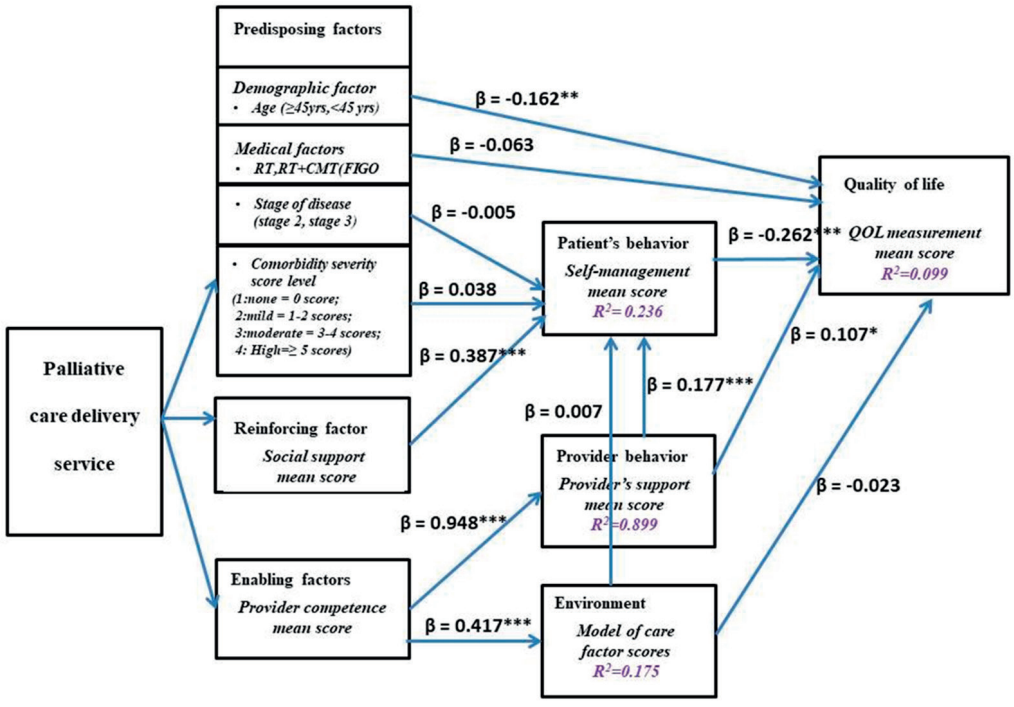


Fig 1. Relationships between patient dimensional factors, palliative care dimensional factors, and QOL of PT2-3CC-PTs of the hypothesized model

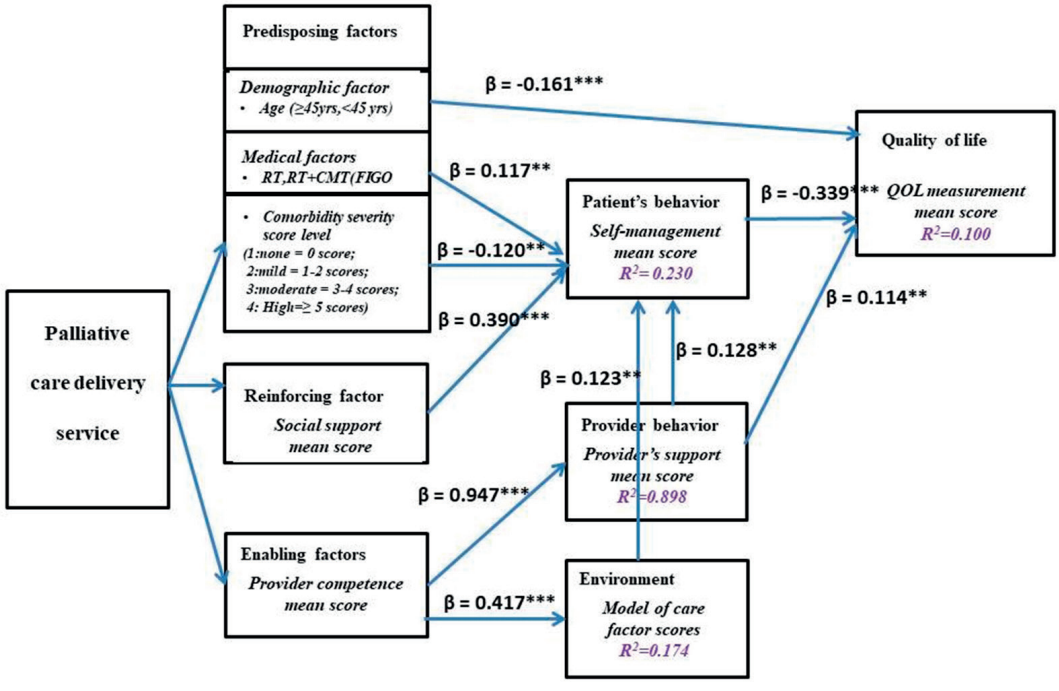


Fig 2. Relationships between patient dimensional factors, palliative care dimensional factors, and QOL of PT2-3CC-PTs of the modified model

diagnosis difference ($\beta = 0.032$, $p < 0.01$), and social support difference ($\beta = -0.103$, $p < 0.001$). The difference of provider competence had a minimal indirect effect on QOL difference through the model of care, provider support, and patients' SM ($\beta = 0.095$, $p < 0.001$). Model of care difference had no direct effect on patients' QOL but had the minimal indirect effect on the difference of QOL through patients' SM ($\beta = -0.033$, $p < 0.01$).

DISCUSSION

The results showed that PT2-3CC-PTs who completed response to cancer treatment had poor QOL due to unsupportive health system. In particular, the health system was not sensitive to sexual health needs, resulting in a lack of engagement of patients, family, and healthcare providers. For instance, the findings revealed no relationships between patients and family

and providers who provided SM support in response to the patients' health problems. Hence, cooperation among patients, family, and healthcare provider is an important strategy to improve QOL of the patients as shown in Fig 2.

This study also found that patients could not live well because of functioning problems, general symptom problems, sexual health problems, and economic problems, as shown in Table 4. The results were correlated with previous studies that PT2-3CC-PTs who had functioning problems, general symptom problems, and sexual health problems would have poor QOL.[3,7,9,19,22,31]

The results in this study indicated that PC in Thailand was mainly developed by considering mainly physical functioning of the patients. As such, the system overlooked patients' age, sexual health related to CC treatment, and severity of comorbidity prior to CC diagnosis. These factors were associated with patients' SM, resulting in poor QOL of the majority of the patients. For example, the presents study found no relationship between patients and family and providers who provided SM support in response to the patients' health problems. Hence, supportive health system is an important strategy to improve QOL of the patients, as shown in Fig 2.

Support from family is the strength of Thai society.[32] The strategy to encourage patients' family to collaborate in PT2-3CC-PTs' HC is significant for improvement of QOL for the patients.[7] Recently, the strategy to provide PC as early as possible by integrating PC services into cancer treatment services is promoted to enhance patients' QOL.[17] In this study, the results showed that the patients could not live well because of their health problems, especially sexual health problems, which, in turn, impacted their emotional, role, and social functioning, as shown in Table 4. The difference of PC dimensional factors associated with poor QOL in the patients in this study is shown in Fig 2. Poor QOL of the patients implied that although the patients had accessed to HC delivery service (follow-up care), they did not receive the PC service as needed. Moreover, PC delivery system in Thailand was not effective enough to encourage patients' family collaboration in PT2-3CC-PTs' HC; thus, the patients had poor QOL (Fig 2). The findings were consistent with previous studies which found that CC patients undergoing complete care for cancer treatment could not live well because HC providers mostly alleviated only physical health problems[9] without considering the differences in age[18,22], comorbidity severity prior to cancer diagnosis[3], and sexual health problems of the patients.[33,34] As a result, the current service could not enhance patients' self-management, causing the patients to continue suffering from the disease and decreased QOL.

CONCLUSION

In Thailand, family is a key component of PC. SS by family members who collaborate with HC delivery service is a promising strategy to develop PC dimensional factors. Another important strategy is to increase the number of providers who understand sexual health care and PC to support both women in the reproductive age and aging women. PT2-3CC-PTs are women with different sexual health problems who still have several roles to play in daily life such as a wife, a mother, and a woman who have their roles for themselves, family, and society. Enabling PT2-3CC-PTs to manage care for themselves requires the support system that directly serves their needs. In addition, they also require the support from family and HC providers who understand their HC needs, especially sexual health problems that can differ in accordance with their age, severity of comorbidity prior to cancer diagnosis, and types of cancer treatment. Therefore, HC providers have an important role to support the patients' ability to SM by improving their ability to manage their health problems, while simultaneously encouraging the patients' family to promote their SM. In addition, competency of nurses who provide care for the patients is an essential component of HC delivery service systems that should be developed urgently. The persons in charge of organizing HC delivery service systems should consider nurses as an important bridge to link, transfer knowledge, and develop skills in sexual health care to the patients. Besides this, policy makers should be careful when devising a policy on PC delivery services for PT2-3CC-PTs. It is suggested that a longitudinal study should be conducted to shed more light on the continuity of relationships between PC dimensional factors and patient dimensional factors. Moreover, further studies should be carried out to confirm that the factors identified as being related to QOL of PT2-3CC-PTs in this study including patient dimensional factors such as age and SM and PC dimensional factors such as provider support actually have an influence on QOL of PT2-3CC-PTs.

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The Accuracy of Cervical Length for Prediction of Delivery in Term Pregnancy Patients Presenting with Labor Pain

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ABSTRACT

Objective: To investigate the relationship between cervical length (CL) at gestational age (GA) 37 to 41+6 weeks and delivery within 7 days in term pregnancy patients who presented with labor pain.

Methods: Term pregnancy subjects who attended antenatal clinic and delivered at Bhumibol Adulyadej Hospital, between September 2017 and June 2018 were recruited in this study. Participants who met the inclusion criteria received transvaginal ultrasound to measure CL. Clinical and delivery outcomes were followed. Sensitivity, specificity, negative predictive value (NPV) positive predictive value (PPV) and accuracy were calculated to assess the relationship between CL and delivery within 7 days.

Results: A total of 106 pregnant women were included in the analysis. The mean age was 26 years. Three-quarters of the cases were nulliparous. The average gestational age at delivery and newborn birth weight were 39 complete weeks and 3,100 grams, respectively. Seventy-six cases successfully delivered within 7 days while 30 patients had to wait for more than 7 days before delivery. The receiver operating characteristic (ROC) curve was used to assess the optimal cutoff of CL. The CL less than 25 mm. gave sensitivity and specificity at 69% and 73%, respectively and gave accuracy of 70.75% in prediction of delivery within 7 days.

Conclusion: Transvaginal CL measurement was useful to predict the time of spontaneous delivery and help clinicians to advise the patients about their delivery plans.

Keywords: Cervical length; term gestation; labor (Siriraj Med J 2019; 71: 278-283)

INTRODUCTION

Labor pain at term was one of the most reported clinical presentations that brought term pregnant women to the delivery room.[1] At our facility, if the patient was not in an active phase for delivery[2], she would be placed in clinical observation for 4 hours and then re-evaluated via pelvic examination. Pregnant women with no cervical progression would then be discharged from the observation. However, such a procedure did not allow the attending physician to estimate time to delivery.

Cervical length (CL) is an ultrasonographic assessment of the cervix. It has been used widely in contemporary obstetrics. It was used to predict the risk of preterm delivery[3,4] and in women before induction of labor to

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predict induction outcome.[5,6] Few studies have examined cervical length at term and attempted to correlate a related cervical length with duration of spontaneous labor.[7]

The aim of the present study was to assess the relationship between cervical length measurement by transvaginal ultrasonography and time to delivery within 7 days in term pregnancy with presenting labor pain.

MATERIALS AND METHODS

Term pregnant women who had labor pain and visited labor rooms at Bhumibol Adulyadej Hospital from September 2017 to June 2018 were recruited. The ethics of the study were approved by the Hospital Ethics Committee, Bhumibol Adulyadej Hospital (IRB 52/60). Informed consent was obtained prior to transvaginal ultrasonographic examination. Labor pain was defined as regular uterine contraction (≥ 4 times/20 min).

Inclusion criteria were defined as: singleton pregnancy, term pregnant women with gestational age (GA) ranging from 37 to 41+6 weeks, cephalic presentation, intact membranes and certain estimated delivery dates.[8] Transvaginal ultrasonographic (TVUS) cervical length measurements and pelvic examinations were performed by obstetrics and gynecology residents who trained on proper CL measurement technique at time of labor room visit. CL measurements performing the TVUS, using a LOGIQ V3 (General electric company, USA) machine equipped with a 8 MHz transvaginal probe.

The participant was placed in the dorsal lithotomy position. A vaginal probe at 8 MHz was used to perform an ultrasonic reading after the participant's bladder was emptied. Endocervical canal length was measured as the distance from the internal and external os in a straight line. If funneling was presented, the cervical length was measured as the distance between the apex of funneling and the external os parallel to the cervical canal. Three images were collected in each patient and the image with the shortest CL was chosen for analysis. All recruited patients were monitored until delivery.

Demographics and obstetrics variable data was collected including patient's age, race, height, body mass index (BMI), CL, gravidity, parity, onset of labor pain, GA at CL measurement, date and time of CL measurement, GA at birth, date and time of birth, time from CL measurement to delivery, fetal weight and route of delivery.

The data was processed using SPSS statistical software version 18 (IBM, Armonk, NY, USA). for analysis. Continuous variables were presented as mean and standard deviation (SD). The *p*-value of less than or equal 0.05 was used for statistical significance. Curves of cervical length for predication of delivery within 7 days were generated using receiver operating characteristic (ROC) curves. Diagnostic accuracy of CL was subcategorized and used for analysis of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likely hood ratio (LR+), negative likelihood ratio (LR-) and accuracy.

RESULTS

A total of 120 pregnant women were enrolled. Fourteen cases were excluded due to patients choosing to deliver at other facilities. One hundred and six cases were interviewed and followed up until delivery. All cases that met inclusion criteria were included in the study.

Of the remaining participants, 76 successfully delivered within 7 days, whilst the remaining 30 cases, delivered outside the 7 days window. There were no statistically significant differences between groups in age, BMI and parity as represented in Table 1.

The participants who delivered at more than 7 days had longer CL, longer time to delivery after visit and higher fetal birth weight than women who delivered within 7 days with ratios of: 29/21.8 mm, 272/54 hours and 3,202/3,061 grams.

ROC curve of cervical length for predicting delivery within 7 days was presented in Fig 1. The appropriate cut off point was chosen from ROC curves that gave a suitable value. CLs less than 25 mm gave the sensitivity and specificity in prediction delivery within one week at a percentage of 69 and 73, respectively. The other cut-off points are also represented in Table 2.

DISCUSSION

The main outcome of this study was the correlation between CL and delivery date within 7 days prediction of term pregnancy cases that presented at the hospital with labor pain. Optimal CL cut-off was suggested at less than 25 mm which gave appropriate sensitivity and specificity (69% and 73%, respectively). All cases with CL less than 15 mm had delivered their newborns within 7 days.

Bayramoglu et al[12] reported from France that sensitivity and PPV of spontaneous labor within 7 days by using CL cut off point at 24.5-29.5 mm were 75-82.9 and 54.8-95.5%, respectively. His work was conducted in vertex and singleton term pregnancy. Half of participants were nulliparous and CL cut off point decreased with the higher GA (29.5 mm at GA 37 weeks, 27.5 mm at GA 38 weeks, 25.5 mm at GA 39 weeks and 24.5 mm at GA 40 weeks). Comparison to the present study at cut off point

TABLE 1. Demographic data of the study population.

	Within	More	*P*-value
Age (years)	26.43±6.29	25.60±6.16	0.538
BMI (kg/m^2)	26.39±4.63	27.00±3.44	0.510
CL (mm)	21.8±7.4	29.0±6.3	<0.01
Time (hours)	53.92±42.26	271.99±91.49	<0.01
GA (days)			
Visit	274.08±6.35	268.93±6.82	<0.01
Delivery	276.42±6.26	280.40±6.43	0.04
FBW (gm)	3061.84±393.22	3202.23±249.56	0.03
Nulliparous	51(76.1%)	16(23.9%)	0.18
Multiparous	25(64.1%)	14(35.9%)	

Data were shown as mean ± SD (standard deviation), Within: delivery within 7 days from pelvic examination, More: delivery more than 7 days from pelvic examination

Abbreviations: BMI: body mass index, CL: cervical length, Time: time from examination to delivery, GA: gestational age, Visit: gestational age at examination, Delivery: gestational age at delivery, FBW: fetal birth weight.

TABLE 2. Diagnostic accuracy of CL to predict delivery within 7 days.

	CL (mm)			
	< 15	< 20	< 25	< 30
Sensitivity	19.7	40.7	69.7	85.5
Specificity	100	96.6	73.3	36.6
PPV	100	96.8	86.8	77.3
NPV	32.9	39.1	48.8	50.0
LR+		12.2	2.6	1.3
LR-	0.8	0.6	0.4	0.4
Accuracy	42.45	56.60	70.75	71.7

Data were shown as %,

Abbreviations: CL: cervical length, PPV: positive predictive value, NPV: negative predictive value, LR+: positive likelihood ratio, LR-: negative likelihood ratio

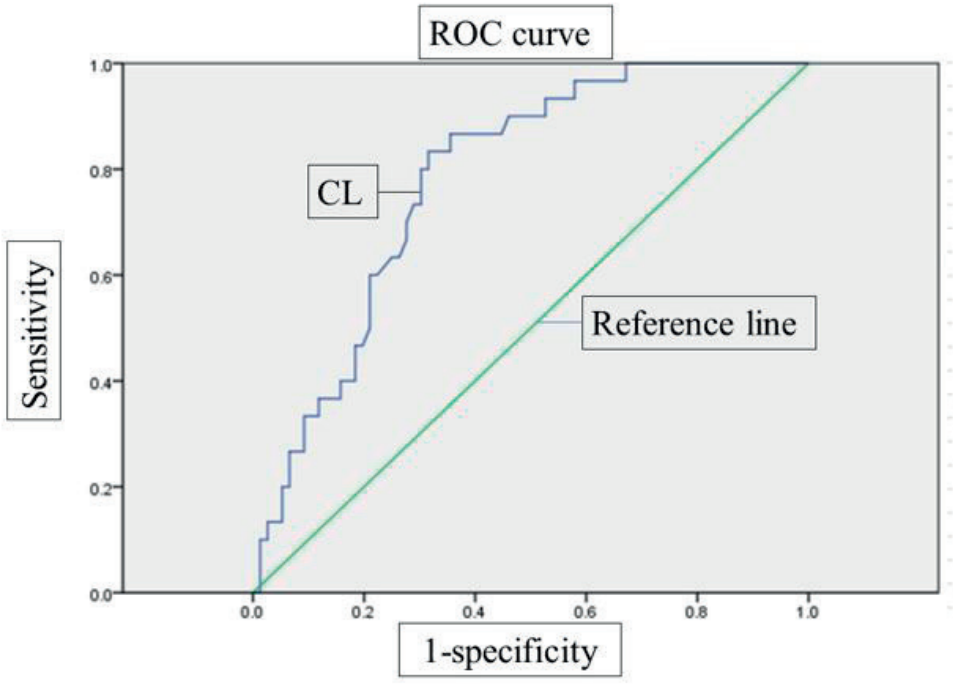


Fig 1. ROC curve of CL to predict delivery within 7 days.
Abbreviations: ROC = receiver operating characteristic, CL= cervical length (mm)

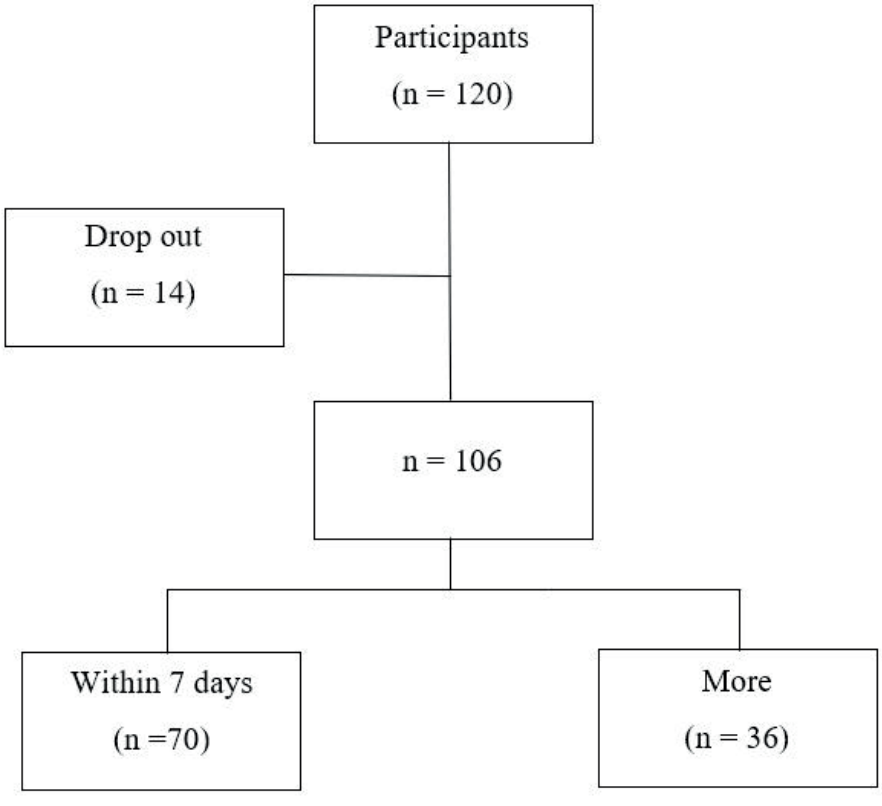


Fig 2. Subject selection and exclusion.
Participants: Term pregnancy who had labor pain, within 7 days: delivery within 7 days from pelvic examination, More: delivery more than 7 days from pelvic examination, Drop out: Term pregnancy who had delivery at other hospitals.

at 25 mm, sensitivity and PPV of Bayramoglu were higher than the present study (75.5/69.5,90.9/73%, respectively). The discrepancy may be due to differences in patient population. The population in Bayramoglu's study was majority French, whilst this study was conducted on a majority Thai population (with 63% nulliparous cases).

Tolaymat et al[9] performed transvaginal ultrasonography to measure CL in 120 pregnant women with singleton and gestations at 37 to 40 weeks to assess the relationship between CL and spontaneous labor within 7 days. Tolaymat suggested CL less than 25 mm that gave sensitivity and PPV of 77.5 and 50.8%, respectively. Our study suggested a cut-off point at the same value as Tolaymat's work (less than 25 mm). The present study had less sensitivity than the Tolaymat's work at of 69.7/77.5 %, while PPV of the present study was higher than Tolaymat's work at of 86.8/50, respectively. The difference was due to differences in patients between the two studies. Three quarters of subjects in Tolaymat's study were of Hispanic race and half of cases were nulliparous women. While this study was conducted in Thai women and all participants had labor pain that increased chances of imminent delivery, compared to pregnant women who had not yet presented with labor pain. The overall prevalence of spontaneous labor within 7 days in Tolaymat's work was low (32.8%) while the present study was 71.6% due to subjects enrolled in this study having presented labor pain prior to the research registration.

In the year 2010, Miura et al reported the CL prediction of labor in Japanese pregnant women. Parity and gestational age of Miura's work were similar to the present study. His work recruited the cases who had no labor pain like Bayramoglu's and Tolaymat's work.[9,12] Miura's work concluded that CL measurement could predict the spontaneous labor within 7 days. His work supported our study.

Systematic review study by Saccoon et al.[7] assessing the accuracy of TVU CL in the prediction of spontaneous onset of labor in singleton gestations revealed the accuracy of CL for prediction of spontaneous labor within 7 days. Pooled sensitivities and specificities yielded the conclusion that the higher CL had better sensitivity; the lower CL had better specificity. Saccoon's work consisted of European cases (90%) who had the same inclusion criteria with this study. All cases in his work had no clinical presentation of labor pain. The present study recruited pregnant women with the same criteria who had clinical labor pain. However, the Saccoon's work still supported the present study that CL was an important factor to predict spontaneous delivery.

Mukherji et al[13] conducted the serial ultrasound for CL measurement in pregnant women at GA 36-40 weeks. Mukherji's population consisted of Indian nulliparous pregnant women. His literature concluded that a single CL could not predict spontaneous labor. CL cut of point at GA 38 weeks from transabdominal and transvaginal ultrasonography in Mukherji's study were 35 mm and 31 mm, respectively can predict post-dated pregnancy. Mukherji conducted his investigation in pregnant women who had no labor pain. In the present study, we studied women who had labor pain. Our study showed that single CL measurement in any gestational age of term pregnancy can predict delivery.

Most CL studied in prediction of spontaneous onset of labor were done in term pregnancy with no labor pain.[9-12] This study was the study that evaluated term pregnancy with labor pain and a wide range of gestational age (37–41+6 weeks). This study suggested a CL value that predicted delivery within 7 days for patients 37+ week gestation with acceptable robustness.

Pregnant population using obstetric service at Bhumibol Adulyadej hospital could be divided into two subgroups, normally local residents and people who work in the area but originated upcountry. The results from our investigation can be used to advise patients for their delivery plan. Those who are discharged from labor rooms were normally concerned about how long would it be before their time to deliver. Women with short CL should be adviced to prepare to stay near the hospital or notify their care givers to stand by for future visit to a labor room. A long CL can be advised that the labor might take longer than one week.

Expecting mothers sometimes choose to deliver their offspring in their hometown so as to benefit from family care and support. A few patients had left our unit after their initial reports of labor pain to deliver elsewhere. Our CL cut-off allowed a good prediction of if the baby would be due within 7 days or not. Armed with this certainly, patients can choose if they would stay in Bangkok to deliver or allow them enough time to travel to their hometown destination for the birth.

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Conflict of Interests: None

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Diagnostic Performance of Short MR-Neurography Protocol for Brachial Plexus Injuries

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ABSTRACT

Objective: To study the diagnostic performance of MR neurography (MRN) for brachial plexus injuries and to optimize the protocol using clinical contexts as the reference standard.

Methods: There were 21 patients with brachial plexus injury who were scheduled for conventional myelography. A brachial plexus MRN including T2-weighted image-high resolution (T2WI/HR), mDIXON and diffusion weighted image was performed prior to a conventional myelography on the same day. The results of the conventional myelography and the MR imaging were recorded and compared, with the clinical contexts as the reference standard. The sensitivities, specificities, accuracies, false positive and false negative were calculated and compared.

Results: The accuracy, sensitivity, specificity, false positive and false negative of the conventional myelography were 69.52%, 73.61%, 60.61%, 19.70% and 48.72%, respectively. The diagnostic performance of T2WI/HR were 72.00%, 78.26%, 58.06%, 19.40% and 45.45% for T2WI/HR, respectively which were comparable to those of conventional myelography. The accuracy, sensitivity, specificity, false positive and false negative of the combination of T2WI/HR and mDIXON were 78.00%, 97.10%, 35.48%, 22.99% and 15.38%, respectively which yielded the highest accuracy.

Conclusion: MRN with the combination of T2WI/HR and mDIXON was superior to conventional myelography for the evaluation of brachial plexus injuries due to its shorter processing time, the lack of a need for contrast medium administration, its noninvasive nature, and the provision of information about both preganglionic and postganglionic injuries.

Keywords: MR-neurography; high-resolution MRI; brachial plexus injury; nerve root avulsion (Siriraj Med J 2019; 71: 284-289)

INTRODUCTION

Traumatic brachial plexus injuries in adults mostly occur in young people aged between 20 and 30 years.[1] Preganglionic lesions result from the avulsion, or the tearing off, of the insertion of the nerve root from the spinal cord, while more-distal nerve ruptures within the brachial plexus are defined as postganglionic lesions. The management and prognosis of brachial plexus injuries depend on the degree of damage and the site of the injuries, with a poor prognosis for preganglionic injuries. Many imaging modalities are available to not only differentiate between preganglionic and postganglionic lesions (such as standard myelography, CT myelography, conventional MRI, MR myelography and MR neurography), but also determine the severity of the injuries. Conventional myelography and CT myelography have long been used

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for the assessment of preganglionic root injuries. However, myelography is an invasive procedure, exposes patients to radiation, and carries the risk of adverse reactions to the iodinated contrast medium. Because of its non-invasive nature and ability to evaluate both the proximal and distal parts of the brachial plexus, MR neurography (MRN) has recently been introduced. MRN comprises a set of evolving protocol techniques to evaluate many abnormalities of the brachial plexus.[2] To achieve the objectives of the MRN, good and clear anatomical or structural information on the entire brachial plexus needs multiple planes and pulse sequences. The high-quality of MR imaging, provided by its high resolution, good fat suppression, and 3D imaging (short inversion-recovery sequence or mDIXON), results in excellent images of the peripheral brachial plexus structure. Furthermore, diffusion-weighted neurography can be used to evaluate postganglionic brachial plexus lesions. However, to evaluate preganglionic brachial plexus injuries, a high-resolution heavily T2-weighted pulse sequence offers comparable information to CT myelography.[3]

The purposes of this study were to optimize the protocol of the brachial plexus MRN used by our institute for brachial plexus injuries, and to study the diagnostic performance of the protocol, with clinical contexts used as the reference standard.

MATERIALS AND METHODS

Patient selection

This prospective study was performed between February 2015 and August 2016. It was approved by the ethics committee of the institute before patients were enrolled (Si 427/2015). A total of 21 patients fitted the inclusion criteria, which including age over 18 years, diagnosed with a brachial plexus injury, and scheduled for conventional myelography. Written informed consents were obtained from all patients before enrolment in the MRI study.

MR imaging

All patients underwent an MRI just prior to conventional myelography. All MRI examinations were performed on a 3.0-T MR unit (Ingenia, Philips Medical Systems, Best, the Netherlands), with a 16-element, head and neck matrix coil. We designed three pulse sequences of MRN brachial plexus protocol for the setting of brachial plexus injury and covering C4-T1 levels. The 3 MR pulse sequences acquired were axial T2-weighted image-high resolution (repetition time = 3000; echo time = 140; matrix, 180 x 178; field of view, 180 mm x 180 mm; turbo spin echo factor, 38; Sense factor, 1.7; slice thickness, 2.0 mm, no gap; number of signal average, 2); coronal T2-weighted image-mDIXON (repetition time = 2721; echo time = 90; matrix, 444 x 217; field of view, 400 mm x 252 mm; Sense factor, 2; slice thickness, 2.0 mm, gap, 0.2 mm; number of signal average, 2); and axial diffusion weighted image (repetition time = 9000; inversion time = 250; echo time = 67; matrix, 112 x 112; field of view, 300 mm x 300 mm; Sense factor, 2.5; slice thickness, 3.0 mm, no gap; number of signal average, 6; b factor = 0 and 800 s/mm^2; directions of gradient sampling, 16). The scan time took 13 minutes for T2-weighted image-high resolution, 5 minutes for mDIXON and 8 minutes for diffusion weighted image; the total scan time was therefore 26 minutes.

Conventional myelography

All patients underwent conventional myelography. Under a sterile technique, the subarachnoid space at the L3-L4 intervertebral level was punctured by a spinal needle. Then, 10 ml of water-soluble, non-ionic contrast medium (iopamiro) was injected via the spinal needle. The cervical myelography was performed with fluoroscopic guidance for the AP, lateral and both oblique views. After that, patients had to rest with their head elevated to observe for any immediate complications. It took about 90-120 minutes to perform the conventional myelography.

The results of the conventional myelography and MR imaging were recorded as a normal or abnormal nerve from C5-T1 levels, bilaterally. With the conventional myelography, abnormal nerve roots were defined as the loss of normal configuration (i.e. blunting) of nerve roots and/or demonstrable pseudomeningocele (Fig 1). As for the MR imaging, abnormal nerves were defined as the loss of normal nerve alignments, distributions and/or architectures in either the preganglionic or postganglionic portions (Fig 1, Fig 2, Fig 3). The preganglionic nerve root was interpreted from T2-weighted image-high resolution, and the postganglionic nerve root was observed by using T2-weighted image-mDIXON and diffusion weighted image. The abnormality of the nerve roots was interpreted and compared with the normal contralateral side in both the conventional myelography and MR imaging.

Two neuroradiologists separately reviewed the MRN study and the conventional myelography, and they were blind to the clinical data. Disagreements between the readers were resolved by consensus.

Statistical analysis

The results of conventional myelography and each sequence of MR imaging were correlated, with the clinical contexts being used as the gold standard. The accuracies,

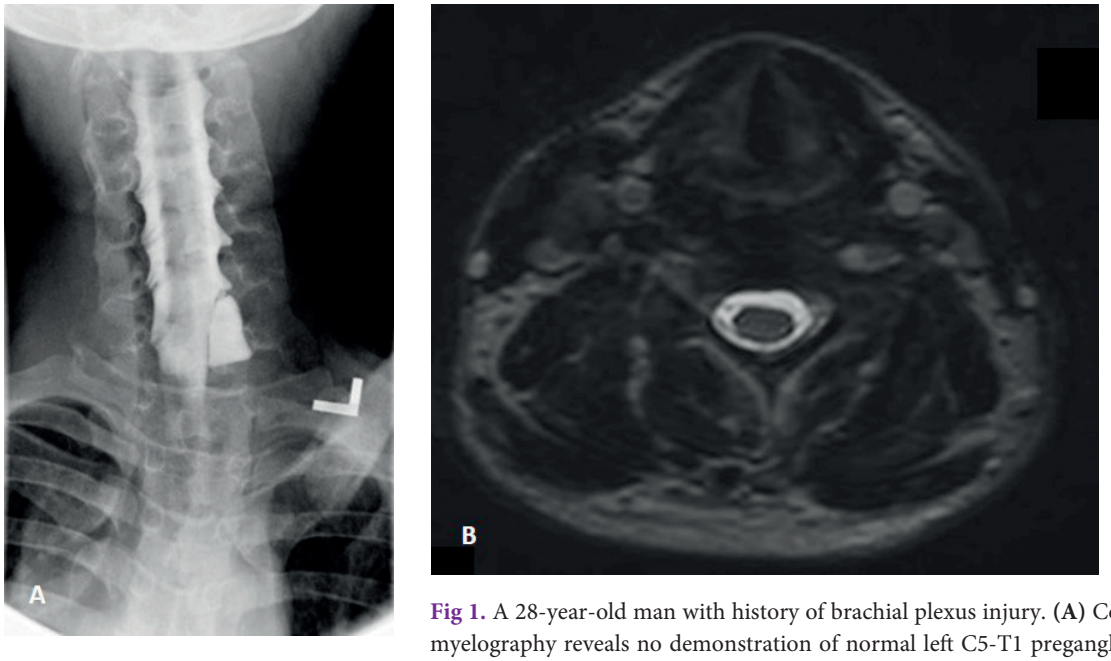


Fig 1. A 28-year-old man with history of brachial plexus injury. **(A)** Conventional myelography reveals no demonstration of normal left C5-T1 preganglionic nerve roots with pseudomeningocele at left C8 nerve root. **(B)** T2-weighted image-high resolution, no detectable normal ventral and dorsal left C5 nerve roots, representing nerve root avulsion.

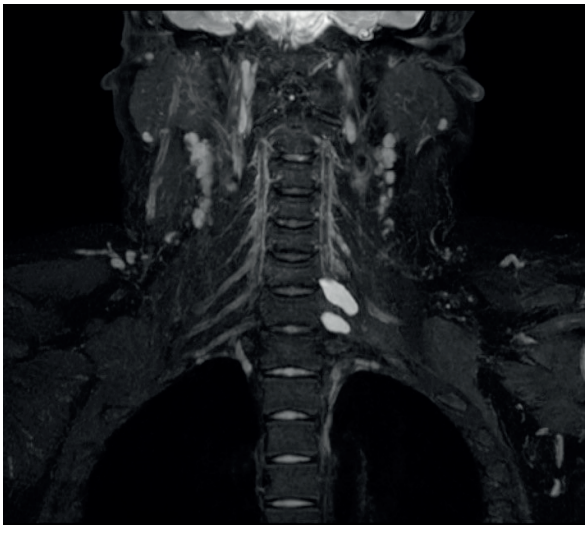


Fig 2. Coronal MIP image of mDIXON of a 20-year-old man reveals abnormal contour with irregularity of left C5 and C6 roots and total avulsion of left C7 and C8 roots with associated pseudomeningoceles at left C7 and C8 roots.

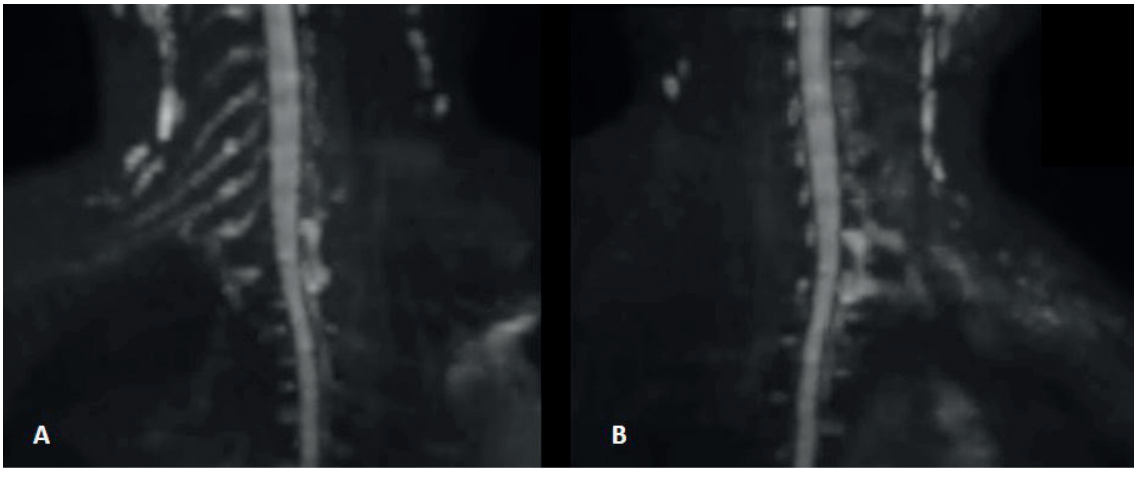


Fig 3. Coronal MIP image of diffusion weighted image of a 28-year-old man reveals abnormal contour with total irregularity of left C5-T1 nerves (B) as compared with the contralateral normal appearance (A)

sensitivities, specificities, and the false positive and false negative values were calculated. All data analyses were performed using SPSS software version 18.0 (SPSS Inc., USA).

RESULTS

The 21 patients with brachial plexus injury in this study were investigated 2 to 13 months after injury (mean: 5.1 months). The mean age of the patients was 27.1 years, with an age range of 16 to 39 years; 19 were male, and 2 were female. A total of 210 nerves of the brachial plexus (bilateral C5-T1) were interpreted for their individual modalities/MR sequences. In the case of T2-weighted image-high resolution, one patient was excluded due to motion artifact during imaging, leaving 200 nerve roots. The number of nerve abnormalities evaluated for each nerve level and for the different modalities are at Table 1.

Table 2 summarizes the diagnostic performance (specifically, the accuracy, sensitivity, specificity, false positive and false negative values) of each diagnostic tool (conventional myelography, T2-weighted image-high resolution, mDIXON, diffusion weighted image, and the combination of T2-weighted image-high resolution and mDIXON and T2-weighted image-high resolution and diffusion weighted image). The diagnostic performances of conventional myelography and T2-weighted image-high resolution were similar. The combination of T2-weighted image-high resolution and mDIXON had the highest accuracy for the diagnosis of brachial plexus injury.

A comparison of the critical performance factors of the conventional myelography and the MRI study is at Table 3. The benefits of the MRI study over the conventional myelography were its shorter processing time, lack of radiation exposure, lack of the need for contrast medium administration, and the ability to evaluate both pre- and postganglionic lesions. However, the cost of using an MRI study was much higher than that for conventional myelography.

TABLE 1. Number of nerve abnormalities, by nerve level, for different modalities.

Diagnostic tool (total patients)	Number of nerve abnormalities				
	C5	C6	C7	C8	T1
Clinical (21)	17	19	15	11	10
Myelography (21)	5	17	18	16	10
T2WI/HR (20)	9	15	17	16	10
mDIXON (21)	17	21	20	18	9
DWI (21)	14	19	21	20	10

Abbreviations: T2WI/HR = T2-weighted image-high resolution, DWI = diffusion weighted image

TABLE 2. Diagnostic performance of imaging modalities in brachial plexus injury compared with clinical contexts.

Diagnostic tool	Accuracy	Sensitivity	Specificity	False positive	False negative
MYELOGRAHY	69.52%	73.61%	60.61%	19.70%	48.72%
T2WI/HR	72.00%	78.26%	58.06%	19.40%	45.45%
mDIXON	76.19%	91.67%	42.42%	22.35%	30.00%
DWI	67.62%	84.72%	30.30%	27.38%	52.38%
T2WI/HR + mDIXON	78.00%	97.10%	35.48%	22.99%	15.38%
T2WI/HR + DWI	71.00%	91.30%	25.81%	26.74%	42.86%

Abbreviations: T2WI/HR = T2-weighted image-high resolution, DWI = diffusion weighted image

TABLE 3. Comparison of the critical performance factors of conventional myelography and MRI study.

Factor	Conventional myelography	MRN study
Time [Minutes]	90-120	26
Cost [Baht]	3300	17 600
Contrast medium	Yes	No
Radiation exposure	Yes	No
Evaluation	Preganglionic injury	Both pre- and postganglionic injury

DISCUSSION

Most Thai patients with brachial plexus injuries are male and of a younger age because the injuries commonly occur in motor vehicle accidents, as has been reported in multiple studies.[4-6] Brachial plexus injuries are classified into three categories: preganglionic lesions, postganglionic lesions, and a combination of both.[7] Multiple root injuries are also seen in most patients. Adequate surgical technique requires the differentiation of preganglionic lesions from postganglionic lesions. This is because the surgical procedure for preganglionic lesions consists of neurotization (nerve transfer), whereas postganglionic lesions may be treated by neurolysis or repair with nerve grafting.[8,9] The accurate diagnosis of brachial plexus injuries before surgery remains challenging. Many methods are used to evaluate the injury pattern, including physical examination, a nerve conduction study, electromyography, conventional myelography, CT myelography, and MRI. However, none of those methods is considered the reference standard.[10] Some studies have used the results of operative findings or have combined them with intraoperative electrodiagnostic studies to establish a reference standard.[4,8,11] Some studies have also used CT myelography as the gold standard for the imaging of nerve root avulsion.[7,9] However, in experienced surgeons at our institute use physical examination to diagnose brachial plexus injuries in combined modality with a nerve conduction study or an electromyogram test in some cases. Sometimes, surgeons cannot identify the entire course of the nerves, probably due to fibrosis, so making a definite diagnosis by using operative findings is not possible. Therefore, we used the clinical contexts as the reference standard in our study.

For the evaluation of preganglionic root injuries, conventional myelography is the diagnostic tool currently used by our institute. However, it is an invasive procedure, and it takes considerably longer to perform than an MRI study. D. Somashekar et al. found that a high-resolution MRI had a similar sensitivity to CT myelography when evaluating neonatal brachial plexus palsy.[3] According to our results, T2-weighted image-high resolution was also comparable to conventional myelography in terms of its accuracy, sensitivity, specificity, and false positive and false negative values. In addition, T2-weighted image-high resolution is noninvasive and needs a noticeably shorter performance time (approximately 13 minutes) than conventional myelography (approximately 90-120 minutes). Furthermore, the patients are not exposed to the contrast medium, have no risk of iodine contrast allergy, and do not suffer from any side effects or radiation exposure. Therefore, we suggest that T2-weighted image-high resolution replace conventional myelography for the diagnosis of brachial plexus injuries. However, in our study, both conventional myelography and T2-weighted image-high resolution had a diagnostic accuracy of preganglionic nerve root injury of only 69.52% and 72.00%, respectively. The inaccurate interpretations are probably due to partial nerve root avulsions, intradural fibroses, scars, or postganglionic lesions.

Conventional myelography and T2-weighted image-high resolution demonstrate preganglionic injuries, whereas mDIXON and diffusion weighted image detect postganglionic injuries. In our study, mDIXON had a slightly higher diagnostic yield than diffusion weighted image in the diagnosis of postganglionic brachial plexus injuries. In addition, mDIXON can provide accurate, indirect signs of root avulsion injuries, namely, the regional denervation of muscle changes which are seen as muscle atrophy, or a high T2 signal change, consistent with the article by A. Chhabra et al.[12] Therefore, mDIXON may have more benefits than diffusion weighted image in the detection of postganglionic lesions. However, it is also feasible to apply diffusion tensor imaging by improving the spatial resolution in order to obtain better information

on nerve abnormalities than diffusion weighted image, including microstructural changes and fiber tractography. By contrast, mDIXON only provides information on the structural changes of nerves. The combination of T2-weighted image-high resolution with mDIXON or diffusion weighted image provided better results for the detection of brachial plexus injuries than mDIXON or diffusion weighted image alone because a combination can detect lesions in both pre- and postganglionic injuries. Given that the combination of T2-weighted image-high resolution and mDIXON had the highest diagnostic yield, we recommend it be used as the diagnostic tool for brachial plexus injuries in preference to conventional myelography.

The present study used the clinical contexts as the reference standard. The low specificities and high false-positive values in the results were probably due to the following:

1. At our institute, expert hand orthopedists use the clinical contexts as the gold standard, and only total avulsion tears are considered as abnormal findings. In other words, partial tears are excluded. However, there is a view that the clinical contexts might be inaccurate. Some believe that surgery might be more accurate, but in practice, orthopedists cannot explore the brachial plexus for each root level in all patients. This is because some patients need no surgery, and if surgery is performed, the brachial plexus still cannot be well identified, not only due to the anatomical defect but also fibrosis. Thus, there is still doubt as to what should be used for the definition of the gold standard.

2. There might be overinterpretation by the radiologists as the study defined abnormal findings in the myelography and MRI as a loss of normal nerve root alignment, distribution and/or architecture relative to the normal contralateral side, which may have included a partial tear at the site of the nerve injuries.

LIMITATIONS

The reference standard in our study only used a physical examination, which might be an inaccurate reference. Using a combination of physical examination, surgical findings, and electromyogram as the reference standard might improve the diagnostic yield.

In addition, the reference standard used in our study could not differentiate preganglionic from postganglionic lesions.

CONCLUSION

We recommend that the combination of T2-weighted image-high resolution and mDIXON be adopted as the diagnostic tool for the diagnosis of brachial plexus injuries in preference to conventional myelography. This is because of its faster processing time, the lack of the need for contrast medium administration, and its usefulness in evaluating both preganglionic and postganglionic injuries.

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The Determinants of Quality of Life in Thai Family Caregivers of Stroke Survivors

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ABSTRACT

Objective: Stroke survivors suffer from multiple health problems, leading to physical and psychological impairments or disabilities. Largely, family caregivers encounter stressful situations when providing stroke care at home, however, little is known about their quality of life (QOL) and its determinants. This study aimed to identify the determinants of QOL among Thai family caregivers of stroke survivors.

Methods: The sample consisted of stroke caregivers from two tertiary hospitals in the central region of Thailand. Data collection using a set of questionnaires was performed at the out-patient department of each hospital. Data analysis included descriptive statistics and path analysis to examine the hypothesized relationship between the study variables and QOL.

Results: A total of 300 stroke caregivers were recruited. Their age ranged from 20-84 years old, and mostly were female (76%). Determinants of QOL among family caregivers were caregivers' age, caregivers' income and care burden. Care burden was the strongest predictor which explained 64 % of the total variance ($p < .001$).

Conclusion: Sociodemographic factors impact on QOL among Thai family caregivers of stroke survivors. Caregivers' burden remains a serious issue, especially for those at an advanced age with low income who provide the care for severely dependent stroke survivors. Therefore, nurses and health care team should be aware of these determinants and develop a family intervention program to support them so as to improve their QOL.

Keywords: Family caregiver; stroke survivor; quality of life; determinants (Siriraj Med J 2019; 71: 290-296)

INTRODUCTION

Stroke is a serious global health problem. Each year, more than 6.5 million adults die from stroke and another 5 million are left permanently disabled.[1] Family caregivers provide most of the home-based care for stroke patients. Previous studies in other countries suggest that the provision of stroke care can be a significant stressor in the lives of family caregivers, negatively affecting their quality of life (QOL). The definition of QOL as proposed by the World Health Organization[2] (an individuals' perception of their physical health, psychological well-being, level of independence, and social relationships in the context of their sociocultural environment) was used to guide this study. Previous cross-national literature involving family caregivers of stroke survivors reported a negative relationship between measures of QOL and perceived caregiver burden.[3,4,5] Some but not all studies have also reported a relationship between dependency for activities

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of daily living (ADLs), age, income, social support and decreased QOL scores.[3,4,6] Cultural beliefs and values may account for some of the discrepant findings across studies.[7] Currently, little data are available regarding QOL in the context of Thai family caregivers of stroke survivors, providing little for health care providers and policymakers to develop strategies to develop family-centered support.

Similar to an American study with caregivers of stroke survivors[8], we used the Stress Process Model (SPM)[9] to frame this study. This model is composed of four domains, including background and context, stressors, mediators, and outcomes. Within a Thai context, we considered the stressor to be the degree of dependency for ADLs, potential mediators to be age, income, coping style and social support, and the measured outcome was the family caregiver's QOL score. The primary aim of this study was to examine family caregivers' QOL within a Thai context and its relationship with factors that have been previously reported to influence QOL in family caregivers from other countries who provide daily care to their family member who has survived a stroke.

MATERIALS AND METHODS

A cross-sectional study design was used to examine the variables of interest and their potential impact on family caregivers' QOL. Approval for this study was obtained from the Institution Review Board for the protection of human subjects from Mahidol University (Si 251/2558). The inclusion criteria for family caregivers were adults aged 18 years and older; self-identified as a primary caregiver that lived with the survivor and provided unpaid continuous care for a family member that had experienced a stroke at least 6 months prior to the study; and those able to speak, read, and understand Thai. The calculated sample size, using the method proposed by Hair and colleagues[10], to meet our primary objective was estimated as requiring 300 participants.

Data were collected from family caregivers at the out-patient department (OPD) of two tertiary care hospitals located in an urban area in the central region of Thailand. The first hospital is a tertiary hospital under the Ministry of Education whereas the second hospital is a tertiary hospital under the Ministry of Public Health. Both hospitals are selected because they are teaching hospitals, referral centers with certified stroke centers that could represent characteristics of stroke survivors and family caregivers throughout the country. A single interview was completed in a private area of the OPD in each hospital, either before or after the patient and family caregiver were seen in follow-up by their physician. After obtaining informed consent participants were asked questions from a sociodemographic form and asked each item from a series of standardized questionnaires. Sociodemographic data included age, marital status, and perceived income sufficiency. The Barthel Activities of Daily Living Index (BAI)[11] Thai version[12] was used to assess the ADL dependency of the stroke survivors. It is composed of 10 items, with the total score ranging from 0 to 20. Lower scores indicate high dependency. The Burden Interview (BI) developed by Zarit[7] and translated into Thai by Mapi Research Trust[13] was used to measure caregiver burden. Total BI scores range from 0 to 88, with higher scores indicative of greater perceived burden. Coping strategies used by the family caregiver were identified using the Jalowiec Coping Scale (JCS),[14] which had been previously translated into Thai.[15] The JCS is divided into three subscales: confrontive coping (constructive problem solving; 13 items), emotive coping (expressing emotions as a stress reliever; 9 items), and palliative coping (activities to make one feel better; 14 items). Total coping scores range from 36 to 180; higher scores indicative of more frequent use of that coping strategy. The Social Support Questionnaire (SSQ)[16] was translated and modified for cultural relevance[17] and was used to assess perceived social support from three potential sources: family members (5 items), relatives and friends (5 items), and healthcare providers (5 items). Total scores range from 0 to 60, with higher scores indicative of greater social support. QOL was measured by the World Health Organization Quality of Life Instrument BREF (WHOQOL-BREF) Thai version.[18] The first two items rate general health satisfaction and overall QOL, while the other 24 items gather information about physical health (7 items), psychological health (6 items), social relationships (3 items), and the environment (8 items). The total QOL scores range from 26 to 130; higher scores indicative of greater perceived QOL. Reliability was tested for each of the instruments used in the study; with Cronbach's alpha coefficients calculated for each (BAI = 0.89; BI = 0.94; JCS = 0.84; SSQ = 0.94; and WHOQOL-BREF = 0.88).

Data analysis

The data in the present study were analyzed using descriptive statistics to delineate the sociodemographic characteristics of the family caregivers and the stroke survivors. Student t-tests were used to examine for gender and age group differences in the study variables. This was followed by calculating Pearson's correlation coefficients to examine the relationships between each variable of interest and the QOL score. Finally, path analysis [using

the Linear Structural Relationship (LISREL) 8.72 Program (Student version, Scientific Software International, Chicago, IL, USA)] was used to develop a best fit model. The indicators that were used to establish model fit, included: 1) the non-significant value of chi-square (χ^2); 2) the ratio of chi-square (χ^2) / degree of freedom (df) less than 2; 3) goodness of fit (GFI) greater than 0.9; 4) adjusted goodness of fit (AGFI) greater than 0.9; 5) comparative fit index (CFI) greater than 0.95; 6) root mean square error of approximation (RMSEA), and standard root mean square residual (SRMR) less than 0.05.[10] Of note, the study variables in this study were not normally distributed. Therefore, the robust maximum likelihood (RML) method using an asymptotic covariance matrix was used for input10 and the Satorra-Bentler scaled chi-square was used to indicate the value of the chi-square (χ^2) for measuring the model fit with the empirical data.

RESULTS

The ages of the participants reflected a broad range from 20 - 84 years old (M = 52.32, SD = 13.59). When examining the number of participants in each age group, the result showed that 67.7% were adults (20 - 59 years old) and 32.3% were older persons (60 years old and older). Age group differences between adults and older persons were not significant in the scores associated with coping, caregiver burden and QOL. Similar to the majority of other studies regarding caregivers, most of the participants in this study were female (76%) and married (69.7%). Two-thirds of the caregivers considered they had sufficient income and also indicated that they had secondary caregivers that helped them (mainly other family members). More than half of the participants (56%) reported physical health problems (musculoskeletal pain, stress and anxiety, and insomnia were the most frequent concerns). Table 1 summarizes the data from the standardized questionnaires. Significant gender differences were observed in the scores obtained in the measures of coping, caregiver burden and QOL. Almost half (49%) of the stroke survivors had experienced their stroke between 6 to 12 months prior to the study.

The modified model fit well with the data at $\chi^2 = 0.43$, df = 11, χ^2 /df = 0.03, p = 1.00, GFI = 0.99, AGFI = 0.98 (Fig 1). The contributions of the variables to the scores on the WHOQOL-BREF, in terms of direct, indirect, and total effects, are displayed in Table 2. Specifically, the model illustrates that the caregivers' age and income had a positive direct effect on their WHOQOL-BREF QOL scores, and the caregivers' age had a significant indirect effect on the scores through social support. Caregiver burden had a negative direct effect on the WHOQOL-BREF QOL scores and an indirect effect through coping. Social support was more powerful than coping as a mediator of WHOQOL-BREF QOL scores among the stroke caregivers. ADL dependency scores did not have a significant direct or indirect effect on the caregivers' WHOQOL-BREF QOL scores (Table 2). This best fit model explained 64% of the variance in QOL, 10% of the variance in coping, and 4% of the variance in social support.

TABLE 1. Overall and gender differences in characteristics of stroke caregivers (n = 300).

	Overall		Male (n = 72)		Female (n = 228)		P value*
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	
Caregiver burden	44.65	17.59	39.81	1.84	46.18	1.12	0.007
Coping	92.60	13.74	87.84	1.17	94.10	0.87	0.001
Confrontive	42.36	7.99	28.61	0.64	32.10	0.36	
Emotive	17.22	3.98	21.62	0.51	19.69	0.43	
Palliative	33.01	5.72	39.54	0.87	40.37	0.43	
Social support	32.45	12.21	31.79	1.28	32.66	0.83	0.597
Family	11.79	6.11	12.09	0.74	11.69	0.40	
Relative	10.49	5.83	9.29	0.63	10.86	0.39	
Health care provider	10.13	4.33	10.40	0.46	10.10	0.29	
Overall QOL	75.88	14.44	79.81	1.69	74.64	0.94	0.008
Physical health	21.22	4.69	22.79	0.54	20.73	0.30	
Psychological health	18.47	3.73	19.26	0.37	18.22	0.25	
Social relationship	7.64	2.01	8.00	0.26	7.52	0.12	
Environment	22.99	4.40	23.79	0.52	22.73	0.28	

Note: * the results of the t-tests comparing male and female caregivers

TABLE 2. Direct effect, indirect effect and total effect of study variables.

Variable & impact	The modified model		
	DE	IE	TE
BETA			
Social support ⟶ QOL	.28***	-	.28***
Coping ⟶ QOL	.10*	-	.10*
GAMMA			
Age ⟶ Social support	-.18***	-	-.18***
Age ⟶ QOL	-.15***	-.05	-.20***
Income ⟶ Social support	.10	-	.10
Income ⟶ QOL	.14***	.03	.17***
ADL ⟶ Coping	.00	.00	.00
ADL ⟶ QOL	.05	-	.05
Burden ⟶ Coping	.31***	-	.31***
Burden ⟶ QOL	-.64***	.03	-.61***

Note: ***p < .001, *p < .05 **Abbreviations:** DE = Direct Effect, IE = Indirect Effect, TE = Total Effect

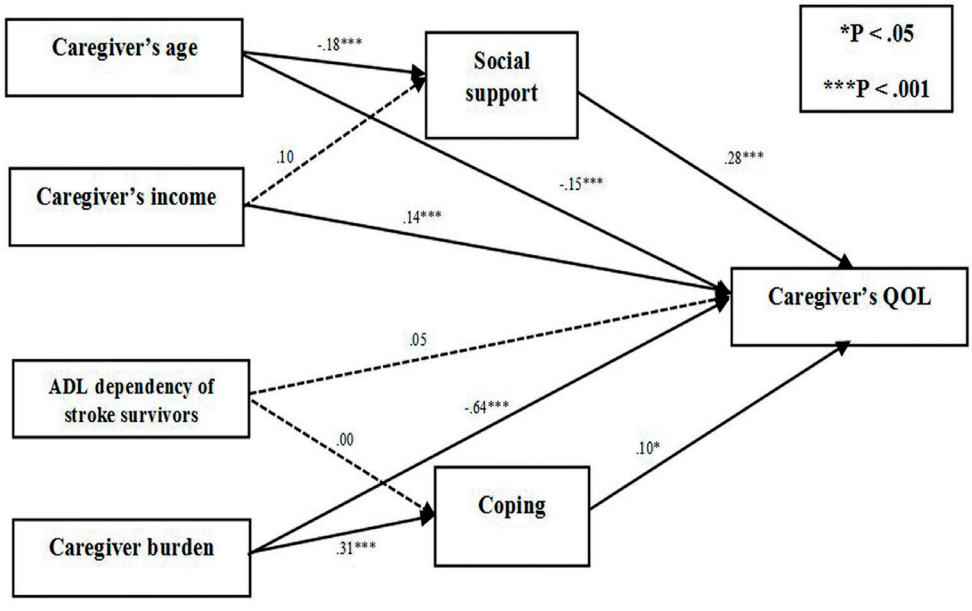


Fig 1. Determinants of quality of life in Thai family caregivers of stroke survivors.

DISCUSSION

In this study, most of the findings were congruent with the Stress Process Model (age, income, care burden). However, ADL dependency did not make a significant contribution to QOL scores. This is in contrast to some previous research[19,20] but consistent with other studies.[5,21]

Although more than 50% of caregivers reporting that they provided most of the hygiene care, mobility and emotional support, and transportation for follow-up medical, this was not related to the caregivers perceived QOL. This is consistent with a previous study that used the same theoretical model and reported that loss of functional capacity in the stroke survivor decreased leisure activities for the caregiver, however this decrease did not affect scores on the QOL measure.[8] Potential contributors to this difference include the duration of

caregiving (all caregivers had been providing care for more than 6 months and 50% for more than 12 months), thus perhaps they had adapted to their caregiving role while caregiving became more structured into routines. In addition, after this time period, there may also have been improvements in ADLs that provided positive reinforcement for caregivers.[20] In addition, most of the participants (64%) had secondary caregivers to help them in providing care for their family member.

In response to the questions from the BI, some participants expressed that they were grateful to have a chance to repay their parent/spouse for past support. This sense of filial responsibility and pride in having that responsibility is consistent with Thai spiritual and cultural beliefs and values and has been noted by other Thai researchers.[22] Indeed, older adults living in care homes in Thailand feel stigmatized, reflecting a belief that others must see them as being poor with no family.[23] In the original article regarding development of the BI, Zarit and colleagues[7] cautioned that culture is important in the concept of caregiver burden. In a recent literature review, caregivers derived meaning in their caregiving from multiple sources (their personal sacrifice, a moral or religious obligation, others' expectations, social norms and a subjective choice based on love, hope, and a sense of reciprocity).[24] Thus, comparing scores obtained from cross-cultural studies must be interpreted with caution, considering interactions among individual, cultural and societal contexts. For example, BI scores reported from studies involving family caregivers of stroke survivors ranged from 29.6 to 34.9 in two Brazilian studies[5,25], 47.4 in a Turkish study[26,27], 21.6 in another Thai study[22] and 34.1 in a Japanese study.[28] In an Indian study 58% of the caregivers had BI scores over 75.20. The mean score (44.7) observed in this study was higher than some other studies and may reflect an increased prevalence of physical health problems reported by caregivers and perhaps a more accurate estimate of caregiver burden, as suggested by other Thai researchers.[29,30] An American study calculated a cutoff score on the BI of 24 - 26 as being predicative of increased risk of depression in caregivers.[31] However, in contrast to the extensive and well-established long-term care system in North America, most Asian countries rely heavily on family members to provide care until the family member's death.[32]

As with other studies[33,34], we found financial security had a significant positive direct effect on the caregivers' QOL. This consistent finding has led to efforts to quantify the cost associated with informal care by families and to consider providing employee benefits or government subsidies to support family caregiving, especially for women who leave employment to care for parents who need care.[35,36,37] In relation to an age issue, the finding in this study revealed that about one third of the participants aged 60 years old and older. Although some previous study[38] found that the more advanced age, the more mature and experienced people have in care providing skills. However, consistent with previous stroke literature[3,4], this study revealed that advanced age had a negative direct effect on QOL. Older people tend to have health decline and therefore require support to cope with care burden for other family members who are ill. Finally, the importance of social support and adaptive coping was affirmed in our study. As reviewed in previous studies, multiple family support interventions have been developed and tested, with positive impact on QOL measures.[37,39,40]

Limitations

This study may have limited generalizability due to a potential bias selection of participants. Based on the selection criteria, the participants were family caregivers who were able to bring their stroke relatives to follow up at the OPD. This means the ADL of their stroke relatives might have been improved. However, there may be a number of stroke survivors that have been bedridden and difficult to bring to follow up at the OPD. In these cases, the ADL dependency may make a significant contribution to the QOL scores. Therefore, further study should investigate more on those caring for stroke survivors who are bedridden at home. Qualitative studies that can yield rich text regarding factors affecting QOL of stroke caregivers would also make an important contribution to further understanding in this issue.

CONCLUSION

This study identified a number of potentially modifiable determinants (socioeconomic of caregiver, perception of care burden, and social support) that could be used to develop and test interventions to improve the QOL among family caregivers of stroke survivors in Thailand. However, our data provide evidence that such development would require consideration of gender. Qualitative studies on the lived experience of Thai male and female caregivers of stroke survivors could provide rich information about their biggest challenges, what resources would be most helpful, and what priority area(s) would improve their QOL. These data could provide further details to optimize potential the development and testing gender-sensitive and/or gender-specific interventions. The topics addressed in such an intervention could focus on improving caregivers' physical health status, providing psychological support, and creating routines

that allow them for more predictability and scheduled time for social activity and for self, leading to grater QOL.

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Clinical Characteristics and Prognosis of Morphea (Localized Scleroderma) in Adults: a Retrospective Study

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ABSTRACT

Objective: To study the clinical characteristics and prognosis of morphea in Thai adult patients.

Methods: The medical records of 81 morphea adult patients who visited Siriraj Hospital, Thailand, between 2006 and 2015, were retrospectively reviewed. The demographics, clinical features, treatments and outcomes were analyzed. Clinical improvement was categorized as excellent (>80%), partial (1%–80%), and no response.

Results: Circumscribed morphea was the most common subtype (34, 42%) of the 81 patients, followed by linear morphea (21, 26%), generalized morphea (14, 17%), en coup de sabre (11, 14%) and Parry–Romberg syndrome (1, 1%). Systemic treatment and ultraviolet A (UVA)1 phototherapy had satisfactory outcomes in 83% and 79% of cases, respectively, providing a partial to excellent response. For overall remission, one year after the treatment, 30% of patients achieved a partial to excellent response. After 2 years, this proportion rose to 50%. The median time to clinical response was 24 months.

Conclusion: Morphea is a difficult-to-treat dermatosis, with the majority of the patients having a partial clinical response and a high recurrent rate. Combination of treatment might be a worthy option.

Keywords: Morphea; prognosis; phototherapy; systemic; treatment (Siriraj Med J 2019; 71: 297-301)

INTRODUCTION

Morphea, or localized scleroderma, is a rare, chronic, autoimmune disease manifested by dermis and/or subcutaneous tissue sclerosis.[1] The incidence of morphea is approximately 2.7 cases/100,000 people.[2] Morphea is divided into five subtypes: (1) circumscribed morphea (including a superficial and deep variant); (2) linear morphea (including a limb/trunk variant and a head variant); (3) generalized morphea; (4) the pansclerotic subtype; and (5) the mixed subtype.[1] The different clinical manifestations of morphea have led to the development of different classifications and progressions of the disease.[1,3] Therefore, this study aimed to elucidate the clinical characteristics, treatment types, results after treatment, and prognosis of adult patients with morphea.

MATERIALS AND METHODS

Subjects

This study was approved by the Institutional Review Board, Faculty of Medicine Siriraj Hospital (Si 690/2015). The medical records of patients age ≥ 18 years diagnosed with morphea at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, between January 2006 and December 2015 were retrospectively reviewed. A total of 81 adult morphea patients, evidenced by clinical and/or pathological findings, were included.

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Demographic data, clinical manifestations, lesion sites, symptoms, treatments and clinical responses at final follow-up were collected. A telephone survey was conducted to follow up the relapse status after the last consultation.

The clinical responses were subjectively categorized as excellent (>80%), partial (1%-80%), and no response. Serial photographs before and after treatment were evaluated for clinical response by two dermatologists. Additionally, the effects of the UVA1 dosage on the clinical responses and recurrence rates were gathered. UVA1 phototherapy was categorized as low-dose (20-40 J/cm^2), medium-dose (>40-80 J/cm^2) and high-dose (>80-120 J/cm^2). UVA1 phototherapy was administered three to five times a week for 30 sessions.

Statistical analysis

Descriptive statistics, including frequency counts and tables, were used for demographic data, clinical manifestations, clinical responses, treatments, and disease recurrence. A Chi-square test or, if there were <5 responses in a cell, a Fisher exact test was used to examine the differences in the proportions and the association strength between the clinical response and disease recurrence, according to the treatment types and UVA1-phototherapy doses. A p value of less than .05 was set as the cutoff for statistical significance. All analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA).

RESULTS

A total of 81 patients, aged 18-83 years and with a median age of 34 years, were included in the analysis. There were 64 (79%) females, and 17 (21%) males, making the female to male ratio 3.8:1. The median time between the initial disease manifestation and diagnosis was one month. The most common subtype of morphea was circumscribed morphea (34, 42%), followed by linear morphea (21, 26%), generalized morphea (14, 17%), en coup de sabre (11, 14%), and Parry-Romberg syndrome (1, 1%).

Morphea lesion was mostly found in the lower extremities, followed by the trunk, head and neck, and upper extremities. In circumscribed morphea, lesions were mostly found in the trunk. However, in the linear and generalized groups, lesions were mostly found in the lower extremities. Skin discoloration (79%), induration (43%) and atrophy (39%) were the top three, most common clinical symptoms of all of the types of morphea. None of the patients progressed to systemic sclerosis during the follow-up period.

The combination therapy was the most often used treatment for generalized morphea and linear morphea (Table 1). Topical corticosteroids (41%) were the most frequently prescribed topical treatment, followed by combined topical corticosteroids with a calcineurin inhibitor (24%), and then by a calcineurin inhibitor alone (11%). In the case of systemic treatment, colchicine (23%), corticosteroid (19%), and methotrexate (14%) were the top three prescribed medicines. Colchicine was the most commonly prescribed drug for systemic treatment in the circumscribed and en coup de sabre groups. As for linear and generalized morphea, oral prednisolone (23.8%) and methotrexate (35.7%) were the most used drugs, respectively.

Fifty-nine percent of patients achieved a partial clinical response, another 18% had no response, while 9% had an excellent response. Generalized morphea (Fig 1) displayed the most favorable response rate at 79%, followed by circumscribed morphea (70%), linear morphea (67%), and en coup de sabre (46%). The linear group had the shortest recurrence time, at 8 months, followed by en coup de sabre (10 months) and generalized (31 months). Circumscribed morphea had the longest recurrence time, at 47 months.

UVA1 phototherapy was administered in 24 (30%) cases. Eighteen (75%) patients received a medium dose (>40-80 J/cm^2) regimen of UVA1 (Table 1). For all types of morphea, the clinical responses did not differ significantly with different doses of UVA1 (p=0.490; Table 2). UVA1 phototherapy combined with systemic treatment (oral prednisolone, methotrexate, colchicine or chloroquine) provided a significantly better response than UVA1 alone (p= 0.044). The recurrence rate did not vary significantly (p=0.674) for morphea patients treated with just UVA1 or with UVA1 plus systemic treatment. Different doses of UVA1 also had no effect on the recurrence rate (p=0.850) (Table 2).

The Kaplan–Meier curve demonstrated the probability of a partial to excellent clinical response for the morphea patients overall. One year after the treatment, 30% of patients achieved a partial to excellent response. After 2 years, this proportion rose to 50%. The median time to clinical response was 24 months.

DISCUSSION

This retrospective study emphasizes the clinical features and prognoses of different types of morphea. We found circumscribed morphea to be the most common type, which was similar to results from the Korea and Netherlands.[4,5] However, a study from the United States found that generalized morphea was the most common subtype among adults.[6]

TABLE 1. Number and type of treatments by morphea subtypes.

	Type of morphea, n (%)				Total, n (%)
	Localized (n=34)	Linear (n=21)	Generalized (n=14)	En coup de sabre (n=11)	(n=80)
Demographics					
Mean age (range)	45 (18-83)	29 (18-52)	35 (21-65)	31 (18-49)	37 (18-83)
Male	6 (18)	5 (29)	1 (7)	5 (46)	17 (21)
Female	28 (82)	16 (76)	13 (93)	6 (55)	64 (79)
Mean age onset (range)	37 (4-81)	19 (2-52)	27 (9-58)	22 (8-37)	28 (18-83)
Mean duration of disease (months) (range)	98 (12-240)	124 (2-276)	93 (6-240)	118 (12-216)	107 (2-81)
Location					
Head and neck	9 (24)	2 (7)	2 (6)	11 (100)	25 (23)
Trunk	13 (35)	3 (11)	9 (27)	0	25 (23)
Buttock	1 (3)	2 (7)	0	0	3 (3)
Upper extremities	6 (16)	9 (34)	10 (31)	0	25 (23)
Lower extremities	8 (22)	11 (41)	11 (33)	0	30 (27)
Intertriginous area	0	0	1 (3)	0	1 (1)
Symptoms					
Tightness	1 (1)	6 (13)	0	0	7 (4)
Pain	1 (1)	2 (4)	0	0	3 (2)
Skin color change	29 (43)	16 (33)	12 (43)	6 (32)	63 (38)
Erythema/edema	5 (8)	6 (13)	5 (18)	1 (5)	17 (10)
Deformity	1 (1)	6 (13)	0	2 (11)	9 (6)
Induration	17 (25)	10 (20)	6 (21)	1 (5)	34 (21)
Atrophy	14 (21)	2 (4)	5 (18)	9 (47)	31 (19)
Type of treatment					
Topical treatment					
Corticosteroids	13 (38)	10 (48)	8 (57)	2 (18)	33 (41)
Calcineurin inhibitor	5 (15)	3 (14)	–	1 (9)	9 (11)
Corticosteroids plus calcineurin inhibitor	10 (29)	4 (19)	2 (14)	3 (27)	19 (24)
Others†	3 (9)	2 (6)	–	2 (18)	7 (9)
Systemic treatment					
Oral prednisolone	6 (18)	5 (24)	4 (29)	1 (9)	15 (19)
Methotrexate	3 (9)	3 (14)	5 (36)	–	11 (14)
Colchicine	9 (27)	3 (14)	4 (29)	2 (18)	18 (23)
Others†	11 (32)	9 (43)	8 (58)	4 (36)	32 (40)
Phototherapy (UVA1)‡					
Low dose	1 (3)	1 (5)	–	–	2 (2)
Medium dose	4 (12)	5 (24)	7 (50)	2 (18)	18 (28)
High dose	–	2 (10)	1 (7)	1 (9)	4 (5)
Other treatments					
Intralesional corticosteroids	1 (3)	–	–	1 (9)	2 (3)
Surgery for reconstruction	–	–	–	1 (9)	1 (1)
Clinical response					
Excellent (>80%)	2 (6)	1 (5)	4 (29)	–	7 (9)
Partial (≤80%)	22 (64)	13 (62)	7 (50)	5 (46)	47 (59)
No response	5 (15)	4 (19)	1 (7)	4 (36)	14 (18)
Loss to follow-up	5 (15)	3 (14)	2 (14)	2 (18)	12 (15)
Recurrence of disease					
Recurrence (months)	7 (29)	6 (43)	3 (27)	3 (60)	19 (24)
Time to recurrence (months) – median (min, max)	47 (4, 93)	8 (2, 26)	31 (19, 32)	10 (4, 15)	17 (2, 93)

† Other systemic treatments included chloroquine, hydroxychloroquine, isotretinoin, pentoxifylline, d-penicillamine and indomethacin

‡ UVA1 phototherapy was categorized as low dose (20–40 J/cm^2), medium dose (>40–80 J/cm^2) and high dose (>80–120 J/cm^2)

Abbreviation: UVA1= ultraviolet A1

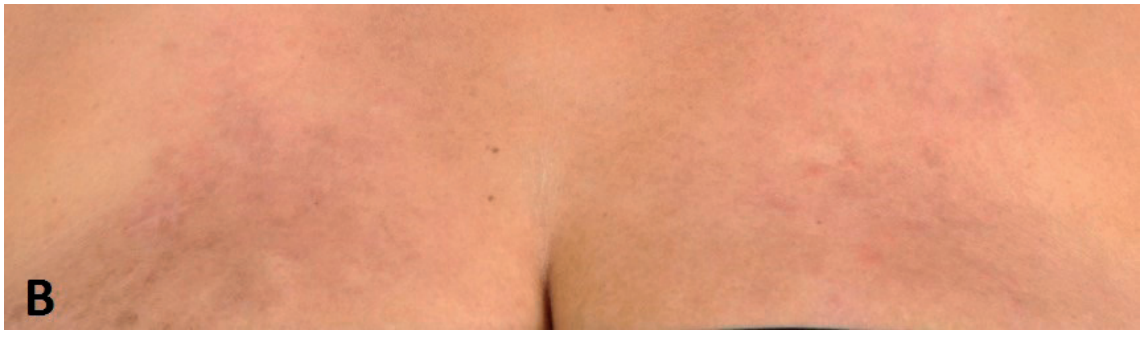
TABLE 2. Clinical response and disease recurrence from UVA1 phototherapy.

	Clinical response, n (%)			*P*-value	Disease recurrence n (%)	*P*-value
	Excellent (>80%)	Partial (≤80%)	No response			
Treatment						
UVA1 plus systemic treatment	3 (33)	6 (67)	–	0.044*	5 (56)	0.674
UVA1	1 (7)	11 (73)	3 (20)		6 (50)	
Dose of UVA1†						
Low dose	–	2 (100)	–	0.490	1 (50)	0.850
Medium dose	3 (17)	12 (66)	3 (17)		8 (53)	
High dose	1 (25)	3 (75)	–		2 (50)	

† UVA1 phototherapy was categorized as low dose (20–40 J/cm^2), medium dose (>40–80 J/cm^2) and high dose (>80–120 J/cm^2)
* p-value ≤ 0.05 considered statistically significant
Abbreviation: UVA1 = ultraviolet A1



1A



1B

Fig 1. Excellent response of generalized morphea on the breast. **A)** Baseline, indurated plaque on the breast. **B)** After treatment with oral prednisolone (30 mg/day) for 6 months, combined with methotrexate 7.5-10 mg/weeks for 12 months and medium dose UVA1 for 30 sessions. The morphea lesion left with postinflammatory hyperpigmentation.

In the present study, clinical responses, including partial to excellent responses, were detected in 59% of the treated morphea cases. The overall level of clinical improvement was similar to the aforementioned Korean study, which showed a 63% improvement.[4] Based on the Kaplan–Meier curve, approximately 50% of treated morphea cases obtained partial to excellent clinical responses within 2 years, regardless of the treatment employed. By comparison, Mertens et al., evaluated the clinical responses after treatment with methotrexate alone; and 62% of patients show a partial to excellent response after 2 years.[7]

UVA1 phototherapy is a commonly-used treatment for morphea.[8] Medium- and high-dose UVA1 phototherapy have proven to provide better outcomes for morphea than low-dose UVA1.[9] Our study showed that 80% of patients had a partial to excellent response to UVA1 (medium dose), similar to the efficacy results found in studies by Vasquez et al. (60%), Su et al. (82.9%) and Andres et al. (82%).[10-12]

Recurrence is common after morphea treatment. Mertens et al., reported a disease recurrence rate of 17% for adult-onset localized morphea, and 27% for pediatric-onset morphea.[5] Linear morphea was the most frequent type.[5] Methotrexate combined with systemic corticosteroids showed a recurrence rate of 30%, with a 6-month mean relapse time after methotrexate discontinuation.[13] Moreover, Vasquez et al., reported a recurrence of 46% for active morphea after successful UVA1 phototherapy.[10] UVA1 phototherapy combined with immunosuppressives may inhibit episodes of recurrence.[10] Similar to another study,[10] the present study found a recurrence rate of 50% after successful treatment with UVA1. Our study supports the view that UVA1 combined with a systemic treatment for morphea provides significantly more benefits than UVA1 alone.

This study is a retrospective chart review and there was a lack of standardized criteria to evaluate the treatment responses; so the evaluation of the effectiveness of the treatments could therefore be subjective. Lastly, there may be a recall bias from the telephone interviews. We recommend a further study should be performed using validated assessments of morphea activity to reduce any bias in collecting data, such as the ultrasound measurements of skin thickness.

CONCLUSION

Morphea is a difficult-to-treat dermatosis, with most patients having a partial clinical response and a high recurrence rate. Overall, the median time to achieve a partial to excellent clinical improvement was 2 years. UVA1 phototherapy combined with systemic treatment was found to be a worthy option for patients.

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Conflicts of interest: None

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A Two-Year Outcome of Intrastromal Corneal Ring Segment Implantation in Keratoconus: Initial Report in Thai Patients

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ABSTRACT

Objective: To determine two-year outcome of intrastromal corneal ring segment (ICRS) implantation in keratoconus in Thai patients

Methods: A retrospective review of medical records of the patients underwent Ferrara-type ICRS implantation (single and two segments) at Siriraj Hospital between November 2013 and December 2017 was conducted. Clinical outcomes were assessed at 1 month, 6 months, 1 year, and 2 years postoperatively.

Results: Of 9 eyes in 8 patients, the mean age of the patients was 24.6 ± 7.5 years. The mean follow-up time was 32.2 ± 9.4 months. Overall, the median visual acuity was significantly improved postoperatively (p value = 0.007). At 2 years, the uncorrected visual acuity (UCVA) improved from 1.00 logMAR to 0.56 logMAR, and the corrected distance visual acuity (CDVA) improved from 0.76 logMAR to 0.10 logMAR. Correspondingly, the median spherical equivalent refraction was significantly improved postoperatively from -7.38 D to -3.13 D ($p < 0.001$). Moreover, the median anterior corneal topographic data significantly changed between visits ($p < 0.02$). The Kmax decreased from 52.65 D to 46.65 D and the Kmean decreased from 48.10 D to 45.40 D at 2 years. Postoperative adverse effects were glare and halos (3 eyes), visually insignificant small white corneal deposits around the segments (2 eyes), extrusion of a ring segment needed removal with reversible to baseline vision (1 eye).

Conclusion: This initial report in Thai patients showed that the ICRS implantation in keratoconus could improve the visual, refractive, and topographic parameters with stability at 2 years. However, appropriate case selection and surgical technique should be considered.

Keywords: Intrastromal corneal ring segment; keratoconus; Thailand (Siriraj Med J 2019; 71: 302-309)

INTRODUCTION

Keratoconus is a progressive ectatic disease resulting in severe visual loss. There is a wide spectrum of treatments for keratoconus including non-surgical options of glasses and contact lenses and invasive surgery of keratoplasty. For the reason to improve spectacle corrected vision or contact lens tolerance and postpone keratoplasty, minimally invasive surgery of keratoconus by intrastromal ring segment (ICRS) implantation was introduced by Colin et al in 2000[1] and has gained wide acceptance in the previous decade. The explanation to correct the myopia was that adding tissue to the periphery of the cornea with small arc-like implants resulted in flattening the central cornea.[2,3]

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Previous studies evaluated the effectiveness of the surgery in their populations.[3-7] To our knowledge, and based on our review of the English-language literature (Ovid, PubMed, ProQuest, Google Scholar, ScienceDirect, and Scopus databases), no previous study has reported on the outcome of the ICRS implantation in keratoconus in Thai patients. We conducted a retrospective record study to demonstrate the clinical outcome and the stability of outcome of the surgery at 2-year follow up.

MATERIALS AND METHODS

Patients

The protocol for this study was approved by the Committee for the Protection of Human Participants in Research at the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (Si 787/2558). The study was a longitudinal retrospective analysis of consecutive patients with keratoconus in which ICSR implantation was performed at Siriraj Hospital from November 2013 to December 2017. The inclusion criteria for ICRS implantation in this study were progressive intolerance to contact lenses and a clear cornea with minimum thinnest corneal thickness of over 300 µm. The exclusion criteria were a significant apical corneal opacity and scarring, corneal hydrops, endothelial count less than 2000 cells/mm^2, history of glaucoma, patients with intense atopy, autoimmune disease or systemic connective tissue disease. All surgeries were performed by four surgeons (P.K., P.P., S.C., and C.C.).

Preoperative examination

Before the surgery, all patients had a complete ophthalmologic examination including uncorrected (UCVA) and best-corrected (CDVA) distance visual acuity, manifest refraction, slit-lamp biomicroscopy, fundoscopy, and Pentacam corneal topography analysis (Oculus Optikgerate GmbH, Wetzlar, Germany). The following topographic data were evaluated: the thinnest corneal thickness, anterior keratometry, and corneal asphericity (Q value) at 8 mm. The grading of the keratoconus was classified according to Amsler-Krumeich classification[8], based on preoperative anterior keratometry; grade I: Kmean ≤ 48 D; grade II: Kmean > 48D to 53 D; grade III: Kmean: > 53 D to 55D; and grade IV: Kmean > 55D.

Surgical technique

The polymethyl methacrylate Ferrara-type ICRS (AJL Ophthalmic, S.A., Spain), which has a triangular cross section (flat basis width = 0.6 mm) that induces a prismatic effect on the cornea, was used in all eyes. The segment has variable thicknesses (150 to 300 µm) and arc lengths (90°, 120°, 140°, 160°, and 210°). The protocol used for ICRS selection was based on the manufacturer-defined nomogram.

The surgery was performed under local anesthesia. The ICRS tunnel was created manually. The center of the visual axis on the cornea was marked for a reference point for centration by asking the patient to fixate on the corneal light reflex of the microscope light. Then, a 5 mm., optical zone was marked and a small radial incision was made at the most curved meridian by a diamond knife for the ICRS to be implanted. The depth of this perpendicular incision was 80% of the corneal thickness. Preparation of the intrastromal pocket for the ICRS was performed at the side of the incision from its base by the spreader and the 270-degree semicircular (clockwise and counterclockwise) dissectors maintaining a uniform depth. After channel creation, the segment was inserted using the modified McPherson forceps with the flat side of the ring downward.

Postoperatively, levofloxacin eye drops were prescribed four times daily for 2 weeks and topical steroid eye drops four times daily for 2 weeks with tapering of the dose over the following 1 month. Non-preservative artificial tear was also prescribed.

Postoperative assessment

Postoperative follow-up visits were at 1 day; 1, 3, 6 months, and then every year following ICRS implantation. We assessed only the clinical outcomes at 1 month, 6 months, 1 year, and 2 years postoperatively to evaluate effectiveness and stability of the surgery. At each of the follow-up visits, the record of UDVA, CDVA, manifest refraction, slit-lamp biomicroscopy, and corneal topography were reviewed. Visual acuity was measured using the Snellen rating and transformed into the logarithm of the minimum angle of resolution (LogMAR)

Statistical analysis

Data analysis was performed using PASW Statistics (SPSS) 18.0 (SPSS Inc., Chicago, IL, USA). A non-parametric Friedman test was used to compare preoperative and postoperative data at all visits. If the difference was statistically significant, a *post-hoc* paired comparison was implemented using the nonparametric two related sample comparison method with adjusting Bonferroni-corrected alpha level. A p value of < 0.05 was considered significant throughout.

RESULTS

Clinical data

Nine eyes in 8 patients were included in the study, and 5 patients were male and 3 patients were female.

One patient received ICRS implantation in both eyes. Four eyes were right eye. The mean age of the patients was 24.6 ± 7.5 years. Considering age group of the patients, 6 eyes were ≤ 30 years and 3 eyes were > 30 years. About grading of keratoconus; 4 eyes were grade I, 2 eyes were grade II, 2 eyes were grade III, and 1 eye was grade IV. The mean thinnest corneal thickness was 442 ± 45.5 µm.

Eight eyes had two segments of ICRS implantation (segment thicknesses of 150 µm and 200 µm, arc lengths of 140°and 160°), whereas 1 eye had single segment (segment thicknesses of 200 µm, arc lengths of 210°). The mean follow-up time of all patients was 32.2 ± 9.4 months. Representative slit-lamp pictures after the surgery were shown in Fig 1. Postoperative symptom of tolerable glare and halos occurred in 3 eyes. Concerning information about scotopic pupil size, centering or depth of the ICRS was not enough to analyze the possible associated factors of those glare and halos. Small white intrastromal deposits which accumulated in the lamellar channel around the segments were found in 2 eyes. There was an extrusion of a ring segment at the incision site in 1 eye at a few weeks after 1 month postoperatively, and both segments in the eye were removed because of the awareness of surgically induced astigmatism. However, 4 months later, her visual acuity and refraction returned back to the baseline before surgery. As the result, eight eyes remained for the data analysis at 6 months, 1 year, and 2 years.

Visual acuity

Visual acuity before and after ICRS implantation at 1 month, 3 months, 6 months, 1 year, and 2 years were presented in Table 1 and Fig 2. Overall, the median UCVA significantly improved after surgery ($p = 0.007$). After *post-hoc* paired comparison, the median UCVA still significantly improved at 2 years postoperatively ($p < 0.02$). Moreover, the median CDVA significantly improved after surgery ($p = 0.001$). After a *post-hoc* paired comparison, the median CDVA significantly improved after 1 year postoperatively ($p < 0.02$). At the last follow up, the median CDVA improved from 0.76 logMAR to 0.10 logMAR.

Manifest Refraction

Manifest refraction before and after ICRS implantation at 1 month, 3 months, 6 months, 1 year, and 2 years were also presented in Table 1 and Fig 2. Overall, the median spherical equivalent of high myopia significantly decreased after surgery ($p < 0.001$). After *post-hoc* paired comparison, the median spherical equivalent significantly decreased at 6 months postoperatively and was still significantly decreased at 2 years postoperatively ($p < 0.02$). Postoperatively, the median spherical equivalent improved from -7.38 D to -3.13 D. The median refractive astigmatism also decreased after the surgery from -8.75 D to -2.25 D, but did not reach statistical significance.

Corneal topography

Anterior corneal topographic data before and after ICRS implantation at 1 month, 3 months, 6 months, 1 year and 2 years were presented in Table 2 and Fig 2. Representative anterior corneal topographic findings before and after surgery were shown in Fig 3. Overall, the median Kmax, Kmean, and keratometric astigmatism significantly decreased postoperatively ($p < 0.02$). At the last visit, Kmax decreased from 52.65 D to 46.65 D, Kmean decreased from 48.10 D to 45.40 D, and keratometric astigmatism decreased from 6.70 D to 1.40 D. After *post-hoc* paired comparison, Kmax and keratometric astigmatism significantly decreased at 6 months postoperatively and remained significantly decreased at 2 years postoperatively ($p < 0.05$). After *post-hoc* paired comparison, Kmean also significantly decreased at 2 years postoperatively ($p < 0.03$). The median Q value of the anterior cornea changed significantly toward prolateness after surgery ($p = 0.01$). At the last visit, Q value changed from -0.83 to -0.04. After *post-hoc* paired comparison, Q value changed significantly toward prolateness after 1 month postoperatively ($p = 0.01$).

DISCUSSION

To investigate the outcome of ICRS implantation in keratoconus in Thai patients, a two-year retrospective review in 9 eyes was conducted. The result showed that the median visual acuity significantly improved after surgery ($p \leq 0.007$). At the last follow up, the median UCVA improved form 1.00 logMAR to 0.56 logMAR, and the CDVA improved from 0.76 logMAR to 0.10 logMAR, which represented approximately 0.40 logMAR change or 4 lines gain of the vison and considered to be clinically significant. Among publications with the same Ferrara type ICRS and similar follow-up time of 6 months to 2 years, the improvement of CDVA in this study was comparable with others which reported the mean improvement ranged from 0.14 logMAR to 0.40 logMAR.[3-7]

Consistent with the visual outcome, the refractive outcome was significantly improved postoperatively in terms of the spherical equivalent ($p < 0.001$). At the last follow up, the median spherical equivalent improved from -7.38 D to -3.13 D. The change of 4.25 D in this study

TABLE 1. Visual acuity and manifest refraction before and after intrastromal corneal ring implantation.

	Examination					
	Pre-operative	Post-operative				
Parameter		1 month	6 months	1 year	2 years	*P* value
UCVA (logMAR)						
Median	1.00	0.50	0.50	0.70	0.56	0.007[*,d]
Interquartile range	0.60, 1.30	0.40, 1.00	0.30, 0.90	0.20, 0.90	0.20, 0.90	
CDVA (logMAR)						
Median	0.76	0.30	0.20	0.10	0.10	0.001[*,c,d]
Interquartile range	0.30, 0.80	0.10, 0.70	0.10, 0.70	0.00, 0.56	0.00, 0.48	
Spherical equivalent						
Median	-7.38	-6.38	-3.13	-5.13	-3.13	<0.001[*,b,c,d]
Interquartile range	-14.13,-4.88	-15.63,-1..75	-10.00, 1.00	-9.13, 0.75	-7.63, 0.50	
Refractive astigmatism						
Median	-8.75	-3.50	-2.75	-1.50	-2.25	0.052
Interquartile range	-11.00, -7.50	-7.75, -2.00	-4.00, -2.25	-3.50, -1.25	-4.75, -1.25	

*statistically significant by non-parametric Friedman test, [b]statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 6 months (p value = 0.013), [c]statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 1 year (p value ≤0.01), [d]statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 2 years (p value <0.02)

TABLE 2. Anterior corneal topographic data before and after intrastromal corneal ring implantation.

	Examination					
	Pre-operative	Post-operative				
Parameter		1 month	6 months	1 year	2 years	*P* value
Kmax						
Median	52.65	47.20	46.80	46.50	46.65	0.005[*,b,d]
Interquartile range	50.93, 59.20	44.20, 53.53	42.45, 52.60	44.28, 52.45	44.05, 52.20	
Kmean						
Median	48.10	45.45	45.75	45.55	45.40	0.014[*,d]
Interquartile range	47.78, 56.03	42.10, 51.55	43.50, 50.60	43.90, 50.40	43.83, 50.55	
Kastigatism						
Median	6.70	2.35	2.20	1.45	1.40	0.005[*,b,c,d]
Interquartile range	5.25, 8.30	1.58, 7.20	0.48, 3.75	0.73, 2.83	0.55, 3.23	
Q value						
Median	-0.83	0.41	0.02	-0.03	-0.04	0.01[*,a,b]
Interquartile range	-1.56, -0.46	-0.96, 0.71	-0.80, 0.55	-0.80, 0.49	-0.81, 0.51	

* statistically significant by non-parametric Friedman test, [a] statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 1 month (p value=0.01), [b] statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 6 months (p value<0.05), [c] statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 1 year (p value<0.05), [d] statistically significant with a post-hoc paired comparison using Dunn-Bonferroni test between preoperative examination and postoperative examination at 2 years (p value<0.03)

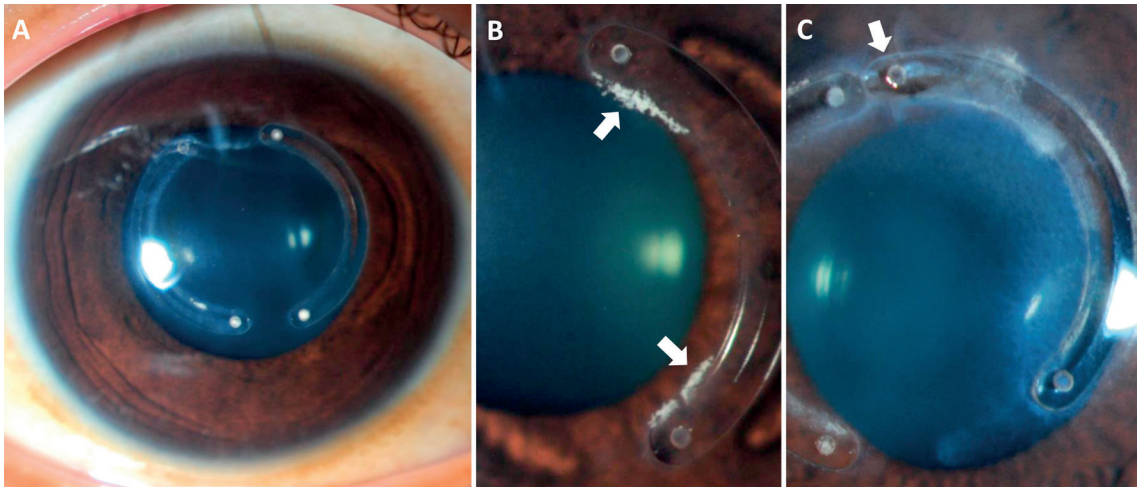


Fig 1. Representative pictures of postoperative intrastromal corneal ring segment implantation. **(A)** Successful two-segment typed surgery. **(B)** Small white deposits around the rings (arrows). **(C)** A complicated case with one segment extrusion (arrow).

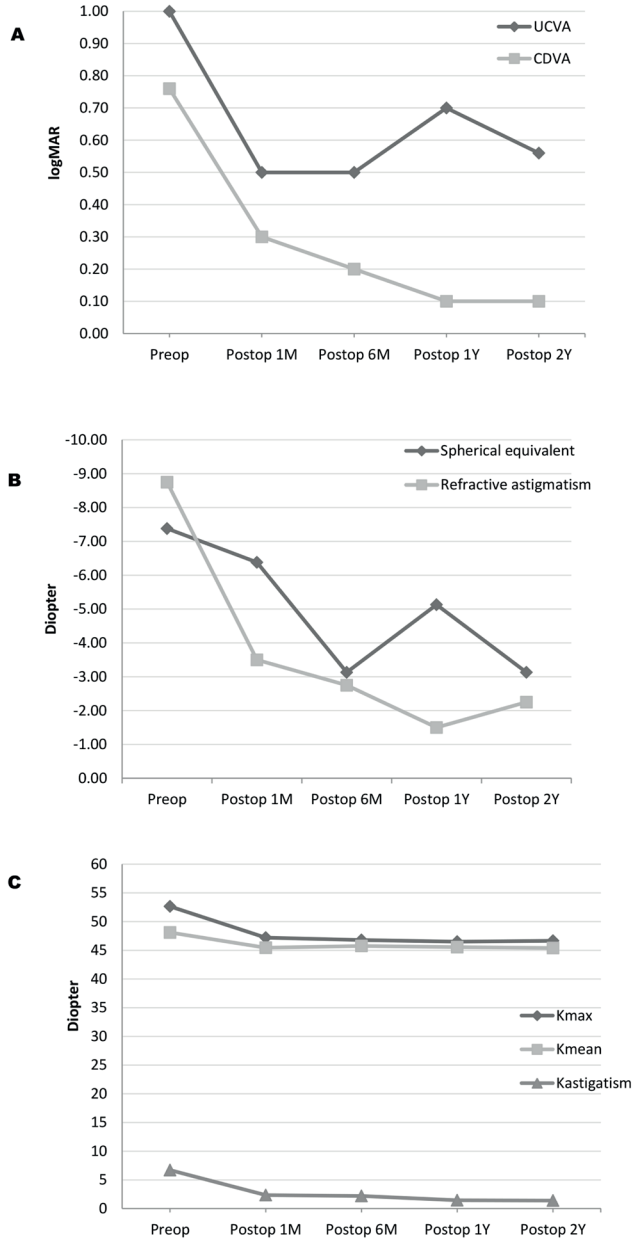


Fig 2. Comparison of **(A)** visual acuity, **(B)** refraction, and **(C)** keratometry between visits.

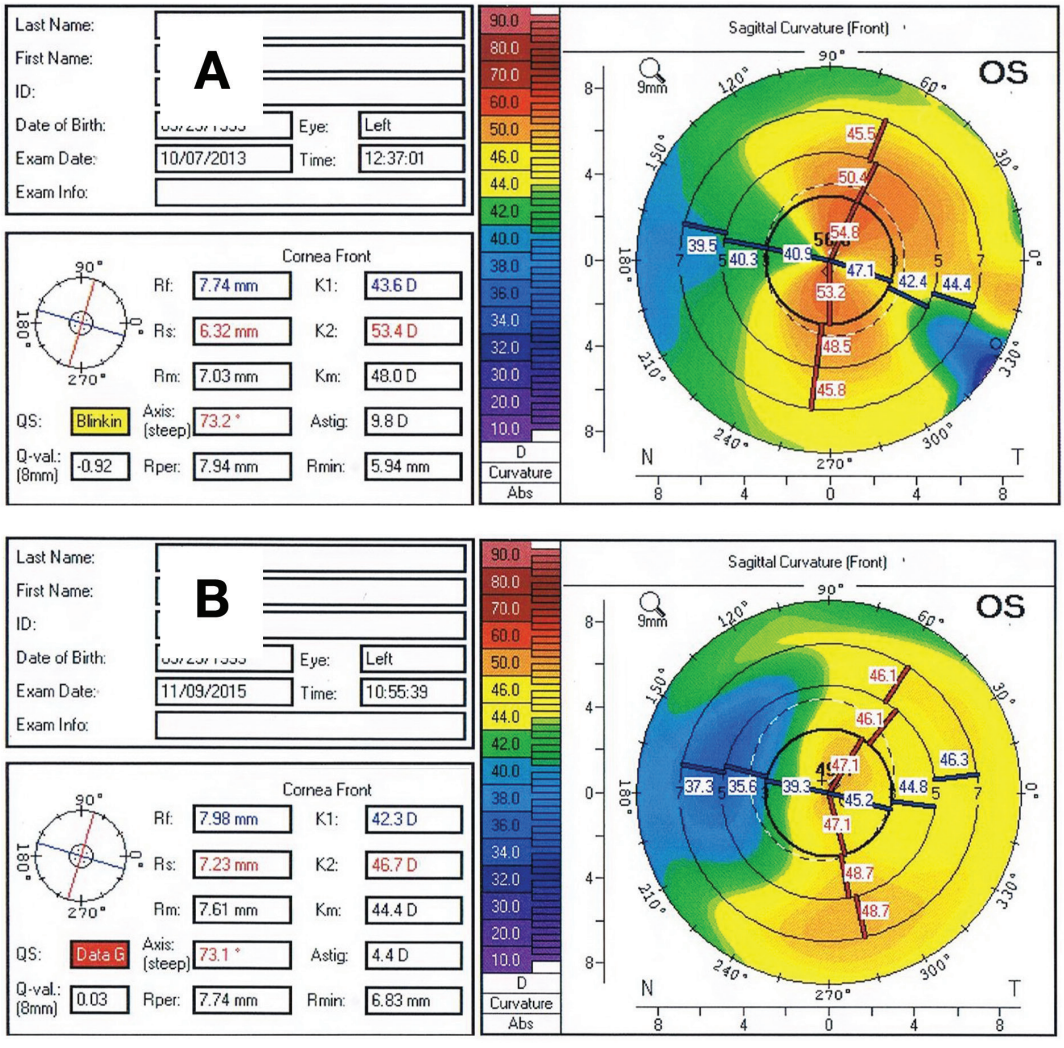


Fig 3. Representative topographic findings **(A)** before and **(B)** 2 years after intrastromal corneal ring implantation. The curvature maps showed flattening effect on the central cornea after the surgery. The parameters of the anterior cornea appeared on the left column were recorded.

was comparable with previous studies which reported the change ranged from 3.36 D to 5.8 D.[3-7]

Because anterior corneal shape is the most important parameter to determine corneal deformation after ICRS implantation[9], anterior corneal topographic outcomes were evaluated. There was significant change of keratometry between visits. At the last visit, the median decrease of Kmax was 6.00 D and the median decrease of Kmean was 2.70 D. The results were comparable with a previous report by Ferrara et al[7] that showed the Kmax change of 5.19 D and the Kmean change of 4.64 D postoperatively. Moreover, other reports of the Ferrara type with 6 months to 2 years follow up found the changes of the Kmean between 0.09 D to 3.82 D.[5,6,10] Considering the other commomly used Intacs type, the changes of the Kmean were 1.94 D to 7.87 D.[10-16]

Besides corneal flattening and improving visual acuity, another goal of the treatment in keratoconus is to improve quality of vision. Corneal asphericity was reported to increase in keratoconus and was proportional to the severity (grading) of the disease.[17] In this study, after the surgery, the median anterior Q value showed significant change between follow-up visits ($p = 0.01$). The preoperative Q value was -0.83, which demonstrated excessive prolateness of the cornea. Then cornea changed towards an oblate cornea for a while at early postoperative 1 month (Q value 0.41). However, after 6 month postoperatively, the Q value changed toward minimal prolateness of the cornea which was from -0.03 to -0.04 at the last visit. Similar to this study, Torquetti et al reported that the Ferrara ICRS significantly reduced the Q value from -0.85 to -0.32 at their 16-month follow up.[18] To illustrate, the anterior corneal asphericity reduced after ICRS implantation to be more similar to the normal physiologic cornea in which the most commonly accepted value in a young adult population is approximately -0.23 ± 0.08.[18]

Considering comparison of the outcomes between visits, we noted that the major parameters including Kmax, keratometric astigmatism, and spherical equivalent refraction were at their significant outcome or relatively highest effect at 6 months ($p < 0.05$), then the outcomes were still stable with no regression at 2 years ($p < 0.03$). This stability was consistent with the previous publications with the long-term follow up.[19,20] Torquetti et al showed the good stability of the outcome with the Kmax significantly decreased of 4.41 D at 5 years and later with no regression at 10 years, consistently, and the Kmean with significantly decreased of 3.13 D at 5 years with no regression at 10 years after surgery.[20] In contrast, Vega-Estrada et al reported that the K reduction was observed only at 6 month after sugery, then after 6 months there was a regression of Kmax for 3.31 D at 1 year and 3.14 D at 5 years, and a regression of Kmean for 3.14 D at 1 year and 3.36 D at 5 years.[21]

Postoperative adverse effects of glare and halos occurred in 3 eyes. These symptoms were also reported in other studies.[22,23] However, none of them requested that their implants to be removed. Small white intrastromal corneal deposits around the segments were found in 2 eyes. This was reported to be frequently found (about 70%) and not resulted in alteration of visual performance.[24] Ly et al elucidated that the mechanical and physiologic stresses introduced by the implantation lead to the accumulation of lipid deposits in the extracellular matrix of the cornea.[25]

One case of extruded ICRS, which needed removal, was reported. However, her visual acuity and refractive status could return to preoperative baseline in months. This reversible status was also reported in other studies.[26-28] In fact, this is an advantage of the surgery that the rings are removable if complicated or poorly tolerated.[29] Ferrara et al suggested that this complication could be minimized after mastering the surgical technique, especially in the deep incision and the well-constructed intrastromal tunnel.[5]

This study has some mentionable limitations. One was the retrospective study design. A second limitation was the small sample size. Prevalence of keratoconus varies in different parts of the world, but may be relatively rare in Thailand (no prevalence study in Thai people). Moreover, only some of the patients were eligible for the benefit of ICRS. The strength of this study is that, ICRS implantation has been one of the internationally approved treatment options for keratoconus and its outcomes were firstly reported in Thai patients. Further study could include larger and wider range of patients with keratoconus such as various preoperative grading and progression. Moreover, the combined treatment of ICRS implantation with the other novel treatment of corneal collagen crosslinking for keratoconus could be another aspect to study.

In conclusion, this initial report in Thai patients with keratoconus showed that the ICRS implantation significantly improved the visual, refractive, and topographic outcomes during the 2-year follow up. The evidence seemed to show that with the appropriate case selection and surgical technique, the ICRS implantation was considered to be an effective and safe procedure in most cases.

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The Prevalence and Factors Associated with Mistreatment Perception among Thai Medical Students in a Southern Medical School

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ABSTRACT

Objective: To assess the prevalence of mistreatment perception among medical students as well as to identify the types of mistreatment and their associated factors.

Methods: This cross-sectional study surveyed all of the 4th to 6th year medical students at the Faculty of Medicine, Prince of Songkla University, from January to April 2017. Three questionnaires were employed: 1) Demographic data 2) Mistreatment perception, and 3) the Patient Health Questionnaire (PHQ)-9 Thai version. The data were analyzed using descriptive statistics. The results were presented as frequency, percentage, average and standard deviation. The factors associated with mistreatment perception were analyzed by means of the chi-square test and logistic regression.

Results: Two hundred and ninety-eight medical students (55.0%) completed the questionnaires, 66.1% of them were female. Their mean age was 22.5+1.1 years. As to the medical students' perception, the majority (63.4%) reported experiencing at least one incidence of mistreatment by attending physicians (53.7%), residents (36.2%) and nurses (16.4%) within the previous year. The majority of mistreatment types were verbal criticism (59.7%) and discriminative behavior (51.4%). The mistreated medical students reported consequences such as experiencing unpleasant feelings (41.3%) and burnout (35.6%). According to the PHQ-9 Thai version findings, 11.1% of all of our students had depression; however, depression did not correlate with the mistreatment perception. The significant factor that correlated with mistreatment perception was the academic year.

Conclusion: More than a half of the surveyed medical students perceived being mistreated and reported experiencing unpleasant feelings as a consequence.

Keywords: Perception; mistreatment; prevalence; medical students (Siriraj Med J 2019; 71: 310-317)

INTRODUCTION

Medical student mistreatment has been recognized for decades; it was initially described in 1982 by Henry Silver, who highlighted its similarities to child abuse.[1] Examples of such mistreatment include inappropriate physical contact, verbal abuse, sexual harassment and power abuse.[2] In 1990, the first document regarding incidence, severity, and significance of medical student mistreatment were conducted, by a major medical school. At same time while enrolled in medical school, 46.4% of all medical students had been abused, and 80.6% of seniors reported being abused by the senior year.[3] The medical student mistreatment is known to adversely impact students both personally and professionally. Similarly,

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burnout has been shown to negatively impact students[4]; 69.1% of those abused reported that at least one of the episodes they experienced was of "major importance and very upsetting" and 49.6% of them indicated that the most serious episode of mistreatment affected them adversely for a month or more, whereas 16.2% of them said that it would "always affect them".[3-6] Concerning discrimination, some studies reported that females were significantly more likely than males to report gender discrimination, exclusion from informal settings and discomfort from sexual humor. Typically, males low in masculinity and females low in femininity were most likely to report abuse.[7] Furthermore, the previous studies have reported that abused medical students develop increased levels of cynicism about medicine; a lack of confidence in performing certain skills; a low opinion of the physician profession, an increase desire to drop out of school; feelings of depression, suicide, anxiety, burnout, anger, and hostility; a drinking problem;[4-6,7-13] a lower career satisfaction;[5,6,12] and become less likely to pursue careers in academic medicine.[14]

In 2011, the Association of American Medical Colleges (AAMC) found that most medical students (57.4% - 88.7%) in the United States were aware of mistreatment at their school.[2] One study reported at least one incident of medical student mistreatment by faculty (64.0%) and residents (75.5%).[4] The mistreatment rates were the lowest for family medicine and the highest for obstetrics-gynecology and surgery specialties. However, the perception of mistreatment in different departments varied significantly by gender and race.[15]

The purpose of this study was to assess the prevalence of mistreatment perception among medical students, as well as identify various types of mistreatment and the association between student perception and teaching behavior. The ensuing data of this study will provide preliminary useful evidence that will hopefully encourage reforms in medical education in order to prevent and manage mistreatment in medical schools appropriately.

Definition

Medical student mistreatment consists of inappropriate physical contact (hitting, pinching, and throwing objects at the student), verbal criticism or humiliation, discriminative behavior, and power abuse or being forced to work outside of one's duty, which the medical students perceived to be significant causes of stress.

Major departments include internal medicine, surgery, obstetrics and gynecology, orthopedic surgery and physical medicine, and pediatrics.

Minor departments include anesthesiology, emergency, otolaryngology head and neck surgery, ophthalmology, radiology, family medicine and preventive medicine, and psychiatry.

MATERIALS AND METHODS

This cross-sectional study was approved by The Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC: 60-472-03-4).

The study surveyed medical students from the 4th to 6th year that studying in the Faculty of Medicine, Prince of Songkla University, Hat Yai Hospital Medical Education Center, and Yala Hospital Medical Education Center at the end (January to April) of the 2017 academic year. The inclusion criterion was being a medical student who could complete the questionnaire.

A medical students were contacted by the research assistant in class, and were provided with the rationale along with an overview of the research. After the self-reporting questionnaires and information sheet were distributed, medical student, they took 5-10 minutes to consider whether to participate in the study or not. After that, the research assistant handed out documentation that assured the volunteers that their identities would be protected. Adhering to a policy of strict confidentiality, the signatures of the participants were not required, and all of the participants retained the right to withdraw from the research at any time. The participants were permitted to finish and return the questionnaires later by 2 options; submitting them in the box at the front of the classroom, or drop them in the box located at the Psychiatry Department. Thus, participant confidentiality was protected.

Instruments

The questionnaire comprised 3 parts:

1) The demographic characteristics questionnaire collected data regarding age, year of medical school, religion, cumulative GPA, hometown, income, and underlying disease.

2) The mistreatment perception and its consequences questionnaire was edited by 5 psychiatrists. It employed 6 questions like, "Since the beginning of your clinical rotations, how many times have you been mistreated in the past year" The response categories were "never", "once or twice", "a few times", "several times", and "numerous times". For the analysis, we classified mistreatment as never, infrequent, or recurrent. Mistreatment was categorized as infrequent if it occurred "once or twice" or "a few times" and recurrent if it occurred "several times" or "numerous times".[4]

3) The patient health questionnaire-9 Thai version

(PHQ-9), consisted of 9 questions and employed a 4-point rating Likert Scale to evaluate depression. The scores for each question were between 0 and 4. The cut-off score was > 9. The sensitivity and specificity were 84.0% and 77.0%, respectively. The positive and negative predictive value were 21.0% and 99.0%, respectively. The internal consistency reliability was assessed with a Cronbach's alpha coefficient of 0.79-0.87. When the score was higher than 9, it indicated depression.[16]

Statistical analysis

The results are presented as percentage, frequency, mean, and standard deviation. The factors associated with mistreatment perception were analyzed using the chi-square test for the univariate analysis and presented using odds ratios.

RESULTS

Demographic data

The total number of medical students who completed the questionnaires was 298; the response rate was 55.0%. The sex proportion and demographic data of the responders were not different from demographic data of the whole population. Of the participants, 197 were female (66.1%) (Table 1). The mean age was 22.5±1.1 years, whereas the mean cumulative grade point average (GPA) was 3.3±0.3, and the median income (IQR) was 8,000 (7,000-10,000) Baht per month.

Perception of mistreatment

In the past year, the prevalence of mistreatment perception among medical students was 63.4%, or 189 of 298 respondents. The gender proportion of mistreatment perception was 58.4% of males and 66.0% of females. According to the medical students' perception, the majority reported experiencing mistreatment by attending physicians, residents and nurses (53.7%, 36.2% and 16.4% respectively) (Fig 1). Most of the departments reporting mistreatment were major departments. Meanwhile, the mistreatment perception in the minor departments was of a lower rate. The most frequently reported types of mistreatment were verbal criticism (59.7%) and discriminative behavior (51.4%) (Fig 2). The mistreated medical students reported experiencing consequences such as unpleasant feelings (41.3%), boredom and burnout (35.6%), anxiety (28.2%) and anger (20.1%) (Table 2).

The medical student's perception of positive teaching behaviors were the giving of encouragement, being praised, and giving advice on how to improve, whereas the unpleasant teaching behaviors were blaming or criticizing, devaluation, looking down or insult, and ignorance (Fig 3).

The internal consistency reliability of our study was 0.62 for perception of mistreatment.

Depression screening

According to the PHQ-9 Thai version results, 11.1% of our medical students had PHQ-9 > 9, that indicated depression (Table 1). The internal consistency reliability of our study was 0.87 for depression screening.

Factors associated with perception of mistreatment

The variables whose p-values from the univariate analysis were lower than 0.2 were included in the initial model; only one variable, academic year, met this criterion (p=0.002) (Table 3). An analysis using odds ratios revealed that, the 5th year medical students had a 2.5 times greater risk for mistreatment perception when compared with 4th year medical students (95% CI = 1.5, 4.3) (Table 4). Moreover, we found that the 5th year medical students had a 2.8 times greater risk for mistreatment perception compared with 6th year medical students (95% CI = 1.2, 6.5). However, the level of depression did not associate with the medical students' mistreatment perception.

DISCUSSION

This study revealed that the prevalence of mistreatment perception among medical students in southern Thailand within 1 year was of the same rate as the data reported from other medical schools. We discovered that the prevalence of medical student mistreatment perception in our population was 63.4% whereas the prevalence of mistreatment among medical students in other countries has been reported at 64.0% by faculty and 75.5% by residents, respectively.[4] The most commonly reported types of mistreatment were verbal criticism (59.7%) and discriminative behavior (51.4%). Our findings concurred with those reported by a 2011 study of 24 difference medical schools in the United States of America.[4] Even though these data may not provide any new information as it regards the worldwide body of knowledge, they constitute the first useful concrete evidence from Thailand on this topic.

Concerning the consequences of mistreatment among medical students, a previous study identified a relationship between verbal mistreatment and confidence in clinical abilities.[17] Moreover, recurrent mistreatment has been associated with a high rate of burnout (57.0%)[4] whereas in this study, the mistreated medical students reported experiencing unpleasant feelings (41.3%) and burnout

TABLE 1. Demographic characteristics (n=298).

Demographic characteristics	Number (%)
Sex	
Male	101 (33.9)
Female	197 (66.1)
Academic year	
4th year	157 (52.7)
5th year	113 (37.9)
6th year	28 (9.4)
Religion	
Buddhism	265 (88.9)
Islam	16 (5.4)
Christianity	7 (2.3)
Other	4 (1.3)
Unreported	6 (2.0)
Home province	
Songkhla	115 (38.6)
Other	178 (59.7)
Unreported	5 (1.7)
Underlying disease	
No	250 (83.9)
Yes	46 (15.4)
Medical illness e.g. allergic rhinitis	31 (10.4)
Psychiatric illness e.g. dysthymia	15 (5.0)
Unreported	2 (0.7)
Depression by PHQ-9	
No depression	238 (79.9)
Depression	33 (11.1)
Unreported	27 (9.1)
Depression categorized by academic year	
4th year	20 (12.7)
5th year	11 (9.7)
6th year	2 (7.1)
Depression categorized by gender	
Male	9 (27.3)
Female	24 (72.7)

Abbreviation: PHQ-9 = Patient Health Questionnaire-9

TABLE 2. Consequence of being mistreated within 1 year (n=298).

Type	Number (%)
Unpleasant feeling but tolerable experience	123 (41.3)
Boredom and burnout	106 (35.6)
Stress and anxiety	84 (28.2)
Anger	60 (20.1)
Sadness and depression	59 (19.8)
Fight or perseverance	34 (11.4)
Escape/ try to terminate study program	33 (11.1)
Low self-esteem and has suicide ideation	11 (3.7)
Need for psychological therapy	5 (1.7)
Felt shame	6 (2.0)

TABLE 3. Crude association between general characteristics and mistreatment perception.

General characteristics	Experience of mistreatment		Chi^2
	Yes (n=189)	No (n=109)	P-value
Sex			0.247
Male	59 (31.2)	42 (38.5)	
Female	130 (68.8)	67 (61.5)	
Academic year			0.002
4^{th} year	88 (46.6)	69 (63.3)	
5^{th} year	86 (45.5)	27 (24.8)	
6^{th} year	15 (7.9)	13 (11.9)	
Cumulative GPA			0.528
<3.00	33 (23.6)	23 (30.7)	
3.01-3.50	70 (50.0)	34 (45.3)	
3.51-4.00	37 (26.4)	18 (24.0)	
Home province			0.637
Songkhla	71 (38.0)	44 (41.5)	
Other	116 (62.0)	62 (58.5)	
Underlying disease			0.447
No	156 (83.0)	94 (87.0)	
Yes	32 (17.0)	14 (13.0)	
Depression (PHQ-9)			0.611
No	151 (86.8)	87 (89.7)	
Yes	23 (13.2)	10 (10.3)	

Note: There were missing values for some variables

TABLE 4. Factors related to mistreatment perception.

Factor	Crude OR (95% CI)	P-value Wald's test
Academic year		
4th year	Reference	
5th year	2.5 (1.5, 4.3)	< 0.001
6th year	0.9 (0.4, 2.0)	0.808

Abbreviation: OR = odds ratio, CI = confidence interval

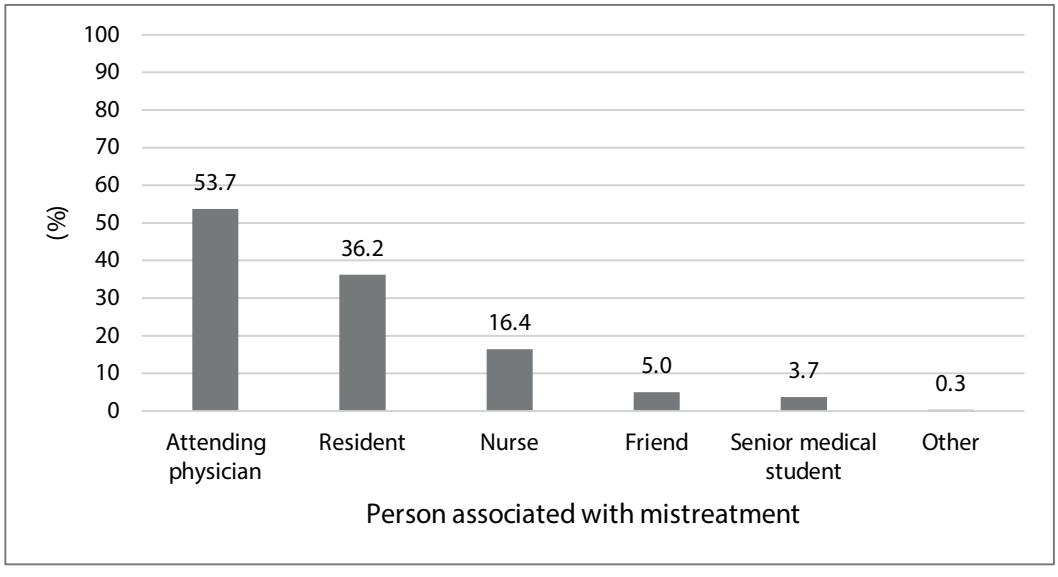


Fig 1. Person associated with mistreatment (can be more than one type)

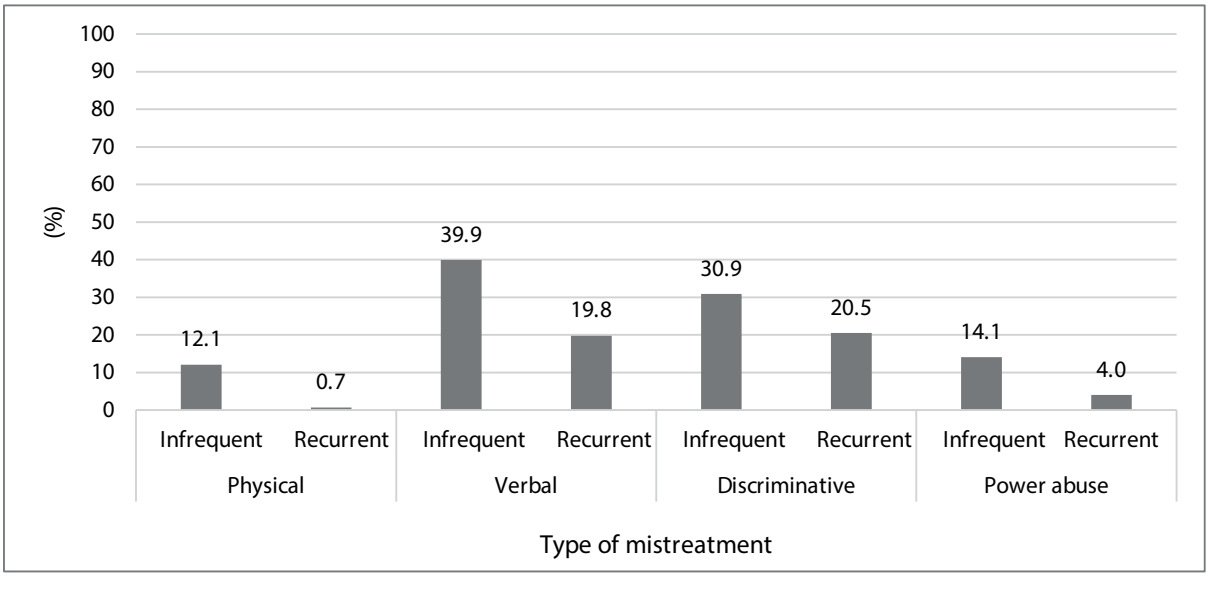


Fig 2. Type of mistreatment (can be more than one type)

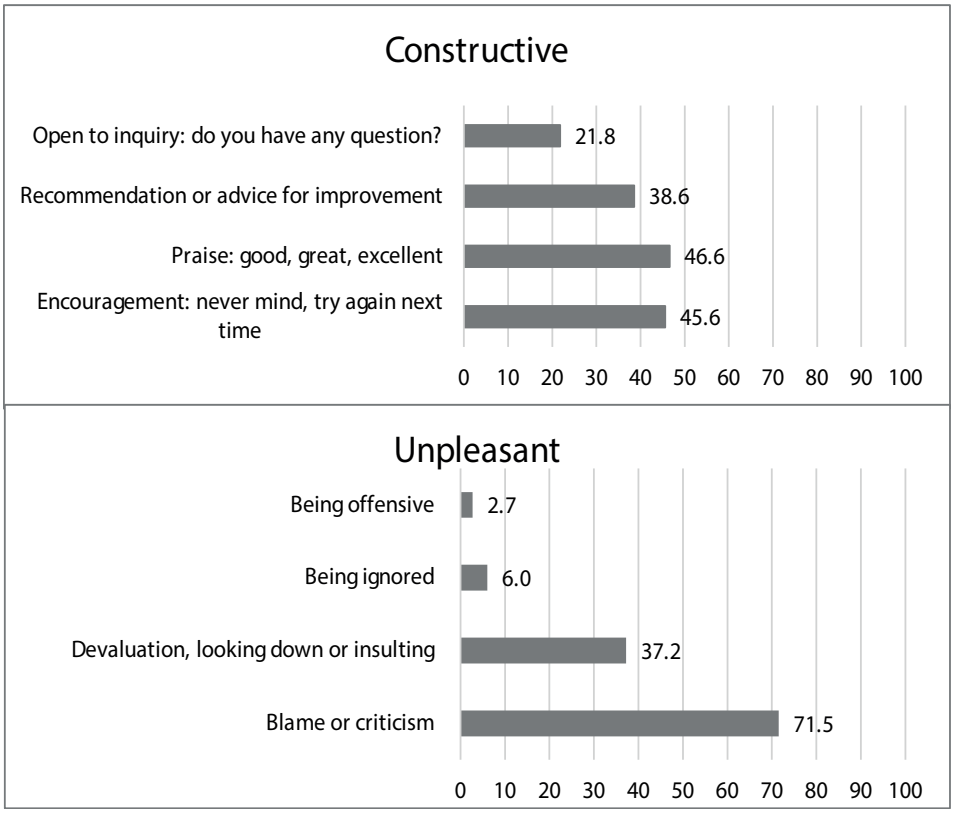


Fig 3 Medical students' perception of positive/constructive and unpleasant teaching behavior (can be more than one type)

(35.6%) as the two most common consequences of mistreatment. This indicates that mistreatment impacts medical students negatively both personally and professionally. Regarding the factor associated with mistreatment perception, this study identified an association between academic year and risk of mistreatment perception. Since no previous study has reported such correlation, future in-depth analyses should be undertaken in order to explain this phenomenon.

Moreover, this study identified positive and unpleasant teaching behaviors on the part of the instructing medical personnel that may be useful for reforming our medical educational system. They suggested that the teaching behaviors they appreciated were receiving encouragement, praise, and recommendations or advice whereas the unpleasant teaching behaviors were blaming, criticizing, devaluation and ignorance. Therefore, we need to ask ourselves the question, "What is the teacher's role?". This study might have reflected the current teacher role in the Thai medical education. Consequently, the reformation of our medical education should be further enhanced. In other words, well-designed curriculum reforms or the adoption of sound concepts regarding the role and conduct of teachers that reflect the highest philosophy and values need to be considered by faculty.

As it is well-known, the processes of teaching for effective learning such as team-based learning, idea sharing and interaction need safe environments. Such environments require the teacher to understand the students, and build strong rapport with them by effective listening and communication. Furthermore, additional necessary skills of teachers include being intentional about constructive interpersonal interaction by offering positive reinforcement and feedback.

An example of an appropriate teacher role is found in preclinical education, where the medical students are educated via the problem-based learning (PBL) process, which requires the teacher to act as a coach. Additionally, even in the clinical-teaching process, our study, revealed that the medical students want the teacher to act like a coach. They suggested that the teacher should be encouraging and offer positive feedback. Therefore, our values and philosophy of teaching should be about the creation of a climate of trust and respect, being open and responsive, and evaluating the needs of medical students.

Limitations

This study had a cross-sectional design and employed self-reporting for individual perception assessment.

Moreover, its response rate was 55.0%, which might have led to information bias. In addition, the sample size was limited to only medical students in the Faculty of Medicine, Prince of Songkla University. Thus, it is too soon to generalize our findings to the nation-wide setting.

Implications and future recommendations

Further studies should employ a more quantitative method and cover more medical schools within Thailand. In so saying, a multi-center study is recommended.

CONCLUSION

More than a half of our medical students perceived having been mistreated and reported experiencing unpleasant feelings. A new philosophy and values regarding teaching and the role of the teacher in the learning process should be adopted in education.

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Surgical Treatment of Myopic Strabismus Fixus by Loop Myopexy Augmented with Scleral Fixation: a Case Report

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ABSTRACT

Objective: To present the clinical findings, surgical procedure and long-term outcome of a Thai patient with myopic strabismus fixus.

Case presentation: The patient presented with recurrent progressive esotropia and hypotropia. Two strabismus surgeries were performed 20 years ago. Magnetic resonance imaging (MRI) findings indicated the etiology which was secondary to inferiorly deviated lateral rectus (LR) muscle and medially deviated superior rectus (SR) muscle. The patient had undergone loop myopexy of lateral rectus and superior rectus muscles augmented with scleral fixation and satisfactory result was achieved up to six years after the operation.

Conclusion: The patient with myopic strabismus fixus should be evaluated by MRI to confirm the etiology of this disorder. Marked esotropia and hypotropia can be safely aligned by simple loop myopexy augmented with scleral fixation.

Keywords: Myopic strabismus fixus; heavy eye syndrome; high myopia; loop myopexy (Siriraj Med J 2019; 71: 318-321)

INTRODUCTION

Myopic strabismus fixus, also known as heavy eye syndrome, is an acquired progressive esotropia and hypotropia associated with high axial myopia. Typically, this condition tends to develop esotropia with restricted abduction which is often accompanied by hypotropia and limited abduction. Various theories about the etiology of this clinical entity have been postulated including the increased weight of the eyeball or forward movement of the center of globe; that is 'heavy eye syndrome'[1], myopathic paralysis of lateral rectus (LR) muscle by pressure from the lateral orbital wall[2], and the mechanical restriction limiting motility due to contact between posterior elongated globe and orbital wall.[3,4] Recently, many investigators reported MRI findings of displacement of both LR and superior rectus (SR) muscles pulley system producing this condition.[5-7] Surgical correction of this restrictive motility disorder is difficult. Multiple surgical procedures have been described; for example large bilateral medial rectus (MR) recession and recession-resection procedure, but results were unsatisfactory.[8] Yokoyama et al[9] proposed the loop myopexy technique of SR and LR muscle as an alternative treatment for this disorder. This report demonstrates the clinical and radiological findings as well as outcome of surgical treatment with loop myopexy augmented with scleral fixation of a patient with myopic strabismus fixus.

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CASE REPORT

A 61-year-old man with a 30-year history of esotropia and high myopia presented with increasing esotropia and hypotropia. Twenty years ago, the patient underwent MR muscle recession 9 mm, LR muscle resection 10 mm, superior oblique tenectomy on the right eye and MR recession 6 mm on the left eye. His right eye gradually increased inward and downward at 6 months after surgery, and thereafter the patient was lost to follow up. On examination, best-corrected visual acuity was hand motion OD, 6/24 OS with left eye fixation preference. Both eyes revealed unremarkable anterior segment examinations except cataract and myopic degeneration on dilated fundus examination. Posterior segment on the right eye could not be evaluated due to extreme adduction and depression position of the right eye. In primary position, the right cornea was shown only 2 mm of superolateral part as Fig 1a. Ocular movement on the right eye was severely limited to abduct (-4) and elevate (-4) beyond the midline while only mildly limited to abduct (-trace) on the left eye as shown in Fig 1b. On coronal view of MRI orbit displayed a nasally deviated SR muscle and an inferiorly deviated LR muscle on the right eye as shown in Fig 2. Orthoptic examination revealed an esotropia of 95 prism diopters (PD) and a right hypotropia of 25 PD with the left eye fixing.

At the time of operation, forced duction testing showed marked restriction of MR muscle, moderate restriction of inferior rectus (IR) muscle on the right eye and mild restriction of MR muscle on the left eye. Also, a nasally displaced course of SR muscle and an inferiorly displaced course of LR muscle on the right eye were confirmed. On the right eye, MR muscle insertion was found 7 mm from limbus whereas LR and SR muscle insertions were attached at the normal position. Strabismus surgery performed for the right eye consisted of looping of SR and LR muscles together and anchoring to the sclera 15 mm behind the limbus using a 5/0 polyester and MR muscle was re-recessed 12 mm from the limbus.

On the first postoperative month, the patient had satisfactory alignment with a 12 PD exotropia and 8 PD right hypotropia as shown in Fig 3. Motility markedly improved in abduction, but limited in adduction (-2) on the right eye. Although visual acuity on the right eye improved to 6/24 after strabismus surgery, the patient still had significant cataract on both eyes. Axial length measurements confirmed after strabismus surgery were 31.35 mm OD and 31.94 mm OS. Hence, 4 months later cataract surgery was performed on both eyes and vision reached 6/7.5 OU. Fig 4 disclosed the first year postoperative alignment. The patient had no double vision, no stereopsis on Fly test and alternate suppression on Worth-4-dot testing. These outcomes were stable 6 years postoperatively.



Fig 1. **(A)** Preoperative appearance in primary position, left eye fixating, **(B)** Preoperative photograph of ocular motility

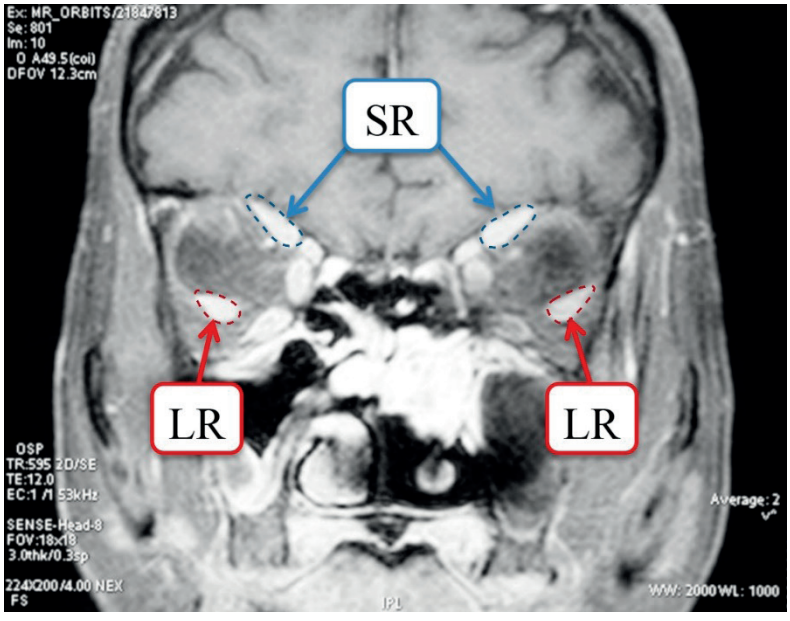


Fig 2. MRI of the orbit before surgery: bilateral displacement of superior recti nasally and lateral recti inferiorly and the oval distortion of the globe



Fig 3. Postoperative photograph of this case, 1 month after surgery



Fig 4. Postoperative photograph of this case, 1 year after surgery

DISCUSSION

Several reports have demonstrated pathogenesis of restricted strabismus in myopic strabismus fixus including displacement of LR and SR muscle pulley system[5] or the mechanical limitation of rectus muscles due to the contact between the posterior elongated globe and the orbital apex.[4] Many surgical procedures to correct the alignment in this condition have been reported[10]; for example, simple recession-resection procedures, and disinsertion or large recession of MR muscle. These procedures showed effective results in the early stages, but later esotropia and hypotropia gradually returned. Likewise, our patient had esotropia and hypotropia again after previous large MR recession and LR resection. Recent findings showed shifting of LR muscle inferiorly and SR muscle nasally caused by a posterior prolapse of an elongated eye beyond the muscle cone due to superior, posterior and lateral protrusion of posterior eyeball.[6,11] The deviant paths of the SR and LR muscles in our case were confirmed with both MRI preoperatively and at the time of surgery. Therefore, the goal of surgical correction was to reestablish the physiological muscle plane by binding the LR and SR muscles to each other and with or without suturing to sclera at equator. Recent studies

have described the effectiveness of this surgery including simple loop myopexy with or without anchoring to sclera, muscle belly union of half tendon of the SR and LR muscles combined with MR recession.[8,12-14] Outcomes showed improved alignment and motility.

Loop myopexy of the SR and LR muscles was performed to normalize their course in our case. A suture looped around the two muscles was secured to the sclera to stabilize the muscle path and to avoid risk of suture migration. Also, the use of a nonabsorbable suture supports the stability of suture placement over time. According to pathogenesis of this disorder, this technique is more effective than the conventional recess-resect procedures because it moves the deviant path of extraocular muscles to the desired position to straighten the eye in primary position. Also, this technique minimizes the risk of anterior segment ischemia since both LR and SR muscles were not disinserted. However, the risk of scleral perforation may be encountered in this procedure due to scleral suture. After extraocular muscle surgery, the patient underwent cataract extraction with intraocular lens implantation in both eyes and vision reached 6/7.5 in both eyes. Both ocular alignment and visual results were favorable and stable throughout 6 years of follow-up.

In summary, patients with high myopia, progressive esotropia and hypotropia should be assessed by MRI preoperatively to confirm the cause of this condition. Loop myopexy augmented with scleral fixation was sufficient to correct both large horizontal and vertical deviation and maintain ocular alignment for a longer period. Hence, this surgical method is recommended in myopic strabismus fixus.

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Pseudohyperkalemia Caused by EDTA Contamination: a Not Uncommon Pre-analytical Error

To the Editor,

Pseudohyperkalemia from potassium ethylene-diaminetetraacetic acid (EDTA) contamination has been reported for decades. The mechanism of this anticoagulant is chelation of calcium, which is a divalent cation that is essential for the proper function of the clotting cascade. EDTA contamination is most often caused by inappropriate order of blood draw, and it can be recognized by the apparent presence of spurious coexisting hyperkalemia and hypocalcemia.[1]

We report the case of a 93-year-old cachexic Thai male who was diagnosed as having diabetes mellitus in a hyperosmolar hyperglycemic state. His laboratory test results showed markedly hyperkalemia and hypocalcemia. Electrocardiogram (ECG) showed sinus rhythm without tall peak T wave or widening of the QRS complex. The discordance between the ECG result and the reported hyperkalemia prompted a second blood draw to rule out pseudohyperkalemia in the first sample (Table 1). Thereafter, 20 ml of 10% calcium gluconate was pushed intravenously to treat the patient's hypocalcemia.

At our central laboratory and due to the abrupt change in potassium level, total calcium was performed in the second specimen which showed normocalcemia. No significant hemolysis was observed in either the first or second specimen. The patient had no known underlying medical conditions that could have been the cause of pseudohyperkalemia, such as thrombocytosis or marked leukocytosis. From these evidences together with the coexisting spurious hyperkalemia and hypocalcemia in the first sample, the most likely cause of pseudohyperkalemia was judged to be potassium EDTA contamination.

The mechanisms of EDTA contamination can be described, as follows: syringe needle contamination due to the filling of blood into the EDTA sample tube before other tubes, pouring the blood from EDTA sample tube into other tubes[1-3], and mistakenly switching the cap of EDTA sample tubes with others. The person who took the first blood specimen claimed that there was no transfer of blood or switching of tube caps from one tube to another, but could not confirm that the proper order of blood draw had been followed. According to European Federation of Clinical Chemistry and Laboratory Medicine guidelines, the order of blood draw should be, as follows: blood culture tubes, coagulation tubes, serum tubes, heparin tubes, EDTA tubes, glycolytic inhibitor tubes, and then other tubes.[4] In our case, the first blood draw included lithium heparin tube, K2EDTA tube, and sodium fluoride tube. There was, therefore, a high probability that blood was collected in the K2EDTA tube first, followed by the lithium heparin tube, which would have resulted in K2EDTA contamination in the lithium heparin tube.

TABLE 1. Patient blood glucose and electrolyte results.

Test	Unit	1st sample	2nd sample	Normal range
Blood glucose	mg/dl	1,031	869	74-99
Sodium	mmol/L	150	153	136-145
Potassium	mmol/L	9.9	4.2	3.4-4.5
Chloride	mmol/L	109	115	98-107
Bicarbonate	mmol/L	22.0	19.0	22-29
Total calcium	mg/dl	3.5	9.08	8.2-9.6

The failure of our laboratory staff to recognize coexisting distinct hyperkalemia and hypocalcemia in the first sample result caused misinterpretation and inappropriate calcium replacement in our patient. Fortunately, the patient showed no sign of hypercalcemia afterwards, and the follow-up calcium level was within normal range.

Recognition of coexisting hyperkalemia and hypocalcemia in the same sample strongly suggests an EDTA contaminated sample. A campaign designed to remind and reinforce appropriate blood collection procedures would help to decrease the frequency, but not totally eliminate EDTA contamination.[1,5] Furthermore, it only takes a very small amount of EDTA contamination to influence a pseudohyperkalemia and pseudohypocalcemia result, and the presence of EDTA can be difficult to identify.[1-3] Three previous studies reported that a lack of routine EDTA measurement as a screening protocol would result in 36-42% of pseudohyperkalemic samples going undetected and being reported as true hyperkalemia.[1,2,5] Thus, a cost-effective strategy would be to implement a routine EDTA analysis protocol.[1-3]

In conclusion, lack of awareness about EDTA contamination and clue for how to identify it can lead to misinterpretation and inappropriate treatment. We would like to highlight the need for ongoing reinforcement of the importance of blood draw protocols, and the need for implementation of EDTA assay for routine EDTA screening.

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