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(Only published in printed version)

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The Thai Journal of Surgery is the official publication of The Royal College of Surgeons of Thailand and is issued quarterly.

The Thai Journal of Surgery invites concise original articles in clinical and experimental surgery, surgical education, surgical history, surgical techniques, and devices, as well as review articles in surgery and related fields. Papers in basic science and translational medicine related to surgery are also welcome.

Aim & Scope

The Thai Journal of Surgery is dedicated to serving the needs of the members of The Royal College of Surgeons of Thailand, specifically the younger researchers and surgical trainees who wish to have an outlet for their research endeavors. The Royal College strives to encourage and help develop Thai Surgeons to become competent researchers in all their chosen fields. With an international outlook, The Thai Journal of Surgery welcomes submissions from outside of Thailand as well.

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2. Corporate Author:

- The Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology. Recommended method for the determination of gamma glutamyltransferase in blood. Scand J Clin Lab Invest 1976; 36:119-25.
- American Medical Association Department of Drugs. AMA drug evaluations. 3rd ed. Littleton: Publishing Sciences Group, 1977.

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- o Chirappapha P, Arunnart M, Lertsithichai P, et al. Evaluation the effect of preserving intercostobrachial nerve in axillary dissection for breast cancer patient. Gland Surg 2019;8:599-608. doi:10.21037/gs.2019.10.06.

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Use only standard abbreviations of commonly used approved abbreviations. Avoid abbreviations in the title. The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement.

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All statistical analyses and the statistical software used must be concisely described. Descriptive statistics for quantitative variables must include an appropriate central tendency measure (e.g., mean or median) as well as a corresponding measure of spread (e.g., standard deviation or range or interquartile range). Categorical variables must be summarized in terms of frequency (counts) and percentage for each category. Ordinal variables can be summarized in terms of frequency and percentage, or as quantitative variables when appropriate. Statistical tests must be named and p-values provided to 3 decimal places. P-values less than 0.001 should be written "< 0.001" and p-values approaching 1 should be written "0.999".

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Randomized controlled trials should be analyzed using the intention-to-treat principle, and as treated analysis should be applied as well if there are significant cross-overs. Further details of statistical issues are available here (http://www.icmje.org/icmje-recommendations.pdf).

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(see Format https://bit.ly/3IaP4ZB)

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literature review of previous published, related results. These related results must be compared with those of the authors' study, and the differences clearly stated along with plausible explanations. New unexpected findings, especially from subgroup analyses or those for which the research was not designed, should be considered hypothetical and stated as such. Any plausible, relevant clinical application should be indicated. Finally, any significant limitations of the study must be mentioned and possible extensions of research should be briefly provided. **Conclusion,** which should be concerned with answering the research question posed by the current study, should not be summarizing results of previous studies or recommendations. An **Acknowledgement** section can be added at the end of the article. The Reference list should be in the format as described previously.

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Use the common format. Emphasis is on clinician comprehension. The **Abstract** uses the same common structured format. In the **Main text,** the **Introduction,** in addition to the usual context setting and rationale, should also contain explanations and descriptions of basic science concepts at the level of the educated layman. The **Methods** section should still be concise with sufficient detail for others to replicate the experiment, but one or two paragraphs in between explaining basic processes in plain English would be helpful. In the **Results** section, similar conciseness is still the rule, but a brief simplified summary of the findings should be provided. In the **Discussion,** clinical implications should be clearly stated. The **Conclusion,** again, should answer the research question.

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We encourage publication of case series or case reports if a comprehensive review of the literature is included, with the aim of helping the clinician manage rare and challenging diseases or conditions based on best available evidence in conjunction with practical, local experience. For the Thai Journal of Surgery, this implies that the case report format differs somewhat from that of the common format for research articles.

Abstract: Need not be structured. State objective of the case presentation, present a summary of the case, the outcome and learning points in one concise paragraph.

Main text: An **Introduction** is required to set the importance or relevance of the case within the current clinical context, based on a comprehensive literature review. A brief review of anatomy and pathology, or pathophysiology can be provided. **Report of the case** then follows with sufficient details on clinical presentation, diagnostic work up, interesting features, and decision making, to be useful for other surgeons. Surgical management should be concisely described and should be accompanied by high-resolution photographs or high-quality drawings and diagrams, if possible. Unique features of the case, and typical or general features should be distinguished. **Results** of management and follow-up information should be provided. **Discussion** then places the clinical, diagnostic, surgical and pathological features of the case within current knowledge or context and provides reasons for decision making and surgical management or otherwise. Wider implications of the case should be emphasized; for example, when management contradicts existing guidelines or when feasibility of some never-before performed surgery has been demonstrated. The **Conclusion** simply summarizes the case in terms of management implications.

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Abstract: No structure is required. A description of the aims of the article and contents should be sufficient.

Main text: An **Introduction** serves to set the rationale or objective of the review. While systematic reviews focus on narrow research questions with aims of obtaining generalizable knowledge, the narrative review is education-based. The **main content** can be structured in anyway as is necessary for adequate comprehension. Finally, a **Conclusion** summarizes the content in greater detail than the abstract, emphasizing recent developments or future research.

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Abstract: A brief description of aims and content is sufficient.

Main text: An **Introduction** to set the aims of the article. The **main content** can be structured in any way. A **Conclusion** to summarize the content should be helpful, as well as to place some personal reflections.

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Editorial

Doonyapat Sa-Nguanraksa, MD
Editor of The Thai Journal of Surgery

In the current issue of the Thai Journal of Surgery, there are 4 original articles and 2 case reports that cover various subspecialty surgical fields and demonstrate a commitment to improving patient care.

For trauma surgeons, the development of a prediction score to inform decision-making about colonic injuries might help newly graduated surgeons decide whether to divert or repair the injury. Plastic surgeons from Malaysia demonstrate the satisfying outcome of the non-invasive treatment of lower limb lymphedema using a customized pressure device. The colorectal surgery team from Rajavithi Hospital, one of the largest hospitals of the Ministry of Public Health of Thailand, reports that the new treatment strategy for locally advanced rectal cancer, total neoadjuvant therapy, resulted in a promising outcome in terms of pathological complete response. The use of mobile mammography units increases access to breast cancer screening in limited-resource situations. Two case reports are also presented: a rare case of self-insertion of a foreign body in the bladder and retroperitoneal extraosseous Ewing's sarcoma in a young infant.

This issue of the Thai Journal of Surgery also includes a total of 55 abstracts from the 50th Annual Scientific Congress of The Royal College of Surgeons of Thailand, presented by surgical residents, emphasizing the advances in surgical knowledge originating from the next generation of surgeons. These young researchers' contributions are essential to the ongoing development of surgical techniques and will surely spur more advancement in the area.

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Original Article

Continuation Development Santichatngam's Colonic Injury Prediction Score (SCOPES) for Decision Making in Colonic Injuries due to Trauma

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Abstract

Background: Primary repair, a method involving direct repair of colonic injuries, has emerged as a preferred treatment option. The development of the SCOPES scoring system has significantly enhanced decision-making regarding primary repair versus diversion procedures. SCOPES version I effectively predicts optimal patients for primary repair, while version II accurately identifies those requiring diversion. By providing a more systematic approach, SCOPES has reduced variability in clinical decision-making. Given the lack of a gold standard for managing colonic injuries, this study seeks to assess the clinical utility of SCOPES versions I, II, and III in patients with colonic injuries.

Patients and Methods: A four-year retrospective study was conducted involving 34 patients with colonic injuries from Pranangklao Hospital and Maharat Nakhon Ratchasima Hospital. Medical records were reviewed from October 2020 to September 2024.

Results: The majority of patients were working-age males with an average age of 38 years. Motor vehicle accidents were the primary cause of injuries, resulting in blunt trauma more frequently than penetrating trauma. The right colon was the most common site of injury. A comparison of primary repair and diversion procedures revealed that primary repair was associated with better outcomes and fewer complications. The study found that SCOPES version I was effective in predicting patients suitable for primary repair, although it had certain limitations. SCOPES versions II and III were more effective in predicting patients who required diversion compared to SCOPES version I. These versions demonstrated 100% sensitivity, specificity, accuracy, positive and negative predictive values, and had a significant impact on positive and negative likelihood ratios, diagnostic odds ratios, and posttest odds.

Conclusion: SCOPES versions II and III, designed for diversion procedures, outperformed SCOPES version I, which was developed for primary repair. These versions exhibited significantly better predictive accuracy compared to relying solely on clinical judgment or surgical judgment.

Keywords: Clinical prediction score, Colonic injury

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Introduction

Current surgical management of colonic injuries has shifted away from routine colostomy.[1-11] Santichatngam's 2017 study introduced the Santichatngam's COlonic injury PrEdiction Score (SCOPES) as a tool to aid in surgical decision-making between primary repair and diversion procedures.[12] SCOPES version I (for primary repair) includes < 2 factors: delayed surgery time (> 6 hours), gross fecal contamination, left-sided colonic injury, and duodenum/ureter injury (grade > 3). A retrospective study by Banpot Wattakawanich and Prinya Santichatngam, conducted between 2013 and 2017 at Maharat Nakhon Ratchasima Hospital, evaluated the performance of the SCOPES in predicting outcomes of primary repair in patients with colonic injuries. While SCOPES demonstrated high sensitivity, specificity, and negative predictive value for predicting successful primary repair, its positive predictive value was relatively low. To improve the comprehensiveness of treatment recommendations, the study adjusted the Colonic Injury Severity Score (CIS) cutoff from ≥ 4 to ≥ 3.[13] A subsequent study by Prinya Santichatngam in 2022 evaluated the performance of both SCOPES versions I and II in patients with grade 3 or higher colonic injuries.[14] For SCOPES version II, diversion was recommended if more than one major factor was present, or if one major factor was accompanied by one or more minor factors. Major factors included gross fecal contamination and duodenum/ureter injury, while minor factors included delayed time to surgery (> 6 h) and left-sided colonic injury. The study compared the two versions, considering four factors for SCOPES version I. A primary repair was recommended if only one factor was present. For SCOPES version II, diversion was suggested if more than one major factor was present or if one major factor was accompanied by one or more minor factors. The study found that SCOPES version I had a sensitivity of 81%, specificity of 86%, positive likelihood ratio of 5.7, positive predictive value of 96%, and accuracy of 82% for predicting successful primary repair. SCOPES version II, on the other hand, demonstrated a sensitivity of 43%, specificity of 100%, positive likelihood ratio of greater than 10, positive predictive value of 100%, and accuracy of 90% for predicting the need for diversion. Overall, the use of both SCOPES versions could assist in making treatment decisions for up to 74% of patients with colonic injuries, potentially offering advantages over clinical judgment alone. The optimal management of colonic injuries remains a subject of ongoing debate, as there is no established gold standard treatment. This study aimed to determine the benefits of using SCOPES versions I, II, and III for patients with colonic injury in terms of sensitivity, specificity, accuracy, positive predictive value, and positive likelihood ratio.

Patients and Methods

A retrospective chart review was conducted at Pranangklao Hospital in Nonthaburi Province, a Level 2 Trauma Center under the Ministry of Public Health, and Maharat Nakhon Ratchasima Hospital in Nakhon Ratchasima Province, a Level 1 Trauma Center under the same ministry. The purpose of the study was to evaluate the diagnostic accuracy of SCOPES in patients with colonic injuries (ICD-10 codes: S365, S3650, S3651). The study included a total of 34 patients diagnosed between October 1, 2020, and September 30, 2024. Of these, 13 patients were from Pranangklao Hospital and 21 patients were from Maharat Nakhon Ratchasima Hospital.

Inclusion criteria

1. Age 15 years or older.
2. Underwent exploratory laparotomy.
3. Had a confirmed intraoperative diagnosis of grade 3 or higher colonic injuries.[9]

Exclusion criteria

1. Underwent damage control surgery.
2. Sustained iatrogenic injuries.
3. Had isolated rectal injuries (ICD-10: S36.6).

Baseline demographic data and clinical characteristics were collected, including type of injuries, underlying diseases, time to operation, colonic injuries score (CIS) according to the American college of surgeons (ACS),[9] degree of fecal contamination, sites of colonic injuries, grade of duodenal or ureteral injuries,[15,16] damage control surgery, details of the operative procedure, and operative complications. The criteria for SCOPES version III (for diversion) are as follows: These criteria are used in conjunction with SCOPES version II, meaning that if gross fecal contamination is present, diversion is recommended. All patients were assessed by two trauma surgeons who are board-certified, each having over two years of experience and subspecialty certification in trauma from the Medical Council of Thailand. These surgeons reviewed both the patient's condition and the operative notes. This study employed a peer review process requiring consensus between these two surgeons to establish a reference

standard for optimal treatment selection. In cases where the consensus of the peer reviewers differed from the treating physician's decision, the peer reviewers' joint assessment was considered the more suitable treatment option. The actual surgical treatments performed and the treatment recommendations generated by the SCOPES prediction score for colonic injuries were then compared against this reference standard (based on intraoperative findings and the final diagnosis). The predictive accuracy of the SCOPES scoring system for colonic injuries was assessed using a diagnostic test accuracy analysis. Sensitivity, specificity, positive and negative likelihood ratios, diagnostic odds ratio, overall accuracy, prevalence, and pretest and posttest odds were computed to evaluate the system's diagnostic performance. The research protocol has been reviewed and approved by the ethics committees of both Pranangklao Hospital, Nonthaburi, and Maharat Nakhon Ratchasima Hospital, ensuring adherence to ethical guidelines.

Results

Table 1 Demographic Data (N = 34)

Age (years) (mean) (SD) (range)	38.4 (16.02) (15-71)
Sex: male: female (%)	31 (91.2) : 3 (8.8)
Underlying disease	
HT (%)	1 (2.9)
DM (%)	3 (8.8)
Cause of injuries	
Blunt injuries	23 (67.6)
Penetrating injuries	
Non-gunshot or shotgun injuries	4 (11.7)
Gunshot or shotgun injuries	7 (20.6)
Length of stay (days) (median) (Interquartile range Q1-Q3)	11.5 (6.25-16)
Injury to operation (hours) (mean) (SD) (range)	13.35 (9.16) (2-41)
Preoperative shock (%)	1 (2.9)
Intraoperative shock (%)	0 (0)
Operative Time (hours) (mean) (SD) (range)	2.1 (0.88) (1-5)
Colonic injury grade: Grade 3 : Grade 4 : Grade 5 (%)	16 (47.1) : 8 (23.5) : 10 (29.4)
Side of colonic injuries: Right : Left : Both (%)	16 (47.1) : 15 (44.1) : 3 (8.8)
Associated intra-abbdominal organ injuries (Grading ≥ 3)	
Liver (%)	3 (8.8)
Stomach (%)	2 (5.9)
Duodenum (%)	3 (8.8)
Small bowel (%)	(23.5)
Degree of fecal contamination	
Mild to moderate contamination (%)	31 (91.2)
Gross or severe contamination (%)	3 (8.8)
Intraoperative blood transfusion* (units) (median) (Interquartile range Q1-Q3)	1 (0-2)
Estimate blood loss (ml) (median) (Interquartile range Q1-Q3)	425 (200-925)
Colonic management	
Primary repair (%)	28 (82.4)
Diversion procedure (%)	6 (17.6)
Outcome	
Survive (%)	32 (94.1)
Colonic-related complication	2 (5.9)

* Intraoperative blood transfusion refers to the administration of whole blood or packed red blood cells during a surgical procedure.

The number of patients with colon injuries (CIS > 3) from Pranangklao Hospital was 13, while Maharat Nakhon Ratchasima Hospital reported 21 patients. The average incidence of such injuries was 3.3 patients per year at Pranangklao Hospital and 5.3 patients per year at Maharat Nakhon Ratchasima Hospital. Of the total patients, 20 (58.8%) sustained injuries from road traffic accidents, 7 (20.6%) from gunshot wounds, 3 (8.8%) from sharp objects, 2 (5.9%) from falls from heights, 1 (2.9%) from being struck by a tree, and 1 (2.9%) from a saw. The locations of the colon injuries were as follows: cecum (7 patients, 20.6%), ascending colon (1 patient, 2.9%), hepatic flexure (1 patient, 2.9%), transverse colon (10 patients, 29.4%), splenic flexure (3 patients, 8.8%), and sigmoid colon (3 patients, 8.8%). Associated intra-abdominal injuries included liver injuries (grade 3 : 3 patients, 8.8%; grade 1: 1 patient, 2.9%), gastric injuries (grade 3 : 3 patients, 8.8%; grade 1: 1 patient, 2.9%; grade 2: 1 patient, 2.9%), duodenal injuries (grade 3 : 2 patients, 5.9%; grade 1: 1 patient, 2.9%), and small bowel injuries (grade 3 : 3 patients, 17.6%; grade 5 : 2 patients, 5.9%). Additional associated injuries included retroperitoneal hematoma (3 patients, 8.9%), diaphragmatic injuries (2 patients, 5.9%), pelvic fractures (2 patients, 5.9%), head injuries (2 patients, 5.9%), and a knee injury (1 patient, 2.9%). Please note that some patients have sustained injuries to multiple organs. Colonic-related complications observed included anastomotic leakage (1 patient, 3.6%) and stomal necrosis (1 patient, 16.7%). Causes of death among the patients included hospital-acquired pneumonia (1 patient, 2.9%), septic shock (1 patient, 2.9%), and severe head injury (1 patient, 2.9%).

Table 2 Comparison of actual colonic management and PEER review recommendations (N = 34)

		Actual surgical management	
		Diversion procedure	Primary repair
Reference Standard (PEER review)	**Diversion procedure**	2	1
	Primary repair	4	27

The actual management accuracy compared to PEER review recommendations was 85.29%.

Table 3 SCOPES version I (for primary repair) (N = 34)

		Reference Standard		Sensitivity (for primary repair)	Specificity (for primary repair)	Accuracy (for primary repair)	Positive predictive value	LR+
		Diversion	Primary repaired					
SCOPES version I	**Diversion procedure**	3	5	76.47	100	85.29	100	> 10 (large impact)
	Primary repair	0	26					

LR+: positive likelihood ratio

Negative predictive value is 37.50%. The negative likelihood ratio is 0.16, indicating a moderate impact. The diagnostic odds ratio exceeds 10, suggesting a large impact. The prevalence for primary repair is 91.18, with pretest odds of 10.34 and posttest odds indicating a large impact.

Table 4 SCOPES version II, III (for diversion procedure) (N = 34)

		Reference Standard		Sensitivity (for diversion procedure)	Specificity (for diversion procedure)	Accuracy (for diversion procedure)	Positive predictive value	LR+
		Diversion	Primary repaired					
SCOPES version II, III	**Diversion procedure**	3	0	100	100	100	100	> 10 (large impact)
	Primary repair	0	31					

LR+: positive likelihood ratio

Negative predictive value is 100%. The negative likelihood ratio is 0, indicating a large impact. The diagnosis odds ratio is greater than 10, also indicating a large impact. The prevalence of the diversion procedure is 8.82, while the pretest odds are 0.09. The posttest odds indicate a large impact.

Discussion

This study found that colonic injuries predominantly occurred in working-age individuals, with a mean age of 38.4 ± 16.02 years. Males were more frequently affected (91.2%) compared to females (8.8%), consistent with the findings of Brady and Oosthuizen.[17,18] Those with multiple comorbidities exhibited inferior treatment outcomes, corroborating the findings of Chamieh et al.[19] Blunt trauma was identified as the predominant mechanism of injury in this study, comprising 67.6% of cases. Road traffic accidents constituted 58.8% of the overall injuries. These findings deviate from previous research,[17,18] which has emphasized the significance of penetrating trauma. The majority of injuries were situated in the right side of the large bowel, with the transverse colon (29.4%), cecum (20.6%), ascending colon (2.9%), and hepatic flexure (2.9%) being the most frequently affected segments. This distribution is consistent with the observations reported by Sağıroğlu et al.[20] Falcone et al.[21] identified a constellation of risk factors associated with increased morbidity and mortality rates, including hypotension, massive transfusion, the extent of intra-abdominal contamination, concomitant organ injuries, shock, injuries to the left side of the colon, and the presence of multiple comorbidities. Within this study, preoperative shock was documented in 2.9% of patients, with no instances of intraoperative shock. The median volume of intraoperative blood transfusion was 1 unit, corresponding to a median estimated blood loss of 425 ml. Gross or severe fecal contamination was observed in 8.8% of cases. A significant proportion of patients (8.8%) sustained duodenal or ureteral injuries graded ≥ 3 in this study. Previous research has advocated for diversion procedures as a management strategy for injuries of this severity.[3,20] Colonic-related complications occurred in 3.7% of patients who underwent primary repair and 16.7% of those who underwent diversion procedures. These findings align with previous studies, which reported lower complication rates in the primary repair group, supporting the use of primary repair.[21-23] This study found an overall mortality rate of 5.9%, which is lower than the 9.9% reported by Burch JM and colleagues.[24] The accuracy of the surgical procedures executed by surgeons, as evaluated against the PEER review, was determined to be 85.29%. A previous study by Prinya Santichatngam[12] in 2017 identified factors affecting treatment diversion procedure or primary repair in colonic injuries, including delayed time to surgery, gross fecal contamination, left-sided colonic injuries, and duodenal or ureteral injuries (grade ≥ 3). The SCOPES version I, with factors > 2, demonstrated a sensitivity of 88.24% and specificity of 83.51%. A 2022 report revealed that SCOPES version I, designed for primary repair, exhibited a sensitivity of 81% and a specificity of 86%. In contrast, SCOPES version II, developed for diversion procedures, had a sensitivity of 43% and a perfect specificity of 100%.[14] This study demonstrated that while SCOPES version I (for primary repair) achieved a sensitivity of 76.47%, specificity of 100%, and accuracy of 85.29%. A study by Durham et al.,[25] identified gross or severe fecal contamination as a primary factor influencing treatment outcomes. In a more recent study by Jinescu et al.,[26] surgical judgment continues to play a pivotal role in decision-making. A multicenter study by Zeineddin et al.[27] proposed the use of the American Association for the surgery of trauma colon organ injury scale (OIS) to guide the management of colonic injuries. Studies by Durham,[25] Jinescu,[26] and Altiok[28] have proposed various scoring systems, including the abdominal trauma index (ATI) ≥ 30, colonic injury scale (CIS) ≥ 4, injury seriousness score (ISS), revised trauma score (RTS), and trauma injury severity score (TRISS), to guide treatment decisions for patients with colonic injuries. While these scoring systems aim to standardize treatment approaches, their implementation in clinical practice has encountered significant challenges. As a novel study, SCOPES versions II and III have demonstrated unparalleled accuracy and consistency in predicting outcomes for diversion procedures. With perfect sensitivity, specificity, positive or negative predictive value, positive or negative likelihood ratio or diagnosis odds ratio, or posttest odds, and accuracy, these models have significantly outperformed version I and traditional clinical judgment. This study provides strong evidence that SCOPES versions II and III offer a more reliable and consistent approach compared to traditional clinical judgment. applications.

Limitation

This hospital-based study was conducted at a trauma center to develop a new scoring system for surgical decision-making in colonic injuries with a colon injury scale (CIS) score > 3. Given the absence of a universally accepted gold standard for treatment recommendations, the study employed a PEER review process as the reference standard. As each participating hospital manages only approximately 3-5 such patients annually, refining surgical expertise through this system aims to facilitate the selection of more appropriate surgical treatments.

Conclusion

SCOPES versions II and III, developed for diversion procedures, have demonstrated exceptional performance in predicting outcomes, with perfect sensitivity, specificity, and accuracy. In contrast to primary repair surgery, which showed superior overall outcomes, SCOPES versions II and III significantly outperformed SCOPES version I, which was designed for primary repair. These findings highlight the reliability and accuracy of SCOPES versions II and III, making them valuable tools for clinical decision-making compared to traditional clinical or surgical judgment.

Conflict of Interest

No authors have any potential conflict of interest to disclose.

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Original Article

Efficacy of Customized Pressure Device in Treating Lower Limb Lymphedema: An Observational Study

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Abstract

Objectives: Lymphedema is a chronic, progressive, debilitating disease characterized by the accumulation of protein-rich interstitial fluids in the subcutaneous tissue due to the failure of the lymphatic drainage system. This study sought to evaluate the efficacy of customized pressure devices in treating lower limb lymphedema.

Materials and Methods: 5 patients with lower limb lymphedema who are on customized pressure devices were recruited in this study. The severity of the lymphedema limb(s) was evaluated over 5 months based on both objective and subjective measures. An objective measure was evaluated using limb circumference at different levels measured from the heel, supplemented with the lower extremity lymphedema (LEL) index. Subjective measures were evaluated using the Lymphedema Functionality, Disability and Health Questionnaire for Lower Limb Lymphedema Reliability and Validity (Lymph-ICF-LL).

Results: The study group includes 4 male patients and 1 female between 40 and 55 years old. 2 patients have bilateral lower limb lymphedema, 2 patients have right lower limb lymphedema, and 1 patient has left lower limb lymphedema. Through the LEL index, all patients have significant improvement except 1 patient. Whereas utilizing the Lymph-ICF-LL questionnaire, clinically relevant improvements were observed in 1 patient in the mental function and mobility domain. Minor improvements were identified in others. No patient experiences reduced in functionality. Most patients with lower limb lymphedema experienced a positive effect with the use of customized pressure devices.

Conclusion: Our study demonstrated the role of customized pressure devices in managing lower limb lymphedema. There is a significant decrease in LEL in 80% of our patients. Only 20% reported clinically significant improvement in their Lymph-ICF-LL score. Further evaluation is needed to determine the long-term outcomes of patients with lower limb lymphedema, especially regarding the long-term effects of customized pressure devices on LEL index and the ability to return to physical activities.

Keywords: Lymphedema, Lower limb lymphedema, Lymph-ICF-LL questionnaire, LEL Index, Compreflex

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Introduction

Lymphedema is a chronic, progressive, debilitating disease characterized by the accumulation of protein-rich interstitial fluids in the subcutaneous tissue due to failure in the lymphatic drainage system.[1] The failure can either be due to structural or functional abnormalities of lymphatic channels in the form of obstruction or hypoplasia.[2] Lymphedema can be classified into primary lymphedema, which is the malformation of lymphatic channels, or secondary lymphedema, which is destruction or obstruction of previously formed channels.[3,4] It can affect any part of the body, but is commonly observed affecting the upper and lower limbs.[1] In Malaysia, lymphatic filariasis is the most common cause of lower limb lymphedema.[5] Lymphatic filariasis has infected approximately 120 million people globally, and approximately 40 million have become incapacitated due to the disease.[5] Approximately 65% of the patients live in Southeast Asia, 30% in Africa, and the remaining patients in other tropical areas.[5] Globally, approximately 90% of lymphatic filariasis infections are caused by Wuchereria bancrofti, and Brugia malayi and B. timori cause the rest.[5] In Malaysia, lymphatic filariasis is caused by W. bancrofti and B. malayi and is transmitted by mosquitoes of the genus Anopheles and Mansonia. It occurs mainly in a few states in Malaysia, namely Sabah and Sarawak (East Malaysia) and Terengganu, Kelantan, Pahang, Selangor, and Johor (Peninsular Malaysia).[5]

Lymphedema can cause severe physical and psychological morbidity and is commonly associated with limb pain and heaviness, skin tightness, recurrent soft tissue infection, decreased range of movement, and secondary malignancy.[1] Psychologically, patients with lymphedema have a higher risk of having body image disturbances, anxiety, and depression. Consequently, lymphedema significantly decreases the quality of life in patients by affecting the ability to work and engage in social activities, reducing the workforce within the community.[1]

Diagnosis of lymphedema in our setting is usually established clinically, followed by blood investigations and imaging studies. Imaging modalities for disease confirmation, like radionuclide lymphoscintigraphy, magnetic resonance contrast lymphography, and indocyanine green lymphangiography, are unavailable in our setting, limiting the team to rely solely on magnetic resonance imaging (MRI).[3,4] In terms of lymphedema quantifications and progress monitoring, a variety of noninvasive methods like the water displacement method, perometry, tissue tonometry, bioelectrical impedance spectroscopy (BIS), computed tomography (CT) scan, magnetic resonance imaging (MRI), and ultrasonography can be used, but are not applicable in our setting.[6] Progress of disease is monitored via limb circumference measurements and monitoring of quality of life through subjective questions.[1]

Treatment of lymphedema is initiated with complex decongestive therapy (CDT) followed by surgical intervention (physiological and ablative surgery) if indicated.[1,3,4] Complex decongestive therapy remains the mainstay of lymphedema treatment worldwide to date and aims to decrease the excessive fluid in the lymphedematous limbs. It consists of skin care, exercise, compression therapy, and manual lymphatic drainage combinations.[1,3,4] Due to the lack of lymphedema paramedics and resources, our center does not offer multilayer bandaging (compression therapy) and manual lymphatic drainage. Self-bandaging challenges our patients due to their restricted mobility and limited resources. Customized pressure devices (Compreflex) were recently available in our setting (Figure 1). This device is more user-friendly, and the comprehensive services offered by the pressure device team and the availability of medical aid funding for the device have greatly benefited patients and lymphedema services in various ways. This device allows easy self-donning with a front stretch panel to secure the garment in place and straps that roll back. The pressure implied by the device is self-adjustable by patients using measuring tapes (Accutab) that come along with the device, which have pre-labeled pressure ranges labeled on them, as shown in Figures 2 and 3. This encourages a patient's self-management and adherence to treatment. In our study, all 5 patients are using the pressure range of 30-40 mm Hg as the pressure device team suggested. This study aims to evaluate the efficacy of customized pressure devices in treating lower limb lymphedema.

Figure 1 A patient wearing customized pressure devices (Compreflex)

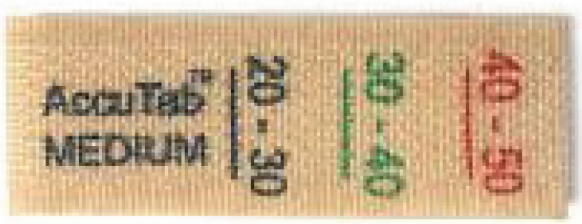

Figure 2 Pre-labelled measuring tape (Accutab)

Figure 3 Customized pressure devices (Compreflex) and Pre-labelled measuring tape (Accutab)

Materials and Methods

The duration of this study is five months from July 2024 until November 2024. 12 patients with lymphedema of the limb who are on customized pressure devices were identified. 2 patients with upper limb lymphedema were excluded from this study. 5 patients with lower limb lymphedema were unable to participate in this study due to various reasons (non-compliance, defaulting on follow-up, uncontactable). 5 patients with lower limb lymphedema (unilateral and bilateral) were recruited in this study. The severity of the lymphedema limb(s) was evaluated based on both objective and subjective measures.

Objective measurements were evaluated in terms of limb circumference at different levels measured from the heel: 5 cm, 10 cm, 15 cm, 20 cm, 25 cm, 30 cm, 35 cm, and 40 cm, taken twice over 3 months, and were supplemented using the lower extremity lymphedema (LEL) index.[7] LEL index was calculated by taking the sum of the squares of all the limb circumferences, then dividing by the respective patients' BMI. The calculation formula is shown in Figure 4.

$$\text{LEL} = \frac{\text{Sum of [Measured limb circumferrences]}^2\ (\text{cm}^2)}{\text{Patient's BMI}\ (\text{kg/m}^2)}$$

Figure 4 Formula for calculation of lower extremity lymphedema (LEL) index

Subjective evaluation was carried out by interviewing patients using the Lymphedema Functionality, Disability and Health Questionnaire for Lower Limb Lymphedema Reliability and Validity (Lymph-ICF-LL) during the first and third clinic visits. It is a descriptive, evaluative tool containing 28 questions about impairments in function, activity limitations, and participation restrictions in patients with lower limb lymphedema.[8] Full questionnaire is shown in Appendix 1.

Both objective and subjective evaluations were taken pre-treatment and 3 months after commencement of the customized pressure device. No surgical intervention has been done for these patients over this period of time.

Results

Demographics of patients and a summary of data obtained from this study were shown in Tables 1, 2, and 3. Lower limb circumference measurements for patients

were shown in Tables 4A to 4E. A total of 5 patients with lower limb lymphedema were recruited in this study. 2 patients had bilateral lower limb lymphedema, 2 patients had right lower limb lymphedema, and 1 patient had left lower limb lymphedema. Through the lower extremity lymphedema index, all patients have significant improvement except 1 patient. Whereas utilizing the Lymph-ICF-LL questionnaire, clinically relevant improvements were observed in 1 patient in the mental function and mobility domain. Minor improvements were still observed in other patients. No patient experiences a decrease in functionality. The majority of patients with lower limb lymphedema experienced a positive effect with the use of customized pressure devices.

Table 1 Demographics of patients

Patient	Age	Gender	Weight (kg)	Height (cm)	BMI (kg/m^2)	Co-morbidities	Affected lower limb(s)	Cause of lymphedema
A	46	Male	158	163	59	Obesity class 3 Hypertension	Bilateral	Lymphedema precox
B	44	Male	85	172	28.7	Pre-obesity	Right	Lymphedema precox
C	48	Female	72	164	30.4	Obesity class 1 Dyslipidemia	Right	Lymphedema precox
D	38	Male	125	165	45.9	Obesity class 3 Hypertension	Bilateral	Lymphedema precox
E	40	Male	95	169	33.2	Obesity class 1	Left	Lymphedema precox

Table 2 Objective outcome following customized pressure device, Lower extremity lymphedema (LEL) index

Patient	Lower Limb (S)	LEL Index 1st Measurement	LEL Index 2nd Measurement	LEL1 -LEL2	Outcome (%)
A	Right	289	286	3	- 1.04
	Left	582	571	11	- 1.89
B	Right	526.5	455.4	71.1	- 13.50
C	Right	383	342	41	- 10.70
D	Right	597.5	506.6	90.9	- 15.21
	Left	1,157.3	1,070.5	86.8	- 7.50
E	Left	654	612	42	- 6.42

Table 3 Subjective outcome following customized pressure device Lymphedema Functionality, Disability and Health Questionnaire for Lower Limb Lymphedema and Validity (Lymph-ICF-LL)

Patient	Physical function		Outcome	Mental function		Outcome	General task/ household		Outcome	Mobility		Outcome	Life domain/ social life domain		Outcome	Total of Outcome
	Pre	Post		Pre	Post		Pre	Post		Pre	Post		Pre	Post		
A	28	26	-2	52	48	-4	23	21	-2	67	65	-2	60	59	-1	-11
B	9	3	-6	36	16	-20 Clinically relevant improvement	17	17	-	48	27	-21 Clinically relevant improvement	30	16	-14	-61
C	19	9	-10	23	14	-9	3	2	-1	25	21	-4	23	16	-7	-31
D	29	18	-11	38	29	-9	17	14	-3	58	51	-7	42	37	-5	-35
E	28	24	-4	8	6	-2	3	0	-3	18	16	-2	15	12	-3	-14

Table 4A.1 Right lower limb circumference measurements for patient A

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Right	**5 cm**	41	1,681	41	1,681
	10 cm	39	1,521	38	1,444
	15 cm	37	1,369	39	1,521
	20 cm	39	1,521	39	1,521
	25 cm	44	1,936	42	1,764
	30 cm	44	1,936	45	2,025
	35 cm	56	3,136	57	3,249
	40 cm	63	3,969	61	3,721
Sum of square of limb circumference (cm^2)			17,089		16,926
LEL index			289		286

Table 4A.2 Left lower limb circumference measurements for patient A

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Left	**5 cm**	55	3,025	53	2,809
	10 cm	55	3,025	56	3,136
	15 cm	59	3,481	59	3,481
	20 cm	63	3,969	63	3,969
	25 cm	65	4,225	63	3,969
	30 cm	68	4,624	67	4,489
	35 cm	79	6,241	78	6,084
	40 cm	76	5,776	76	5,776
Sum of square of limb circumference (cm^2)			34,366		33,713
LEL index			582		571

Table 4B Right lower limb circumference measurements for patient B

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Right	**5 cm**	32	1,024	36	1,296
	10 cm	36.5	1,332.25	34	1,156
	15 cm	44.5	1,980.25	38	1,444
	20 cm	48.5	2,352.25	40	1,600
	25 cm	48	2,304	44	1,936
	30 cm	49	2,401	43	1,849
	35 cm	46	2,116	45	2,025
	40 cm	40	1,600	42	1,764
Sum of square of limb circumference (cm^2)			15,109.75		13,070
LEL index			526.5		455.4

Table 4C Right lower limb circumference measurements for patient C

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Right	**5 cm**	34	1,156	32	1,024
	10 cm	30	900	29	841
	15 cm	29	841	29	841
	20 cm	39	1,521	36	1,296
	25 cm	41	1,681	40	1,600
	30 cm	44	1,936	41	1,681
	35 cm	42	1,764	40	1,600
	40 cm	43	1,849	39	1,521
Sum of square of limb circumference (cm^2)			11,648		10,404
LEL index			383		342

Table 4D.1 Right lower limb circumference measurements for patient D

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Right	**5 cm**	48.1	2,313.61	46	2,116
	10 cm	48	2,304	44	1,936
	15 cm	45.2	2,043.04	45	2,025
	20 cm	45.5	2,070.25	45	2,025
	25 cm	63.3	4,006.89	60	3,600
	30 cm	72	5,184	63	3,969
	35 cm	73	5,329	65	4,225
	40 cm	65	4,225	58	3,364
Sum of square of limb circumference (cm^2)			27,425.79		23,260
LEL index			597.5		506.6

Table 4D.2 Left lower limb circumference measurements for patient D

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Left	**5 cm**	71	5,041	72	5,184
	10 cm	74	5,476	73	5,329
	15 cm	73.6	5,416.9	75	5,625
	20 cm	76	5,776	78	6,084
	25 cm	87	7,569	80	6,400
	30 cm	86.3	7,447.69	84	7,056
	35 cm	92.6	8,574.76	84	7,056
	40 cm	89	7,921	80	6,400
Sum of square of limb circumference (cm^2)			53,122.35		49,134
LEL index			1,157.3		1,070.5

Table 4E Left lower limb circumference measurements for patient E

Affected limb	Measurements from heel	Limb circumference (cm)	Square of limb circumference (cm^2)	Limb circumference (cm)	Square of limb circumference (cm^2)
Left	**5 cm**	41.5	1,722.25	41	1,681
	10 cm	40.5	1,640.25	39	1,521
	15 cm	44	1,936	44	1,936
	20 cm	48	2,304	46	2,116
	25 cm	52	2,704	49	2,401
	30 cm	63	3,969	58	3,364
	35 cm	62	3,844	62	3,844
	40 cm	60	3,600	59	3,481
Sum of square of limb circumference (cm^2)			21,719.5		20,344
LEL index			654		612.8

Discussion

Lymphedema management has always posed challenges in terms of diagnosis, classification, and management. Measuring the circumference is the most common method for objectively evaluating lymphedema.[7] However, this method is inconsistent due to the variability of a reference point for measurement.[7] This is due to anatomical distortion caused by the lymphedema, rendering fixed points such as the patella or malleolus undetectable. Lymphedema also has volumetric changes on top of circumferential increase. Volume is more difficult to quantify due to the asymmetrical distribution of lymphatic fluid.[6] Yamamoto et al. developed the lower extremity lymphedema (LEL) index in 2011, which incorporates the cross-sectional area of the affected limb and patients' BMI.[7] It can be used to assess the severity of the lymphedema through a numerical rating, regardless of body habitus, and for comparison between different patients.[7] It is calculated by using the sum of the squares of circumference in 5 areas of the lower limbs (10 cm above the patella, superior edge of the patella, 10 cm below the patella, lateral malleolus, dorsum of the foot) and divided by the respective patients' BMI.[7] In our study, we modified the calculation of the LEL index using the heel as a reference point and measured the limb circumference at intervals of 5 cm. These measurements are done to get a more accurate representation of the lymphedema throughout the lower limb. All 5 patients recruited in our study are of Campisi clinical stage 4, and due to severe anatomical distortion, a reference point for measurement was difficult to obtain. Thus, instead of using the patella as a landmark for measurement, we measure the circumference of the lower limb at 5 cm, 10 cm, 15 cm, 20 cm, 25 cm, 30 cm, 35 cm, and 40 cm from the heel. The sum of the squares of all the values is then divided by the respective patients' BMI to obtain the LEL index.

The Lymph-ICF-LL questionnaire was developed by Devoogdt et al in 2014 and was tested as reliable and valid for assessing problems in functioning in patients with lower limb lymphedema.[8] The Lymph-ICF-LL is a descriptive, evaluative tool containing 28 questions about impairments in function, activity limitations, and participation restrictions in patients with lower limb lymphedema.[8] The questionnaire has 5 domains: physical function, mental function, general tasks/household activities, mobility activities, and life domains/social life.[8] Patients must complete the questionnaire by themselves and were asked to score the same hobbies and social activities each time.[8] According to Devoogdt et al, for the interpretation of follow-up assessment with the Lymph-ICF-LL questionnaire, a change (increase/decrease) of 20 or more is considered a clinically relevant change for all domains except the life domain/ social life.[8] For the life domain/ social life domain, a change (increase/decrease) of 40 is considered a clinically relevant change.[8] Only 1 of our patients reported clinically significant mental function and mobility changes in Lymph-ICF-LL. However, all of the patients have reported improvement throughout all aspects of the Lymph-ICF-LL questionnaire. This study was conducted in a short period of 5 months, and most patients have not had adequate time to return to their daily activities yet due to various reasons, such as excessive

weight and lower limb weakness. Long-term follow-ups are needed on these patients.

No significant relationship is observed between the decrease in lower limb lymphedema and patients' functionality, disability, and health. This is observed when we compare the LEL1-LEL2 scores to the Lymph-ICF-LL scores. A higher LEL1-LEL2 score does not improve the Lymph-ICF-LL score further. This can be multi-factorial as patients' pre-morbid function, mental health, and existing medical conditions can affect the scores in the Lymph-ICF-LL questionnaire. There is also no relationship between the severity of lymphedema and patients' functionality, disability, and health, as the high LEL1 or LEL2 scores do not cause a lower score in the questionnaire.

Last but not least, obesity was observed in all 5 of our patients. Multiple recent clinical studies have established the significant relationship between obesity and lymphedema.[9] Case of obesity-induced lymphedema of the lower extremities was reported and concluded that lymphedema can develop once a patient's body mass index (BMI) exceeds 50.[10] Unlike other co-morbidities such as diabetes, hypertension, and sleep apnea, which may improve with massive weight loss, obesity-induced lymphedema may not resolve, even with weight reduction due to the irreversibility of lymphatic dysfunction.[10] Several studies have shown that obesity increases the risk of secondary lymphedema following damage to the lymphatic system.[9] Recent research also indicates that morbidly obese individuals can develop lymphedema even without prior surgery or injury, highlighting that obesity alone can impair lymphatic function and lead to the development of lymphedema.[10] Growing evidence suggests a reciprocal relationship between obesity and lymphedema, where obesity impairs lymphatic function, and impaired lymphatic drainage, in turn, promotes fat deposition, but this is limited to animal models for now.[10]

Conclusion

Results from our study demonstrated the role of customized pressure devices in lower limb lymphedema management. There is a significant decrease in LEL in 80% of our patients, hence proving that there is a significant physical and volumetric decrease in lower limb lymphedema. Only 20% of our patients reported clinically significant improvement in their Lymph-ICF-LL score. This is possibly due to the short course of this study, the patient's pre-morbid physical conditions, and existing medical conditions. Patients with chronic malnutrition and anemia were less likely to get back to physical activities. Although treatment with a customized pressure device showed promising results, there is still a need to evaluate the long-term outcomes further.

Conflict of Interest

All authors have nothing to disclose.

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Informed consent

Informed consent and consent to publish the outcomes were obtained from all the individual participants included in this study.

Consent to publish

All individual participants included in the study have consented to the submission of this original article to the journal.

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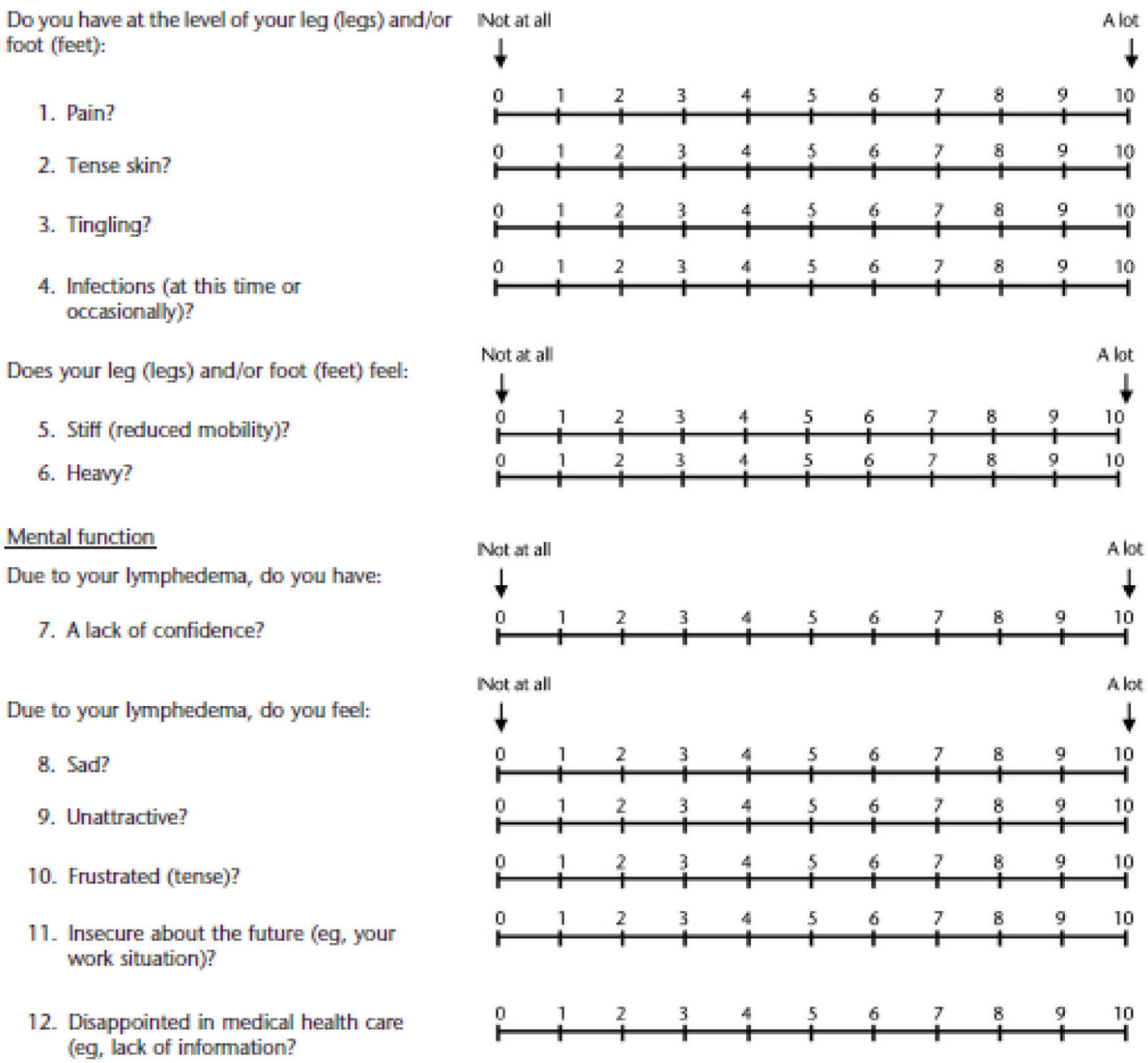
Appendix 1 Lymphedema Functionality, Disability and Health Questionnaire for Lower Limb Lymphedema Reliability and Validity (Lymph-ICF-LL)



General tasks/household

Due to your lymphedema, have you:

13. Become more dependent on others? (Not at all – A lot; 0 1 2 3 4 5 6 7 8 9 10)

Due to your lymphedema, do you have difficulties with:

14. Organizing different matters (eg, chores, appointments)? (0 1 2 3 4 5 6 7 8 9 10)

15. Completing household chores? (0 1 2 3 4 5 6 7 8 9 10; Not applicable)

Mobility

Due to your lymphedema, can you: (Very well – Not at all; 0 1 2 3 4 5 6 7 8 9 10)

16. Sit for a prolonged period of time?

17. Stand for a prolonged time?

18. Kneel?

19. Walk (>2 km)?

20. Ride a bicycle?

21. Drive a car?

22. Take the stairs (or get on and off a bus)? (Not applicable)

Life domains/social life

Due to your lymphedema, can you: (Very well – Not at all; 0 1 2 3 4 5 6 7 8 9 10)

23. Fulfill your job (paid work)?
My job: _____

24. Practice sports?
My sport(s): _____

25. Carry out leisure-time activities?
My leisure-time activities: _____

26. Carry out social activities with friends (eg, go to a party, go out for dinner)?
My social activities: _____

27. Wear clothes and/or shoes you like to wear?

28. Go on a holiday? (Not applicable)

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Original Article

Efficacy of Total Neoadjuvant Therapy (TNT) Versus Concurrent Neoadjuvant Chemoradiotherapy (CCRT) Alone for Locally Advanced Rectal Cancer in Rajavithi Hospital: A Retrospective Study

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Abstract

Background: Conventional therapy for locally advanced rectal cancer included concurrent chemoradiotherapy (CCRT) followed by surgery and adjuvant chemotherapy. An alternative strategy known as total neoadjuvant therapy (TNT) involves the administration of neoadjuvant chemotherapy plus CCRT before surgery. The studies before suggest that TNT is a promising strategy in locally advanced rectal cancer with a superior rate of PCR compared with conventional therapy. The purpose of this study is to compare the rate of PCR using these 2 approaches in patients at Rajavithi Hospital.

Objective: To determine the differences in rates of pathologic complete response (PCR), R0 resection, and 30-day mortality between patients receiving TNT vs conventional CCRT.

Materials and Methods: We performed a retrospective study of patients with clinical stage II/III rectal cancer within Rajavithi Hospital. All patients who received TNT and conventional CCRT were collected between 2019 and 2024, and the rates of pathological complete response (pCR) were compared between the two arms.

Results: Of the 135 patients in the cohort, 102 (76%) received conventional treatment and 33 (24%) received TNT. At baseline, patients in both groups were more likely to have clinical Stage 3 disease. There were 5 (15.2%) TNT patients who achieved pCR after surgery, compared to 8 (7.8%) conventional CCRT patients ($P = 0.305$), with no significant difference. There were no significant differences in the rate of positive margins after surgery (3% vs. 8.8%, $P = 0.45$). Only one patient in the standard arm has mortality within 30 days.

Conclusion: In the TNT group, PCR was found to be higher than the standard group (15.2% vs 7.8%, $p = 0.305$), although PCR was not significantly different, the real pCR rate was consistent with previous studies that suggest TNT is a promising strategy in locally advanced rectal cancer, with superior rates of PCR compared to standard CCRT.

Keywords: Total neoadjuvant chemotherapy (TNT), Concurrent chemoradiotherapy (CCRT), Locally advanced rectal cancer (LARC), Pathological complete response (PCR)

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Introduction

Rectal cancer has been increasingly diagnosed over the years in Thailand, with an incidence of 14.1 per 100,000 in men and 10 per 100,000 in women.[1] In 2018, there were 17,534 new cases of rectal cancer, accounting for 10.3% of all newly diagnosed cancers in Thailand.[2] For patients with locally advanced rectal cancer (LARC), locoregional recurrence rates have declined in recent years due to advances in surgical techniques and the adoption of neoadjuvant chemoradiation. As a result, the most common cause of death is now distant metastasis.[3,4] This risk can be reduced through the use of systemic chemotherapy.

However, the optimal timing for administering systemic chemotherapy in these patients remains unclear. Historically, patients with LARC have undergone neoadjuvant chemoradiation and surgery, followed by adjuvant chemotherapy. Nevertheless, intolerance to chemotherapy following surgery leads to poor compliance, with only 40%-50% of patients completing the adjuvant treatment course in clinical trials.[5,6]

In recent years, a new treatment strategy known as total neoadjuvant therapy (TNT) has emerged. In this approach, patients receive both systemic chemotherapy and chemoradiation prior to definitive surgical resection.[7] TNT is theoretically associated with improved treatment compliance, higher rates of R0 resection, and increased pathologic complete response (pCR) rates.

Many trials of TNT have been previously studied,[8-16] demonstrating excellent compliance rates and tolerability. However, the unclear result of the pathological complete response rate. One small phase 2 trial directly compared neoadjuvant CAPOX (TNT) to adjuvant CAPOX and found no difference in pCR after surgery.[12] Recently, a single institution retrospective study found that TNT increased rates of pCR.[17]

In the COVID-19 ERA, due to limited access to surgical facilities, we initiated total neoadjuvant therapy (TNT) as a treatment strategy for LARC patients at Rajavithi Hospital. We performed a single retrospective study at Rajavithi Hospital to examine whether the TNT approach is associated with improved pathological complete response (pCR) to conventional historical CCRT.

Materials and Methods

A retrospective study was conducted at Rajavithi Hospital, focusing on the period from January 2019 to June 2024. The initial query included all adult patients diagnosed with rectal cancer who received chemotherapy between 2019 and 2024 (N = 567). Patients with clinical stage 1 or 4, who have undergone no definitive surgery, upfront surgery, received post-op RT, and who have received an incomplete dose of chemotherapy were excluded.

The study included patients diagnosed with rectal cancer at American Joint Committee on Cancer (AJCC) clinical stage II or III who received all three of the following treatments: (1) systemic chemotherapy, (2) neoadjuvant chemoradiotherapy, and (3) surgery.

Data were obtained from the Rajavithi Hospital database, including patient age, gender, ASA score, tumor characteristics (both clinical and pathological AJCC TNM stage), chemotherapy regimen, surgical margin status, surgical approach and type, pathological complete response (pCR), and 30-day postoperative mortality.

Patients in the conventional arm were defined as those who received concurrent chemoradiation (CCRT) prior to surgery. TNT patients were defined as those who received neoadjuvant chemotherapy either before or after chemoradiation, followed by surgery. The exclusion criteria were clinical I or IV, the patient did not undergo definitive surgery, an incomplete course of chemotherapy, the patient underwent upfront surgery, or the patient received postoperative radiotherapy. The definition of incomplete course chemotherapy is failure to receive the planned full course of systemic chemotherapy, either due to premature discontinuation, dose omission, or early termination before completing the scheduled cycles.

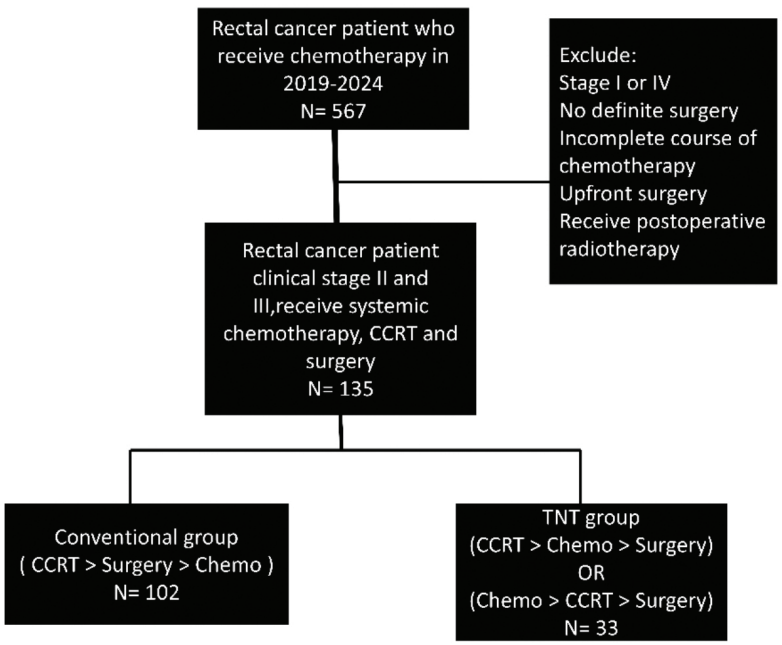

Figure 1

The primary outcome was to determine the difference rate of pathological complete response (pCR) between patients receiving total neoadjuvant therapy (TNT) and those receiving conventional concurrent chemoradiation (CCRT). pCR was defined based on pathological T and N staging.

The secondary outcomes were to compare the rates of R0 resection and 30-day postoperative mortality between the two treatment groups.

Statistical analysis

Data were analyzed using SPSS version 26.0. Univariate analysis was performed using the $\chi 2$ test for dichotomous variables and the Student's *t*-test or Wilcoxon rank sum test for normal and non-normal continuous variables, respectively, with a *p*-value of less than 0.05 defined as statistically significant.

Results

Patient Demographics and Clinical Characteristics (Table 1)

A total of 135 patients were included in the study, with 102 patients receiving conventional concurrent chemoradiation therapy (CCRT) and 33 patients receiving total neoadjuvant therapy (TNT). The participants consisted of 63% males and 37% females, with a mean age of 55.48 years. The majority of patients were classified as ASA class II (59.3%), followed by class I (38.5%) and class III (2.2%).

Regarding tumor characteristics, 80% of patients had AJCC clinical stage III disease, and 20% had stage II disease. The most common clinical T stages were cT3 (65.2%) and cT4 (28.9%). Clinically positive lymph nodes (cN+) were present in 79.3% of patients, while 20.7% were cN0. Pathological T stage was mostly ypT3 (47.4%) and ypT4 (25.9%), and pathological N stage was mostly ypN0 (62.2%).

The overall pathological complete response rate was 9.6%, R0 resection was achieved in 92.6% of patients, and only 1 patient died (0.7%) within 30 days postoperatively. Among the TNT group, the most commonly used chemotherapy regimen was FOLFOX (73%), followed by CAPOX (27%).

Table 1 Demographic and Clinical Characteristics between TNT gr and conventional gr.

Characteristics	Group		*p*-value
	TNT patients n (%) = 33	Conventional patients n (%) = 102	
Gender			0.357
Male	23 (69.7)	62 (60.8)	
Female	10 (30.3)	40 (39.2)	
Age (year)			0.893
Mean ± SD	55.85 ± 11.23	55.36 ± 11.02	
ASA score			0.666
I	38 (37.3)	14 (42.4)	
II	62 (60.8)	18 (54.5)	
III	2 (2)	1 (3)	
Tumor characteristics			
AJCC clinical staging			0.089
Stage 2	10 (30.3)	17 (16.7)	
Stage 3	23 (69.7)	85 (83.3)	
Clinical T classification			0.828
cT1	0	1 (1)	
cT2	1 (3)	6 (5.9)	
cT3	23 (69.7)	65 (63.7)	
cT4	9 (27.3)	30 (29.4)	
Clinical N classification			0.119
cN0	10 (30.3)	18 (17.6)	
cN+	23 (69.7)	84 (82.4)	
Pathological T classification			0.72
ypT0	5 (15.2)	8 (7.8)	
ypT1	0	1 (1)	
ypT2	5 (15.2)	17 (16.7)	
ypT3	14 (42.4)	50 (49)	
ypT4	9 (27.3)	26 (25.5)	
Pathological N classification			< 0.001
ypN0	30 (90.9)	54 (52.9)	
ypN1	3 (9.1)	36 (35.3)	
ypN2	0	12 (11.8)	
Pathological complete response (pCR)			0.305
Yes	5 (15.2)	8 (7.8)	
No	28 (84.8)	94 (92.2)	
Chemotherapy Regimen			
CAPEOX	9 (27)	-	
FOLFOX	24 (73)	-	
Surgical approach			1.0
Open	16 (48.5)	48 (47.1)	
Laparoscopic	16 (48.5)	50 (49)	
Lap convert to open	1 (3)	4 (3.9)	
Surgical type			0.695
AR/LAR/ISR	21 (63.6)	61 (59.8)	
APR/Hartman/Pelvic ex	12 (36.4)	41 (40.2)	
R0 resection margin			0.45
Yes	32 (97)	93 (91.2)	
No	1 (3)	9 (8.8)	

Values were represented as n (%), mean ± SD, and median (min-max). The p-value from the student *t*-test and chi-square test * significant at $p < 0.05$

Comparison of TNT vs. Conventional CCRT

Compared to patients who received conventional therapy, patients in both the TNT and conventional groups were likely to have non-different clinical stage III disease. The mean age was comparable between the TNT and the conventional group, as were sex distribution, ASA score, clinical T stage (cT), and clinical N stage (cN).

Following surgery, the pathological T0 stage (pT0) was observed in 15.2% of TNT patients and 7.8% of conventional neoadjuvant CCRT patients ($P = 0.72$), while the pathological N0 stage (pN0) was significantly higher in the TNT group (90.9% vs. 52.9%, $P < 0.001$). Notably, all patients with pT0 also achieved pathological complete response (pCR).

There was no statistically significant difference in the rate of positive surgical margins between the two groups (3.0% vs. 8.8%, $P = 0.45$). Thirty-day postoperative mortality occurred in only one patient, who was in the conventional group.

There was no significant difference in the type of surgical approach (laparoscopic vs. open) between the TNT and conventional group.

In the TNT group, the FOLFOX regimen was more commonly used than CAPOX (73% vs. 27%).

Pathological complete response

A total of 5 patients (15.2%) in the TNT group achieved pathological complete response (pCR) after surgery, compared to 8 patients (7.8%) in the conventional neoadjuvant CCRT group; this difference was not statistically significant ($P = 0.305$).

However, the nodal conversion rate from clinically positive nodes (cN+) to pathologically negative nodes (ypN0) was significantly higher in the TNT group compared to the conventional group (90.9% vs. 52.9%, $P < 0.001$).

Discussion

In the COVID-19 era, physicians at Rajavithi Hospital are increasingly using TNT in practice due to limitations in the operating room and this strategy has favorable tolerability profile, including a shorter ostomy duration, as demonstrated in previous studies.[8-13] Additionally, TNT has not been shown to negatively affect overall survival (OS), which supports its growing use as an alternative to conventional neoadjuvant therapy in LARC.[18,19]

In this retrospective cohort study conducted at Rajavithi Hospital, we compared the efficacy of total neoadjuvant therapy (TNT) versus conventional neoadjuvant concurrent chemoradiotherapy (CCRT) in patients with locally advanced rectal cancer (LARC). Our primary outcome was the rate of pathological complete response (pCR), with secondary outcomes including R0 resection rates and 30-day postoperative mortality. Among 135 patients, 33 received TNT and 102 received conventional neoadjuvant CCRT. The pCR rate was higher in the TNT group compared to the CCRT group, at 15.2% and 7.8%, respectively, but no statistically significant difference ($P = 0.305$). Notably, the nodal conversion rate was significantly higher in the TNT group, 90.9% and. 52.9%, $P < 0.001$. Rates of R0 resection and 30-day mortality were similar between two groups.

About the pCR rate, our study was concordant with previous reports in recent meta-analyses and randomized controlled trials (RCTs), which generally report pCR rates between 14% and 36% for TNT and 7–22% for conventional neoadjuvant CCRT.[20-24]

There are several factors that are associated with pathological complete response after TNT. Two studies demonstrate that the predictors of pCR are total neoadjuvant treatment.[25,26] Patient-related factors, such as young age (less than 60 years) and better performance status (ECOG 0-1), are associated with a higher pCR rate.[25,26] Tumor-related factors, including non-mucinous adenocarcinoma, are associated with a higher pCR rate; conversely, mucinous adenocarcinoma and signet-ring cell carcinoma are associated with a lower pCR rate.[25,26] Biological marker: CEA level < 5 ng/mL before treatment predicts a higher pCR rate, although the relationship between post-treatment CEA level and pCR remains unclear.[25] Receiving a complete course of chemotherapy without interruption and a longer interval between completion of neoadjuvant chemoradiotherapy (nCRT) and surgery shows an increased pCR rate.[26,27] But it should be noted that Yacoub H, etal, reported this study with total neoadjuvant treatment using short-course radiotherapy, commonly used in European countries.[26]

Although the pCR rate in our study was not statistically significant, this outcome remains clinically relevant. pCR is considered a surrogate marker for improved long-term survival, with previous studies showing better outcomes in patients who achieve pCR.[18] In our study, the pCR rate was higher in the TNT group compared to the conventional group (15.2% vs. 7.8%; $P = 0.305$), which is concordant with previous reports.[18-26] Kong et al. reported a pCR rate of 22.3% in the TNT group versus

14.2% in the conventional group ($P < 0.001$), and there was a significantly better 3-year disease-free survival and overall survival in the TNT compared to the conventional neoadjuvant CCRT group.[23] Similarly, Gabbani et al. conducted a meta-analysis of 14 randomized controlled trials and found a pCR rate of 23.6%, with 3- and 5-year overall survival rates of 93% and 81.6%, respectively.[24] A systematic review and meta-analysis by Kasi et al. in 2020 reported a pooled pCR rate of 29.9% (range, 17.2%–38.5%) in the TNT group versus 14.9% (range, 4.2%–21.3%) in the conventional group. The authors concluded that TNT is a promising strategy in LARC, associated with a significantly greater chance of achieving pCR (odds ratio [OR], 2.44; 95% CI, 1.99–2.98).[20]

The rationale for TNT is to reduce a patient's risk of distant metastasis, which is a major cause of death in rectal cancer. Early systemic chemotherapy can eradicate micrometastases before they become distant metastases and improve overall survival.[22] TNT consists of induction chemotherapy and consolidation chemotherapy. Both induction and consolidation chemotherapy improve pCR rate and disease control compared to CCRT. A recent meta-analysis does not show evidence that induction or consolidation is better.[21,22] The pCR rate for induction and consolidation is similar in the meta-analysis.[20,21,22] Induction chemotherapy may be better for early systemic control. Consolidation chemotherapy may maximize tumor shrinkage before surgery and better selection for the organ preservation strategy.[22]

Our study shows a significantly higher nodal conversion rate in the TNT group, at 90.9%, compared to 52.9% in the CCRT group ($P < 0.001$). This observation is consistent with the hypothesis that early and intensified systemic chemotherapy, as delivered in TNT, is more effective at eradicating micrometastatic disease and achieving nodal downstaging, aligning with results from the RAPIDO and PRODIGE-23 trials. Other studies have similarly reported that TNT increased nodal downstaging and reduced rates of distant metastasis.[18,22]

Systematic review and meta-analysis from Kong et al. showed that Patients who received TNT were less likely to have residual nodal disease on final pathology (pooled OR 0.87, 95% CI 0.73–1.03, $p = 0.122$, I 2 = 67.7%), sub meta-analysis showed that there is significantly nodal conversion in induction chemotherapy group (OR 0.56, 95% CI 0.41–0.77, $p < 0.001$, I 2 = 33.5%).[22] The author concluded that TNT is associated with downstaging of both the primary site and nodal basin, which also added benefit in the rate of anal preservation, distant recurrences, disease-free survival, and 3-year overall survival.[22]

Regarding the primary outcome, our study did not demonstrate a statistically significant difference in pCR rate between the TNT group and the conventional group. The pCR rate is consistent with previously published data.[8,10-14,17-26] The absence of statistical significance is likely attributable to the small sample size of the TNT arm (N = 33), which limited the statistical power to detect the differences.

Limitations

This study is limited by its retrospective design, which may introduce selection bias and confounding factors between the treatment groups. Although the sample size calculation for the TNT group indicated that at least 73 patients would be required to achieve adequate statistical power, only a small population of about 33 patients met the inclusion criteria during the study period at Rajavithi Hospital (January 2019 to June 2024). As a result, the study may have been underpowered to detect a statistically significant difference in outcomes between the groups.

Another limitation of our study is the exclusion rate between groups. Patients in the CCRT group were excluded more frequently than those in the TNT group due to lower compliance with completing the planned chemotherapy regimen. This may have introduced a selection bias.

Conclusion

In the TNT group, the pathological complete response (pCR) rate was no different compared with the conventional CCRT group (15.2% vs. 7.8%, $P = 0.305$). This may be attributed to the limited sample size in the TNT group at Rajavithi Hospital. A future multicenter study with a larger population is warranted to increase statistical power and validate these findings.

Additionally, significantly greater nodal downstaging was observed in the TNT group, which reflects patterns seen in larger trials and meta-analyses. These findings support the continued investigation and possible adoption of TNT as a conventional strategy for LARC, particularly in patients at high risk of systemic disease.

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Original Article

Evaluation of Breast Cancer Screening Services Using Mammograms and Ultrasounds via Mobile Mammography Units

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Abstract

Objective: Breast cancer is a major public health concern in Thailand, ranking as the most common cancer among Thai women, with an annual incidence of 17,043 cases and 4,753 deaths. Proactive screening methods, such as breast self-examination (BSE), clinical breast examination (CBE), mammograms, and ultrasounds, are crucial in reducing mortality rates. However, access to these technologies remains limited, particularly in remote areas, due to insufficient mammography machines nationwide. This study aims to evaluate breast cancer screening outcomes among at-risk populations and improve access to medical services in underserved areas.

Materials and Methods: This retrospective study analyzed data from 525 women aged 14-82 who underwent mammograms and ultrasounds via mobile screening units between April and August 2024.

Results: The results showed that 121 participants (23.05%) presented abnormalities requiring follow-up, classified under BIRADS 3–5 risk categories. The estimated number of breast cancer cases from this study is higher than the national average incidence rate.

Conclusion: The findings highlight the effectiveness of mobile screening units in detecting abnormalities and increasing access to services in underserved areas. The incidence of breast cancer in the population studied was approximately 20.02-31.34 per 1,000 individuals. The research underscores the need to expand access to advanced screening technologies and consider extending mammogram and ultrasound benefits to high-risk populations. Further cost-effectiveness and long-term outcomes studies are recommended to support policy development and enhance national breast cancer screening strategies.

Keywords: Screening breast cancer high risk, Mammography, Ultrasound mobile units

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Introduction

Breast cancer is a significant public health issue in Thailand. The incidence of breast cancer among Thai women has shown a continuous upward trend, rising from the third most common cancer in 1990 to currently being the leading cancer affecting Thai women. Each year, approximately 17,043 new cases are reported,[1] equivalent to about 47 cases per day, with mortality rates reaching 4,753 deaths annually.[2] This critical issue demands urgent attention.

Proactive breast cancer screening is a key measure to reduce mortality rates. Although breast cancer can potentially affect all women, it is also a preventable disease through modifications of risk behaviors. Furthermore, breast cancer is treatable and curable if detected in its early stages.

Guidelines for the Diagnosis and Treatment of Breast Diseases and Breast Cancer in Thailand are as follows:[3]

Women aged 20 years and above:

Monthly breast self-examinations (BSE) are recommended, and individuals should be informed of both the benefits and limitations of BSE. Proper training in performing BSE correctly should also be provided. If any suspicious symptoms arise, women should undergo examinations by trained medical personnel.

Women aged 40–69 years without symptoms:

In addition to regular BSE, these women should have annual clinical breast examinations (CBE) conducted by trained medical personnel.

Women aged 70 years and above:

Screening for this group should be individualized, taking into account the potential benefits and risks of mammographic imaging based on their current health status and life expectancy.

Since 1999, Thailand has initiated breast cancer screening programs. By 2024:

Breast Self-Examinations (BSE): 8.7 million women have undergone screening, accounting for 72.63% of the 12 million target population.

Clinical Breast Examinations (CBE): 9.2 million women have been screened, achieving 92.67% of the 10 million targets.

In addition, screening benefits have been extended for high-risk groups, including:

1. *BRCA1/BRCA2* genetic testing in 2022
2. Mammography with ultrasound for high-risk women in 2024

However, mammography and ultrasound screenings are not yet standard benefits for the general population. Among Thai women aged 40-70, the population is approximately 14.5 million.[4] Yet, Thailand only has 331 mammography machines, with some provinces lacking these machines altogether. Consequently, mammography and ultrasound screening are insufficient for population-level screening.

For high-risk groups, mobile mammography and ultrasound units have significantly improved access to screening services in remote areas. The National Cancer Institute has been operating mammography and ultrasound mobile units since 2009, serving a total of 16,257 individuals and detecting abnormalities in 1,563 cases, as shown in Table 1.

Table 1 Summary of the breast cancer screening results using a digital mobile mammography unit and automatic ultrasound year 2009-2024.

No.	Fiscal Year	Case No.	(BI-RADS)					
			1	2	3	4	5	Only U/S
1	2009	969	420	373	136	35	5	
2	2010	528	250	209	58	9	2	
3	2011	317	134	124	49	9	1	
4	2012	959	471	410	41	36	1	
5	2013	2,011	1,112	704	131	62	2	
6	2014	1,335	894	346	53	37	5	
7	2015	1,692	917	667	67	41	0	
8	2016	1,363	695	556	76	34	2	
9	2017	1,270	634	571	47	15	3	
10	2018	1,270	680	537	31	22	0	
11	2019	1,303	775	477	25	18	0	8
12	2020	746	150	414	137	28	2	15
13	2021	139	25	81	29	4	0	
14	2022	266	54	176	15	12	2	7
15	2023	849	143	622	55	23	5	1
16	2024	1,240	266	772	143	48	7	4
Total		**16,257**	**7,620**	**7,039**	**1,093**	**433**	**37**	**35**
						1,563		

This study involves collecting data on breast cancer screening results across various provinces and designing an optimal and cost-effective screening approach for population-level breast cancer screening. The research is a part of the project titled *"Taking Doctors to the People"*, conducted in honor of His Majesty the King on the auspicious occasion of His 72nd birthday anniversary on July 28, 2024. The study aims to lay the groundwork for future plans, should advanced technologies and tools become available and feasible.

This study aims to analyze the results of breast cancer screenings in high-risk populations and to enhance access to medical services for people in remote areas.

Material and Methods

We conducted a retrospective descriptive study by collecting data from 525 women aged 14–82 who underwent mammograms and ultrasounds via mobile screening units between April and August 2024.

Population and sample

The study targeted women aged 40 years and older who underwent mammography and ultrasound breast cancer screenings via mobile digital mammography and automated ultrasound units as part of the "Taking Doctors to the People" project. This initiative, which honored His Majesty the King on the occasion of His 72nd birthday anniversary, was conducted from April to August 2024 and included a total of 525 participants. Participants were asymptomatic and selected based on screening criteria specifically developed by the research team.

Screening event locations:

1. In Buri Hospital, Singburi Province
2. Wat Bang Phli Yai Community Health Center, Samut Prakan Province
3. Om Noi Municipality, Samut Sakhon Province
4. Pho Thong Hospital, Ang Thong Province
5. Dan Chang Kindergarten School, Suphan Buri Province
6. Phayao Hospital, Phayao Province
7. Lad Yao Hospital, Nakhon Sawan Province
8. Somdej Phra Yupparat Loeng Nok Tha Hospital, Yasothon Province
9. Phon Thong Hospital, Roi Et Province

Subject selection and allocation

Inclusion criteria were women aged 35-39 years with abnormal findings from Clinical Breast Examination (CBE) or with a first-degree relative diagnosed with breast cancer before age 50, and women aged 40 years and older with abnormal findings from Clinical Breast Examination or with a first-degree relative diagnosed with breast cancer.

Exclusion criteria were women under 40 years of age with normal findings from Clinical Breast Examination conducted by medical personnel and individuals who had undergone breast cancer screening within the past two years.

Table 2 Criteria for providing breast cancer screening services using a mobile digital mammography unit and automated ultrasound

Age	CBE Results	Screening	Remark
≥ 40	Abnormal	MMG + U/S	Providing services to all
≥ 40	Normal, but have a close relative with breast cancer	MMG + U/S	Providing services to all
35 - 39	Abnormal	MMG + U/S	Providing services to all
35 - 39	Normal, but have a close relative with breast cancer < 50 years old	MMG + U/S	Providing services to all
< 35	Abnormal	Only U/S	Mammography may be considered in a case-by-case

Table 3 BIRADS category & estimated breast cancer risk[3]

BI-RADS	Likelihood of Malignancy	Findings/Examination	Recommendation
1. Negative	Essentially 0%	Normal examination	Routine mammography screening
2. Benign	Essentially 0%	Benign findings: benign calcification, cyst	Routine mammography screening
3. Probably benign	≤ 2%	Non-calcified circumscribed solid mass, focal asymmetry, or single group of punctate calcifications, cluster of microcysts, single complicated cyst	Short interval follow-up in 6 months
4. Suspicious	> 2% but < 95%	Palpable mass, complex solid-cystic mass, suspicious calcifications	Tissue diagnosis
4A: low	> 2% but ≤ 10%	Palpable circumscribed mass, palpable complicated cyst, suspicious of breast abscess	
4B: moderate	> 10% but ≤ 50%	Group of amorphous or fine pleomorphic calcifications, an ill-defined mass	
4C: high	> 50% but < 95%	New group of fine linear calcifications, irregular solid mass with an ill-defined border	
5. highly suggestive of malignancy	≤ 95%	Irregular, spiculated mass with associated microcalcifications and new fine linear and branching calcifications in segmental distribution	Tissue diagnosis
6. Known proven malignancy			Surgical excision when clinically appropriate

Research Instruments

1. Patient Information Record Forms
2. Mammogram and Ultrasound Results

Data Collection

1. Data collection from mammogram result records
2. Classification of results according to BIRADS criteria

Data Analysis

The data was analyzed to calculate the percentage of participants in each BIRADS category and summarize the outcomes as a formula:

Example Calculation:

BIRADS 1: Number of Participants in Each Group/ Total Number of Participants

Abnormal detection rate calculation:

The abnormal detection rate was calculated to assess the proportion of participants requiring further diagnostic evaluation (BIRADS 3 or higher) as formula:

Example Calculation:

Abnormal cases: Number of Participants in Each Group/ Total Number of Participants

Results

Between January and August 2024, a total of 525 participants aged 14-82 years (median age: 42 years) were screened. Out of these, 121 participants (23.05%) required follow-up medical attention due to abnormal results.

Discussion

From the age distribution, it was observed that individuals aged between 18 and 82 years underwent ultrasound and mammography screenings. These screenings were initiated due to abnormalities detected during clinical breast examinations by medical personnel. Both ultrasound and mammography results for these individuals were normal. Additionally, four individuals underwent ultrasound only, as they were unable to undergo mammography, and no abnormalities were found.

Out of the total 525 screened individuals, 121 cases (23.05%) required follow-up due to detected abnormalities. Based on the data, the initial risk of breast cancer can be estimated by categorizing cases according to the BIRADS system, which indicates the likelihood of breast cancer based on imaging findings. The risk interpretation by BIRADS classification is as follows:

1. BIRADS 3: Low risk (< 2%) — follow-up required every six months.

2. BIRADS 4: Moderate to high risk (approximately 2–95%):

2.1 4A: Low risk (2–10%).

2.2 4B: Moderate risk (10–50%).

2.3 4C: High risk (50–95%).

3. BIRADS 5: Very high risk (> 95%).

The number of individuals categorized by BIRADS risk levels is as follows:

4. BIRADS 3: Low risk (< 2%) = 94 individuals.

Estimated breast cancer cases: approximately 1.88 cases (94 × 2%).

5. BIRADS 4 (including 4A, 4B, and 4C): Moderate to high risk (2-95%) = 23 individuals.

5.1 4A (2–10%): Approximately 0.2–1 case (10 × 2-10%).

5.2 4B (10–50%): Approximately 0.6–3 cases (6 × 10-50%).

5.3 4C (50–95%): Approximately 3–5.7 cases (6 × 50-95%).

6. BIRADS 5: Very high risk (> 95%) = 5 individuals.

Estimated breast cancer cases: approximately 4.75 cases (95% of 5).

Table 4 Distribution of BIRADS Categories

Result	Number	Percentage
BIRADs 1*	147	28
BIRADs 2*	253	48.19
BIRADs 3**	94	17.9
BIRADs 4A***	10	2.62
BIRADs 4B***	6	1.14
BIRADs 4C***	6	1.14
BIRADs 5***	5	0.95
Only U/S#	4	1.76
Total	**525**	**100**

* BIRADs 1, 2: Advise performing BSE (Breast Self-Examination) every month and CBE (Clinical Breast Examination) annually.

** BIRADs 3: Advise performing BSE every month, with a follow-up appointment for mammogram and ultrasound in the next 6 months.

*** BIRADs 4, 5: Schedule an appointment for tissue diagnosis.

For those who are unable to have a mammogram.

Estimated total breast cancer cases:

Minimum Estimate:

1.88 + 0.18 + 0.6 + 3 + 4.75 = 10.41 cases 1.88 + 0.18 + 0.6 + 3 + 4.75 = 10.41 cases

Maximum Estimate:

1.88 + 0.9 + 3 + 5.7 + 4.75 = 16.23 cases 1.88 + 0.9 + 3 + 5.7 + 4.75 = 16.23 cases

Thus, for the 521 individuals screened, the potential number of breast cancer cases ranges from approximately 10 to 16 cases.

The incidence rate of breast cancer in this study was calculated relative to the total population screened. Compared to the national breast cancer incidence rate in Thailand, which is 34.2 per 100,000 people.

The formula for incidence rate:

$$\left[\text{Incidence rate} = \left(\frac{\text{Number of study}}{\text{Number of cancer)}} \times 100{,}000\right)\right]$$

$$6.1 \quad \left[\text{Incidence rate} = \left(\frac{(10}{521} \times 100{,}000\right)\right] = 1{,}919.38$$

$$6.1 \quad \left[\text{Incidence rate} = \left(\frac{(16}{521} \times 100{,}000\right)\right] = 3{,}071.98$$

The incidence of breast cancer in this study was estimated to range between 1,919.38 and 3,071.98 per 100,000 population, significantly higher than the national average incidence (34.2 per 100,000 population).

However, this study may have targeted a high-risk population, such as individuals with a family history of breast cancer in direct relatives, those with abnormalities detected during physical examinations, or individuals aged 40 years and older. The study of Sripaiboonkij et al. (2016) reported that the incidence of screening for breast cancer in this group was found to be 10 per 1,000 individuals.[5]

When comparing the calculated incidence rate in this study to the rates of abnormalities detected. The incidence of breast cancer in the population studied was approximately 20.02–31.34 per 1,000 individuals, significantly higher than the established average of 10 per 1,000 individuals.

Among cancers in women in Thailand, breast cancer ranks first. A hospital-based cancer registry showed that among Thai women with all forms of cancer, the proportion of new patients with first-stage breast cancer declined from 13.6% in 2016 to 7.6%.[6] We believe that the breast cancer screening in the group we designed will prove to be valuable and will lead to the detection of more early-stage cancers. This screening process can assist in evaluating the current benefits of ultrasound and mammogram screenings for individuals with a family history of direct relatives affected by breast cancer. In the future, it may be considered worthwhile to expand these benefits further, increasing accessibility beyond the current target of 28,000 cases per year.

The recommendations are as follows:

Enhancing access to services

Consider expanding mobile units equipped with mammograms and ultrasound machines to cover remote areas.

Support the increase in the number of mammogram machines nationwide.

Supporting healthcare benefits

Propose mammogram and ultrasound screenings for high-risk groups, such as individuals with a family history of breast cancer, as a healthcare benefit available to the general public.

Developing screening strategies

Promote awareness of Breast Self-Examinations (BSE) and Clinical Breast Examinations (CBE), particularly among high-risk populations.

Improve the integration of data collection, ensuring coverage from initial BSE and CBE screenings through confirmed cancer diagnoses.

Utilize findings from this study as a proposal for shaping future screening policies to ensure comprehensiveness and cost-effectiveness.

Further research

Study the cost-effectiveness of advanced screening technologies in high-risk populations and evaluate their long-term impact to refine screening guidelines.

Conclusion

This research emphasizes the importance of proactive breast cancer screening, particularly among high-risk populations. It highlights opportunities for developing the public health system to reduce mortality rates and improve the quality of life for the population.

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Case Report

A Self-Insertion of 26 High-Strength Neodymium Magnetic Beads in the Bladder: A Case Report

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Abstract

Background: The presence of a foreign object inside the urinary bladder is a rare occurrence in urological emergencies. These objects can enter the bladder through various routes, including medical procedures (iatrogenic causes), self-insertion for sexual stimulation, sexual abuse, physical assault, or migration from nearby organs. Gathering a thorough patient history can be particularly difficult when the insertion was done for sexual gratification. Commonly encountered foreign bodies include everyday items like electrical wires and pencils, medical devices such as intrauterine contraceptive devices (IUDs) and catheter components, or, as seen in this case, high-strength neodymium magnetic beads.

Case Presentation: We describe a rare occurrence where a 24-year-old man inserted 26 high-strength neodymium magnetic beads into his urethra for sexual gratification. The clinical presentation with management outline is discussed. The patient underwent two cystoscopic procedures for complete removal of the intravesical foreign body. During the initial intervention, seven neodymium magnetic beads were successfully extracted. A second cystoscopy was performed the following day, resulting in the complete retrieval of the remaining 19 beads. While treatment's main objective is the removal of the foreign object, it is essential to take into account both immediate and long-term complications that may arise.

Conclusion: Bladder foreign bodies are rare, requiring individualized management. This case highlights the challenges of managing magnetic bead insertion, emphasizing the importance of prompt diagnosis and staged endoscopic removal.

Keywords: Magnetic beads, Foreign Body, Cystoscopy, Bladder, Case report

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Introduction

Foreign bodies in the lower genitourinary tract are an uncommon but potentially dangerous urological emergency. These occurrences may stem from a variety of factors, such as impulsive actions, psychological conditions, sexual experimentation, assault, or abuse.[1] Commonly inserted objects can range from everyday items like electrical wires and pencils to medical devices like intrauterine contraceptive devices and catheter parts, or, as seen in our case, high-strength neodymium magnetic beads. Diagnosis can be challenging unless the insertion is disclosed early on. The condition is often presented late due to feelings of shame and embarrassment. Failure to remove the foreign body may result in complications such as dysuria, hematuria, urinary retention, and the development of secondary calculi. Cases of foreign body insertion are often either not reported or misdiagnosed. Al-Heeti et al., in a retrospective study on foreign bodies in the urinary bladder during a period of 10 years in a teaching hospital, only reported 21 cases, of which the most common cause is iatrogenic (42.9%) followed by self-insertion (33.3%), migration from outside the bladder (14.3%) and external trauma (9.5%).[2] As far as we know, such research has not been done yet in Malaysia, and to the best of our knowledge, this is the first such case documented in our region. Magnetic foreign bodies are especially worrisome because they can compress the urethral or bladder wall, potentially leading to ischemia. Their removal is often challenging due to the strong magnetic attraction between the objects.[3] We emphasize the importance of prompt diagnosis and intervention, which is why we have chosen to present this case. In our patient, a total of 26 high-strength neodymium magnetic beads were successfully removed from the bladder.

Case Presentation

A 24-year-old male without notable medical comorbidi ties presented with a 48-hour onset of dysuria, urinary hesitancy, and burning sensation over the penile area. Upon further investigation, it was disclosed that he had inserted 26 high-strength neodymium magnetic beads into his urethra. The patient was unable to specify the precise dimensions of the magnetic beads and admitted to inserting them into his urethra to heighten sexual stimulation. This indicates a lack of awareness regarding the potential medical complications associated with such behaviour. At that time, he had no prior history of any diagnosed mental or psychiatric conditions. The physical examination of the patient showed normal results, with no evidence of trauma to the external genitalia. Blood tests, including white cell count, hemoglobin, platelet count, and renal function, were all within normal limits. Additionally, urinalysis did not reveal any signs of bacterial infection, but there were red blood cells. An anterior-posterior pelvic X-ray showed a cluster of radio-opaque shadows in the pelvic region, with the shape consistent with magnetic beads that are adhered to one another (Figure 1). Given the patient's stable hemodynamic status, absence of peritoneal irritation, and lack of clinical indication of foreign body migration, advanced imaging modalities such as a computed tomography (CT) scan were not pursued. A plain pelvic radiograph was deemed sufficient for evaluation. The patient was brought to the operating room, where a cystoscopy was performed under general anesthesia. The presence of magnetic foreign bodies is especially concerning due to the risk of pressure-induced ischemia in the bladder or urethral walls. Cystoscopic examination revealed the presence of magnetic beads within the bladder (Figure 2). Removing all the magnetic beads in a single surgical session proved challenging, as they were tightly attached to one another. This posed a significant risk of increased morbidity due to prolonged operating time and the potential for repeated instrumentation of the urethra, which could result in epithelial damage. The patient underwent a transurethral cystoscopy to remove the foreign body using forceps on two separate occasions. In the first procedure, only 7 magnetic beads were successfully extracted (Figure 3A). The following day, the procedure was repeated, and the remaining 19 magnetic beads were removed entirely (Figure 3B). While treatment's primary goal is removing the foreign body, it is crucial to consider both short-term and long-term complications that may arise. These complications can include, but are not limited to, urethral strictures, urinary incontinence, and the formation of urethral diverticula. The likelihood and severity of these complications depend on various factors such as the depth of the initial insertion, the frequency of foreign body insertion, and the method employed for extraction. Postoperatively, he made a smooth recovery and subsequently received an outpatient psychiatric evaluation at the clinic, where he was diagnosed with obsessive-compulsive disorder. He continued to do well throughout his follow-up visits at our urology clinic, which were scheduled at the first and third months. He has established normal voiding without any complications.

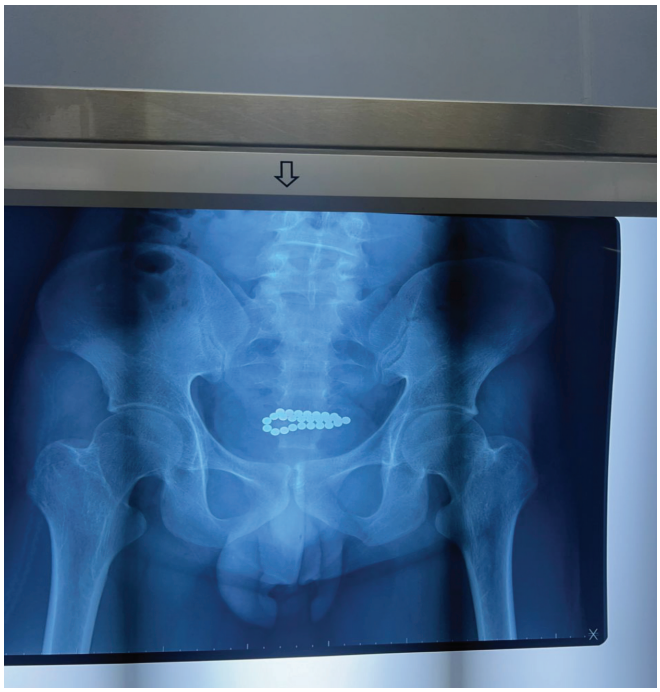

Figure 1 An anterior-posterior pelvic X-ray showed a cluster of radio-opaque shadows in the pelvic region, with the shape consistent with magnetic beads.

Figure 2 Cystoscopic examination revealed the presence of magnetic beads within the bladder.

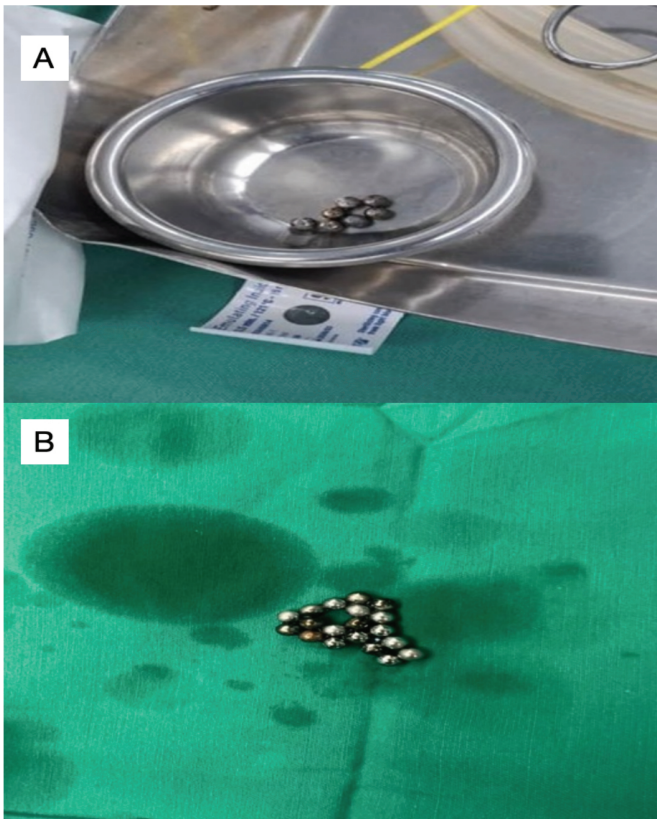

Figure 3 Intraoperative retrieval of magnetic beads (A) 7 Magnetic beads on the first cystoscopic retrieval (B) 19 Magnetic beads on the second cystoscopic retrieval

Discussion

A genitourinary foreign body is uncommon, although the incidence has increased in recent decades. Among the various genitourinary structures, the urethra and bladder are the most frequent sites for foreign body insertion and are typically linked to a condition called polyembolokoilamania. This disorder involves individuals inserting objects into various bodily orifices for a variety of reasons, including psychopathological motives, urological procedures, self-stimulation, enhancement of erections, seeking attention, or merely out of curiosity. Urologists have been dealing with this issue for years, as it presents considerable challenges in both diagnosis and management.[4] Due to frequent under-reporting, the true prevalence remains largely uncertain. Accidental insertion is most commonly observed in children, whereas in adolescents and adults, it typically results from curiosity-driven behaviour, underlying psychiatric conditions, or paraphilic tendencies linked to sexual gratification.[5] In certain instances, like the present one, underlying

motivations can be multifactorial—where auto-erotic activities coincide with compulsive behaviours. Patients often withhold information due to the stigma surrounding this behaviour, which makes the diagnosis difficult to establish. When assessing a suspected foreign body, it is crucial to carefully consider the patient's medical history, symptoms, clinical examination results, and imaging findings comprehensively and coordinately. For non-radiopaque foreign bodies, plain radiography provides a straightforward method for visualization, allowing direct evaluation of their shape and size. With a specificity of up to 91%, plain radiography is generally sufficient to identify both metallic and non-radiopaque foreign bodies, assisting in their localization and confirming their presence or movement. Ultrasound has become an increasingly reliable and popular choice, with an 81% sensitivity for detecting urogenital foreign bodies. It is a safe, radiation-free, non-invasive, and cost-effective imaging technique, particularly well-suited for pediatric patients. A CT scan, on the other hand, offers enhanced soft tissue imaging and greater diagnostic accuracy when ultrasound or conventional radiography are unable to detect or characterize the foreign body.[6] Plain radiography can provide a general overview of a foreign body, but ultrasonography or computed tomography (CT) may be necessary for precise localization. CT is particularly useful when there is suspicion that a foreign body has migrated into adjacent structures. As noted, in this case, plain radiography was the preferred imaging modality since the patient was hemodynamically stable and showed no signs or symptoms pointing towards the migration of a foreign body. Managing a retained foreign body should focus on its complete removal while aiming to reduce the risk of complications as much as possible. Treatment options for bladder foreign bodies include endoscopic, percutaneous, open, and laparoscopic procedures. The choice of extraction technique depends on the size and mobility of the foreign body within the bladder. Nonetheless, endoscopic removal is typically the method of choice for most urologists.[2]

In the case mentioned above, a total of 26 high-strength neodymium magnetic beads were removed over two separate procedures. The staged removal technique, as performed in our case, is preferred in cases with strong magnetic adherence to minimize trauma. Alternative approaches, such as suprapubic cystostomy, have been reported in cases with larger objects or failed endoscopic retrieval. Endoscopic techniques are widely utilized to remove foreign bodies from the bladder in urological practice. Using a cystoscope, clinicians can directly visualize the bladder cavity and accurately retrieve the object with specialized instruments such as baskets, forceps, graspers, and clamshell devices. Although cystoscopic retrieval is often effective, the success rate can vary considerably, ranging between 50% and 90%.[7] Striving for complete removal in a single procedure could have led to additional complications, such as prolonged general anesthesia time and the risk of repeated urethral instrumentation, which could cause epithelial damage and potentially result in future strictures. The optimal management approach depends on the characteristics of the foreign body, its location, the surgeon's expertise, and the available equipment at that point in time.

Conclusion

The insertion of high-strength magnetic beads is rare and poses a significant hazard. Often, it poses a diagnostic challenge due to the unclear or incomplete medical history provided by the patient. A comprehensive approach to patient management is crucial in these cases. To determine the precise location, size, shape, and quantity of foreign bodies, imaging techniques such as plain radiography, ultrasound, or CT scan can be used, each with its own advantages and limitations. Surgical intervention should be considered promptly once the foreign body is confirmed. The main goal of surgery is to remove the foreign body successfully while minimizing the risk of complications. The choice of removal technique depends on factors such as the location, size, and configuration of the foreign body, the surgeon’s expertise, and the available instruments. Surgical options typically include cystoscopic removal or open surgery. Management should be tailored to the specific circumstances of each case. Given the high prevalence of mental illness in these patients, it may be beneficial to conduct thorough assessments. The primary motivation for ruling out mental illness is to reduce the likelihood of recurrence.

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Contributions:

(I) Conception and design: Hemanathan Praemanathan

(II) Administrative support: All Authors

(III) Provision of study materials or patients: Hemanathan Praemanathan

(IV) Collection and assembly of data: All Authors

(V) Data analysis and interpretation: N/A

(VI) Manuscript writing: Hemanathan Praemanathan

(VII) Final approval of manuscript: All Authors

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Ethical statement

The authors are accountable for all aspects of the work and ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient to publish this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal. Patient confidentiality and anonymity were maintained during the publication.

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Case Report

Retroperitoneal Extraosseous Ewing's Sarcoma in a Young Infant: A Case Report and Literature Review

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Abstract Ewing's sarcoma (ES) is a rare malignancy primarily affecting bone and soft tissue in children and adolescents. While often presenting with palpable masses and bone pain, extraskeletal Ewing's sarcoma (EES) can manifest with diverse symptoms depending on the location. Accurate diagnosis and prompt treatment of EES are crucial for minimizing recurrence and improving survival outcomes. This case report describes a young infant presenting with a palpable left-sided abdominal mass, ultimately diagnosed as retroperitoneal EES. An initial computed tomography (CT) scan of the abdomen revealed a necrotic mass on the left side, arising from the pancreatic body and tail, leading to a suspicion of pancreatoblastoma. An unexpected finding during surgical exploration revealed a large, well-circumscribed, yellowish, hypervascular retroperitoneal mass attached to the tail of the pancreas. Histopathological examination of the resected tumor confirmed the diagnosis of Ewing's sarcoma. The infant was subsequently treated with a combination of chemotherapy and radiation therapy due to a tumor attached to the tail of the pancreas. This report highlights the diagnostic challenges and management strategies for retroperitoneal EES in infants, contributing to the limited existing literature on this rare clinical entity.

Keywords: Ewing's sarcoma, Pediatric sarcoma, Pediatric tumor

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Introduction

Ewing's sarcoma family of tumors (ESFS) is a group of rare and aggressive malignancies that predominantly affect bone and soft tissue in children and adolescents.[1,2] ESFS was divided into four types based on the origin of cancer: Extraosseous Ewing's sarcoma or extraskeletal Ewing's sarcoma (EES), Ewing's sarcoma of bone (ES), peripheral primitive neuroectodermal tumor (pPNET) and Askin's tumor. EES, including the paravertebral spaces, lower extremities, head and neck, and pelvis, occurs in about 20% of all Ewing's sarcoma cases.[3] EES arises in various locations and accounts for approximately 10-15% of all Ewing's sarcoma cases, with the retroperitoneum being an uncommon primary site.[4] These tumors often present with nonspecific symptoms, such as abdominal pain, palpable mass, and distention, making early diagnosis challenging. Furthermore, the proximity of retroperitoneal EES to vital organs and structures can complicate surgical resection and increase the risk of complications. The incidence of EES is 0.4 per million individuals.[5] Moreover, previous reports revealed that EES has a bimodal distribution, which has the occurrence rate among children (< 5 years) and adults (> 35 years).[1] This report describes a rare case of retroperitoneal EES in a young infant presenting with a palpable left-sided abdominal mass. The diagnostic workup found that the mass arose from the pancreatic body and tail, but surgical management and histopathological findings confirmed Ewing's sarcoma, highlighting the importance of a multidisciplinary approach in managing this rare entity. This case contributes to the limited literature on retroperitoneal EES in infants and emphasizes the need for heightened awareness among clinicians to ensure prompt diagnosis and treatment.

Case Report

This case report was informed consent from the patient for publication of this case report and accompanying images.

A 1-year-old boy presented with a palpable painless abdominal mass that had been progressively enlarging for over one month. The mass was located in the left upper quadrant and was not associated with any other significant symptoms, such as anorexia, weight loss, fever, obstipation, vomiting, or hematuria.

At a local hospital, an abdominal examination confirmed a large, non-tender mass in the left upper quadrant. A computerized tomography (CT) scan of the abdomen revealed a heterogeneously enhanced mass with internal necrosis measuring $8.2 \times 8.6 \times 9.9$ cm at the left anterior pararenal space. The pancreatic body and tail were posteriorly displaced without normal fat plane separation, raising suspicion of a pancreatoblastoma originating from the pancreatic body and tail. The adjacent spleen was compressed with a hypodense area, suggesting perfusion abnormality. The left kidney was also posteriorly displaced without invasion. No liver or adrenal metastasis was identified (Figure 1). Based on these findings, a differential diagnosis of pancreatic tumor or retroperitoneal tumor was considered, and the patient was then referred to our hospital for further management.

Upon admission to our hospital, a physical examination revealed a large, non-movable, non-tender mass in the left upper quadrant, measuring approximately 8×8 cm. The remainder of the physical examination was unremarkable. Laboratory investigations, including liver function tests, complete blood count, and electrolytes, were all within normal ranges. Tumor markers, including CA19-9, β-HCG, AFP, and NSE, were all negative. A review of the abdominal CT scan confirmed the previous findings. To further evaluate metastatic disease, a CT scan of the chest and a bone scan were performed, both of which were negative for evidence of metastasis.

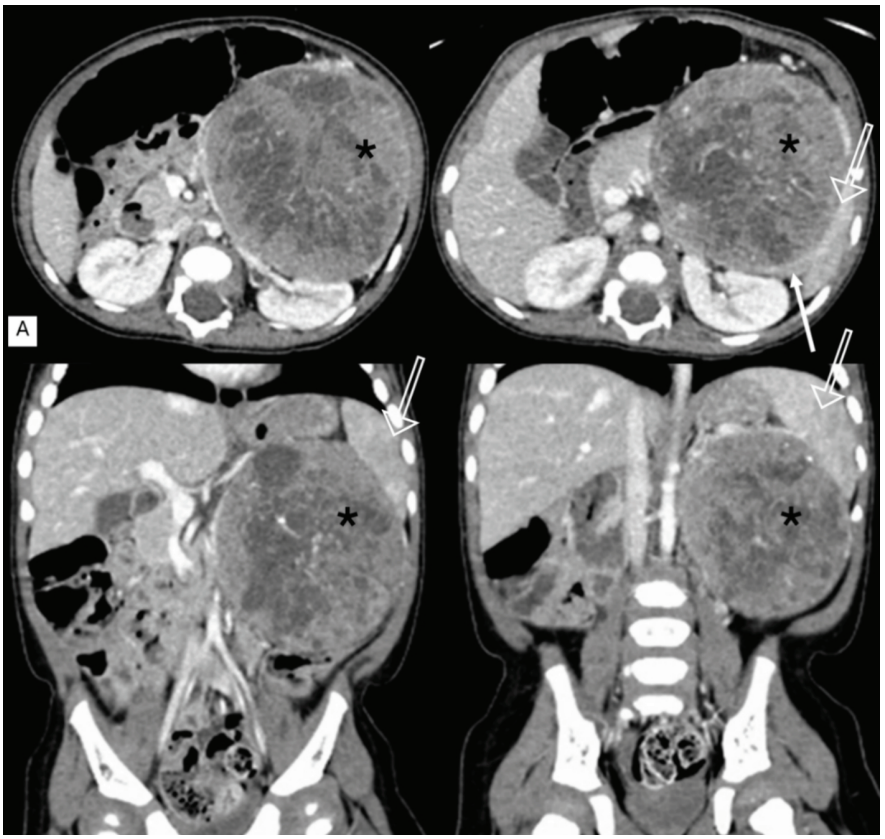

Figure 1 Computerized tomography scan of the whole abdomen (CTWA) axial view (A, B) and coronal view (C, D) demonstrated a heterogeneously enhanced mass with internal necrosis at the left anterior pararenal space (asterisk). There was a mass effect to posteriorly displace pancreatic body and tail (white arrow), laterally displace spleen with perfusion abnormality (open arrow)

Preoperative planning and surgery

Given the close proximity of the tumor to the splenic vessels, as demonstrated on the CT scan, preoperative pneumococcal vaccination against encapsulated organisms was administered to mitigate the risk of post-splenectomy sepsis in the event of accidental splenic injury. The tissue biopsy was not performed because the primary suspicion was pancreatoblastoma, and the gold standard management was complete resection of the tumor. Neoadjuvant chemotherapy was obtained when primary surgical resection was not possible.[2] The case was discussed at the multidisciplinary meeting, and the decision was made to proceed with surgery for tumor removal.

The patient underwent exploratory laparotomy. We performed a transverse incision in the left upper abdomen to allow easy access to the tumor. The left side of the colon was then mobilized to expose the mass. Unexpectedly, the intraoperative findings revealed a large, well-circumscribed retroperitoneal mass measuring 10 × 10 cm on the left side of the abdomen. The mass was attached to the tail of the pancreas but did not appear to originate from it. Notably, the mass was also adherent to the splenic vessels (Figure 2). Careful dissection allowed for complete separation of the tumor from the tail of the pancreas and splenic vessels, enabling total tumor removal with preservation of the pancreas and spleen. The tumor was resected with close margins to the pancreas, so a biopsy of the pancreatic tail was performed to evaluate for pancreatic invasion. There were no intraoperative complications.

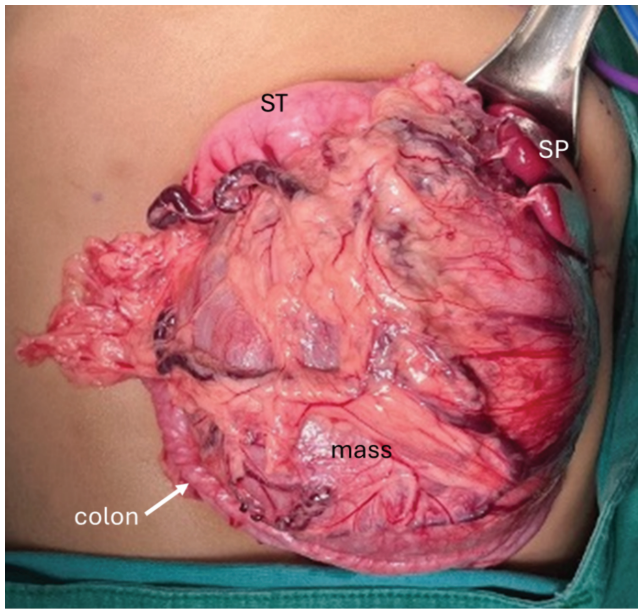

Figure 2 Intraoperative findings show a large hypervascularized retroperitoneal mass attached to the stomach at the superior margin (ST), splenic vessel, and spleen at the lateral margin (SP).

Pathological examination

Gross examination of the resected specimen revealed a yellowish, well-circumscribed, hypervascular mass measuring 10 × 10 cm. There was no evidence of tumor rupture (Figure 3). Cut sections of the mass showed pale-yellow, rubbery tissue with small areas of cystic degeneration. A small 2 cm satellite lymph node was identified at the lower pole of the main tumor mass (Figure 3).

Microscopic examination (H&E stain) showed uniform, small, round cells arranged in sheets separated by dense fibrous tissue (Figure 4). The tumor cells had round nuclei, finely stippled chromatin, indistinct nucleoli, and scant clear to pale eosinophilic cytoplasm. Homer-Wright rosettes (tumor cells arranged around a central area of fibrillary material) and patchy areas of necrosis were observed in the small satellite nodule. Periodic acid-Schiff (PAS) stain was positive and diastase-sensitive, indicating the presence of intracytoplasmic glycogen. Immunohistochemical stains demonstrated diffuse membrane staining for CD99 and focal positivity for neuron-specific enolase (NSE). The tumor cells were negative for AE1/AE3, EMA, CD56, S100, desmin, SMA, MyoD1, WT-1, chromogranin, and synaptophysin. Pancreatic tissue was not involved by tumor cells. These histomorphological and immunohistochemical findings were consistent with the diagnosis of Ewing's sarcoma, and resection margins were clear.

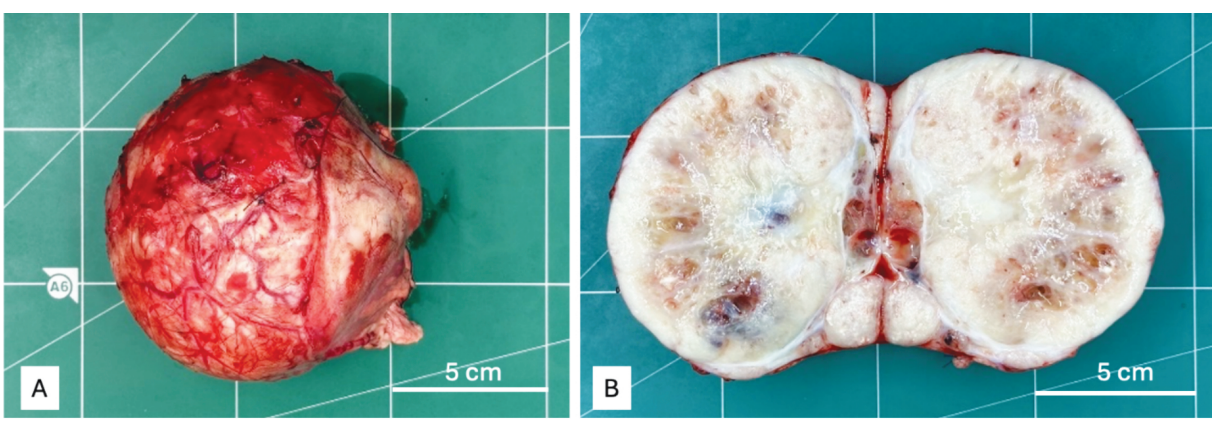

Figure 3 (A) Gross pathology revealed yellowish and hypervascular well-circumscribed mass. (B) Cross section of the mass showed two pale-yellow rubbery tissues with slight cystic degeneration (black arrow).

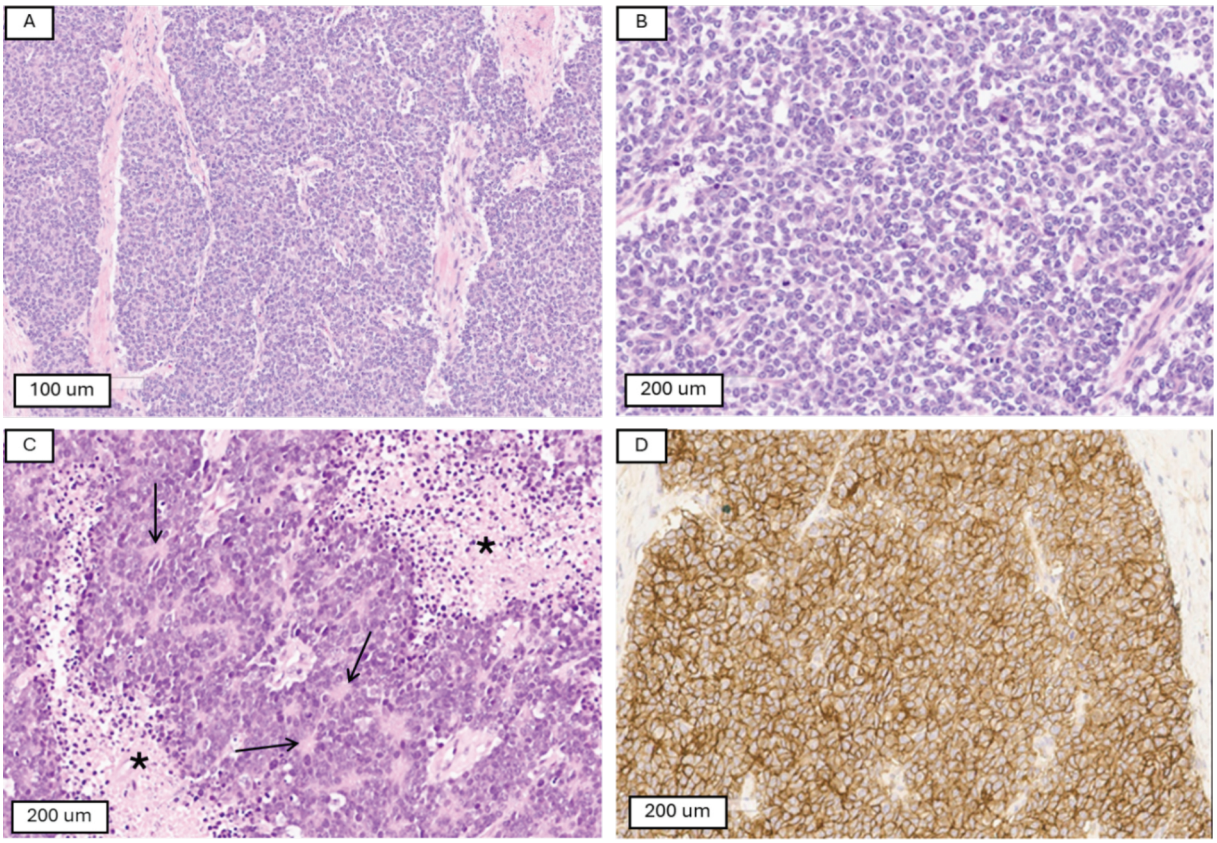

Figure 4 Morphologic features of the tumor. (A) and (B) H&E section (100× and 200× original magnification) Sheets of uniform round cells separated by fibrous tissue. (C) Homer-Wright rosettes (arrow) and tumor necrosis (asterisk). (D) Intense membrane immunostaining for CD99 (200×).

Postoperative management and outcome

Following surgery, a postoperative CT scan of the abdomen at one month showed no gross residual tumor at the resection margins. The patient received interval-compressed adjuvant chemotherapy consisting of vincristine (2 mg/m²), doxorubicin (37.5 mg/m²/day), cyclophosphamide (1,200 mg/m²), and mesna (300 mg/m²/dose) alternating with ifosfamide (1,800 mg/m²/day) and etoposide (100 mg/m²/day) every 2 weeks for a total of 14 cycles for systemic control.[15]

A patient with localized EES underwent surgical resection. Intraoperatively, we found a tumor close to the margin of the pancreas, but the pathological report revealed Ewing's sarcoma and resection margins were clear. The case was discussed at the multidisciplinary meeting, and the decision was made to receive the local control by external beam radiation therapy (45 + 5.4 Gy/28 fractions) over a total of 6 weeks to avoid the recurrence of Ewing's sarcoma. The patient is under regular follow-up care and remains cancer-free at 1-year post-treatment.

Discussion

EES accounts for approximately 10-15% of all Ewing's sarcoma cases. While EES can occur anywhere in the body, the most common locations include the paravertebral region, chest wall, lower extremities, and the retroperitoneum.[4] Diagnosing Ewing sarcoma in such atypical sites is challenging and usually requires an integrated approach combining histology, immunohistochemistry, and molecular techniques.[1] Differential diagnoses of retroperitoneal mass near the tail of the pancreas in an infant include teratoma, neuroblastoma, rhabdomyosarcoma, and other non-rhabdomyosarcoma soft tissue tumors. We can differentiate the diagnosis of a retroperitoneal mass by its location and other markers, such as rising AFP levels in yolk sac tumors, rising β-HCG levels in choriocarcinoma, bone involvement in Ewing sarcoma, and bone marrow involvement in neuroblastoma. However, the definitive diagnosis is based on histologic results from percutaneous biopsy or resection.[5] Our patient had previously been diagnosed with a

pancreatic tumor based on imaging, so we considered the potential for surgical resection. Unfortunately, intraoperative findings revealed that the mass did not arise from the pancreas but from the retroperitoneum, attaching to the tail of the pancreas. Therefore, we performed a complete resection with pancreatic tail biopsy to obtain the specimen for histopathological study. The pathologic reports showed Ewing's sarcoma and resection margins were clear.

The hallmark of Ewing's sarcoma is a monotonous population of small, round cells with scant cytoplasm and high nuclear-to-cytoplasmic ratios, typically arranged in sheets or nests.[6] The nuclei are round and uniform in size, with finely dispersed chromatin and inconspicuous nucleoli. Areas of necrosis and hemorrhage are common, reflecting the tumor's rapid growth and vascularity. Homer-Wright rosettes (cells arranged in a circle around a central fibrillary space) may be present but are not as common as in other small round blue cell tumors. The diagnosis of ES in our patient was based on this typical histopathology. It was supported by positive immunostaining of CD99, which was the most sensitive marker for Ewing's sarcoma, showing strong and diffuse membrane staining in almost all cases. The genetic hallmark of Ewing's sarcoma is the translocation-fusion between the EWS RNA binding protein 1 (EWSR1) gene or the fused in sarcoma/translocated in sarcoma (FUS) gene and a member of the ETS family of transcription factors, which the most common is the FLI1 gene on chromosome 11.[3,7,8] Recent studies have found other somatic mutations in ES patients, such as mutations in tumor protein 53 (TP53) and stromal antigen 2 (STAG2). The benefit of somatic mutation in Ewing's sarcoma patients is to identify appropriate treatment because patients with increased somatic mutations are more aggressive and treatment-resistant than tumors with minimal mutations.[9] In our case, we could not perform the fusion gene analysis because the RNA quality of the collected specimen was limited.

EES may be presented as localized or metastatic disease. Localized EES carries a better prognosis, with 10-year event-free survival (EFS) and overall survival (OS) rates of 77.5% and 85.5%, respectively, compared to 11.1% and 29.5% for metastatic disease. This difference persists despite both groups receiving surgery, radiotherapy, and chemotherapy, except for patients with small, completely resected tumors who may not require radiotherapy.[10]

The current treatment recommended by the National Comprehensive Cancer Network (NCCN) for EES involves local and systemic control.[5] Local control is achieved through surgery and/or radiotherapy, with complete surgical resection being the gold standard for localized disease. Systemic treatment relies on chemotherapy, typically combined with doxorubicin, cyclophosphamide, vincristine, actinomycin-D, ifosfamide, and etoposide.[11-14] While EES is radiosensitive, surgery is the preferred method for local control to minimize radiation-associated risks. Wide resection without radiation is ideal for localized lesions with no evidence of microscopic residual disease. The overall 5-year survival rate is better in patients who undergo complete resection, with wide surgical margins compared with suboptimal margins.[5] However, if the tumor is not resectable with clear margins or if the surgery involves vital fixed structures, postoperative radiotherapy may be added for incomplete resection.[5,15] Some reports, such as by R. AL Rashed et al., describe retroperitoneal EES invading the left adrenal gland, which was completely resected, and a partial left adrenalectomy with negative margin resection. The patient then received adjuvant chemotherapy without radiotherapy.[16] However, Wu et al. reported a case of large retroperitoneal EES with a mass effect on the left kidney. The patient underwent exploratory laparotomy with tumor resection and left radical nephrectomy. The pathological report showed free margin resection, but the patient received adjuvant chemotherapy and radiotherapy to avoid recurrence.[17] Both cases showed good outcomes with no recurrence. In our case report, a patient with localized EES underwent surgical resection. He received adjuvant chemotherapy and radiotherapy by an oncologist and radiation oncologist because of the intraoperative finding of a tumor close to the margin of the pancreas to avoid the recurrence of EES. The patient will undergo surveillance imaging every 2-3 months for the first three years, which is the recommended follow-up for localized, non-metastatic EES.[13] Our patient was followed up.

Conclusion

We report a case of EES in a male infant who presented with an abdominal mass. The patient underwent successful surgical resection, but intraoperatively, the tumor was found to be close to the margin of the pancreas. As a result, the patient received adjuvant chemotherapy and external radiation to avoid the recurrence of EES.

The study suggests that EES should be considered as one of the differential diagnoses for retroperitoneal masses during infancy and highlights the role of external radiation therapy in cases of close-margin resection to avoid the recurrence of EES.

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