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EDITORIAL

ORIGINAL ARTICLES

CASE REPORT

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About the Journal

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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References must be listed on a separate sheet in numeric order as referred to in the article, not alphabetically. A simplified Vancouver system is used. Only references mentioned in the text should be listed and should be selective with no more than 30 references except under unusual circumstances. Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and legends by Arabic numerals (in superscript). The references must be verified by the author(s) against the original documents. Example forms of references are given below.

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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.

3. Personal Author(s):

- Osler AG. Complement: mechanisms and functions. Englewood Cliffs: Prentice - Hall, 1976.

4. Editor, Compiler, Chairman as Author:

- Rhooder AJ, Van Rooyen CE, comps. Textbook of virology: for students and practitioners of medicine and the other health

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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.

Abbreviations

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.

Statistics

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".

All statistical estimates (e.g., mean differences, odds ratios, risk ratios, hazard ratios, regression coefficients, and so on) must have corresponding 95% confidence interval limits. All statistical models used must be briefly described. Uncommon or unusual methods used should be referenced. Authors should refrain from over-modeling their dataset; for example, multivariable analyses of datasets with small sample sizes (e.g., < 100), or few outcomes (e.g. < 10), could be unreliable. Relative risks of categories in a categorical risk factor should be compared to its own reference category, which must be indicated, for example, in a table of multivariable analysis.

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)

Abstract: should be no more than 300 words in length, and written in a structured format, including the following headings: **Objective,** which can include some background material of 1 to 2 sentences in length, but mainly describing the research question; **Methods,** concisely describing the research design and data procurement; **Results,** describing the main findings of the study; and **Conclusion,** which should concisely answer the research question, and no more. Below the abstract, a list of keywords should be provided.

Main text: should be written in a structured format, including the following headings. **Introduction** should describe the rationale of the study within the context of current knowledge; the gap in knowledge with which the research study will fill must be clearly pointed out and a research question explicitly stated. **Methods (and patients, if applicable)** should clearly describe the details of research methodology and patient or research volunteer recruitment according to Guidelines for each type of research as listed above (…), and how the data was collected and analyzed. A short description of statistics used, and the software and references if appropriate, must be provided. A note on Ethics Committee approval, if applicable, must be given. **Results** should include data or summaries of patient or volunteer characteristics, summaries of risk factors or covariates and outcomes, presented in tabular, graphical or descriptions in the text as appropriate, without significantly duplicating one another. Results of statistical analyses must be clearly displayed and should include point estimates, standard errors, statistical tests, *p*-values, and 95% confidence intervals as detailed (…). Analyses not shown but referred to must not change the conclusions or outcomes. **Discussion,** which must fully describe the implications of the research results, should include a concise

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.

Basic Science and Translational Research

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.

Case Series and Case Reports

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.

Narrative Review Articles

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.

Surgical Techniques

Abstract: A short description of what the techniques is about.

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Editorial

Suphakarn Techapongsatorn, MD, PhD

Editor of The Thai Journal of Surgery

Welcome to the first issue of The Thai Journal of Surgery, 2025. As we step into another year, we are pleased to present a diverse selection of articles that cover key developments in surgical research and practice. This issue reflects our continued commitment to showcasing high-quality research that contributes to both academic knowledge and clinical excellence.

This edition features six articles spanning a range of surgical topics. The first article discusses the challenges and learning curve in laparoscopic liver resections, providing valuable insights for surgeons adapting to this minimally invasive approach. The second article explores the clinico-epidemiological patterns of penile emergencies in a Nigerian hospital, emphasizing the importance of early intervention in urological trauma.

The third study presents a comparative analysis of palliative gastrectomy and non-gastrectomy approaches in advanced gastric cancer, highlighting the survival benefits and surgical outcomes. The fourth article evaluates laparoscopic gastric resection for submucosal tumors in difficult locations, comparing it to open surgery and demonstrating the advantages of minimally invasive techniques.

The fifth article examines risk factors that influence complications in patients with gallstone-related inflammation, emphasizing the importance of early identification and surgical prioritization to improve patient outcomes. Lastly, a fascinating case report details the fungal necrotizing fasciitis of the face, its complications, and the reconstructive strategies employed.

With the growing complexity of surgical cases and the integration of new technologies, our journal remains a platform for sharing innovations, clinical experiences, and evidence-based practices. We encourage all surgeons, researchers, and trainees to contribute their work, fostering knowledge exchange within the surgical community.

We extend our gratitude to our dedicated authors, reviewers, and readers for their continued support. As always, ethical research and sound methodology remain the foundation of high-quality publications. We hope this issue provides valuable insights and inspires future research endeavors.

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Original Article

A Rookie in Laparoscopic Liver Resections: Initial Performance of 22 Cases at Lampang Regional Hospital

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Department of Surgery, Lampang Regional Hospital

Abstract

Objective: To review the initial 22 cases of laparoscopic liver resections (LLRs) by a general surgeon to enhance the quality of patient care and implementation for the broader medical community in the northern region of Thailand.

Materials and Methods: This descriptive retrospective study analyzes the author's liver surgery registry data from August 2018 to December 2023. Patients included underwent LLRs for various provisional diagnoses. All received computed tomography (CT) triple-phase liver protocol scans to assess provisional diagnosis and resectability. The IWATE score was used to evaluate procedural difficulty, and inflow control techniques were identified.

Results: A total of 22 patients underwent LLRs between August 2018 and December 2023, with a mean age of 63.8 ± 13.8 years; 68.2% were male. Most patients were classified as Child Turcotte Pugh (CTP) A. The most common preoperative and postoperative diagnosis was hepatocellular carcinoma (HCC). The mean IWATE score was 5.6 ± 2.2, and 40.9% of the surgeries were classified as major procedures. The most common resection was left hepatectomy, while the procedure with the highest difficulty score was anterior sectionectomy for HCC. Estimated blood loss was 125 [100, 300] milliliters, and the mean operative time was 4.1 hours ± 105.9 minutes. One patient died postoperatively due to a ruptured abdominal aortic aneurysm (rAAA).

Conclusion: LLRs are feasible for surgeons with a learning curve. IWATE difficulty scoring can assist surgeons in deciding on minimally invasive surgery, albeit with some limitations.

Keywords: Laparoscopic, Liver resection, Minimally invasive surgery, Resources

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Introduction

Laparoscopic liver resection (LLR) emerged as a groundbreaking surgical technique in 1991 and has since been accepted as an alternative operation in liver surgery.[1] By 1996, formal LLRs were revolutionized by a Japanese group, making a significant advancement in hepatobiliary surgery.[2] A comprehensive review has outlined the historical evolution of LLRs, highlighting key milestones and challenges encountered in the first 25 years, which paved the way for modern surgical innovations.[3]

Despite these advancements, the adoption of laparoscopic techniques in liver resection has progressed more slowly compared to other areas of laparoscopic surgery. The primary challenges include technical difficulties, particularly in controlling bleeding. To aid decision-making, various scoring systems have been developed to assess the complexity of LLRs. These systems typically consider factors such as tumor location, size, liver function, and proximity to major vessels, stratifying cases into different levels of difficulty.[4-6] Over the past two decades, LLRs have demonstrated their safety, resulting in reduced bleeding, shorter hospital stays, and fewer complications.[7-9] As a result, new-generation surgeons are encouraged to practice LLRs, though mastering the learning curve remains essential.

This study provides a comprehensive analysis of the first 22 patients who underwent LLRs in Lampang Regional Hospital by a general surgeon. The aim is to enhance the quality of patient care and facilitate the broader implementation of LLR techniques within the medical community in northern Thailand.

Materials and Methods

Participants

This descriptive study retrospectively reviewed data from the author's personal liver surgery registry, covering the period from August 2018 to December 2023. All patients included in the study were admitted to the general surgical ward at Lampang Regional Hospital. Data were collected from electrical medical records (EMR). The study received Ethical approval from the institutional review board (IRB) number EC 012/67.

Eligible participants in the study included all patients who underwent LLRs. There were no exclusion criteria. Demographic characteristics and laboratory findings were collected from each patient. All patients underwent a computed tomography (CT) triple-phase liver protocol scan to assess provisional diagnosis and resectability.

Operative considerations

The difficulty of each operation was classified by the IWATE criteria score,[10] which ranges from 0 to 12, based on six clinical parameters: tumor location, extent of hepatic resection, tumor size, proximity to a major vessel, liver function, and the use of hand-assisted laparoscopic surgery (HALS) or hybrid techniques. The difficulty levels were stratified into four categories: low (0 - 3), intermediate (4 - 6), advanced (7 - 9), and expert (10 - 12). Each patient's CT scan was evaluated, and an IWATE score was recorded to determine the feasibility of undergoing LLRs, with informed consent obtained from the patients.

Patients undergoing LLRs were positioned supine under general anesthesia (GA). Central lines were used in major hepatectomies for close hemodynamic monitoring. The surgical technique employed was developed during fellowship training, complemented by novel techniques from the literature, and adapted to the hospital's available resources.

A 12-mm camera port was inserted using an open technique at the vertical line above the umbilicus, followed by sequential placement of 5-mm, 12-mm, and 5-mm subcostal ports. After completing the cholecystectomy, an additional port was adjusted along the left costal margin under laparoscopic visualization. Carbon dioxide (CO2) gas insufflation was maintained at 12 - 15 mmHg. The working port position was adjusted by direct visualization depending on liver position and parenchymal transection line. The variation of the port placement is demonstrated in Figure 1. A 12-mm working port was positioned at the transection line for intraoperative ultrasound (IOUS), and a Cavitron ultrasonic surgical aspirator (CUSA: Sonoca300, Soring GmbH), with a 5-mm port at another location. IOUS was used to assess transection margins, hepatic venous guidance, and any remaining lesions in the liver parenchyma.

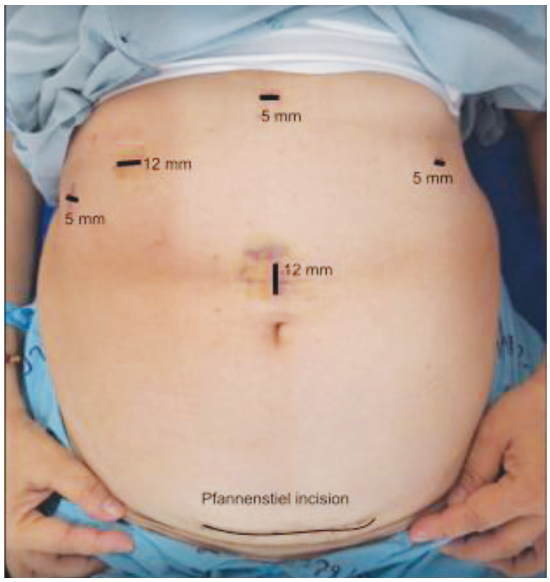

Figure 1 Port position for standard hepatectomy procedure; Right subcostal 5 mm and 12 mm port primarily performing cholecystectomy and parenchymal transection. Epigastric port 5 mm is employed for dissecting around the hepatocaval confluence and conducting parenchymal transection in the cephalad direction. The left subcostal 5 mm port serves the purpose of liver traction. When using an Endostapler for transecting the portal pedicle or hepatic vein, both 12mm ports (the camera port and the right subcostal port) are utilized to ensure the Endostapler is properly positioned.

For inflow control, Pringle's maneuver was prepared for inflow control by occluding the hepatoduodenal ligament. Inflow control approaches varied based on anatomical variations: the extrahepatic Glissonean pedicle method for standard hepatectomy and anterior sectionectomy (Figure 2), hilar dissection for lymph node dissection, and transfissural approach for lateral sectionectomy or masses near the Glissonean pedicle (Figure 3).

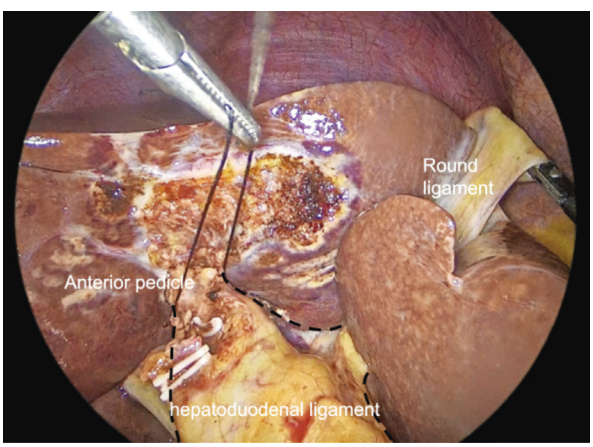

Figure 2 Extrahepatic glissonean approach in anterior sectionectomy

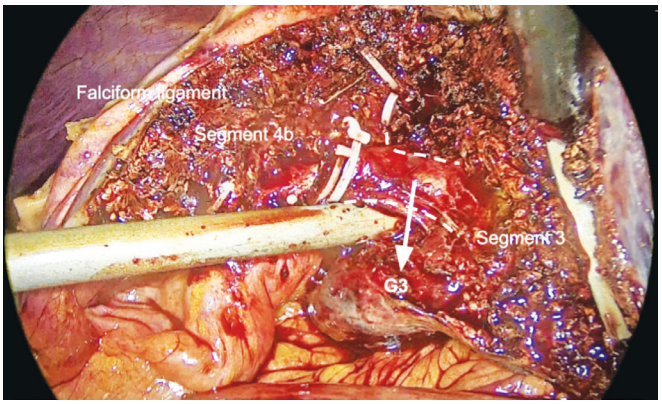

Figure 3 Transfissural approach in lateral sectionectomy. G3 = Glissonean pedicle of segment 3.

The inflow was effectively controlled by the Huang loop, eliminating the need for an Endobulldog. Huang loop was particularly useful for selective inflow control, especially the right and left portal pedicles.

After achieving inflow and mobilizing the liver, parenchymal transection was performed by CUSA, a bipolar sealing device (LIGASURE, Medtronic), and ultrasonic scissors for clamp crushing techniques. During this phase, patients were repositioned by the anesthesiologist, with their heads and legs elevated to reduce back bleeding from the outflow. The positive end-expiratory pressure (PEEP) was set to zero, and central venous pressure (CVP) was lowered to 3 – 5 mmHg while ensuring urine output and maintaining systolic blood pressure. The Glissonean pedicles and hepatic veins were divided using Echelon 60 Flex (Ethicon Endosurgery), With the Hepatic vein serving as a parenchymal guide in major hepatectomy (Figures 4 and 5). The smaller inflow vessels and hepatic veins were secured with double Hem-O-lock clips. Endostapler tools were essential for the safe and efficient division of vascular structures during the operation. The thick cartridges (ECHELON blue cartridge and COVIDIEN tri-stapler purple cartridge) were used for hepatic portal pedicle division, while thinner cartridges (ECHELON white cartridge and COVIDIEN tri-stapler gray cartridge) were employed for smaller hepatic veins.

Specimens were enclosed in plastic bags and extracted through the camera port extension. For larger specimens, a Pfannenstiel incision was made to facilitate removal. Negative pressure drains were placed intraperitoneally in all cases.

Figure 4 Hepatic vein guidance parenchymal transection in left hepatectomy. The Dot line is the transaction line that follows the medial aspect of the middle hepatic vein. (MHV=middle hepatic vein)

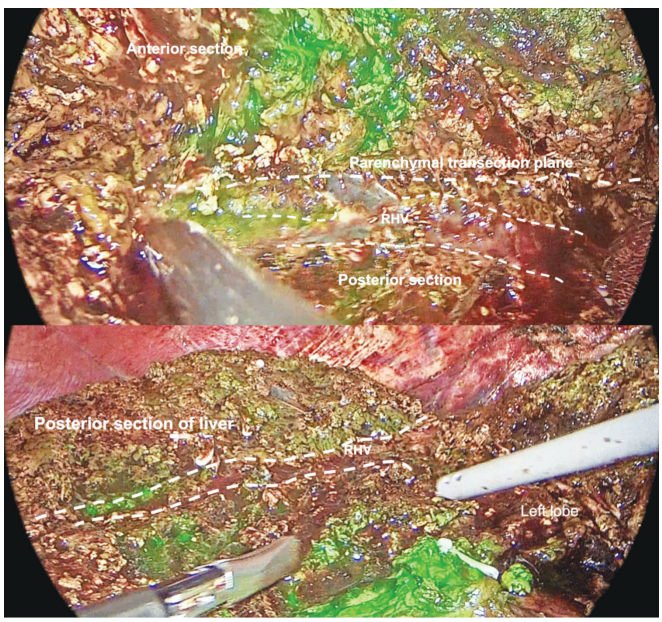

Figure 5 Demonstrated RHV guidance in anterior sectionectomy. Indocyanin green dye (Diagnogreen) was injected intravenous intraoperatively after selective portal pedicle clamping with a negative staining technique. After complete transection in midplane, the liver was transected from medial to lateral, guided by the right hepatic vein (upper). The right hepatic vein was barely seen after complete transection (lower). RHV = right hepatic vein.

Statistical Analysis

Categorical data were presented as frequencies and percentages. For data with a normal distribution, we calculated the mean and standard deviation (SD). Skewed data were reported using median and interquartile range (IQR). All statistical analyses were conducted using STATA version 16 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC).

Results

Data were collected between August 2018 and December 2023 by the author, who also served as the operating surgeon. A total of 22 patients underwent laparoscopic liver surgery. The mean age of the patients was 63.8 ± 13.8 years, and 68.2% of them were male. Most patients were classified as Child Turcotte Pugh (CTP) class A, with only one patient classified as CTP class B. Details of underlying diseases and laboratory findings are presented in Table 1.

Table 1 Baseline characteristics of the patients who underwent laparoscopic liver resections

Parameters	Missing data, n (%)	Total, n = 22
Age, years (mean ± SD)	1 (4.6)	63.8 ± 13.8
Male sex, n (%)	0 (0.0)	15 (68.2)
Diabetic mellitus type 2, n (%)	1 (4.6)	5 (23.8)
Cirrhosis, n (%)	0 (0.0)	8 (36.4)
Laboratory findings:		
Albumin, g/dL (mean ± SD)	1 (4.6)	4.0 ± 0.5
Total Bilirubin, mg/dL [median, IQR]	1 (4.6)	0.5 [0.5, 0.7]
INR (mean ± SD)	1 (4.6)	1.1 ± 0.1
BUN, mg/dL (mean ± SD)	1 (4.6)	15.5 ± 6.1
Creatinine, mg/dL (mean ± SD)	1 (4.6)	1.0 ± 0.5

SD = standard deviation; g = gram; dL = deciliter; IQR = interquartile range; INR = international normalized ratio; BUN = blood urea nitrogen

The major preoperative diagnosis was HCC, accounting for 63.7% of cases, followed by IPNB and CRLM. The most common postoperative diagnosis remained HCC, at 54.6%. Detailed characteristics of diseases are provided in Table 2.

Table 2 Disease characteristics of the patients who underwent laparoscopic liver resections

Parameters	Missing data, n (%)	Total, n = 22
Preoperative diagnoses:	0 (0.0)	
HCC, n (%)	-	14 (63.6)
IPNB, n (%)	-	4 (18.2)
CRLM, n (%)	-	2 (9.1)
ICCA, n (%)	-	1 (4.6)
Liver nodule, n (%)	-	1 (4.6)
Postoperative diagnoses:	0 (0.0)	
HCC, n (%)	-	12 (54.6)
ICCA, n (%)	-	2 (9.1)
CRLM, n (%)	-	2 (9.1)
Liver nodule, n (%)	-	1 (4.6)
Abscess, n (%)	-	1 (4.6)
Chronic cholangitis, n (%)	-	1 (4.6)
Biliary cyst, n (%)	-	1 (4.6)
Adenoma, n (%)	-	1 (4.6)
Dilated duct with inflammation, n (%)	-	1 (4.6)

HCC = hepatocellular carcinoma; IPNB = intraductal papillary neoplasm of bile duct; CRLM = colorectal liver metastasis; ICCA = intrahepatic cholangiocarcinoma

The mean IWATE score for procedural difficulty was 5.6 ± 2.2. The difficulty levels were classified as low (27.3%), intermediate (45.5%), advanced (22.7%), and expert (4.6%). Major procedures accounted for 40.9% of operations. The most common resection performed was left hepatectomy (27.3%), followed by wedge resections (18.2%) and anatomical resections (18.2%). The procedure with the highest difficulty score was anterior sectionectomy for HCC, measuring 4.7 cm in segments 5 and 8. The median tumor size was 2.6 cm [1.8, 5.4], with a maximum size of 9 cm. The median waiting time was 36 days [32, 42].

During surgery, the surgeon achieved inflow control in 15 out of 22 cases (68.2%) using extrahepatic Glissonean pedicles (46.7%), transfissural approaches (40.0%), and hilar dissection (13.3%). All hilar dissections were performed for patients diagnosed with ICCA. Initially, extracorporeal Pringle's maneuver was performed using umbilical tape encircling the hepatoduodenal ligament, with both tape ends externalized through an 18 French nasogastric tube alongside a 5 mm working port channel.[11] Later, it was modified using a Foley catheter sling.[12] The median Pringle time was 30 minutes [25, 60]. The estimated blood loss during operation was 125 mL [100, 300], and the mean operative time was 4.1 hours ± 105.9 minutes. Intraoperative findings revealed no macroinvasion. Detailed operative characteristics are presented in Table 3.

Table 3 Operative characteristics of the patients who underwent laparoscopic liver resections

Parameters	Missing data, n (%)	Total, n = 22
IWATE score:	0.0	
Mean ± SD	-	5.6 ± 2.2
Low, n (%)	-	6 (27.3)
Intermediate, n (%)	-	10 (45.5)
Advanced, n (%)	-	5 (22.7)
Expert, n (%)	-	1 (4.6)
Operations:	0 (0.0)	
Major, n (%)	-	9 (40.9)
Left hepatectomy, n (%)	-	6 (27.3)
Wedge resection, n (%)	-	4 (18.2)
Anatomical resection, n (%)	-	4 (18.2)
Lateral sectionectomy, n (%)	-	3 (13.6)
Right hepatectomy, n (%)	-	2 (9.1)
Segmentectomy, n (%)	-	2 (9.1)
Anterior sectionectomy, n (%)	-	1 (4.6)
Tumor size, cm [median, IQR]	6 (27.3)	2.6 [1.8, 5.4]
Waiting time, days [median, IQR]	13 (59.1)	36 [32, 42]
Pringle time, minutes [median, IQR]	0 (0.0)	30 [25, 60]
Estimated blood loss, ml [median, IQR]	0 (0.0)	125 [100, 300]
Operative time, minutes (mean ± SD)	0 (0.0)	265 ± 105.9
Macroinvasion, n (%)	1 (4.6)	0 (0.0)

SD = standard deviation; cm = centimeters; IQR = interquartile range; ml = milliliters

Postoperative outcomes are detailed in Table 4. The mean length of stay was 6.9 ± 2.7 days. The median ICU stay was 1 day [0, 1], with a maximum stay of 3 days. There were no cases of post-hepatectomy liver failure or recurrence. The most common postoperative complication was atelectasis (13.6%), which required physiotherapy. One patient was converted to open surgery due to uncontrolled portal pedicle bleeding with associated hypotension.

Ascites developed in one patient post-surgery, which was resolved with prolonged drainage and diuretic therapy. Another patient experienced a Class II complication involving bile leakage, which was treated with antibiotics and extended drainage. Eight patients required postoperative critical care in the surgical intensive care unit (ICU). No patients received neoadjuvant treatment before surgery.

Most resection margins in final pathological reports were free from malignancy, except for one case with a positive hepatic duct margin indicating malignant IPNB. Mortality occurred in 1 of 22 patients (5.3%) due to rupture abdominal aortic aneurysm (rAAA).

Table 4 Postoperative characteristics of the patients who underwent laparoscopic liver resections

Parameters	Missing data, n (%)	Total, n = 22
Length of stay, days (mean ± SD)	1 (4.6)	6.9 ± 2.7
ICU stay, days [median, IQR]	0 (0.0)	0 [0, 1]
Posthepatectomy liver failure, n (%)	2 (9.1)	0 (0.0)
Recurrence, n (%)	2 (9.1)	0 (0.0)
Clavien-Dindo Complication Classification[13]	2 (9.1)	
No complication, n (%)	-	15 (75.0)
Grade I, n (%)	-	1 (5.0)
Grade II, n (%)	-	3 (15.0)
Grade III, n (%)	-	1 (5.0)
Grade IV, n (%)	-	0 (0.0)
Mortality, n (%)	3 (13.6)	1 (5.3)

SD = standard deviation; ICU = intensive care unit; IQR = interquartile range

Discussion

Laparoscopic surgery has long been recognized as safe and feasible[14] for various abdominal procedures, including liver resections. It offers advantages such as reduced hospital stay, less postoperative pain, and quicker recovery time.[15] Importantly, LLRs did not increase mortality or readmission rates and proved to be cost-effective. Since 2009, the popularity of LLRs has surged, with over 9,000 cases performed worldwide.[7] The Enhanced Recovery after Surgery (ERAS) Society recommends minimally invasive surgery combined with multimodal analgesia to reduce postoperative complications.[16] However, LLRs demand expertise in hepatobiliary anatomy, experience in controlling intraoperative hepatic vascular bleeding, and proficiency with laparoscopic equipment.[17] The learning curve for major laparoscopic hepatectomy is estimated to be 45-60 cases.[18]

At our institution, surgeons perform over 50 open liver resections annually, with a total of 250 cases conducted by the author, who initiated LLRs with the first 22 cases since 2018 during the early learning curve. This study aims to review the safety of LLRs at a resource-limited institute, improve patient care quality, and share experiences with young surgeons interested in establishing LLRs in their practices.

The author began with patients diagnosed with resectable HCC due to its high prevalence and lower procedural complexity compared to CCA, which requires lymphadenectomy. The IWATE difficulty scoring system was employed in this study to stratify the difficulty level and aid in decision-making. Most cases were classified as low to intermediate difficulty, yielding satisfactory outcomes, including acceptable estimated blood loss (EBL), operative time, length of stay, and mortality. Complication-free recovery was observed in 75% of patients, with only one case converted to open surgery due to bleeding. There were no reoperations.

The author recommends that young surgeons start with patients who have a low IWATE score to build competency. The learning curve for surgeons performing LLRs with low IWATE scores warrants further study.

This study has limitations. Firstly, being retrospective in nature, there was some missing data and potential recall bias. Secondly, the small sample size limited the potential for more advanced statistical analyses. Future studies should explore external validation of difficulty scoring systems and include time-to-event or decision analysis based on registry data. Lastly, since the operations were performed by a single surgeon, future research could include LLRs from multicenter to help generalize the impact of surgical skills.

Conclusion

LLRs are a feasible option for surgeons who are on the learning curve, and the IWATE difficulty scoring system can assist them in deciding whether to perform minimally invasive surgery, although it has some limitations.

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Original Article

Clinico-Epidemiological Pattern of Penile Emergency in a Nigerian Hospital

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Abstract

Objective: Acute penile condition is a relatively uncommon urological emergency. This condition may lead to penile organ dysfunction if intervention is delayed. The commonly seen penile emergencies are priapism, penile fracture, and traumatic penile injury, among others. Our objective was to review all cases of penile emergencies managed over a period of four years (2021-2024) at our center.

Patients and Methods: This was a retrospective review of all cases managed for penile emergencies over a period of four years. The case files of the patients were retrieved from the hospital record department. The information extracted was written in a designed proforma. A descriptive statistic was carried out on the data.

Results: A total number of 19 cases of penile emergencies were managed during the years under review. The age range of the study group was 0.08-46 years, with a median of 23.9 ± 11.44 SD. The median duration of symptoms at presentation was 64.4 ± 123.2 SD with a range of 2 hours -504 hours. About half of the cases were traumatic (10 patients, 52.6%). The review of the underlined etiology showed sickle cell anemia, coital trauma, self-inflicted genital mutilation, circumcision injury, blunt penile trauma, and Fournier gangrene. Twelve patients (63.2%) had surgical intervention, while the rest were managed non-operatively. Post-intervention evaluation of erectile function done in three priapic patients with partners showed severe erectile dysfunction.

Conclusion: The most common (nontraumatic) penile emergency from this series was low-flow priapism. The majority of them had successful nonoperative measures with diluted adrenaline. Adrenaline may be an alternative sympathomimetic drug to the more preferred phenylephrine when not available. Other acute penile conditions noted were penile fracture and penile amputation, some of which had successful emergency interventions.

Keywords: Penile emergency, Priapism, Penile fracture

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Introduction

Acute penile condition is a relatively uncommon urological emergency.[1] This condition may lead to penile organ dysfunction if intervention is delayed. The commonly seen penile emergencies are priapism, penile fracture, and traumatic penile injury, among others.[2] Acute penile pain is one of the most common symptoms at presentation. Penile emergencies may be traumatic or nontraumatic. Some of the traumatic penile emergencies are penile fracture, penile amputation, and penile soft tissue injury, among others, while some of the non traumatic are priapism, phimosis, and paraphimosis. The global incidence of penile emergencies depends on the etiology. The overall incidence of priapism is estimated at 0.73-5.4/100,000 men/year, while the overall yearly incidence of penile fracture in the United States was reported to be 1 case per 175,000 men.[3] Diagnosis is usually clinical; however, ambiguous cases may require imaging evaluation, such as penile ultrasound, magnetic resonance imaging, and laboratory investigation. Immediate intervention is important for organ functional and anatomical preservation.[4] The type of surgical intervention depends on the type of penile emergency. The management of ischaemic priapism includes therapeutic corporeal aspiration and saline irrigation. Some may resolve with these measures, while others may require intracavernosal injection of sympathomimetic drugs and surgical shunting before resolution.[5] The management of penile amputation depends on the grade of the injury. Some of them may benefit from immediate macroscopic or microscopic reattachment, while others in which reattachment is not feasible may undergo refashioning plus urethrostomy or suprapubic urinary diversion.[6] Penile fracture is managed by surgical exploration and repair of ruptured tunica albuginea. Post-intervention evaluation of erectile function is of paramount importance. Our objective was to review all cases of penile emergencies managed over a period of four years (2021-2024) at our center.

Patients and Methods

This was a four-year retrospective review of all cases managed for penile emergencies. The patient's case files were retrieved from the hospital record department. The information extracted included the patients' ages, type of penile emergency, etiology of penile emergency, duration of symptoms at presentation, and type of surgical or medical intervention. Patients with incomplete data were excluded from the study. This was written in a designed proforma. Data was entered into SPSS version 23 for descriptive analysis.

Results

A total number of 19 cases of penile emergencies were managed during the years under review. The age range of the study group was 0.08-46 years, with a mean of 23.9 ± 11.44 SD. The mean duration of symptoms at presentation was 64.4 ± 123.2 SD with a range of 2 hours -504 hours. About half of the cases were traumatic (10 patients, 52.6%). Others were nontraumatic. The most common (nontraumatic) penile emergency was low flow priapism (8 patients, 42.1%). Others were penile fracture (4 patients, 21.1%), penile amputation (4 patients, 21.1%) and, penile laceration, penile Fournier gangrene, & penile ring impaction (1 patient each, 5.3%) (Table 1). Three (75%) out of the cases of penile amputation were grade iii, while the fourth case was grade iv (Table 2). Two of the cases of penile amputation were as a result of self-mutilation. These were complete amputations, but the penile stump could not be retrieved, while the other two cases, as a result of circumcision injury, presented with gangrenous stump. The review of the underlined etiology showed sickle cell anemia, coital trauma, penile self-inflicted genital mutilation, circumcision injury, blunt penile trauma, and Fournier gangrene (Table 3). Twelve patients (63.2%) had surgical intervention, while the rest were managed non-operatively. Concerning priapism, six (75%) out of the eight patients had successful medical interventions with diluted adrenaline following the failure of therapeutic corporeal aspiration. In contrast, the remaining two had open distal surgical shunting (Al-Ghorab technique) following the failure of medical intervention. These two cases were drug (Viagra) induced ischemic priapism. There were two cases of recurrent low-flow priapism in patients with sickle cell anemia. This was managed non-operatively. There was no case of high flow priapism. No patient was placed on anti-androgen for the prevention of priapism. All the cases of penile amputation had corporeal refashioning plus urethrostomy and catheterization, except one that had suprapubic urinary diversion. Patients with penile amputation were referred for phalloplasty. Post-intervention evaluation of erectile

function done in three priapic patients with partners showed severe erectile dysfunction. The erection hardness score was zero following combined injection and stimulation with papaverine. Two out of these three cases were drug-induced, while the third one was a case of sickle cell anemia. The patients were referred for penile prosthesis. All the patients with penile fractures reported satisfactory erectile function on follow-up.

Table 1 Showing the frequency of acute penile conditions

S/N	Penile emergency	Frequency (n = 19)	Percentage (%)
1	Priapism	8	42.1
	Penile fracture	4	21.1
	Penile amputation	4	21.1
	Ring impaction	1	5.3
	Penile laceration	1	5.3
	Fournier gangrene	1	5.3

Table 2 Showing the etiology and grade of penile amputation among the study group

S/N	Etiology	Grade
1	Self-mutilation	iii
2	Self-mutilation	iii
3	Circumcision injury	iii
4	Circumcision injury	iv

Table 3 Showing the basic and clinical data of the study group

S/N	Age (years)	Penile emergency	Etiology	Duration of symptoms (hours)	Type of surgical intervention
1	29 days	Penile amputation	Circumcision injury	2	Suprapubic cystostomy
2	45 days	Penile amputation	Circumcision injury	3	Urethrostomy plus catheterization
3	32	Ischemic priapism	Viagra, tramadol-induced	504	Surgical shunting
4	22	Penile amputation	Self-inflicted genital mutilation (Psychosis disorder)	3	Urethrostomy plus catheterization
5	26	Penile laceration	Blunt trauma	96	Primary suturing
6	28	Ring impaction	Penile ring	5	Removal with bone cutter
7	32	Penile fracture	Coital trauma	24	Repair
8	36	Penile fracture	Coital trauma	6	Repair
9	24	Penile fracture	Coital trauma	4	Repair
10	28	Penile fracture	Coital trauma	96	Repair
11	22	Ischemic priapism	Sickle cell disease	24	Medical therapy
12	20	Ischemic priapism	Sickle cell disease	24	Medical therapy
13	21	Ischemic priapism	Sickle cell disease	8	Medical therapy
14	20	Ischemic priapism	Sickle cell disease	2	Medical therapy
15	18	Ischemic priapism	Sickle cell disease	48	Medical therapy
16	15	Ischemic priapism	Sickle cell disease	4	Medical therapy
17	40	Fournier gangrene	Diabetes mellitus	264	Healing by secondary intention
18	46	Penile amputation	Self-inflicted genital mutilation (Psychosis disorder)	4	Urethrostomy plus catheterization
19	32	Ischemic priapism	Viagra induced	168	Surgical shunting

Discussion

This review has further established the rarity of penile urological emergencies. A review of 19 cases over a period of four years in a referral center may be a pointer to its rarity. The overall incidence of penile emergency is largely unknown due to the rarity of the condition.[7] Some of the studies on penile emergency are largely case reports.[8] These cases were either penile fracture priapism or penile amputation, among others. In a study conducted in France on urological emergencies, the only penile emergency observed was priapism, and it was among the least.[9] Similarly, in a review by Salako et al. in Nigeria, priapism was the least core urological emergency.[10] All these have given credence to the rarity of penile emergencies.

The establishment of priapism as the most common nontraumatic penile emergency followed by penile fracture from this study is in agreement with similar series in the medical literature.[11] Other types of penile emergencies are less frequently reported. Generally, the incidence of priapism is around 0.3-1.5/100,000 compared with penile fracture, which is around 0.2-1.3/100,000.[12]

It was observed that traumatic penile emergency was slightly higher than non-traumatic type. This was in consonance with similar previous studies.[13] Although there are several causes of low-flow priapism, sickle cell anemia has been described as the most frequent cause, and this study did not observe otherwise. We observed two of the cases of priapism were as a result of intake of Sildenafil (Viagra). Sildenafil is an uncommon inducer of priapism.[14] The report on Viagra-induced priapism is scanty in the medical literature.[15] This study has shown the risk of priapism following Viagra. Some of the commoner drugs that have been associated with ischemic priapism are psychotropic drugs, antihypertensive drugs, and heparin, among others.[16]

The etiology of penile fracture noted in this review was in accordance with the existing literature. Although coital trauma has been reported to be the most frequent cause in a previous meta-analysis study, forced flexion, masturbation, and rolling in bed on an erect penis have also been implicated.[8]

We observed four cases of penile amputation, two in adults secondary to self-mutilation and the other two noted in neonates as a result of circumcision injury. The findings from this study agree with the most commonly reported etiology of penile amputation in adults, which are self-mutilation and trauma. Similarly, in children, our findings agree with the frequent causes of penile amputation, which are traumatic circumcision and automobile accidents.[17] The incident of penile self-mutilation is very rare. It was noted by Vishal Mago in 2011 that only 57 cases of penile self-mutilation existed in the English literature.[18] The two cases noted in this study were the only cases ever seen in our environment. In a study conducted by Oranusi et al.[19] in Nigeria on traumatic penile injury, it was noted that penile self-mutilation accounted for six out of 23 cases of penile injury. This is in contrast to what was observed in this study.

All the cases of priapism reviewed in this study were low flow. This finding was not different from some other previous reviews in a similar setting.[20] This may be a pointer to the relative rarity of high-flow priapism in our environment. This was in contrast to the findings from a similar study conducted by Toshihiro et al., who had two cases of high-flow priapism out of five cases reviewed.[21]

The majority of the patients with priapism were managed non-operatively with either corporeal aspiration alone or, in addition, with sympathomimetic injection. Although phenylephrine is preferred because of its lower side effect profile,[22] epinephrine was used because phenylephrine was not readily available. Some of the patients were managed successfully, and no adverse effects were reported. Some authors have reported similar experiences on the use of epinephrine in priapism. Surgical shunting was necessary in only two patients following the failure of non-operative measures. The failure of medical therapy in these two cases may result from extensive thrombus formation within the cavernosal sinusoids due to delayed presentation, as noted. This was different from what was reported by Ugumba et al. and Badmus et al., where a larger number of the cases investigated had surgical shunting.[23,24] Erectile dysfunction was noted in these two cases that had surgical shunting, perhaps due to delayed presentation. This may be linked to poor healthcare-seeking behavior in our environment.

No consideration was given to conservative management of penile fracture in this study as all the patients had immediate surgical repair. Conservative management has been reported in the literature to be associated with more morbidity compared with surgical care. This review did not observe any morbidity following surgical repair, as all the patients reported satisfactory erectile function.

The approach to penile amputation depends on the grade of the injury. Grades iii and iv were noted in this series, and none of them had an attempt at replantation because amputated penile stumps could not be retrieved in some of them while others were already gangrenous.

Other relatively rare etiologies of penile emergency noted in this review were penile Fournier gangrene and penile ring impaction. Penile Fournier gangrene was managed conservatively, but some authors have reported the need for penile soft tissue reconstruction. This is probably dependent on the level of tissue disruption.

Conclusion

The most common penile emergency from this series was low-flow priapism, and the most common presentation was acute penile pain. The majority of the patients with priapism had successful non-operative measures with diluted adrenaline. Adrenaline may be an alternative sympathomimetic drug to the more preferred phenylephrine when not available. Other acute penile conditions noted were penile fracture and penile amputation, some of which had successful emergency interventions. Erectile dysfunction may complicate priapism, especially when presentation is delayed. Sexual activity remains the most common cause of penile fracture.

Early presentation and prompt intervention are key to penile function preservation and prevention of long-term complications such as penile curvature and peyronies disease following acute penile condition. Regular public enlightenment on acute penile conditions is imperative to early presentation and prompt care.

Limitation

1. This study is prone to recall bias due to its retrospective nature.

2. The findings from this study may not be generalized due to the low sample size and single-center study, even though this clinical condition is uncommon.

Conflict of interest

All authors declare no conflict of interest.

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Nil.

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Original Article

Comparison of Palliative Gastrectomy and Non-Gastrectomy in Advanced and Metastatic Gastric Cancer

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Abstract

Objective: A study was conducted to evaluate the efficacy of palliative gastrectomy (PG) compared to non-palliative gastrectomy (non-PG) in patients diagnosed with advanced or metastatic gastric adenocarcinoma, with an emphasis on survival outcomes and surgical complications.

Materials and Methods: A retrospective cohort study was conducted involving patients diagnosed with advanced or metastatic gastric adenocarcinoma between January 2015 and August 2024 at Buri Ram Hospital, Buri Ram, Thailand. The patients were categorized into two groups: the PG group and the non-PG group (palliative surgical bypass or feeding enterostomy). Data analysis was performed, and a p-value of less than 0.05 was considered statistically significant.

Results: A total of 136 patients were diagnosed with advanced or metastatic gastric cancer. The patients were divided into two groups: 61 patients in the PG group and 75 patients in the non-PG group. Chemotherapy was administered to 75 patients (55.2%). Among those who received chemotherapy, a higher proportion were from the PG group compared to the non-PG group, and this difference was statistically significant. ($p < 0.001$) Surgical complication was found in 24%. There was no significant difference in surgical complications between the two groups. ($p = 0.757$) The median survival time was 13 months for the PG group and 4 months for the non-PG group (HR: 0.28; 95% CI: 0.13-0.57; $p = 0.001$).

Conclusion: Survival outcomes are markedly improved in patients who undergo PG without complications and receive subsequent chemotherapy.

Keywords: Gastric cancer, Gastrectomy, Advance, Metastasis, Palliative

Introduction

Gastric cancer is the fifth most common cancer and a significant cause of death worldwide as of 2022.[1,2] The incidence is particularly high in Eastern Asia, especially Japan and Korea. Although the overall incidence and mortality rates of gastric cancer have been declining for several decades, it remains a leading cause of mortality and death, especially in advanced and metastatic stages.[2,3] Patients who present with advanced or metastatic gastric cancer are recommended to receive systemic therapy as the first line of care, according to the National Comprehensive Cancer Network (NCCN) guidelines and the Japanese Gastric Cancer Treatment Guidelines 2021.[4,5] Unfortunately, the outcome in these patients was a very poor prognosis. The 5-year survival rate for advance and metastasis stage of gastric cancer is typically less than 10%.[6,7] Although palliative systemic therapy remains the standard of care, growing evidence suggests that palliative surgery can offer both prognostic and symptomatic benefits.

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The Japanese Gastric Cancer Guidelines 2021 recommend that palliative gastrectomy (PG) may be performed in cases of advanced gastric cancer where complications such as bleeding or gastric obstruction are present. The previous studies have shown that PG was performed in patients with advanced gastric cancer, with the aim of increasing survival rates.[3,8-10] However, the impact on survival remains unclear. Li Q et al.[8] found that PG was associated with improved overall survival in patients with metastases to a single site who also received chemotherapy. However, PG did not improve survival rates for patients with metastases to multiple sites. An H et al.[3] observed that patients who underwent PG had a better median survival rate than those who did not receive the surgery. Kamarajah SK et al.[10] compared outcomes in patients with advanced gastric cancer who underwent PG with those who did not. They found that PG was associated with better survival rates, even when patients received other adjuvant treatments, such as chemotherapy, regardless of whether they had the surgery. Luo XF et al.[9] recommended PG for patients experiencing complications from cancer, such as obstruction or bleeding. However, it is important to note that this procedure can be associated with a range of surgical complications. Based on the previous, there remains some uncertainty and no definitive conclusions regarding the treatment of patients with advanced and metastatic gastric cancer. However, it appears that surgery, particularly PG, tends to improve the quality of life in advanced patients. It can help alleviate complications such as bleeding or obstruction, thereby providing symptomatic relief. On the other hand, surgery can be associated with various complications, such as blood loss, anastomotic leakage, abdominal collections, and infections.[11]

However, achieving a longer survival rate in cancer treatment is crucial. Therefore, this study aims to evaluate the survival benefit of palliative gastrectomy (PG) compared with non-PG in patients with metastatic gastric cancer, focusing on survival outcomes and surgical complications.

Materials and methods

A retrospective cohort study was performed involving all patients diagnosed with advanced or metastatic gastric adenocarcinoma between January 2015 and August 2024 at Buri Ram Hospital, Buri Ram, Thailand.

Study Population

All patients were 18 years or older at the time of diagnosis. Gastric adenocarcinoma was confirmed pathologically following esophagogastroduodenoscopy (EGD) and gastric mucosal biopsy. Advanced or metastatic gastric cancer was defined based on findings from computed tomography (CT) scans or magnetic resonance imaging (MRI). Patients with advanced or metastatic cancer were characterized by primary tumor progression, invasion into adjacent organs, matted of intra-abdominal lymph nodes (LNs), or distant tumor metastases or stage IV patients, including those to the liver, lungs, bones, para-aortic LNs, peritoneum, or ovaries. However, patients who underwent PG were staged based on pathological status, while those who underwent non-PG were staged using imaging techniques such as CT scans or MRI. For LNs staging via imaging, N1 was defined as the identification of 1 to 2 enlarged perigastric LNs, N2 as the identification of 3 to 6 enlarged LNs along major vessels, and N3 as the identification of 7 or more enlarged or bulky LNs metastasized along major vessels.[12,13] Patients who received systemic chemotherapy prior to surgery were included in this study. The patients were divided into two groups: those who underwent PG and those who did not undergo PG or non-PG. Patients with a second primary cancer or those who experienced recurrence or metastasis from gastric cancer after surgery and treatment were excluded. The functional status of patients was evaluated using the associated disease and the Eastern Cooperative Oncology Group (ECOG) score.

Surgery

PG was performed in patients with tumor-related symptoms, such as bleeding or obstruction, as well as in asymptomatic patients. The procedure involved removing only the tumor while leaving lymph nodes and metastatic sites intact. All PG procedures were performed via open surgery. The type of operation depended on the tumor's location. Distal or subtotal gastrectomy was performed if the tumor was located in the middle or lower part of the stomach. In contrast, total gastrectomy was performed if the tumor was located in the upper part of the stomach.

The non-PG group included procedures such as gastrojejunostomy bypass, gastrostomy, or jejunostomy and also comprised asymptomatic patients. The choice of surgical procedure was based on the surgeon's decision prior to surgery, intraoperative tumors assessment, and the patient's condition. Postoperative complications were assessed using the Clavien-Dindo classification system.

Systemic treatment and follow-up

All patients were staged according to the AJCC 8th edition.[14] For patients who underwent PG, staging was based on pathological results. In contrast, staging for the non-PG group was determined through clinical examination, imaging, or intraoperative evaluation in patients who underwent gastrojejunostomy bypass, gastrostomy, or jejunostomy. Systemic treatment after surgery is determined based on the patient's performance status according to the Eastern Cooperative Oncology Group (ECOG) scale. The chemotherapy (CMT) regimens included those based on 5-Fluorouracil (5-FU), oxaliplatin, irinotecan, paclitaxel, and cisplatin. Patients were followed up until death or their last visit. Overall survival was observed and analyzed.

Ethics consideration

This study was reviewed and approved by the Buri Ram Hospital Ethics Committee under reference number BR0033.102.1/74.

Statistical analysis

The baseline characteristics of patients, tumors, complications from surgery, and chemotherapy treatments were compared using the Chi-square or Fisher's exact test for categorical variables and the *t*-test for continuous variables. The Cox regression proportional hazard model was used to analyze the relationship between PG, non-PG, systemic chemotherapy treatment, and complications after surgery. The Kaplan-Meier method was used to analyze survival curves. The comparison between survival curves was performed by the Log-rank test to analyze the overall survival between groups. A *p*-value of less than 0.05 was considered statistically significant.

Results

A total of 136 patients were diagnosed with advanced or metastatic adenocarcinoma of the stomach. The patients were divided into two groups: 61 patients in the PG group and 75 patients in the non-PG group. In the non-PG group, 43 patients underwent surgical procedures, including feeding enterostomy (gastrostomy or jejunostomy) in 22 patients (29.3%) and gastrojejunostomy in 21 patients (28.0%). Baseline characteristics, tumor location, cancer staging, and histologic types are presented in Tables 1 and 2.

Table 1 Baseline characteristics of patients

Factors	Total n = 136 (%)	PG n = 61 (%)	non-PG n = 75 (%)	*p*-value
Age (years), mean (± SD)	63.5 (± 8.7)	65.3 (6.2)	62.0 (10.1)	0.985
Sex Male	93 (68.4)	41 (67.2)	52 (69.3)	0.791
Female	43 (31.6)	20 (32.8)	230 (30.7)	
BMI (kg/m^2), mean (± SD)	20.7 (± 0.1)	20.7 (± 0.3)	20.8 (± 0.2)	0.589
Underlying diseases		55	63	
Diabetes mellitus	21 (17.8)	11 (20.0)	10 (15.9)	0.558
Hypertension	32 (27.1)	17 (30.9)	15 (23.8)	0.386
Dyslipidemia	38 (32.2)	18 (32.7)	20 (31.7)	0.909
Coronary artery diseases	12 (10.2)	3 (5.5)	9 (14.3)	0.113
Cerebrovascular diseases	4 (3.4)	2 (3.6)	2 (3.2)	0.890
Chronic kidney diseases	8 (6.8)	3 (5.5)	5 (7.9)	0.592
Liver cirrhosis	3 (2.5)	1 (1.8)	2 (3.2)	0.640
ASA classification				
ASA I	92 (67.7)	45 (73.7)	47 (62.7)	0.168
ASA II	41 (30.1)	15 (24.6)	26 (34.7)	0.202
ASA III	3 (2.2)	1 (1.7)	2 (2.6)	0.684
ECOG Status				
ECOG 0	93 (68.4)	49 (80.3)	44 (58.7)	0.006
ECOG 1	32 (23.5)	7 (11.5)	25 (33.3)	0.002
ECOG 2	7 (5.2)	4 (6.6)	3 (4.0)	0.502
ECOG 3	4 (2.9)	1 (1.6)	3 (4.0)	0.417

SD: standard deviation, BMI: Body mass index, ASA: American Society of Anesthesiologists, ECOG: Eastern Cooperative Oncology Group

Table 2 Tumors location, cancer staging, and histology type of tumors

Factors	Total n = 136 (%)	PG n = 61 (%)	non-PG n = 75 (%)	*p*-value
Tumor location				
Upper	28 (20.6)	9 (14.8)	19 (25.3)	0.129
Middle	47 (34.6)	20 (32.8)	27 (36.0)	0.695
Lower	61 (44.8)	32 (52.4)	29 (38.7)	0.107
TNM staging				
T2	2 (1.5)	1 (1.6)	2 (2.7)	0.684
T3	78 (57.3)	19 (31.2)	59 (78.7)	< 0.001
T4	56 (41.2)	41 (67.2)	14 (18.6)	< 0.001
N0	5 (3.7)	3 (4.9)	2 (2.7)	0.487
N1	37 (27.2)	10 (16.4)	27 (36.0)	0.010
N2	73 (53.7)	27 (44.3)	44 (58.6)	0.094
N3	21 (15.4)	21 (34.4)	2 (2.7)	< 0.001
M0	11 (8.1)	9 (14.8)	2 (2.7)	0.010
M1	125 (91.9)	52 (85.2)	73 (97.3)	
Number of organ metastasis				
Single	49 (38.9)	22 (42.3)	27 (36.5)	0.509
Multiple	77 (61.1)	30 (57.7)	47 (63.5)	
Metastatic site				
Liver	37 (27.2)	11 (18.0)	26 (34.7)	0.030
Lung	27 (19.8)	13 (21.3)	14 (18.7)	0.701
Peritoneum	68 (50.0)	21 (34.4)	47 (62.7)	0.001
Omentum	27 (19.8)	15 (24.6)	12 (16.0)	0.212
Distant LNs	67 (49.2)	30 (49.2)	37 (49.3)	0.986
Bone	11 (8.1)	6 (9.8)	5 (6.7)	0.500
Ovary	3 (2.2)	0 (0)	3 (4.0)	0.114
Histology type				
Well-differentiated	7 (5.2)	1 (1.7)	6 (8.0)	0.094
Moderated differentiated	28 (20.7)	16 (26.7)	12 (16.0)	0.142
Poor differentiated	38 (28.2)	17 (28.3)	21 (28.0)	0.986
Signet ring cell	62 (45.9)	26 (43.3)	36 (48.0)	0.531

Patients with T3 or N1 staging were more prevalent in the non-PG group, whereas T4 or N3 staging was more common in the PG group, with these differences being statistically significant. Metastatic tumors, particularly liver and peritoneal metastases, were more common in the non-PG group, with these differences being statistically significant. There was no significant difference in histologic types between the two groups.

Chemotherapy was administered to 75 patients (55.2%). Among those who received chemotherapy, a higher proportion were from the PG group compared to the non-PG group, and this difference was statistically significant. There was no significant difference in the use of radiotherapy between the two groups. This data are presented in Table 3.

A total of 104 patients underwent surgery, including 61 patients (58.7%) in the PG group and 43 patients (41.3%) in the non-PG group. Among the non-PG group, 22 patients (21.1%) received feeding enterostomy, and 21 patients (20.2%) underwent gastrojejunostomy. There was no significant difference in surgical complications between the two groups. These data are presented in Table 4. Surgical complications were assessed using the Clavien-Dindo classification system and were primarily classified as Grade I and Grade II. Only 3 patients who experienced anastomosis leakage required re-operation.

Table 3 Systemic treatment and radiotherapy

Factors	Total n = 136 (%)	PG n = 61 (%)	non-PG n = 75 (%)	*p*-value
Chemotherapy	75 (55.2)	47 (77.1)	28 (37.3)	< 0.001
Regimens				
FOLFOX	19 (13.9)	7 (11.5)	12 (16.0)	0.449
Capecitabine-Oxaliplatin	7 (5.2)	7 (11.5)	0 (0)	0.003
FOLFIRI	2 (1.5)	0 (0)	2 (2.7)	0.199
5FU - leucovorin	17 (12.5)	14 (22.9)	3 (4.0)	0.001
Cisplatin/5FU	28 (20.6)	19 (31.2)	9 (12.0)	0.006
Carboplatin/Paclitaxel	7 (5.2)	3 (4.9)	4 (5.3)	0.913
Carboplatin/5FU	6 (4.4)	2 (3.2)	4 (5.3)	0.562
Radiotherapy				
Yes	6 (4.4)	5 (8.2)	1 (1.3)	0.053
No	130 (95.6)	56 (91.8)	74 (98.7)	

FOLFOX: Folinic acid (leucovorin), Fluorouracil (5-FU), Oxaliplatin; FOLFIRI: Folinic acid (leucovorin), Fluorouracil (5-FU), Irinotecan

Table 4 Surgical complications

Factors	Total n = 104 (%)	PG n = 61 (%)	non-PG n = 43 (%)	*p*-value
Surgical complications				
Yes	25 (24.0)	14 (22.9)	11 (25.6)	0.757
No	79 (76.0)	47 (77.1)	32 (74.4)	
Type of complication				
Intra-abdominal collection	6 (5.8)	5 (8.2)	1 (2.3)	0.206
Surgical site infection	7 (6.7)	3 (4.9)	4 (9.3)	0.380
Anastomosis leakage	3 (2.9)	3 (4.9)	0 (0)	0.140
Intra operative bleeding	1 (0.9)	0 (0)	1 (2.3)	0.231
Post-operative ileus	5 (4.8)	2 (3.3)	3 (6.9)	0.385
Pneumonia	16 (15.4)	11 (18.0)	5 (11.6)	0.373
Sepsis	12 (11.5)	8 (13.1)	4 (9.3)	0.549
Clavien-Dindo Classification				
Grade I	5 (20)	3 (21.4)	2 (18.2)	0.840
Grade II	17 (68)	8 (57.2)	9 (81.8)	0.189
Grade III	3 (12)	3 (21.4)	0 (0)	0.356

The follow-up time for this study was 10.2 months. The overall survival for all patients was 6 months. The median survival time was 13 months for the PG group and 4 months for the non-PG group (HR: 0.28; 95% CI: 0.13-0.57; p = 0.001). Survival analysis between the two groups is shown in Figure 1. The median survival for patients with single and multiple metastasis sites was 7 months and 5 months, respectively, and no difference in survival was observed between the two groups (HR: 1.07; 95% CI: 0.59–1.96; p = 0.804). Subgroup analysis by metastasis location is shown in Table 5. PG in patients with bone metastasis was associated with better median survival (16 months) compared to non-PG (9 months), with statistical significance (p = 0.021).

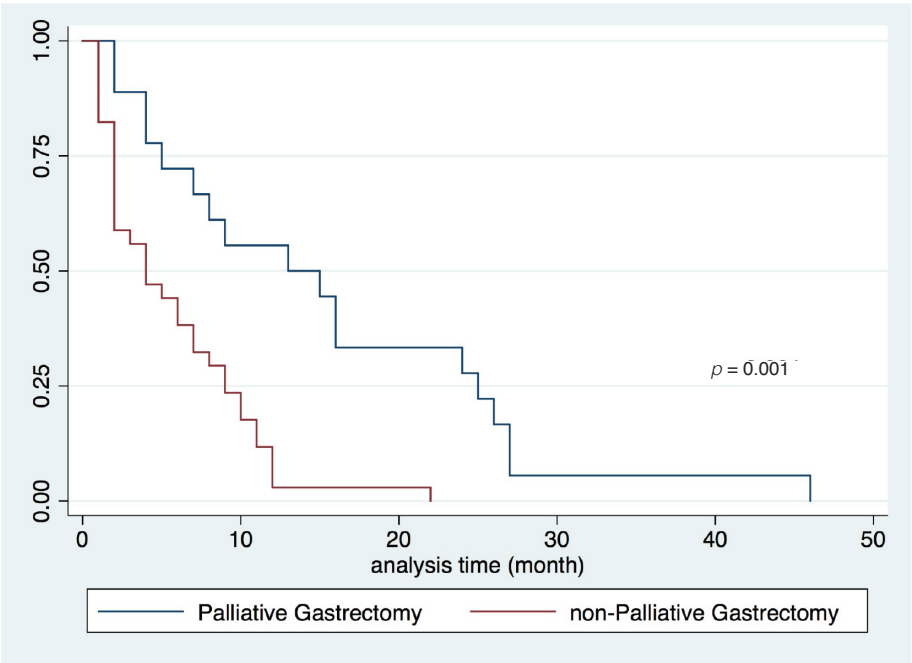

Figure 1 Kaplan-Meier graph shows survival analysis between Palliative gastrectomy (PG) and non-palliative gastrectomy (non-PG)

Table 5 Subgroup analysis by metastasis locations

Location of metastasis	Median survival time (month)		HR	95% CI	*p*-value
	PG	Non-PG			
Liver	6	4	1.07	0.42-2.69	0.885
Lung	8	7	0.61	0.27-1.36	0.229
Peritoneum	8	2	1.47	0.72-3.01	0.285
Distant LN	13	4	1.70	0.83-3.45	0.142
Omentum	8	1	2.48	0.94-6.56	0.066
Bone	16	9	0.25	0.07-0.81	0.021
Ovary	13	10	0.38	0.09-1.52	0.175

HR: Hazard ratio, CI: confidence interval

Survival outcomes were analyzed for patients who received chemotherapy (CMT) and those who underwent surgery. The median survival times were 16 months for the PG + CMT group, 4 months for the PG + no CMT group, 9 months for the non-PG + CMT group, and 2 months for the non-PG + no CMT group. Patients who underwent PG and received CMT had better survival than the other groups (HR: 0.33; 95% CI: 0.16-0.70; $p = 0.004$) (Figure 2). Survival subgroup analysis showed better outcomes in PG + CMT compared to PG + no CMT, non-PG + CMT, and non-PG + no CMT, with $p < 0.001$, 0.002, and < 0.001, respectively. PG + no CMT was compared to non-PG + CMT and non-PG + no CMT, with $p = 0.762$ and < 0.001, respectively. Patients with non-PG + CMT had better survival outcomes compared to non-PG + no CMT ($p < 0.001$).

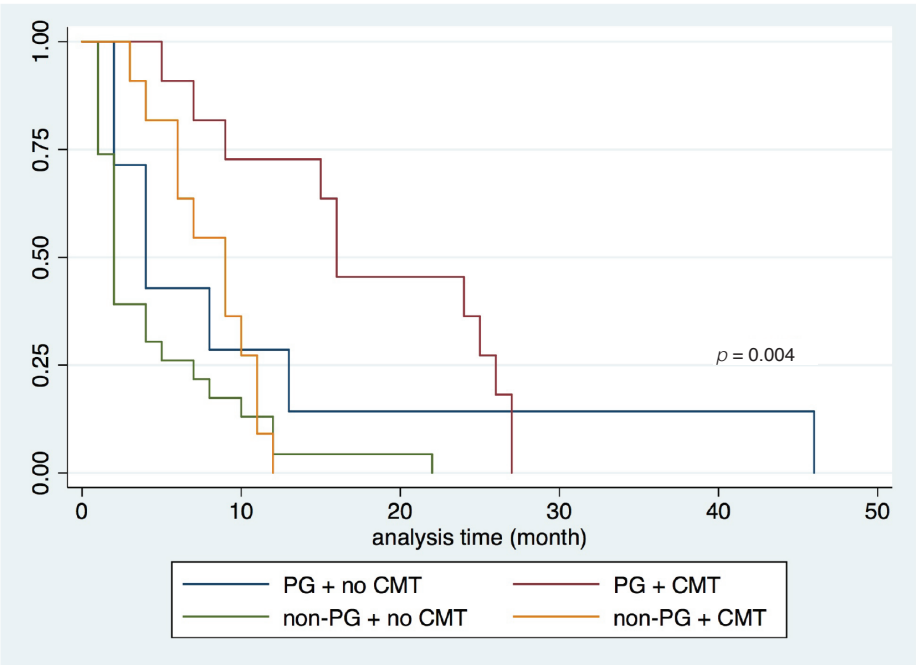

Figure 2 The Kaplan-Meier graph shows the survival analysis for patients in the following groups: PG + no CMT, PG + CMT, non-PG + no CMT, and non-PG + CMT. (PG: palliative gastrectomy, non-PG: non-palliative gastrectomy, CMT: chemotherapy)

The correlation between surgery and complications was evaluated, and survival was found better in the PG group without complications (HR: 0.25; 95% CI: 0.10-0.59; $p = 0.002$). Specifically, survival times were 16 months for PG without complications, 4 months for PG with complications as well as for non-PG without complications, and 2 months for non-PG with complications (Figure 3). Survival subgroup analysis showed better outcomes in PG without complication than PG with complication, non-PG without complication, and non-PG with complication, with $p < 0.001$, < 0.001, and < 0.001, respectively. PG with complication was compared to non-PG with complication and without complication, with $p = 0.005$ and 0.102, respectively. Patients with non-PG without complications had better survival outcomes compared to non-PG with complications ($p < 0.001$).

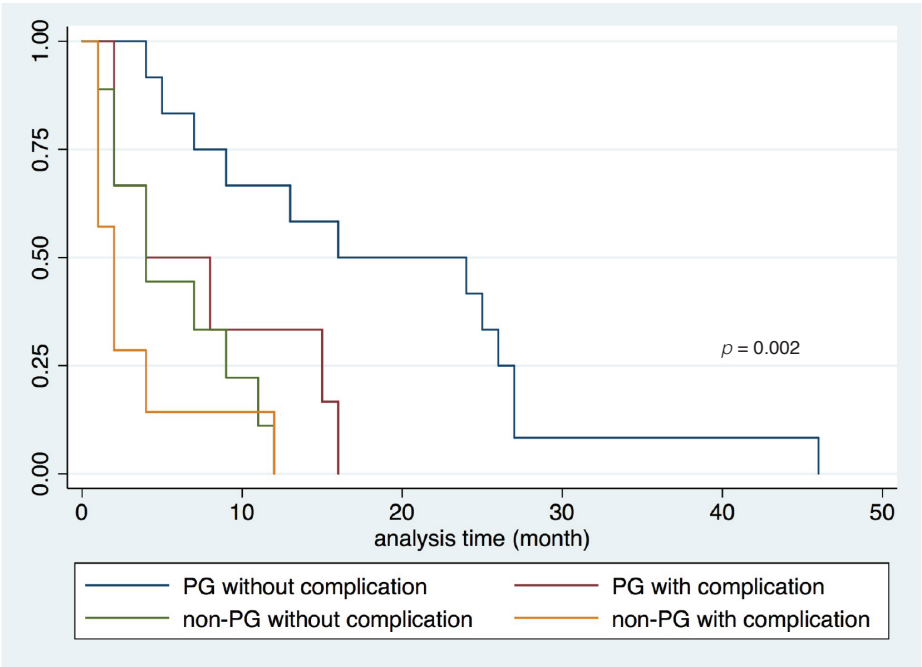

Figure 3 The Kaplan-Meier graph shows the survival analysis for patients in the following groups: PG without complication, PG with complication, non-PG without complication, and non-PG with complication.

Discussion

According to several guidelines, systemic therapy has traditionally been the standard treatment for advanced or metastatic adenocarcinoma of the stomach.[4,5] However, there has been a growing use of PG in these cases. Despite this trend, the effectiveness of this surgery remains inconclusive. This study included patients diagnosed with advanced or metastatic gastric cancer who underwent PG. Notably, none of these patients received systemic treatment prior to the surgery.

For staging in this study, patients who underwent PG were staged based on pathological results. In contrast, patients in the non-PG were staged clinically, using CT scans, MRI, or intra-operative examinations during palliative bypass procedures or feeding enterostomies. This study found that the PG group had more advanced tumor and lymph node stages. In contrast, patients in the non-PG group may have underestimated their staging, as indicated by the higher prevalence of T4 or N3 staging in the PG group compared to T3 or N1 staging in the non-PG group. Several studies have shown that tumor and lymph node metastasis can be aggressive, but most of these studies have relied solely on pathological staging.[3,6,8] This study found that performing PG was insignificant for patients with liver or peritoneal metastases. These metastases were often advanced, unresectable, and associated with a poor prognosis. Consequently, these patients typically underwent only palliative gastrojejunostomy or feeding enterostomy. The GYMSSA trial[15] compared patients who underwent gastrectomy with metastasectomy plus systemic chemotherapy to those who received systemic chemotherapy alone. The results indicated that adding gastrectomy and metastasectomy did not significantly impact overall survival. Granieri S et al.[16] reported that gastrectomy with metastasectomy benefits only patients with liver metastases who do not have extrahepatic disease; surgical removal with curative intent may improve survival in these cases. This study emphasizes the importance of clinical staging in decision-making for operative procedures, providing a broader context for evaluating the extent of the disease.

Chemotherapy plays a crucial role in the treatment of advanced or metastatic gastric cancer and significantly impacts survival outcomes. This study found that patients who underwent PG were more likely to receive systemic treatment than those who did not. This difference was statistically significant and was associated with better patient status in those who underwent PG, particularly in patients with ASA I and ECOG 0 status. Our findings support that the survival outcome of patients who underwent PG and received chemotherapy was 16 months compared with 2 months in patients who did not perform PG and did not receive chemotherapy. An H et al.[3] conducted a comparative study on PG in patients with metastases to other organs. They found that patients who underwent PG had a median survival rate of 13 months, compared to 6 months for those who did not receive the surgery. The study also highlighted the importance of administering appropriate chemotherapy in conjunction with the treatment. Kamarajah SK et al.[10] conducted a study comparing outcomes in patients with advanced gastric cancer who underwent PG with those who did not. They found that PG was associated with better survival rates, even when patients received chemotherapy, either with or without the surgery. Li Q et al.[8] compared patients with metastatic gastric cancer who underwent PG with those who did not. The study found that PG was associated with improved overall survival in patients with metastases to a single site and who received chemotherapy. However, PG did not result in an increased survival rate for patients with metastases to multiple sites. This study found that the benefit of PG was associated with better survival, particularly in patients with bone metastasis. The median survival for patients with bone metastasis who underwent PG was 16 months, compared to 9 months in those who did not undergo PG. Although previous studies[17] have reported poor prognosis in patients with gastric cancer and bone metastasis, with survival of 4-6 months. This study found better survival in patients with gastric cancer and bone metastasis who underwent PG and received chemotherapy. However, a meta-analysis demonstrated that the median survival for patients who underwent PG was 14 months, compared to 7 months for those who did not undergo resection.[18]

Previous data support that patients who undergo gastrectomy for gastric cancer experience improvements in quality of life, including reductions in fatigue, nausea/vomiting, and appetite loss.[19] By reducing tumor burden, PG is associated with enhanced quality of life, which is linked to the patient's status before surgery. This study showed a high prevalence of patients with ASA I and ECOG 0 status in the PG group, contributing to better chemotherapy tolerance post-surgery. Additionally, patients who receive and tolerate chemotherapy may experience improved responses to systemic treatment. On the other hand, some studies have reported that PG is associated with high morbidity and mortality rates.[20] This study found that the overall complication rate for surgery was 24.0%, with 22.9% in the PG group and 25.6% in the feeding enterostomy or gastrojejunostomy group. All complications were classified as minor, and no patients died as a result of the surgery. Previous data indicate that the prevalence of complications after PG ranges from 10% to 38%.[21] Despite the high prevalence of surgical complications, some patients with clinical obstruction or bleeding may require surgery. Luo XF et al.[9] found that PG is recommended for patients experiencing complications from cancer, such as obstruction or bleeding. However, it is essential to note that this procedure can be associated with various surgical complications. Reducing postoperative complications is crucial for decreasing morbidity and mortality and enhancing survival outcomes in patients undergoing PG.

Additionally, initiating chemotherapy as early as possible is essential. Our data support this finding, showing that patients who underwent PG without operative complications had a higher survival rate than those who underwent non-PG with surgical complications. Specifically, the median survival was 16 months for PG without operative complications, compared to 2 months for non-PG with surgical complications.

A Phase 3 randomized controlled trial (REGATTA) investigated patients with advanced or metastatic gastric cancer who received gastrectomy plus lymphadenectomy and chemotherapy compared to those who received chemotherapy alone. The study found no significant difference in survival between the two groups, with a median overall survival of 16.6 months for patients receiving chemotherapy alone and 14.3 months for those undergoing gastrectomy plus lymphadenectomy and chemotherapy. The conclusion suggested that chemotherapy alone might be preferable for advanced or metastatic gastric cancer.[22] Previous studies have reported that patients who underwent PG in conjunction with chemotherapy had better survival outcomes, with median survival

ranging from 8 to 14 months, compared to those who did not undergo surgery.[3,23,24] This study found that the median survival was consistent with previous research. The median survival was 13 months for the PG group and 4 months for the non-resectable group. However, factors influencing survival include the type of surgery, the absence of surgical complications, and the systemic treatment administered after surgery, which plays a crucial role in prolonging patient survival, as shown in this study. Decisions regarding surgery depend on the risk-benefit analysis of complications and the operative outcomes for each patient.

Conclusion

PG in advanced or metastatic gastric cancer can improve survival outcomes, particularly when there are no complications and when patients receive chemotherapy after surgery. Despite the high morbidity associated with the procedure, careful patient selection is crucial for optimizing outcomes.

Limitation of study

Because this study was retrospective, patient selection depended on the surgeon's preference and the aggressiveness of the primary tumor. To reduce selection bias and improve the results, future studies should be conducted through a multicenter approach and designed as prospective studies.

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Original Article

Outcomes of Laparoscopic Gastric Resection for Submucosal Tumors at Difficult Locations: A Prospective Cohort Study

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Abstract

Background: The most common type of submucosal tumor in the stomach is gastrointestinal stromal tumors (GISTs). The standard treatment involves surgical removal with clear margins and without tumor rupture. Current treatment increasingly supports laparoscopic surgery, particularly for tumors located in difficult-to-access locations. This study compares laparoscopic surgery (LapS) and open surgery (OpenS) for gastric submucosal tumors located in such areas.

Objective: This study aimed to evaluate survival analysis and assess the surgical outcomes associated with both techniques.

Materials and Methods: A prospective cohort study was conducted between August 2021 and August 2024 at Buri Ram Hospital. Patients diagnosed with gastric submucosal tumors were evaluated through esophagogastroduodenoscopy (EGD). The tumors were located in challenging stomach areas, including the esophagogastric junction (EGJ), cardia, lesser curvature, posterior wall of the stomach, and pyloric ring of the antrum. The data were analyzed, and a *p*-value of less than 0.05 was considered statistically significant.

Results: Thirty-seven patients were included in the study, with 19 patients assigned to the LapS group and 18 patients assigned to the OpenS group. There were no statistically significant differences in age, sex, or BMI between the two groups. However, the tumors located at the lesser curvature of the stomach were significantly more prevalent in the OpenS group compared to the LapS group ($p = 0.044$). Partial gastric resection was performed more frequently in the LapS group compared to the OpenS group ($p = 0.004$). The LapS group demonstrated better postoperative outcomes, including reduced blood loss, earlier initiation of feeding, earlier passage of flatus, and a shorter duration of hospital stay. The median follow-up time was 19 months. The survival rate in the LapS group was 89.5%, compared to 77.8% in the OpenS group. No significant difference in survival analysis was observed between the two groups (HR 0.54, 95% CI: 0.09-2.98, $p = 0.482$).

Conclusion: For submucosal tumors located in challenging areas of the stomach, laparoscopic surgery offers advantages in terms of minimally invasive approaches and oncologic outcomes compared to open surgery.

Keywords: Gastric submucosal tumors, Gastrointestinal stromal tumors, GIST, Laparoscopic, Difficult

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Introduction

The most common group of submucosal tumors in the stomach is gastrointestinal stromal tumors (GISTs).[1] The standard treatment is the surgical removal of the entire tumor, aiming for curative resection with free margins and without tumor rupture. These factors significantly impact treatment outcomes; complete resection without rupture is associated with lower recurrence rates and improved overall survival.[2,3] In the past, most treatments were performed through open surgery. Lukaszczyk et al. performed the first successful laparoscopic surgical resection of gastric GISTs. This marked the introduction of laparoscopic surgery as a minimally invasive approach to treating GISTs.[4] Liangying Ye et al. conducted a meta-analysis comparing gastric GIST patients undergoing open surgery versus laparoscopic surgery. The results indicated no statistically significant differences between the two surgical methods in terms of survival rates, recurrence, or complications.[5] Current treatment guidelines increasingly endorse laparoscopic surgery, particularly for tumors located in regions amenable to this technique, such as the greater curvature or the anterior portion of the stomach.[6-8] Liao GQ et al. performed a retrospective comparative study of patients undergoing laparoscopic surgery for gastric GISTs. They compared patients with tumors located in easily accessible areas to those with tumors in more challenging positions. The study found that both surgical approaches can be performed safely for patients.[9] Chang-Ming Huang et al. compared patients undergoing laparoscopic and open surgery for gastric GISTs in easily accessible and difficult surgical locations. The results indicated no significant differences between the laparoscopic and open surgery groups, regardless of the tumor's location. Both approaches were found to be safe for patients.[10] Laparoscopic surgery offers the advantage of a minimally invasive approach, leading to reduced postoperative recovery times. In contrast, open surgery provides the benefit of superior palpation and tactile sensation, which can enhance intraoperative decision-making. However, when tumors are located in difficult-to-access areas of the stomach, assessment can be challenging. Current trends increasingly favor laparoscopic surgery, particularly for tumors in such locations.

This study aims to compare laparoscopic surgery and open surgery for gastric GISTs located in difficult-to-access areas. The research employs a prospective data collection methodology to ensure a comprehensive analysis. The objectives of this study are to assess survival analysis and surgical outcomes associated with both surgical techniques.

Materials and Methods

A prospective cohort study was performed between August 2021 and August 2024 at Buri Ram Hospital, Buri Ram, Thailand.

Patients

All patients were 18 years or older at the time of diagnosis. Patients diagnosed with gastric submucosal of the stomach can be evaluated through esophagogastroduodenoscopy (EGD), which may reveal submucosal lesions or allow for tissue biopsy. Additionally, imaging techniques such as computed tomography (CT) scans and magnetic resonance imaging (MRI) can be utilized for assessment. The inclusion criteria were the patients who had American Society of Anesthesiologists (ASA) classification I-II and received neoadjuvant treatment before surgery. Surgical intervention is required, and treatment options include either open surgery or laparoscopic surgery. Postoperative complications were assessed using the Clavien-Dindo classification system. The exclusion criteria for this study included patients with a second primary cancer or those with metastasis at the time of diagnosis. Patients with contraindications for laparoscopic surgery were also excluded from the study. Additionally, all patients were required to sign an informed consent form before being included in the study. The tumor location was identified from EGD, CT scan, or MRI to locate the difficult area of the stomach to approach for surgery, including esophagogastric junction (EGJ), cardia, lesser curvature, posterior wall of the stomach, a pyloric ring of the antrum. For the other location were excluded from the study. The patients included in the study were divided into two groups: the laparoscopic surgery (LapS) group and the open surgery (OpenS) group. The sample size for this study consisted of 16 patients in each group. A dropout rate of 10% was anticipated, with an alpha level of 0.05 and a statistical power of 80%. The study utilized a 1:1 ratio, resulting in a total of 36 patients participating in the study.[10] Patient allocation will follow a 1:1 alternating pattern, as the study is prospective and non-randomized, with participants being assigned after they have been thoroughly informed of the relevant details.

Surgery

The surgical approaches were categorized into LapS and OpenS. The surgical procedure selection was based on the surgeon's judgment and the patient's condition. The technique for gastric resection was determined by the tumor's location and included partial gastric resection, proximal gastrectomy, distal gastrectomy, or total gastrectomy. For the LapS procedure, patients were positioned in reverse Trendelenburg. A trocar was inserted to create 3-4 ports in the anterior abdominal wall. The surgeon positioned themselves on the right side or between the patient's legs, depending on the tumor's location. The assistant or camera operator was positioned either between the patient's legs or on the right side. For the open surgery procedure, patients were positioned in a supine orientation. An upper midline incision was made, followed by the performance of the intra-abdominal procedure. In cases of challenging tumor localization, EGD was utilized. Gastric resection may be performed using gastrointestinal anastomosis (GIA) staplers or hand-sewn techniques. For tumors located near the EGJ or pyloric ring, EGD was conducted to identify potential issues and prevent suture compromise of the gastric lumen. The gastrotomy technique was utilized for tumor resection, ensuring clear margins while preserving the gastric lumen in lesions adjacent to it. In patients who performed distal or total gastrectomy, reconstruction was achieved using the Roux-en-Y gastrojejunostomy or Roux-en-Y esophagojejunostomy techniques. For patients who underwent proximal gastrectomy, esophagogastrostomy was performed for reconstruction. After the completion of the operation, a surgical suction drain was placed near the suture line of the stomach. The data on operative time, blood loss, and intraoperative complications were recorded. The tumors were sent for pathological evaluation, confirming a diagnosis of GISTs in all patients.

Post-operative care

After the patients fully recovered from general anesthesia, a liquid diet was permitted. Pain management was achieved with intravenous morphine injection. Patients without immediate complications were allowed to transition to a soft diet or continue with liquids as tolerated. A surgical suction drain was removed when serous output was observed or prior to patient discharge. The day feeding was initiated, the flatus's first passage and the duration of hospitalization were recorded.

Definitions

The risk of recurrence is determined by the National Institutes of Health (NIH) consensus classification system, which includes tumor size and mitotic count. Tumor size is defined as the maximum diameter of the tumor. The mitotic rate is assessed by counting the number of mitoses per 50 high-power fields (HPF) and is classified into very low, low, intermediate, and high-risk categories.[11]

Adjuvant treatment and follow-up

Adjuvant treatment for gastric GISTs depends on the risk classification. Patients identified as having a high risk of recurrence may receive adjuvant imatinib; however, this is not universally applicable to all high-risk patients, as it depends on the individual patient's financial capacity to support the cost of imatinib. The date of the last follow-up was recorded. The local recurrence and metastasis were observed.

Ethics consideration

This study was reviewed and approved by the Buri Ram Hospital Ethics Committee under reference number BR0032.102.1/37.

Statistical analysis

The baseline characteristics of patients, tumors, and outcome of surgery were compared using the Chi-square or Fisher's exact test for categorical variables and the t-test for continuous variables. The survival and recurrence were analyzed using the Kaplan-Meier curve and logistic regression. A p-value < 0.05 was considered statistically significant.

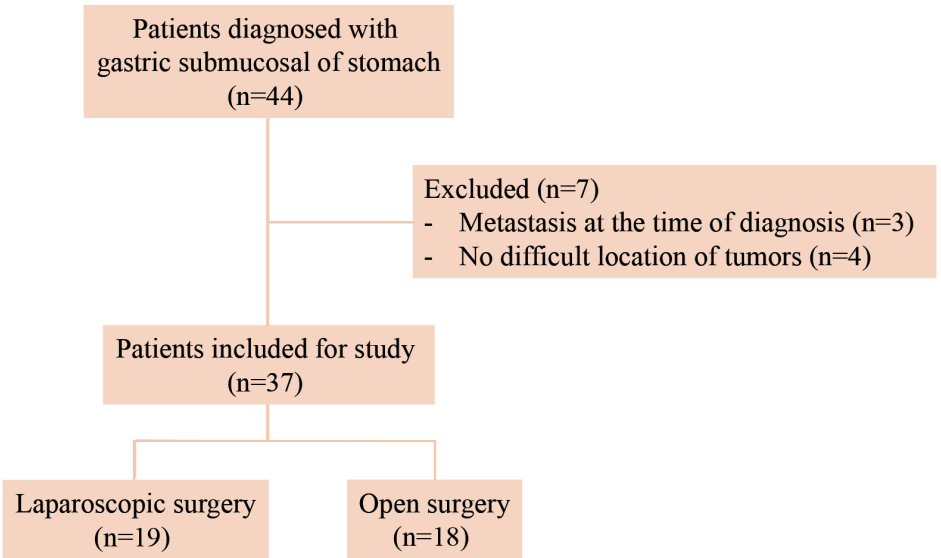

Figure 1 Flow chart diagram of patients

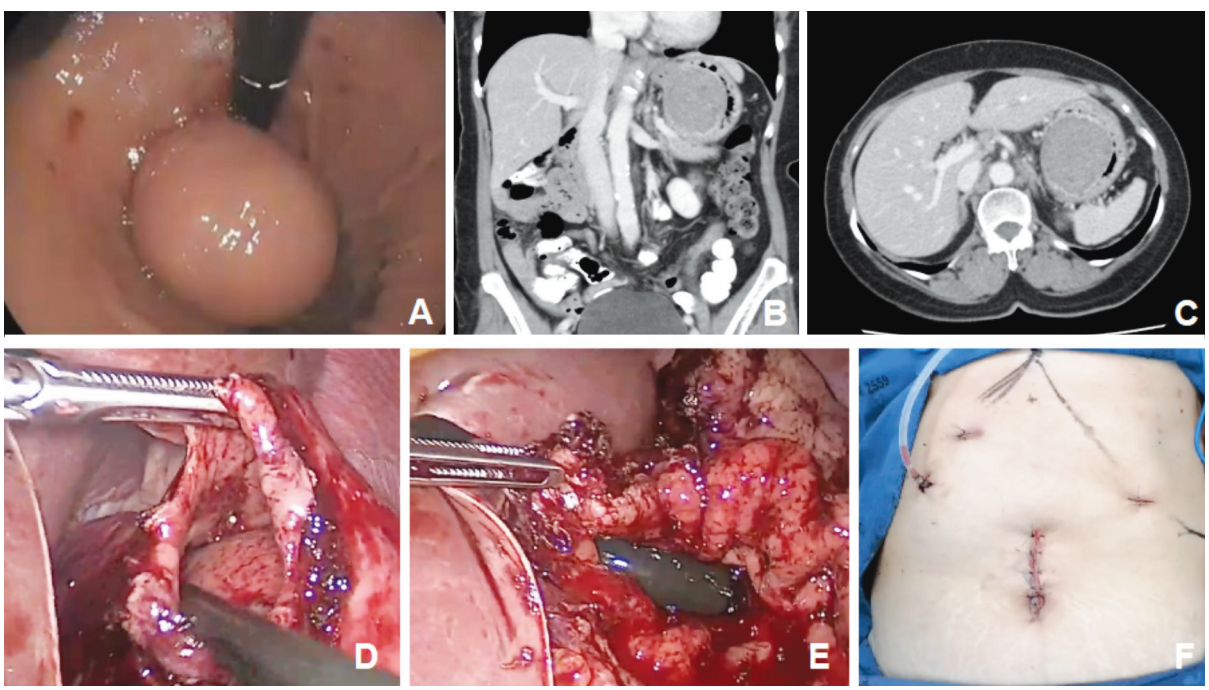

Figure 2 Shows a patient presenting with a gastric GIST at the EGJ.

A: Shows the endoscopic findings of a submucosal lesion at the EGJ.

B, C: The CT scan shows a gastric mass at the EGJ.

D, E: Laparoscopic surgery was performed via gastrotomy, and the gastric defect was closed using an intracorporeal manual running suture.

F: Surgical incision following laparoscopic surgery.

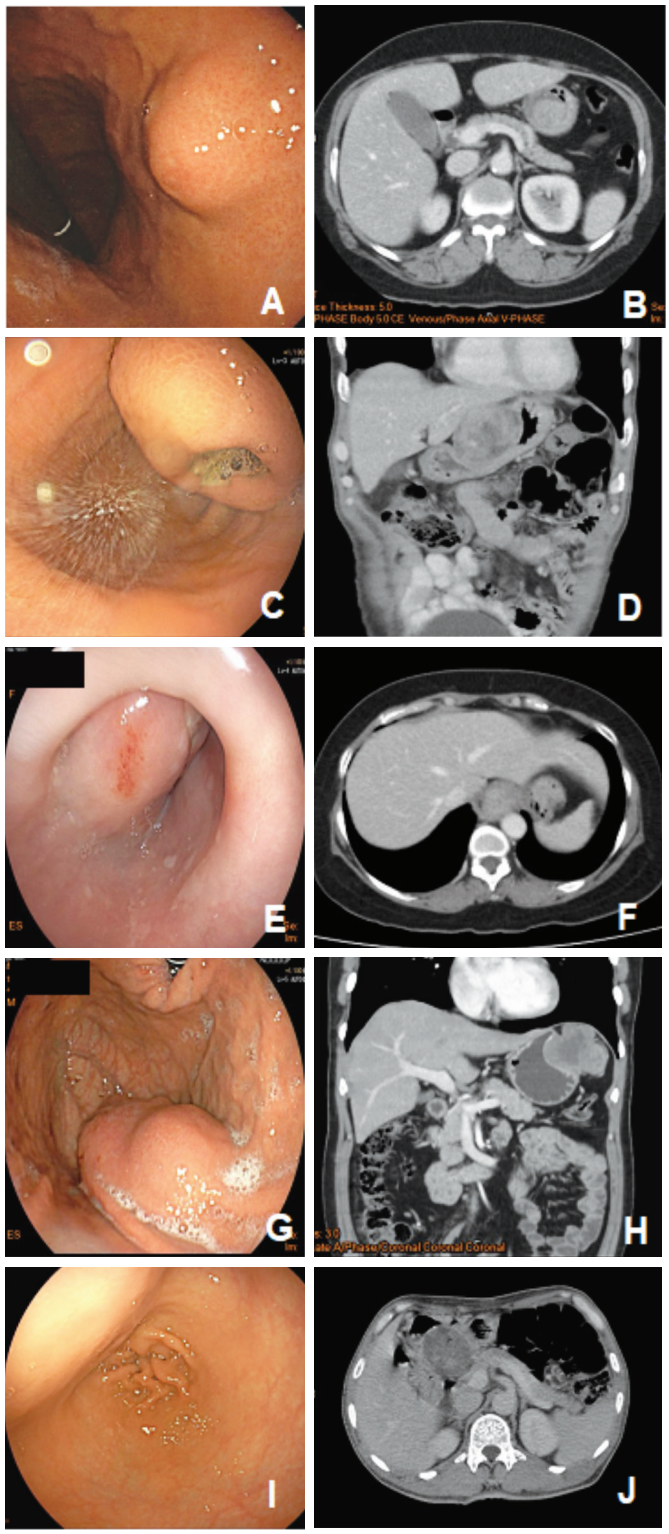

Figure 3 Shows the endoscopic findings and computed tomography (CT) scans of submucosal lesions on the posterior wall of the stomach, lesser curvature, esophagogastric junction (EGJ), cardia, and pyloric ring of the antrum.

A and B: show the submucosal lesion at the posterior wall of the stomach

C and D: show the submucosal lesion at the lesser curvature of the stomach

E and F: show the submucosal lesion at EGJ

G and H: show the submucosal lesion at the gastric cardia

I and J: show the submucosal lesion at the pyloric ring of the antrum

Results

A total of 44 patients were diagnosed with submucosal tumors of the stomach. Seven patients were excluded from the study: three presented with metastasis at the time of diagnosis, and four did not have tumors located in difficult positions within the stomach. Ultimately, 37 patients were included in the study, with 19 patients assigned to the LapS group and 18 patients assigned to the OpenS group. Patient baseline characteristics, including tumor locations, types of surgery, and postoperative outcomes, are presented in Table 1. There were no statistically significant differences in age, sex, or BMI between the two groups. However, the tumors located at the lesser curvature of the stomach were significantly more prevalent in the OpenS group compared to the LapS group ($p = 0.044$). Partial gastric resection was performed more frequently in the LapS group compared to the OpenS group ($p = 0.004$), while no differences were noted for other procedures. The LapS group demonstrated better postoperative outcomes, including reduced blood loss, earlier initiation of feeding, earlier passage of flatus, and a shorter duration of hospital stay. However, the operative time was shorter in the OpenS group compared to the LapS group. No complications were observed in either group.

Table 1 Baseline characteristics of patients, location of tumors, surgery types, and post-operative outcome

Factors	Total n = 37 (%)	LapS n = 19 (%)	OpenS n =18 (%)	*p*-value
Age (years), mean (± SD)	60.3 (12.3)	58.9 (13.1)	61.7 (11.6)	0.254
Sex				0.219
Male	14 (37.8)	9 (47.4)	5 (27.8)	
Female	23 (62.2)	10 (52.6)	13 (72.2)	
BMI, mean (± SD)	22.1 (3.2)	22.5 (3.3)	21.8 (3.1)	0.254
Locations of tumors				
Esophagogastric junction (EGJ)	5 (13.5)	3 (15.8)	2 (11.1)	0.677
Cardia	8 (21.6)	5 (26.3)	3 (16.7)	0.476
Lesser curvature	9 (24.4)	2 (10.5)	7 (38.9)	0.044
Posterior wall of stomach	7 (18.9)	5 (26.3)	2 (11.1)	0.238
Pyloric ring of the antrum	8 (21.6)	4 (21.1)	4 (22.2)	0.931
Surgery type				
Partial gastric resection	23 (62.2)	16 (84.2)	7 (38.9)	0.004
Proximal gastrectomy	3 (8.1)	0 (0)	3 (16.7)	0.063
Distal gastrectomy	9 (24.3)	3 (15.8)	6 (33.3)	0.214
Total gastrectomy	2 (5.4)	0 (0)	2 (11.1)	0.135
Operative outcomes				
Operative time (minutes, ± SD)	147.2 (54.8)	170.8 (56.4)	122.2 (41.5)	0.002
Blood loss (ml. ± SD)	154.6 (210.3)	50 (55.6)	265 (252.9)	< 0.001
Day feeding initiated (day ± SD)	1.9 (1.2)	1.1 (0.2)	2.7 (1.2)	< 0.001
First passage of flatus (day ± SD)	2.8 (0.9)	2.3 (0.6)	3.3 (0.8)	< 0.001
Duration of hospital stay (day ± SD)	7.4 (2.7)	5.6 (1.4)	9.4 (2.5)	< 0.001

SD: standard deviation; BMI: body mass index

Table 2 presents tumor characteristics and systemic treatments. Tumor size and the incidence of tumor rupture were significantly higher in the OpenS group compared to the LapS group ($p = 0.012$ and $p = 0.030$, respectively). However, large tumors, specifically those measuring approximately 10 cm (greater than 9 cm), were analyzed to evaluate the clinical outcomes and the challenges associated with both surgical procedures. No statistically significant difference was observed between the two procedures ($p = 0.310$).

Table 2 Tumor characteristics and systemic treatment

Factors	Total n = 37 (%)	LapS n = 19 (%)	OpenS n = 18 (%)	*p*-value
Size of tumor (cm., ± SD)	6.9 (4.1)	5.5 (1.8)	8.5 (5.3)	0.012
Mitotic count (HPF, ± SD)	8.7 (12.4)	6.9 (10.9)	10.6 (13.8)	0.191
Tumor rupture	4 (10.8)	0 (0)	4 (22.2)	0.030
LVI	1 (2.7)	1 (5.3)	0 (0)	0.324
Metastasis	6 (16.2)	2 (10.5)	4 (22.2)	0.335
Lung	2 (5.4)	0 (0)	2 (11.1)	0.135
Liver	4 (10.8)	2 (11.5)	2 (11.1)	0.954
Neoadjuvant imatinib	3 (8.1)	1 (5.3)	2 (11.1)	0.515
Adjuvant imatinib	11 (29.7)	6 (31.6)	5 (27.8)	0.800

SD: standard deviation; HPF: high-power fields; LVI: lymphovascular invasion

Table 3 The risk of recurrence is determined by the NIH consensus classification system

Factors	Total n = 37 (%)	LapS n = 19 (%)	OpenS n = 18 (%)	*p*-value
Risk category				
Low	15 (40.5)	10 (52.7)	5 (27.8)	0.124
Intermediate	8 (21.6)	5 (26.3)	3 (16.7)	0.476
High	14 (37.9)	4 (21.1)	10 (55.5)	0.031

The risk of recurrence was determined using the NIH consensus classification, as presented in Table 3. A higher proportion of patients in the OpenS group were categorized as high risk for recurrence compared to the LapS group, while no differences were observed in the low and intermediate risk categories between the two groups.

The median follow-up time was 19 months. The median survival analysis was not reached in either group. The survival rate in the LapS group was 89.5%, compared to 77.8% in the OpenS group. No significant difference in survival analysis was observed between the two groups, with a hazard ratio (HR) of 0.54, 95% CI: 0.09-2.98, $p = 0.482$. No local recurrences were detected in either group (Figure 4).

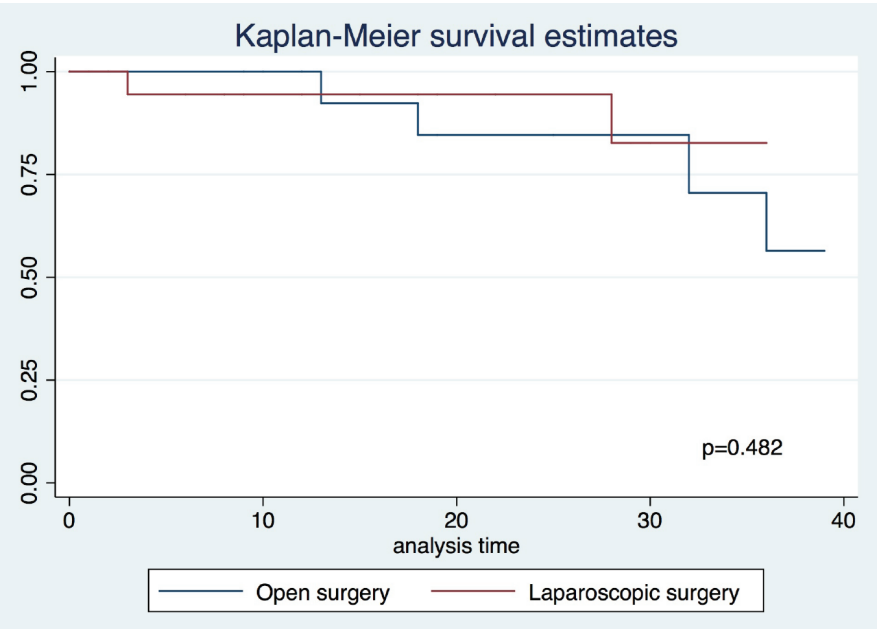

Figure 4 Kaplan-Meier graph shows survival analysis between open and laparoscopic surgery.

Subgroup analysis was performed by risk category based on the surgery type. Median survival was not reached in the LapS group, including the low, intermediate, and high-risk groups, as well as in the OpenS group with the low-risk category. In the OpenS group, the median survival for the intermediate and high-risk categories was 36 and 32 months, respectively. The Log-Rank test for subgroup analysis of survival between Open and laparoscopic surgery by risk category (low, intermediate, and high) showed no statistically significant results, with *p*-values of 0.119, 0.294, and 0.406, respectively (Figure 5).

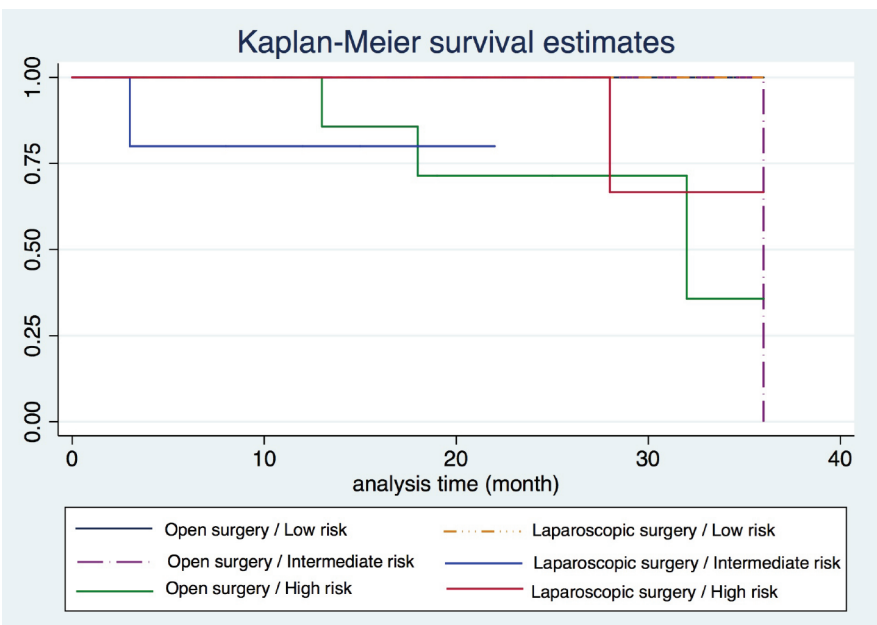

Figure 5 A Kaplan-Meier graph showing subgroup survival analysis between open and laparoscopic surgery, stratified by the risk of recurrence as determined by the NIH consensus classification system.

Discussion

The most common location for submucosal tumors was the stomach, with GISTs being the most prevalent submucosal lesions in this area.[12-14] Surgical resection with clear margins and avoidance of tumor rupture is the recommended treatment for curative intent. Meticulous dissection to prevent tearing of the pseudocapsule is critical in reducing the risk of recurrence and preventing peritoneal seeding.[14-16] In this study, all submucosal tumors of the stomach were diagnosed as gastric GISTs. Laparoscopic surgery is increasingly being utilized for the resection of gastric GIST following the same principles as open surgery. Prior studies comparing laparoscopic surgery with open surgery have shown comparable outcomes, with no significant differences in survival rates, local recurrence, or complications.[4,5] Several treatment guidelines recommend laparoscopic surgery, particularly for tumors located in areas amenable to this technique, such as the greater curvature or the anterior portion of the stomach.[6-8] Karakousis GC et al. reported that laparoscopic surgery for gastric gastrointestinal stromal tumors (GISTs) is appropriate for tumors smaller than 8 cm.[17] Piessen G et al. compared laparoscopic surgery with open surgery for gastric gastrointestinal stromal tumors (GISTs) and found that the outcomes in terms of survival and complications were similar.[18] Some studies suggest that laparoscopic surgery should be performed in favorable tumor locations, such as the anterior gastric wall or lesser curvature of the stomach. Tumors larger than 10 cm are generally not recommended for this approach due to the increased risk of tumor rupture.[15] In this study, tumor size was found to be significantly larger in the OpenS group compared to the LapS group; however, the tumors in both groups were smaller than 10 cm. This suggests that both laparoscopic and open-surgical approaches are suitable for managing these tumors. Tumor locations were classified as follows: esophagogastric junction (EGJ), cardia, lesser curvature, posterior wall of the stomach, and pyloric ring of the antrum. Although the study was prospective, tumors located in the lesser curvature were more frequently managed with open surgery than with laparoscopic surgery. Conversely, partial gastric resection was significantly more common in the laparoscopic surgery group. The risk of recurrence was higher in the OpenS group compared to the LapS group, encompassing factors such as tumor size, incidents of tumor rupture, and high-risk classification, according to the NIH consensus. These data suggest that patients at risk of tumor recurrence, particularly those with larger tumors or unfavorable tumor locations, should undergo open surgery to minimize the risk of recurrence. However, surgery outcomes were more favorable in the LapS group, including reduced blood loss, earlier initiation of feeding, earlier passage of flatus, and a shorter duration of hospital stay, all of which were statistically significant. Huang CM et al.[10] compared patients undergoing laparoscopic and open surgery for gastric GISTs in easily accessible and challenging surgical locations. The findings revealed no significant differences between the laparoscopic and open surgery, irrespective of the tumor's location. Laparoscopic surgery significantly reduced the duration of the operation, minimized intraoperative bleeding, and decreased the time to the first passage of flatus as well as the time to initiate a fluid diet. Additionally, it lowered the rate of postoperative complications, indicating that laparoscopic procedures can offer patients superior short-term outcomes compared to open surgery.

The survival rate in this study was slightly lower than that reported in previous studies, most of which included patients with both favorable and unfavorable tumor locations, as well as those who received adjuvant imatinib according to the NIH consensus classification system.[10,19,20] In contrast, this study focused exclusively on tumors located in challenging areas of the stomach, and the majority of patients did not receive adjuvant imatinib treatment. Nonetheless, there was no significant difference in survival between the LapS and the OpenS groups.

Conclusion

For submucosal tumors located in challenging areas of the stomach, laparoscopic surgery offers advantages in terms of minimally invasive techniques and surgical outcomes compared to open surgery. Ultimately, the choice between laparoscopic and open surgery depends on the surgeon's experience, the risk of tumor recurrence associated with specific tumor locations, and the need to avoid tumor rupture during surgery. Nonetheless, both techniques result in similar short-term oncologic outcomes.

Limitation of study

Although gastric submucosal tumors are rare, the sample size in this study is limited but adequate for statistical analysis. This investigation was conducted at a single center; however, future research could be expanded to a multicenter framework involving a larger patient cohort and designed as a randomized controlled trial with long-term follow-up to detect oncologic outcomes.

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Original Article

Risk Factors Affecting Complications in Patients with Gallbladder Inflammation Due to Gallstones Following Initial Antibiotic Treatment

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Abstract

Background: In 2019, the COVID-19 pandemic limited the timing of surgery in patients with acute calculous cholecystitis (AC), resulting in delayed laparoscopic cholecystectomy (LC) operations for more than three months, according to the FSSA Clinical guide to surgical prioritization during the Coronavirus pandemic, 2022.

Objective: This study aimed to identify the risk factors for gallstone-related complications, including recurrent cholecystitis, cholecystitis with cholangitis, and CBD stone-related complications, within 90 days after conservative treatment for AC.

Materials and Methods: From June 2019 to June 2021, retrospective medical records from a single-center tertiary care hospital were reviewed. A total of 184 patients, aged over 18 years, who were admitted with AC grade I-II according to the Tokyo Guidelines 2018 and treated with conservative therapy were included. Patients with severe cholecystitis, cholangitis, or choledocholithiasis were excluded. Data including age, sex, comorbidities, laboratory results, and imaging findings were collected. Multivariable binary regression was performed to identify risk factors for gallstone-related complications, with results presented as risk ratios (RR) and 95% confidence intervals. Gallstone-related complications were defined as recurrent cholecystitis, cholangitis, choledocholithiasis, and pancreatitis.

Results: Among the 184 patients, thirty-two (17.4%) experienced gallstone-related complications within 90 days after receiving conservation treatment for AC. The risk factors identified were white blood cell counts ≥ 12,000 cells/mL (Adj. RR 2.63, 95% CI 1.35-5.14, $p = 0.005$), gallbladder wall thickness ≥ 10 mm (Adj. RR 3.01, 95% CI 2.01-4.50, $p < 0.001$), and serum bicarbonate < 22 mmol/L (Adj. RR 0.38, 95% CI 0.17-0.87, $p = 0.022$). The model predicted gallstone-related complications with an accuracy of 67% (area under the ROC curve = 0.669).

Conclusion: In the context of delayed surgery for acute cholecystitis, patients with a white blood cell count of less than 12,000 cells/mL, gallbladder wall thickness of less than 10 mm, and bicarbonate levels of 22 mmol/L or higher may be suitable candidates for delayed laparoscopic cholecystectomy. However, concerns regarding gallstone-related complications remain. Definitive treatment should be provided based on the available clinical circumstances.

Keywords: Acute calculous cholecystitis, COVID-19, Gallstones, Laparoscopic cholecystectomy

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Introduction

Acute cholecystitis is associated with gallstones in 95% of cases. Treatment for cholecystitis includes antibiotics and cholecystectomy, which can be performed either as an open surgery or laparoscopic cholecystectomy (LC). Laparoscopic cholecystectomy is the primary treatment method.[1] according to the Tokyo Guidelines 2018. The treatment of acute cholecystitis depends on the severity of the inflammation. The appropriate timing for surgery is divided into early LC, performed within 72 hours of inflammation, and delayed LC, conducted 6-10 weeks after the inflammation.[2]

During the COVID-19 pandemic, surgeries have been delayed more than usual. According to the guidelines of the Federation of Surgical Specialty Associations (FSSA) in the UK, cholecystectomy after acute cholecystitis is categorized as non-urgent surgery, and it is recommended to postpone the procedure for more than 90 days.[3]

The rate of hospital readmission due to complications from gallstones while waiting for laparoscopic cholecystectomy was found to be 28.5%, according to the research by Cheruvu CV, et al. Complications include cholecystitis, gallbladder perforation, cholangitis, and pancreatitis.[4]

The important consequences of developing complications after conservative treatment of acute cholecystitis are increased hospital stays, increased medical costs, and increased morbidity or mortality.[4]

According to research by Loozen C, et al., surgical treatment was successful in 87% of patients with gallbladder disease and 96% of patients with mild gallbladder disease, with a recurrence rate of 20%.[5] The recurrence rate among patients treated with antibiotics alone, with an average age of 62.2 years, was 13.7%. The recurrence rate in patients who received only antibiotic treatment was low.[6] However, in elderly patients with an average age of 80.4 ± 7.2 years, the recurrence rate was 58%, with a possibility of recurrence within two years.[7]

Research Objectives

This research aims to explore the risk factors contributing to gallstone complications and the complications arising from gallstones following cholecystitis after conservative treatment, including recurrent cholecystitis, cholecystitis with cholangitis, and CBD stone-related complications over 90 days.

Materials and Methods

Research Design and Sample Group

The research design was a retrospective cohort study. It involved selecting patients with mild to moderate acute cholecystitis (Grade I-II) who were admitted for inpatient treatment at Nakornping Hospital between June 1, 2019, and June 1, 2021, as shown in Figure 1.

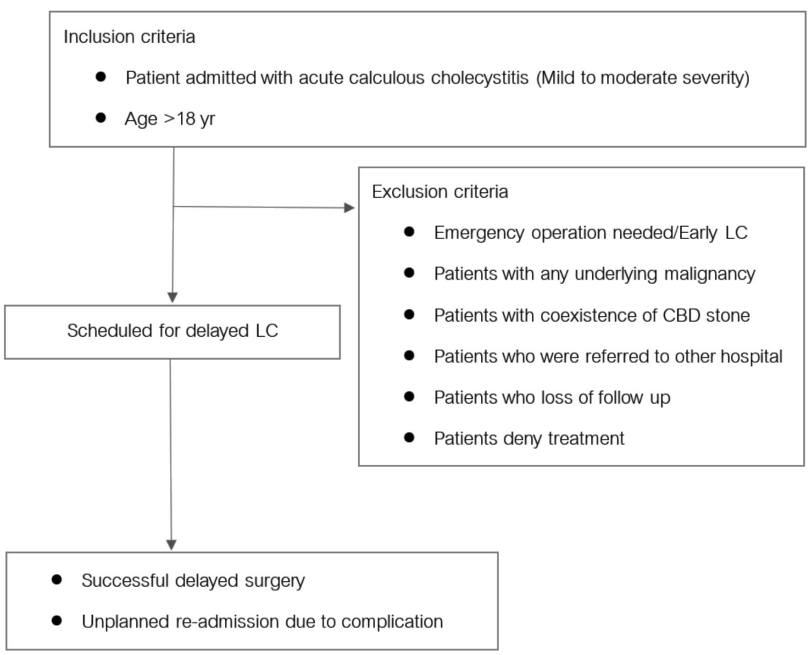

Figure 1 Research implementation plan

Research Location: Nakornping Hospital

Inclusion Criteria

1. Acute calculous cholecystitis
2. Age over 18 years.
3. Patients diagnosed with mild to moderate acute cholecystitis according to the Tokyo Guidelines 2018.
4. Patients scheduled for cholecystectomy at Nakornping Hospital.

Exclusion Criteria

1. Patients with a pre-existing cancer diagnosis.
2. Patients with common bile duct stones identified during initial treatment.
3. Patients referred back to other hospitals.
4. Patients who cannot be followed up.
5. Patients who refused treatment.

The research design was a retrospective cohort study. We included patients over 18 years old diagnosed with mild to moderate acute calculous cholecystitis[8] admitted to the Surgical department, Nakornping Hospital, Chiangmai, during the COVID-19 pandemic between 1 June 2019 and 1 June 2021. After admission, intravenous antibiotics; ceftriazone 2 grams intravenous once daily; metronidazole 500 mg intravenous every 8 hours for 7 - 10 days; then switch to oral antibiotics for 7 days; and general supportive care was given to all patients as a standard treatment. Response to aforementioned treatments was reevaluated on a daily basis. Patients could be discharged when clinical improvement based on stable vital signs, ameliorated abdominal signs, and symptoms were observed. Then, patients would be scheduled for elective LC in the next six to eight weeks. However, the schedules might be extended due to limited resources during the pandemic.

We excluded patients who underwent early LC, as it is also considered to be the first-line treatment for cases of mild form acute calculous cholecystitis.[8] We also excluded patients with pre-existing cancer, coexisting bile duct stones, LC done in other hospitals, loss follow-up, and patients who denied treatment protocol as listed above.

Sample size estimation and key measurements

Based on the calculation for sample size, a total of 162 patients is required when setting α (Type I error) at 0.05 and β (Type II error) at 0.2. Using the calculation for two independent proportions based on gallbladder wall thickness, the minimum sample size required is 162 patients. According to the research by T. Miyata et al. (2021),[9] factors affecting the occurrence of complications include age, white blood cell count (> 13,500/ul), C-reactive protein (CRP), serum albumin level, and gallbladder wall thickness (≥ 5 mm).

Proportion in group 1 (P1) = 0.45, proportion in group 2 (P2) = 0.189, ratio (r) = 5.0, (with ratio 1:5), the sample size for group 1 = 27, and group 2 = 135, adding 20% loss follow-up or completed that sample size for group 1 was 32 and group 2 was 162.

Data analysis

Comparisons of general clinical characteristics are analyzed using Student's *t*-test. Group comparisons and continuous variable cases are generalized linear models: extension to the binomial family resulted in risk ratio; we used risk ratio used to causal relationship analysis to explain the probability of events occurring in the exposed group over the non-exposed group analyzed using Fisher's exact test. Predictive complication factors are analyzed using univariable binary regression, adjusting for confounding factors using multivariable binary regression. The results are presented as adjusted risk ratios, with statistical significance set at 0.05. Data analysis is performed using STATA version 14.0.

Results

From a review of medical records for patients with Grade I-II acute cholecystitis who were admitted to Nakornping Hospital between June 1, 2019, and June 1, 2021, a total of 339 patients met the criteria. After excluding 155 patients who did not meet the criteria, 184 patients were included in the study. Among these, 152 patients were scheduled for surgery as planned, and 32 patients required hospitalization due to complications from gallstones, as shown in Figure 2.

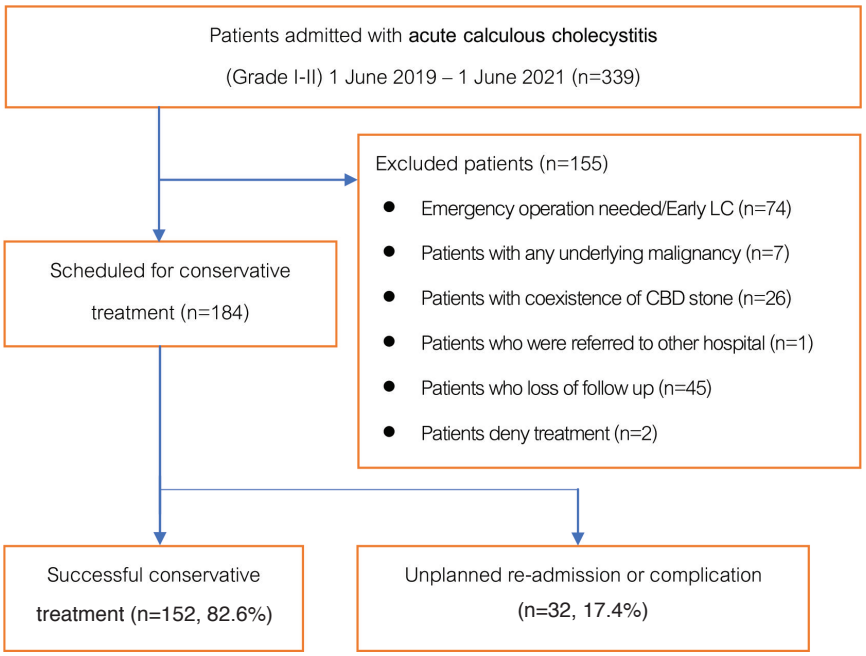

Figure 2 Research implementation plan

Basic Clinical Characteristics

The average age of the patients who were able to undergo surgery as scheduled was 57.08 ± 16.19 years. The average age of the patients who experienced complications before surgery was 56.66 ± 20.72 years. As shown in Table 1, there were no significant differences between the two groups in terms of age, sex, weight, height, body mass index, or pre-existing conditions.

Table 1 Comparison of basic patient characteristics

Patient Characteristics	Gallstone-related complications		
	Yes n = 32, (%)	No n = 152, (%)	*p*-value
Age (years), mean ± SD	56.66 ± 20.72	57.08 ± 16.19	0.701
Age			0.593
< 60	19 (59.38)	78 (51.32)	
≥ 60	13 (40.62)	74 (48.68)	
Sex			0.515
Male	15 (48.88)	69 (45.39)	
Female	17 (53.12)	83 (54.61)	
Weight (kg), mean ± SD	64.72 ± 19.75	64.57 ± 14.51	0.956
Height (metre)	1.61 ± 0.95	1.60 ± 0.95	0.957
BMI (kg/m^2)	24.77 ± 5.26	24.93 ± 5.26	0.874
Diabetes mellitus (DM)			0.210
Yes	3 (9.38)	31 (20.39)	
No	29 (90.62)	121 (79.61)	
Hypertension (HTN)			0.843
Yes	12 (37.50)	63 (41.45)	
No	20 (62.50)	89 (58.55)	
Thalassemia			0.580
Yes	1 (3.12)	7 (4.61)	
No	31 (96.88)	145 (95.39)	
Chronic kidney disease (CKD) stage 3-5			0.378
Yes	2 (6.25)	21 (13.82)	
No	30 (93.75)	131 (86.18)	

Primary Outcome

Single factors that significantly affect the occurrence of complications from gallstones include White Blood Cells (WBC) and Lymphocytes. In the group with WBC ≥ 12,000 cells/ml, 65.63% (21 patients) experienced complications, compared to 34.38% (11 patients) in the WBC < 12,000 cells/ml group, with a statistically significant difference ($p = 0.020$). Additionally, the average Lymphocyte percentage in the group with complications was 11.48 ± 7.82%, compared to 15.56 ± 10.47% in the group without complications ($p = 0.038$),

An imaging study measured the GB wall thickness by ultrasound in 142 patients and by CT scan in 42 patients, as shown in Table 2.

Table 2 Results of the primary outcome

Factors	Gallstone-related complications (n =184)		
	Yes, n = 32 Mean ± SD	No, n = 152 Mean ± SD	*p*-value
Clinical symptoms			
Body temperature (°C)	36.97 ± 0.67	37.02 ± 0.75	0.727
Onset of symptoms (hours)	34.71 ± 31.82	42.90 ± 39.01	0.268
Laboratory studies			
Hb (g/dL)	13.26 ± 2.25	12.89 ± 2.02	0.357
WBC (cells/μL), (%)			0.020
< 12,000	11 (34.38)	87 (57.24)	
≥ 12000	21 (65.63)	65 (42.76)	
Neutrophil	81.94 ± 10.68	77.62 ± 12.30	0.067
Lymphocyte	11.48 ± 7.82	15.56 ± 10.47	0.038
Plt (/uL)	264,719 ± 63,652	261,069 ± 82,596	0.828
Laboratory studies			
BUN (mg/dL)	12.37 ± 4.50	13.97 ± 9.32	0.383
Cr (mg/dL)	0.94 ± 0.29	1.11 ± 1.36	0.558
Sodium (mmol/L)	138.13 ± 3.19	137.41 ± 3.20	0.228
< 140 n, (%)	23 (76.67)	132 (85.71)	
≥ 140 n, (%)	7 (23.33)	22 (14.29)	
Chloride (mmol/L)	103.91 ± 4.38	103.80 ± 4.20	0.894
Bicarbonate (mmol/L)			0.095
< 22 n, (%)	6 (20.00)	57 (37.01)	
22-28 n, (%)	23 (76.67)	86 (55.85)	
> 28 n, (%)	1 (3.33)	11 (7.14)	
Potassium (mmol/L)	3.75 ± 0.39	3.85 ± 0.50	0.289
Albumin (g/dL)	4.02 ± 0.60	3.95 ± 0.56	0.256
Globulin (g/dL)	3.31 ± 0.54	3.25 ± 0.57	0.588
AST (U/L)	100.17 ± 177.54	86.45 ± 187.40	0.731
ALT (U/L)	75 ± 110.68	64.35 ± 107.93	0.642
ALP (U/L)	122.53 ± 90.05	109.48 ± 67.92	0.325
Total bilirubin (mg/dL)	1.35 ± 1.39	1.38 ± 2.67	0.961
Direct bilirubin (mg/dL)	0.79 ± 1.05	0.82 ± 2.05	0.941
Imaging findings			
Gallbladder (GB) wall thickness			0.092
< 10mm n, (%)	27 (87.10)	146 (95.42)	
≥ 10mm n, (%)	4 (12.90)	7 (4.58)	
Diagnosis by CT n, (%)			0.589
Yes n, (%)	7 (22.58)	35 (22.88)	
No n, (%)	24 (77.42)	118 (77.12)	
Gallstones			0.419
Few (1-4) n, (%)	15 (50.00)	92 (59.74)	
Many (≥ 5) n, (%)	15 (50.00)	62 (40.26)	
Severity in Tokyo guidelines			0.541
Grade I n, (%)	23 (71.88)	99 (65.13)	
Grade II n, (%)	9 (28.12)	53 (34.87)	

When factors with a *p*-value < 0.2 were analyzed using Univariable analysis to calculate the risk ratio, statistically significant factors were identified. For WBC ≥ 12,000 cells/ml, the risk ratio was 1.53 (1.12-2.10) with a p-value of 0.023, and for Lymphocytes, the risk ratio was 0.96 (0.92-1.00) with a *p*-value of 0.038, as shown in Table 3.

Table 3 Risk ratio of key variables from univariable analysis

Univariable analysis	Risk ratio	*p*-value
WBC ≥ 12000 cells/μL	1.53 (1.12-2.10)	0.023
Neutrophil	1.03 (1.00-1.06)	0.067
Lymphocyte	0.96 (0.92-1.00)	0.038
Bicarbonate < 22 mmol/L	0.45 (0.19-1.03)	0.600
GB wall thickness ≥ 10 mm	2.22 (0.95-5.22)	0.067

When these factors were analyzed for Adjusted Risk Ratio (Adj. Risk Ratio) using Multivariable binary regression, factors significantly increasing the risk of complications included WBC ≥ 12,000 cells/ml with an adjusted risk ratio of 2.63 (1.35-5.14) and a *p*-value of 0.005, and Gallbladder wall thickness ≥ 10 mm with an adjusted risk ratio of 3.01 (2.01-4.50) and a *p*-value of < 0.001. Conversely, a factor that reduced the risk of complications was Bicarbonate < 22 mmol/L, with an adjusted risk ratio of 0.38 (0.17-0.87) and a *p*-value of 0.022, as shown in Table 4.

Table 4 Adjusted risk ratio of key variables from multivariable analysis

Multivariable analysis	Adjusted risk ratio	*p*-value
WBC ≥ 12000 cells/μL	2.63 (1.35-5.14)	0.005
GB wall thickness ≥ 10 mm	3.01 (2.01-4.50)	< 0.001
Bicarbonate < 22 mmol/L	0.38 (0.17-0.87)	0.022

Secondary Outcome

Among the total of 184 patients in the study, 32 patients (17.4%) experienced complications. These were categorized as follows: recurrent cholecystitis in 10 patients (31.25%), cholecystitis with cholangitis in 4 patients (12.50%), and CBD stone-related complications in 18 patients (56.25%), as shown in Table 5.

Table 5 Results of the secondary outcome

Gallstone-related complication ≤ 90 days	Number of patients n = 32 (%)
Recurrent cholecystitis	10 (31.25)
Cholecystitis with cholangitis	4 (12.50)
CBD stone-related complications	
Cholangitis	6 (18.75)
CBD stone	8 (25.00)
Gallstone pancreatitis	4 (12.50)

Discussion

Acute calculous cholecystitis is one of the most common acute abdomen conditions. Tokyo Guidelines 2018 recommends early LC as the first line treatment for cases of mild form acute calculous cholecystitis, while in moderate form, it can also be managed with intravenous antibiotics and general supportive care, followed with elective LC. Unfortunately, some patients develop gallstone-related complications while waiting for the surgery.

Miyata, et al. found that 20 out of 168 patients with moderate and severe (grade II and III) acute calculous cholecystitis developed acute cholangitis and/or cholecystitis while waiting for surgery. Pre-operative parameters were analyzed, including white blood cell counts, C-reactive protein levels, albumin levels, gallbladder wall thickening (> 5 mm), incarcerated gallbladder neck stones, and peri gallbladder abscess. Compared with our study, similar results are observed, such as white blood cell counts (> 13,500/mL and ≥ 12,000/mL, respectively) and gallbladder wall thickening (> 5mm and > 10 mm, respectively) associated with increased risk of complication while waiting for surgery.

Several studies also demonstrated factors affecting the risk of complications while waiting for surgery. Barak, et al. showed the factors that affected the failure of conservative treatment of AC were age > 70 years, and DM distended gallbladder > 5 cm.[9]

According to the guidelines, elective LC should be scheduled 6-10 weeks after the attack. Our study demonstrates that, in order to avoid gallstone-related complications while waiting for the surgery, patients with WBC ≥ 12,000/ml, gallbladder wall thickness ≥ 10 mm, and bicarbonate > 22 mmol/L should be considered to be the first priority group, and operative scheduled should not be postponed.

However, this study has limitations due to the inability to collect additional data on C-reactive protein, stone incarceration, and lactic acid. Moreover, the study expresses moderate prediction performance, with a ROC of 67% (Figure 3). Therefore, further randomized controlled trials are recommended for additional, comprehensive data to enhance the accuracy of predictive parameters.

In this study, WBC ≥ 12,000 cells/ml, Gallbladder wall thickness, and Bicarbonate < 22 mmol/L were identified as factors that increase the risk of complications. Compared to previous research, the factors that affected the failure of Conservative Treatment of AC were age > 70 years and DM distended gallbladder > 5 cm.[10] Among those treated with antibiotics for acute cholecystitis (AC), the recurrence rate was 13.7, with a higher recurrence rate within 100 days after AC.[6]

This study is a retrospective cohort study, which avoids selection bias but has limitations due to the inability to collect additional data such as C-reactive protein, stone incarceration, and lactic acid. Moreover, the study had only moderate prediction performance, with an ROC of 67%. Therefore, further research using randomized controlled trials is recommended to include additional data and enhance predictive accuracy, as shown in Figure 3.

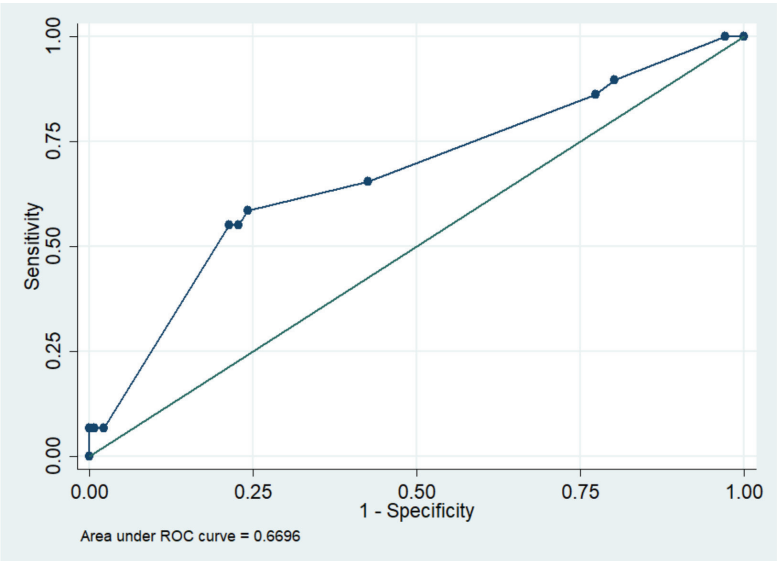

Figure 3 Receiver operating characteristic curve (ROC) derived from the post-estimation probability of gallstone-related complications. The Y-axis shows fractions of true positives, while the X-axis demonstrates false positives of the correspondent prediction from multivariable analysis.

This study found that the factors associated with the above studies were persistently elevated WBC (> 15,000) and gallbladder wall thickening, indicating severe AC inflammation, affecting AC treatment; therefore, follow-up should be performed in this group. However, in cases where surgical limitations arise, patients with risk factors such as WBC ≥ 12,000 cells/ml, Gallbladder wall thickness ≥ 10 mm, and Bicarbonate < 22 mmol/L may benefit from earlier surgery compared to those without risk factors, potentially reducing the likelihood of complications.

Conclusion

In the context of delayed surgery for acute cholecystitis, patients with a white blood cell count of less than 12,000 cells/mL, gallbladder wall thickness of less than 10 mm, and bicarbonate levels of 22 mmol/L or higher may be suitable candidates for delayed laparoscopic cholecystectomy. However, concerns regarding gallstone-related complications remain. Definitive treatment should be provided based on the available clinical circumstances.

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Case Report

Fungal Necrotizing Fasciitis of the Left Hemiface with Subsequent Temporomandibular Ankylosis and Eyelid Lymphedema: A Case Report

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Abstract A 35-year-old female presented with progressive swelling and necrosis of the left cheek after sustaining maxillofacial trauma due to a motorcycle accident. Intravenous antibiotic was given, and emergency debridement was performed. Tissue culture showed ***Aspergillus flavus complex, Acinetobacter baumannii***, and ***coagulase-negative Staphylococci***, so her antibiotics were adjusted to amphotericin B, cefoperazone-sulbactam, and fosfomycin. After the infection was improved, her left hemifacial defect was covered with a skin graft. One month later, she developed a gradually diminishing mouth opening and progressive swelling of her left eyelid that completely obscured her vision. Left temporomandibular joint (TMJ) ankylosis and eyelid lymphedema were diagnosed. Preoperative investigations were performed, and the staged surgical reconstruction strategy was developed. After removing the scar tissues and releasing ankylosis, reconstruction was performed using an anterolateral thigh (ALT) free flap, which directly contacted the left eyelid to facilitate lymphatic drainage. Early postsurgical mouth-opening rehabilitation was introduced. Her swollen left eyelids significantly improved thereafter, and the patient could open her mouth freely with an interincisal gap of 3.5 cm. The second operation involved contouring of the flap, smile reconstruction with a Tensor Fascia Lata sling, and partial resection of the left eyelids to reestablish her vision. The patient can now eat without difficulty, and she has favorably reintegrated into society with good mental health.

Keywords: Fungal infection, Necrotizing fasciitis, Facial reconstruction, Ankylosis, Lymphedema

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Introduction

Necrotizing fasciitis (NF) presents a rapidly progressing infection that affects the fascial layer and subcutaneous tissues. This condition may arise from idiopathic or secondary causes, such as trauma and skin eruptions, potentially leading to life-threatening conditions.[1] In addition to the rare NF of the face compared to other parts of the body, treatment of NF of the face poses a surgical challenge.[2] Only 29 cases of NF of the face have been reported.[3] Due to the thin nature of the skin and muscles, deeper structures, such as facial nerves, may become involved, and debridement may be unavoidable. The surgeon balances the necessity of thorough surgical debridement with the preservation of functional and aesthetic considerations.[4,5]

Case report

A 35-year-old Thai female sustained a right zygomatic complex fracture and multiple facial wounds in a motorcycle accident. The zygoma was treated with internal fixation using miniplates. All wounds were decontaminated and dressed in standard fashion. The patient was discharged one day after the operation and was scheduled for daily wound dressing.

One week after discharge, she developed cellulitis on her left face. The infection progressed to necrotizing fasciitis, which required prompt surgical debridement (Figure 1). She was admitted, intravenous amoxicillin-clavulanate was given, and emergency debridement was performed. Tissue culture showed *Aspergillus flavus complex*, *coagulase-negative Staphylococci*, and *Acinetobacter baumannii*. The antibiotics were then switched to amphotericin B, sulbactam/cefoperazone, and fosfomycin to cover the identified organisms.

Figure 1 (A) Abrasion wound and contusion at left face at 1-week post-accident. (B, C) Progressive swelling and the development of necrotic tissue with fluffy white cotton wool-like growths at the left side of the face two weeks post-accident. (D) Rapidly progressing necrotizing fasciitis.

She underwent a tracheostomy and 14 serial debridement procedures to remove infection and necrotic tissue. The debridement process resulted in a large soft tissue defect on her left face that involved her left forehead, temporal area, cheek, upper neck, and posterior auricular area. The left parotid gland, muscle of facial expression, and left facial nerve were removed during debridement. After gaining control of the infection, the defect on her left face was temporarily closed using the skin graft, and the patient was referred to our center.

At the first visit, she had thin skin coverage with scar tissue and loss of facial contouring over her left face. She had lymphedema of the left eyelid that completely obstructed the vision of her left eye. She had malocclusion and limited mouth opening with an interincisal distance of 1 cm. She also had left facial palsy with total paralysis (House-Brackmann grade VI). Her body mass index (BMI) was 33.7 kg/m^2 without other underlying disease (Figure 2).

Figure 2 (A-C) Patient photos on the first visit, left eyelid was marked swelling due to lymphatic obstruction. (D) Intraoral examination shows limited mouth opening with an interincisor distance of less than 1 cm and malocclusion.

The two times of stage reconstruction were planned. The first operation included the total excision of the scar tissues and skin grafts, then the release of soft tissue ankylosis around the temporomandibular joint (no bony ankylosis was found) and reconstructing the entire defect with anterolateral thigh (ALT) free flap (The ALT free flap size 21 × 13 cm). The intraoperative results demonstrated an interincisal distance of 3.5 cm, and the patient's malocclusion was improved. The edge of the flap was connected with the raw surface of both the upper and lower eyelids to facilitate lymphatic connection and drainage (Figure 3).

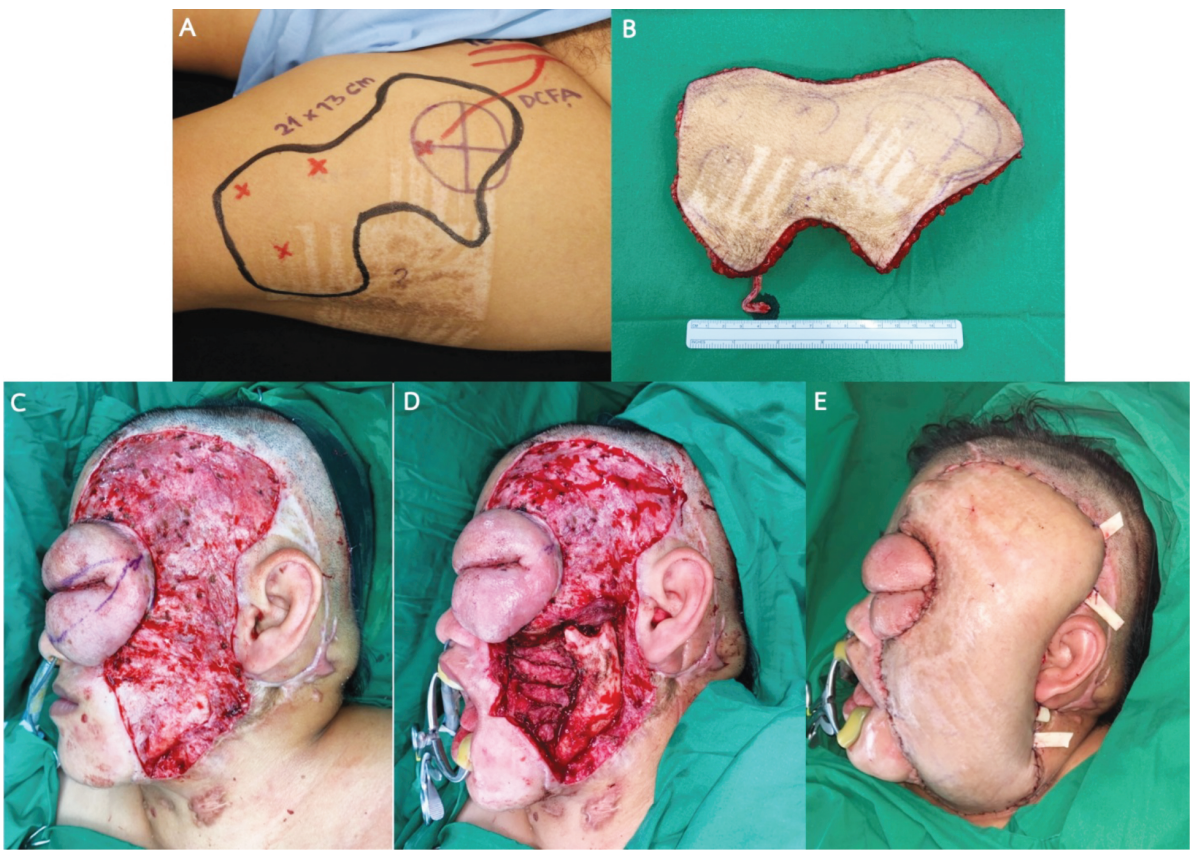

Figure 3 (A) Anterolateral thigh fasciocutaneous flap was designed according to the recipient defect. (B), Flap harvested with the dimension of 20 × 13 cm. (C) Defect after debridement. (D) Temporomandibular joint after exploration and removal of surrounding scar tissue. (E) Immediate postoperative results.

The second operation was performed 6 months later and focused on improving the function and aesthetics. Indocyanine green (ICG) lymphography was performed at the left eyelid, and the results revealed the spontaneous drainage of lymph fluid through the neo-lymphatic connections between the left eyelids and the ALT free flap (Figure 4). The debulking procedure with liposuction and partial resection of excess skin and subcutaneous tissue were performed. Finally, the static smile reconstruction by re-positioning of the left oral commissure was performed by Tensor Fascia Lata (TFL) sling and suture hanging to the periosteum of the left zygoma (Figure 5).

Figure 4 Intraoperative indocyanine green (ICG) lymphography. (A) Immediately after injection. (B) After 10 minutes. (C) After 20 minutes, ICG was spontaneously drained into the reconstructed anterolateral thigh-free flap.

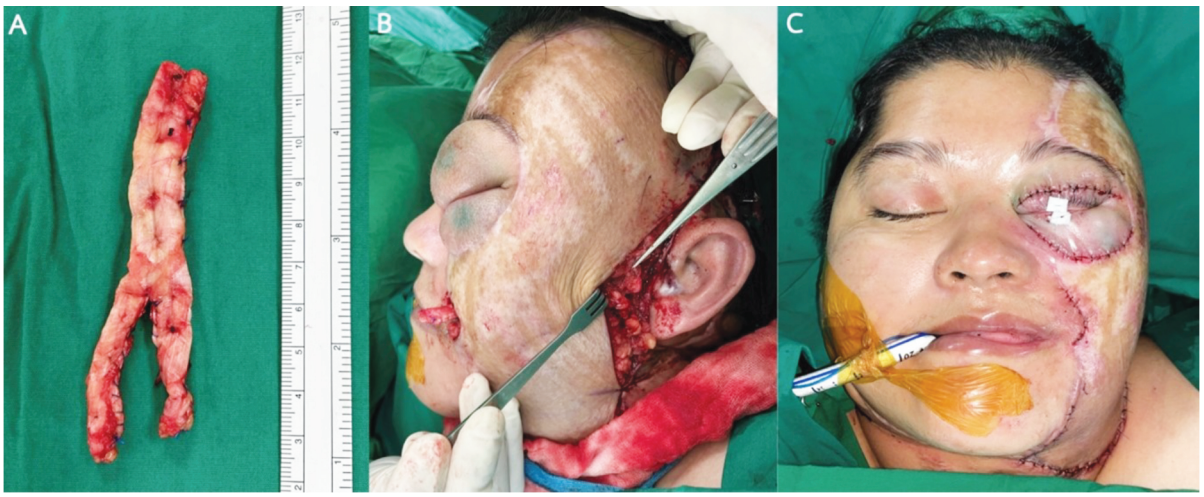

Figure 5 (A) Tensor Fascia Lata (TFL) from the right thigh was prepared. (B) The fascial graft sling was inserted beneath the flap at the left cheek, and the suture hanging for static smile reconstruction. (C) The immediate postoperative outcomes after fascial sling, flap debulking, and partial resection of lymphedema tissue from the left upper and lower eyelids.

At the 1-month postoperative follow-up, the visual field of the patient's left eye was restored, and we plan to correct some ectropion via lateral canthoplasty under local anesthesia in a future procedure (Figure 6).

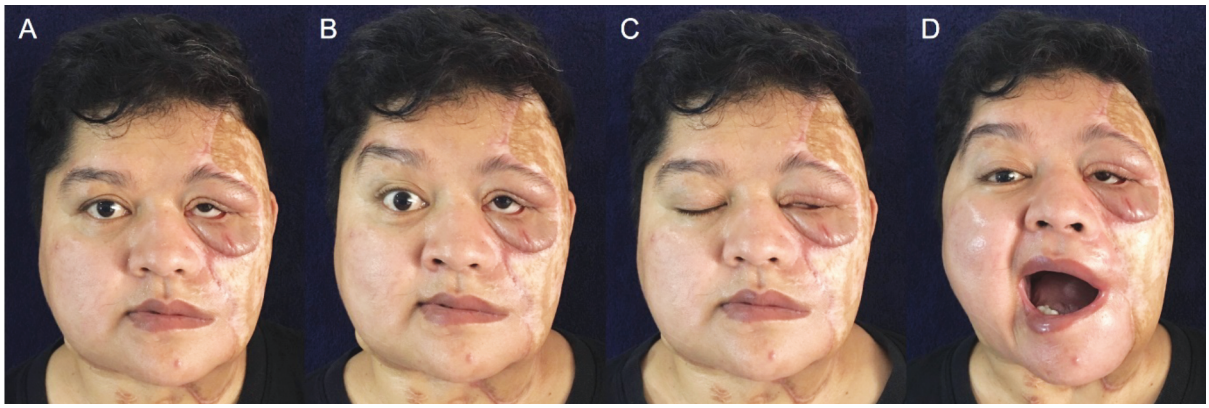

Figure 6 One month after the second operation, (A) Frontal view showed improvement in facial contour. (B, C) The patient can open and close her left eye without difficulty, but she still had some ectropion and scleral show during eye closure. (D) Mouth opening was improved with an interincisal distance of 3.5 cm and good occlusion.

Discussion

Necrotizing fasciitis (NF) of the face is a rare and life-threatening disease.[1] Our patient presented with only an abrasion wound, which later progressed to NF. We found no identifiable predisposing factors, including diabetes, hypertension, or chronic alcohol abuse.[2,6]

The most commonly isolated microorganisms are *Group A Streptococcus, Candida spp.*, and *Enterobacter cloacae*. Polymicrobial infection is more common than monomicrobial infection.[3] Broad-spectrum antibiotics should be given immediately after diagnosis, and adequate surgical debridement should be performed.[7] In this case, tissue culture showed *Aspergillus flavus complex*, *Acinetobacter baumannii*, and *coagulase-negative staphylococci*.

Fungal NF is relatively rare; it may be caused by direct infection by a fungus or as a secondary superimposed infection. A higher prevalence of fungal infection is observed in patients with diabetic mellitus due to decreased neutrophil chemotaxis and phagocytosis.[1,8] Fungal necrotizing fasciitis is characterized by specific signs, including the rapid progression of black tissue necrosis, the formation of cotton wool-like material over the wound, and the absence of clinical response following treatment with broad-spectrum antibiotics. These indicators are crucial in diagnosing and treating this serious condition. A definite diagnosis can be made from tissue culture for fungus and tissue pathology.

Aspergillus flavus, found in soil and outdoor air, is a common cause of fungal infection after trauma.[9] There is a report of NF caused by *A. flavus* in an immunocompromised patient, but this infection in an immunocompetent host has not been previously reported.[10] Amphotericin B is the drug of choice for treating this fungus.[1]

Regarding the outcome of treatment, severe functional deficit and disfigurement of her left hemiface were inevitable. The split-thickness skin graft was employed to cover the entire wound prior to referral temporarily, but the patient developed malocclusion, left TMJ ankylosis, and left eyelid lymphedema. The first stage of the procedure aims to correct the malocclusion and the TMJ ankylosis, to downsize the upper and lower lymphedematous eyelids, and to cover the entire defect with well-vascularized skin and soft tissue.

Concerning facial function and aesthetics, our patient exhibited a diminished left facial expression resulting from multiple aggressive debridements aimed at eradicating the infection and necrotic tissues. Static smile reconstruction with a TFL sling was selected in this case after discussing the pros and cons of each reconstruction technique with the patient.

For left eyelid lymphedema, we managed by creating new lymphatic circulation via a well-vascularized flap. We also partially resected redundant skin and soft tissue. After surgery, our patient can now open her left eye spontaneously, take an oral diet without difficulty, and reintegrate into society with a good mental health status.

Conclusion

Necrotizing fasciitis of the face is a rare and devastating infection. Polymicrobial infection, including fungus, should be suspected. Appropriate surgical debridement should be performed, and proper intravenous antibiotics and antifungals should be given as soon as possible. Wound coverage with subsequent defect reconstruction should be considered after achieving infection control. The well-planned staged reconstruction can yield favorable aesthetic and functional outcomes.

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Conflict of interest

All authors declare no personal or professional conflicts of interest relating to any aspect of this study.

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