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

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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 training who wish to have an outlet for their research endeavors. The Royal College strives to encourage and help develop Thai Surgeons to become competent researchers in all their chosen fields. With an international outlook, The Thai Journal of Surgery welcomes submissions from outside of Thailand as well.

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2. Corporate Author:

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

3. Personal Author(s):

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

4. Editor, Compiler, Chairman as Author:

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6. Agency Publication:

- National Center for Health Statistics. Acute conditions: incidence and associated disability, United States, July 1968-June1969. Rockville. Md.: National Center for Health statistics, 1972. Vital and health statistics. Series 10: Data from the National Health Survey, No. 69: (DHEW publication no. (HSM) 72-1036).

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

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

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

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Editorial

Kaweesak Chittawatanarat, MD, Ph. D

Editor of The Thai Journal of Surgery

Dear Colleagues and Readers,

The landscape of general and specialized surgery continues to balance the necessity of high-acuity emergency interventions with the refinement of elective procedures. These editorial reviews of eight recent studies from diverse surgical fields in this issue highlight how clinical decision-making relies on regional data and precise multi-variable risk analysis.

Strategic Risk Stratification and Surgical Outcomes in Gastrointestinal Malignancies

Gastrointestinal malignancies frequently present a delicate clinical balance between screening efficiency and acute emergency management. On the screening front, Inlao evaluated the diagnostic performance of the Asia-Pacific Colorectal Screening (APCS) risk score and the quantitative Fecal Immunochemical Test (FIT) among 662 patients.[1] While standalone applications of FIT or an APCS score ≥ 4 yielded modest discriminative value (AUROC < 0.60), combining the two modalities improved diagnostic specificity to 79.0%.[1] Crucially, integrating comorbidities like diabetes mellitus and simple laboratory metrics like hematocrit levels yielded a highly robust predictive model (AUROC = 0.86), offering an efficient tool for risk-based colonoscopy referral.[1]

When early detection fails, patients often present with advanced complications such as obstruction or perforation. Orapan conducted a retrospective cohort study comparing emergency and elective resections among 191 patients with colon cancer at Suratthani Hospital.[2] The emergency cohort demonstrated significantly higher comorbidity profiles, a greater necessity for colostomy, and an elevated in-hospital mortality rate (OR 6.8).[2] Long-term surveillance over five years identified bowel perforation and obstruction as independent predictors of worse survival, though adjuvant chemotherapy remained a highly potent protective factor, demonstrating that presentation type carries an intrinsic prognostic burden independent of staging alone.[2]

Even more challenging is the management of ultra-rare gastrointestinal tumors. Tran et al. documented an exceptional case of a 69-year-old female presenting with an acute abdomen secondary to an ileal perforation, combined with a concurrent level III cervical lymph node metastasis from small bowel adenocarcinoma (SBA).[3] This highly aggressive systemic phenotype underscores the diagnostic difficulty posed by deep-seated jejunoileal tumors and highlights the critical role of urgent laparoscopy and immunohistochemistry panels (CK7/EMA positivity with CK20 negativity) in confirming intestinal tumor origin when primary radiologic findings are ambiguous.[3]

Critical Timing and Systemic Burden in Hepatobiliary and Vascular Emergencies.

Optimizing surgical timing remains a foundational debate in acute inflammatory conditions. The disruption of elective healthcare services during the SARS-CoV-2 pandemic provided a unique natural experiment regarding delayed interventions. Alcalá et al. investigated the impact of delayed care by comparing elective laparoscopic cholecystectomies performed before the pandemic (2019) to those delayed until 2021.[4] Delayed surgeries were directly associated with a significant shift in disease severity, resulting in a distinct surge in moderate acute cholecystitis according to the Tokyo Guidelines.[4]

Expanding on this hepatobiliary dilemma, Wiboonkhwan presented a narrative review evaluating early versus delayed laparoscopic cholecystectomy for acute cholecystitis.[5] While early intervention within 72 hours under optimal institutional settings maximizes cost-efficiency and minimizes total hospital stays, real-world data reveal a peak bile duct injury (BDI) rate of up to 2.8% when surgeries are performed during the subacute fibroblastic phase (days 4–7).[5] Consequently, in settings with limited resources or variable surgical volumes, delaying cholecystectomy following conservative management or advanced drainage techniques—such as percutaneous transhepatic gallbladder drainage (PTGBD) or endoscopic ultrasound-guided lumen-apposing metal stents (EUS-LAMS)—serves as a crucial, patient-centered alternative procedure that prioritizes safe cholecystectomy standards.[5]

A parallel imperative for timely clinical intervention and aggressive comorbidity management is evident in peripheral vascular emergencies. Hanaroonsomboon et al. analyzed outcomes in 152 adult patients who underwent open surgical revascularization for Rutherford Class II acute lower-limb ischemia (ALI).[6] The study observed a substantial 17.1% major amputation rate, identifying hypertension, chronic kidney disease, congestive heart failure, sepsis, and a symptom duration exceeding 24 hours as independent risk factors for limb loss.[6] Conversely, the performance of a fasciotomy emerged as an essential, highly protective modifiable aspect of care to mitigate reperfusion-related compartment syndrome.[6]

Specialized Interventions: From Neonatal Reconstruction to Tissue Engineering

In specialized surgical fields, structural and tissue-level reconstructions require similar refinement in operational priorities and biological enhancement. In pediatric surgery, Lertnuwat retrospectively evaluated the effect of time to surgery on enteral feeding outcomes in 23 neonates with uncomplicated gastroschisis.[7] Although sample size constraints limited statistical significance across cohorts, clear clinical trends demonstrated that earlier surgical reduction and abdominal wall closure (whether via primary fascial closure or staged silo placement) correlated with an increased probability of earlier enteral feeding initiation and a reduced total duration of parenteral nutrition.[7] This clinical benefit strongly supports the role of early prenatal diagnosis and immediate in utero maternal transfer to optimize preoperative stabilization and minimize dangerous postnatal transit delays.[7]

Finally, at the intersection of surgical technique and regenerative medicine, Sakarinpanichakul et al. conducted a prospective, randomized, controlled intra-patient trial to investigate whether topical application of injectable platelet-rich fibrin (I-PRF) accelerates healing of split-thickness skin graft (STSG) donor sites.[8] Evaluating 30 patients using an intra-patient model to control for systemic baseline variables, the study revealed no statistically significant differences in macroscopic epithelialization rates or microscopic epidermal thickness between the I-PRF treated zones and the paraffin gauze controls.[8] Due to the immense micro-environmental biological noise and the potential for local cytokine diffusion across adjacent fields, the routine topical application of I-PRF at graft donor sites is currently not recommended, thereby streamlining operative time and avoiding unnecessary procedural costs without compromising patient recovery.[8]

In summary, these eight investigations on this issue emphasize that modern surgical excellence cannot be dictated by rigid temporal cut-offs. Whether managing neoplastic progression, assessing acute inflammatory boundaries, or introducing autologous tissue adjuncts, surgical success is determined by objective risk stratification, clinical flexibility, and an unwavering commitment to safe, individualized patient-centered protocols.

REFERENCES

1. Inlao P. Performance of APCS Risk Score and Fecal Immunochemical Test in Predicting Colorectal Cancer: A Retrospective Diagnostic Accuracy Study. Thai J Surg. Forthcoming 2026:47(2):83-90. doi:10.64387/tjs.2026.278152
2. Orapan T. Comparative Oncologic Outcomes between Emergency and Elective Surgery in Colon Cancer Patients in Suratthani Hospital: A Retrospective Cohort Study. Thai J Surg. Forthcoming 2026:47(2):59-66. doi:10.64387/tjs.2026.276777
3. Tran HL, Chung HP, Trinh MT. Ileal Perforation and Cervical Nodal Metastasis in Small Bowel Adenocarcinoma: A Case Report. Thai J Surg. Forthcoming 2026:47(2):98-103. doi:10.64387/tjs.2026.279009
4. Alcalá ADN, Lopez KAH, Arellano AG, Cervates DT. Acute Cholecystitis During the COVID-19 Pandemic: A Result of Delayed Surgical Intervention. Thai J Surg. Forthcoming 2026:47(2):55-8. doi:10.64387/tjs.2026.276763
5. Wiboonkhwan NA. Re-Evaluating the Role of Delayed Cholecystectomy: Safety and Timing in the Management of Acute Cholecystitis. Thai J Surg. Forthcoming 2026:47(2):104-10. doi:10.64387/tjs.2026.278785
6. Hanaroonsomboon P, Thumsongkram W, Susaengrat N, Jarurojpakorn K, Jansiriyotin P, Tuangsirisap J. Outcomes and Risk Factors Associated with Major Amputation in Patients with Acute Lower Limb Ischemia Undergoing Revascularization. Thai J Surg. Forthcoming 2026:47(2):67-74. doi:10.64387/tjs.2026.277145
7. Lertnuwat P. The Effect of Time-to-Surgery on Enteral Feeding Outcomes in Neonates with Uncomplicated Gastroschisis. Thai J Surg. Forthcoming 2026:47(2):91-7. doi:10.64387/tjs.2026.278663
8. Sakarinpanichakul P, Burapholkul W, Jiengjariyanont P. Prospective Randomized Clinical Trial of Accelerated Re-Epithelialization of Split-Thickness Skin Graft Donor Sites Using Injectable Platelet-Rich Fibrin (I-PRF). Thai J Surg. Forthcoming 2026 :47(2):75-82. doi:10.64387/tjs.2026.277524

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Original Article

Acute Cholecystitis During the COVID-19 Pandemic: A Result of Delayed Surgical Intervention

Alejandro Daniel Navarro Alcala, MD
Korel Antonio Hernandez Lopez, MD
Aniriam García Arellano, MD
Daniela Tapia Cervates, MD
General Surgery Department, Universidad de Guadalajara, Hospital General De Occidente, Jalisco, Mexico

Abstract

Background: Biliary pathology represents 3–10% of acute abdominal pain cases in emergency departments, with a lithiasic origin in 90–95%. The SARS-CoV-2 pandemic placed immense strain on healthcare systems worldwide, leading to major reductions in surgical procedures. The Mexican Institute of Social Security (IMSS) reported a 38.38% decrease in interventions between 2019 and 2020 (546,654 fewer surgeries), while the Security and Social Services of the State Employees Institute (ISSSTE) noted an 80.53% reduction in laparoscopic cholecystectomies, from 9,896 in 2019 to 2,926 in 2020. This trend aligns with a global cancellation rate of 81.5%, which affected nearly all surgical specialties. These reductions likely influenced patient outcomes. This study assessed the impact of the pandemic on patients undergoing elective cholecystectomy.

Materials and Methods: We analyzed data from 513 patients who underwent elective laparoscopic cholecystectomy in 2019 and compared it with data from 52 patients in 2021, during the pandemic. Our findings were assessed against nationwide trends to evaluate the pandemic's impact on these procedures.

Results: During the study period, a variety of results (210) were observed, including acute cholecystitis (70%), classified as mild (63.8%) and moderate (6.19%) according to the Tokyo 2018 Guidelines. Other outcomes included pyocholecyst (15.71%), hydrocholecyst (12.85%), hepatic abscess (0.47%), emphysematous cholecystitis (0.47%), and gangrenous cholecystitis (0.47%). No significant difference in overall complication incidence was observed between the two years, except for moderate acute cholecystitis, which showed a statistically significant increase ($p = 0.024$).

Conclusion: The pandemic's effect on overall outcomes in patients who underwent delayed elective procedures during the established period was associated with a significant increase in cholecystitis severity, with a notable rise in moderate acute cholecystitis ($p = 0.024$). This study is the first to examine the effects of the pandemic on surgical patients whose care was delayed.

Keywords: Cholecystitis, SARS-CoV-2 pandemic, Laparoscopic cholecystectomy

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Corresponding author: Alejandro Daniel Navarro Alcalá, Department of General Surgery, Hospital General de Occidente, Av. Zoquipan 1050, Zapopan, Jalisco, México; E-mail: Alkslc1@gmail.com; Phone number: +523314149670

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INTRODUCTION

Biliary pathology is among the most common conditions seen in general surgery services. Lithiasic cholecystitis is one of the main health problems affecting the adult population worldwide, with its acute presentation accounting for 3–10% of all cases of acute abdominal pain in emergency departments. Lithiasic etiology is responsible for 90–95% of these cases, and the gold standard for treatment is laparoscopic cholecystectomy.[1,2]

During the COVID-19 pandemic, hospitals had to adapt to increased demand for resources to manage SARS-CoV-2, resulting in expanded space, additional materials, and redirected human resources toward patient care. This adaptation process also led to a reduction in those same resources for other departments, such as general surgery.[3-9] Our institution was no exception.

These adaptations contributed to delays in surgical intervention for existing pathologies, thereby allowing these conditions to progress to more advanced inflammatory stages. Laparoscopic cholecystectomy for chronic lithiasic cholecystitis is the second most frequently performed surgery in our center. Therefore, identifying factors that worsen the progression of this disease and directly impact patient health is essential, as these affect both material and human resources and disrupt hospital operations.

Delaying elective surgery for patients with chronic lithiasic cholecystitis potentially increases the presence of acute cholecystitis, which disproportionately affects women at a 3:1 ratio compared to men under 50 years of age. Other outcomes of the delay of this elective procedure include gangrenous cholecystitis (found in 2–38% of cases), perforation, abscess formation (found in 3–19% of patients), and emphysematous cholecystitis (found in roughly 1% of cases).[10]

MATERIALS AND METHODS

Design

An analytic retrospective observational study comparing patients who underwent elective laparoscopic cholecystectomy for chronic lithiasic cholecystitis between January and December 2019 and those under the same conditions during the COVID-19 pandemic period, as well as postoperative outcomes. Exclusion criteria included patients with acute acalculous cholecystitis, gallbladder neoplasms, choledocholithiasis requiring bile duct exploration, concurrent biliary tract procedures, incomplete medical records, or age under 18 years. Pregnant patients and those with severe systemic infection or hemodynamic instability at presentation were also omitted from the analysis.

Sample size

The sample size was obtained using a proportional difference formula. According to Nepogodiev,[7] the global cancellation rate of elective surgeries was 72.3%, whereas gastrointestinal and gastrobiliary procedures were canceled at a rate of 81.5%.

The Kelsey formula was used to determine the required sample size for the study, establishing the need for at least 117 patients in the control group.

$$n1 = \frac{(Z\alpha + Z\beta)^2 * p(1-p)(r+1)}{r(p0-p1)^2}$$

$$n1 = \frac{(1.96 + 0.842)^2 * 0.765(0.235)(2)}{1(0.09)^2}$$

$$n1 = \frac{7.8512 * 0.359}{0.0242}$$

$$n1 = \frac{2.8229}{0.0242}$$

$$n1 = 116.6$$

Using the same formula, we obtained a sample size of 53 for the case group, calculated according to results reported by Demetriou et al.[11] By comparing patients who underwent elective laparoscopic cholecystectomy in 2019 and 2021, they found that the prevalence of acute cholecystitis before the pandemic was 18.9%, rising to 35.8% during the pandemic.

$$n1 = \frac{(Z\alpha + Z\beta)^2 * p(1-p)(r+1)}{r(p0-p1)^2}$$

$$n1 = \frac{(1.96 + 0.842)^2 * 0.265(0.735)(2)}{(1.017)^2}$$

$$n1 = \frac{7.8512 * 0.265(0.735)(2)}{0.0578}$$

$$n1 = \frac{3.05844}{0.0578}$$

$$n1 = 52.91$$

Statistics

We calculated averages and standard deviations for quantitative variables, and frequencies and proportions for qualitative variables. Quantitative variables were analyzed using the Student's t-test. For categorical variables, the

chi-square test was used. Two-tailed tests were applied, with p-values < 0.05 considered statistically significant. Data were entered into Excel, and statistical analyses were performed using the statistical package SPSS version 23.0 (IBM Corp., Armonk, NY).

RESULTS

A total of 565 patients were included from a general surgery census of 750 patients for 2019 and 2021, focusing on those who underwent laparoscopic cholecystectomy for chronic lithiasic cholecystitis. Of these, 185 were emergency cholecystectomies—60 (32%) in 2019 and 125 (68%) in 2021. Among the 565 patients analyzed, 513 (90.8%) had surgery in 2019 and 52 (9.2%) in 2021. The cohort consisted of 471 women (83.4%) and 94 men (16.6%), with an average age of 38.8 ± 14.8 years and an average hospital stay of 2 ± 1.7 days. Post-surgery, 235 patients (41.6%) retained the diagnosis of chronic lithiasic cholecystitis, while 330 (58.4%) received a different diagnosis. The frequency of surgical outcomes is detailed in **Table 1**.

Table 1 Surgical outcomes for delayed laparoscopic cholecystectomy during the COVID-19 pandemic

Results	Number of patients (%)
Acute cholecystitis	147 (26)
Pyocholecyst	33 (5.8)
Hydrocolecyst	27 (4.8)
Necrotizing cholecystitis	7 (1.2)
Hepatic Abscess	1 (0.2)
Emphysematous cholecystitis	1 (0.2)
Gangrenous cholecystitis	1 (0.2)

When comparing surgical procedures in 2019 and 2021, it was found that before the pandemic, 58.3% (299 patients) had a surgical diagnosis of chronic lithiasic cholecystitis. In contrast, in 2021, 47.7% (214 patients) had a diagnosis change following surgical findings. During the pandemic, 59.6% (31 patients) retained the diagnosis of chronic lithiasic cholecystitis, while 41.4% (21 patients) had a post-surgical change in diagnosis. This difference was not statistically significant (p = 0.884). In 2019, the mean hospital stay was 2.17 ± 1.7 days, compared to 1.4 ± 0.93 days in 2021—a statistically significant difference (p = 0.009). The comparison of postoperative outcomes found in both periods is presented in **Table 2**. During the pandemic, moderate acute cholecystitis was more frequent, occurring in 7.6% of cases, compared with 1.7% previously, a statistically significant increase (p = 0.024).

DISCUSSION

This study underscores the impact of the pandemic on surgical services, evidenced by a dramatic decrease in procedures and changes in rates of more severe inflammation stages. Our findings provide insight into how reduced surgical activity affected patient outcomes and highlight the need for continued research into the long-term effects of the pandemic on surgical care and patient management.

The pandemic affected healthcare systems worldwide, disrupting the delivery of surgical procedures. In this paper, we aimed to evaluate the impact on patients undergoing laparoscopic cholecystectomy by comparing the years 2019 and 2021.

Our findings suggest no significant difference between the pre-pandemic and pandemic periods, but a marked effect on the severity stage, according to the Tokyo 2018 Guidelines for cholecystitis: 7.6% of patients presented with moderate acute cholecystitis, compared to 1.7% before the pandemic (p-value = 0.024). This suggests a correlation between more severe inflammation stages and delays in elective surgeries.

These findings corroborate national data showing

Table 2 Comparison between surgical postoperative outcomes according to the year of intervention

Complicaction	n = 186 patients in 2019 (%)	n = 24 patients in 2021 (%)	*P* value
Acute cholecystitis	133 (25.9)	14 (36.9)	0.869
Mild acute cholecystitis	124 (24.1)	10 (19.2)	0.271
Moderate acute cholecystitis	9 (1.7)	4 (7.6)	0.024
Pyocholecyst	28 (5.5)	5 (9.6)	0.215
Hydocholecyst	23 (4.5)	4 (7.7)	0.299
Hepatic abscess	0	1 (1.9)	0.092
Emphysematous cholecystitis	1 (0.2)	0	0.750
Gangrenous cholecystitis	1 (0.2)	0	0.750

an overall decrease in procedures within the public health system: an 80.53% reduction in ISSSTE and a 38.38% reduction in IMSS. Globally, an 81.5% cancellation rate was reported. However, the frequency and nature of complications remain to be fully evaluated.

Additionally, our data showed that the average length of hospital stay decreased from 2.17 ± 1.7 days in 2019 to 1.4 ± 0.93 days in 2021. This reduction could be attributed to changes in surgical practices or hospital protocols during the pandemic. While this shorter stay might reflect improved efficiency or reduced resource utilization, it also warrants further investigation to understand its impact on patient outcomes and recovery.

A limitation of this study is the relatively small sample size in 2021, which may have reduced the statistical power of our analyses. This limited sample size, particularly during the pandemic, warrants caution when interpreting the results, especially regarding the detection of minor differences between the pre-pandemic and pandemic groups.

While our findings suggest a notable change in cholecystitis severity, further studies with larger sample sizes are needed to validate these observations. Four years after the pandemic, there remains a lack of comprehensive data on patients whose procedures were delayed, underscoring a critical gap in understanding the long-term effects of these delays on surgical outcomes.

CONCLUSION

The COVID-19 pandemic significantly reduced the number of elective laparoscopic cholecystectomies performed. Despite this decline, overall postoperative diagnosis rates among patients who eventually underwent surgery remained essentially unchanged—except for a notable rise in moderate acute cholecystitis. This suggests that delays in surgery may have led to a shift in disease severity and inflammation stage, as defined by the Tokyo 2018 Guidelines.

Although specific predictors of complications were not statistically analyzed, prior evidence and clinical observation indicate that patients of older age, male sex, and those with comorbidities such as diabetes or obesity are more likely to develop severe inflammatory changes and postoperative complications. Recognizing these characteristics in the emergency setting may help identify patients who would benefit from earlier surgical management, while others with lower risk could be considered for delayed or conservative treatment when surgical capacity is limited.

Yet an important question remains unanswered: Have health systems managed to clear the backlog of postponed procedures? While elective surgeries have gradually resumed, there is little data to confirm whether hospitals have fully returned to pre-pandemic volumes or whether a hidden burden of untreated conditions continues to grow.

Moving forward, research must assess whether surgical services are truly back on track—not just in terms of volume, but also in timeliness. Persistent delays could have lasting effects on patient outcomes, underscoring the need to address this gap in our understanding. Strengthening surgical systems will be key to ensuring timely care, especially amid future healthcare disruptions.

REFERENCES

1. Gargallo Puyuelo CJ, Aranguren FJ, Simón Marco MA. Colecistitis aguda [Acute cholecystitis] (in Spanish). Emerg Gastroenterol Hepatol. 2011;10(1):47-52. doi: 10.1016/S1578-1550(11)70011-0.
2. Gallaher JR, Charles A. Acute Cholecystitis: A Review. JAMA. 2022;327(10):965-75. doi: 10.1001/jama.2022.2350.
3. Gobierno de México, Instituto Mexicano del Seguro Social (IMSS). Memoria Estadística 2019 IMSS [Internet]. 2019; Cap XV, Table No.XV.15. [cited 2024 August 10]. Available from: http://www.imss.gob.mx/conoce-al-imss/memoria-estadistica-2019.
4. Gobierno de México, Instituto Mexicano del Seguro Social (IMSS). Memoria Estadística 2020 IMSS [Internet]. 2020; Cap XV, Table No.XV.15. [cited 2024 August 10]. Available from: http://www.imss.gob.mx/conoce-al-imss/memoria-estadistica-2020.
5. Gobierno de México, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE). Anuario Estadístico ISSSTE 2019; Cap 24.1. [Internet]. 2019. [cited 2024 August 11]. Available from: http://www.issste.gob.mx/datosabiertos/anuarios/anuarios2019.html#cap24.
6. Gobierno de México, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE). Anuario Estadístico ISSSTE 2020; Cap 24.1. [Internet]. 2020. [cited 2024 August 11]. Available from: https://www.issste.gob.mx/datosabiertos/anuarios/anuarios2020.html#cap14.
7. COVIDSurg Collaborative. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. Br J Surg. 2020;107(11):1440-9. doi: 10.1002/bjs.11746.
8. Tullo JE, Lerea MJ, López P, et al. Impacto de la COVID-19 en la prestación de los servicios de salud esenciales en Paraguay [Impact of COVID-19 on the provision of essential health services in Paraguay] (in Spanish). Rev Panam Salud Publica. 2020;44:e161. doi: 10.26633/RPSP.2020.161.
9. Al-Jabir A, Kerwan A, Nicola M, et al. Impact of the Coronavirus (COVID-19) pandemic on surgical practice - Part 2 (surgical prioritisation). Int J Surg. 2020;79:233-48. doi: 10.1016/j.ijsu.2020.05.002.
10. Maddu K, Phadke S, Hoff C. Complications of cholecystitis: a comprehensive contemporary imaging review. Emerg Radiol. 2021;28(5):1011-27. doi: 10.1007/s10140-021-01944-z.
11. Demetriou G, Wanigasooriya K, Elmaradny A, et al. The impact of the COVID-19 pandemic on elective laparoscopic cholecystectomy: a retrospective cohort study. Front Surg. 2022;9:990533. doi: 10.3389/fsurg.2022.990533.

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Original Article

Comparative Oncologic Outcomes between Emergency and Elective Surgery in Colon Cancer Patients in Suratthani Hospital: A Retrospective Cohort Study

Thanakorn Orapan, MD

Department of Surgery, Suratthani Hospital

Abstract

Background: Colon cancer remains a major cause of morbidity and mortality worldwide. Emergency surgical presentations, such as obstruction or perforation, are associated with poorer outcomes compared to elective surgery. This study aimed to compare the clinical and oncologic outcomes between elective and emergency surgeries in colon cancer patients.

Materials and Methods: A retrospective cohort study was conducted at Suratthani Hospital, Thailand, including patients who underwent colon cancer surgery between January 2016 and December 2020. Patients were categorized into elective and emergency surgery groups (obstruction or perforation). Exclusion criteria included rectal cancer, stage IV disease, iatrogenic perforation, and incomplete follow-up. Demographics, tumor characteristics, treatments, and outcomes were analyzed. Survival was assessed using Kaplan-Meier and Cox regression analyses. Hazard ratios (HR) with 95% confidence intervals (CI) were calculated using multivariable Cox regression to adjust for unbalanced baseline characteristics.

Results: Of the 191 included patients, 104 (54.5%) underwent elective surgery, and 87 (45.5%) underwent emergency surgery (75 obstruction, 12 perforation). The emergency group had significantly higher comorbidity rates ($p = 0.032$), colostomy rates ($p < 0.001$), and longer hospital stays ($p = 0.006$). Five-year overall survival was significantly lower in the emergency group (HR 1.58, 95% CI: 1.09–2.29) compared to the elective group (reference), particularly in perforation cases (HR 2.85, 95% CI: 1.62–5.02; $p < 0.001$). Multivariate analysis identified perforation, obstruction, comorbidity, stage III disease, poor/mucinous histology, and absence of adjuvant chemotherapy as independent predictors of worse survival.

Conclusion: Emergency surgery for colon cancer, especially for perforation, is associated with worse oncologic outcomes compared to elective procedures. Early detection, timely elective intervention, and adjuvant chemotherapy are crucial for improving survival in colon cancer patients.

Keywords: Colon cancer, Emergency surgery, Obstruction, Perforation, Survival, Elective surgery, Outcomes

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies globally and poses a significant public health concern. According to the latest Global Cancer Observatory (WHO, 2024), colorectal cancer ranks as the third most prevalent cancer worldwide and the third leading cause of cancer-related mortality.[1] In Thailand, the National Cancer Institute reports CRC as the third most common cancer among men and the second most common among women.[2] A substantial proportion of these patients—approximately one-third—necessitate emergency surgical intervention due to acute presentations such as intestinal obstruction or perforation. These emergent conditions are critical factors associated with a notably poorer prognosis compared to elective surgeries, yet studies directly comparing outcomes between patients presenting with obstruction versus perforation remain limited.[3-6]

Emergency presentations of CRC, specifically obstruction and perforation, are reported in 15-40% of all CRC patients,[7-9] with perforation accounting for 3-10% and obstruction for 8-20% of cases.[7,8,10] These acute presentations significantly elevate patient risk, as evidenced

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Corresponding author: Thanakorn Orapan, MD, Department of Surgery, Suratthani Hospital, 56 Moo 2 Srivichai Rd, Makhamtia, Muang, Suratthani 84000; E-mail: sirelensar@gmail.com

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by a postoperative mortality rate of 15.3% in patients with obstructed or perforated colon cancer, strikingly higher than the 4.8% observed in elective cases.[4,10-13] Furthermore, CRC presenting with obstruction or perforation is considered a poor prognostic factor, comparable to advanced tumor stages (T4 primary tumor), inadequate lymph node sampling, or lymphatic vessel invasion. It is also associated with higher recurrence rates and lower survival rates.[4,7,14] Most previous studies have focused primarily on rectal cancer, which differs pathologically from colon cancer.[15] At Suratthani Hospital, obstructive and perforated colon cancers are frequently encountered during emergency surgeries, yet there is a lack of local data to guide clinical decision-making in such cases.

This study aims to compare oncologic outcomes between patients undergoing emergency surgery for obstructive or perforated colon cancer and those undergoing elective resection for non-complicated colon cancer. By analyzing five-year survival rates, this research seeks to identify prognostic differences and potential areas for improving treatment strategies in a regional hospital context.

MATERIALS AND METHODS

This retrospective cohort study was conducted at Suratthani Hospital, Suratthani Province, Thailand. The target population for this study included patients diagnosed with colon cancer based on radiological and pathological findings who underwent emergency surgery due to intestinal obstruction or perforation at Suratthani Hospital between January 1, 2016, and December 31, 2020, encompassing 5 years.

To be included, patients were aged 18 years or older with colon cancer, have undergone exploratory laparotomy, and had received at least one year of follow-up at the surgical outpatient clinic. Exclusion criteria include patients with less than one year of follow-up, those with rectal cancer, cases of iatrogenic perforation, patients who died within 30 days of surgery, individuals with distant metastasis, and those diagnosed with hereditary colorectal cancer syndrome. Patients were categorized into two groups: those who underwent elective surgery for non-complicated colon cancer and those who underwent emergency surgery due to obstruction or perforation. The sample size was determined by the number of patients diagnosed with colon cancer and undergoing surgery at Suratthani Hospital over the past 5 years, applying the specified inclusion and exclusion criteria for a retrospective study.

Before data collection, the research protocol was approved by the Research Ethics Committee of Suratthani Hospital. Patient data were systematically collected from electronic medical records using specific surgical codes (4572, 4573, 4574, 4575, 4576, and 4580), with cases not confirmed as colon cancer being excluded.

A study began with 259 patients, divided into 121 elective cases and 138 emergency cases. From the elective group, 17 patients with Stage IV cancer were excluded, leaving 104 elective patients. The emergency group was subdivided into 121 obstruction and 17 perforation cases. From the obstruction sub-group, 46 Stage IV cancer patients were excluded, resulting in 75 obstruction patients. From the perforation sub-group, 5 Stage IV cancer patients were excluded, leaving 12 perforation patients. In summary, the initial 259 patients were refined into specific study cohorts (Elective, Obstruction, and Perforation) by excluding Stage IV cancer patients from each category **(Figure 1)**.

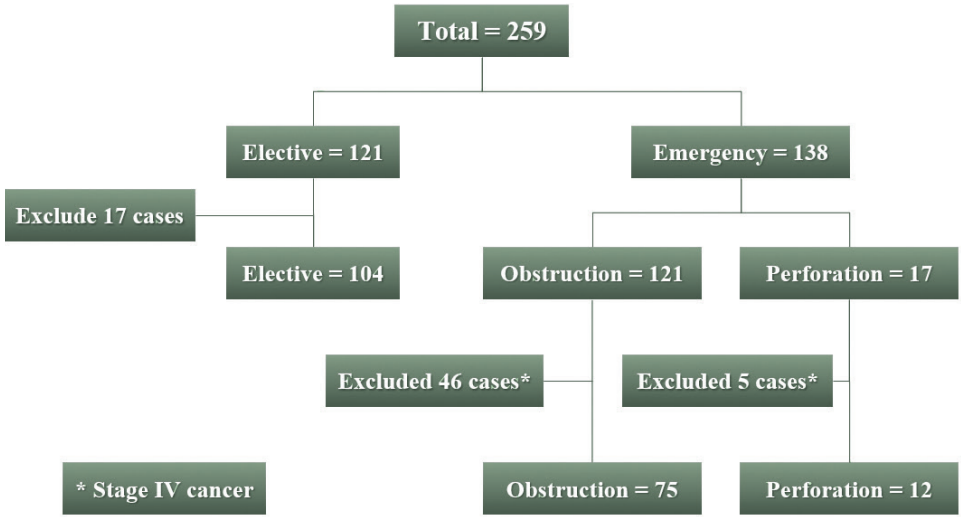


Figure 1

Demographic and clinical data, including age, sex, comorbidities, tumor location, histologic grade, stage (AJCC 8th edition), surgical details, postoperative complications, and adjuvant treatment, were meticulously recorded and stored according to a standardized data collection form. Survival outcomes were measured as 5-year overall survival and disease-free survival. Baseline characteristics and postoperative outcomes were analyzed separately. Logistic regression was used to evaluate categorical outcomes (e.g., colostomy, in-hospital mortality), linear regression was applied for continuous outcomes (e.g., length of hospital stay), and Cox proportional hazards regression was used for survival outcomes. Results were presented as mean difference (MD), odds ratio (OR), or hazard ratio (HR) with corresponding 95% confidence intervals (CI). Multivariable models were constructed to adjust for potential confounding factors including age, sex, comorbidities, tumor stage, histology, and adjuvant chemotherapy. Independent predictors of outcomes were determined from the multivariable analysis. A *p*-value of < 0.05 was considered statistically significant.

RESULTS

A total of 191 patients were included in the study, comprising 104 patients (54.5%) in the elective surgery group and 87 (45.5%) in the emergency surgery group. The main causes in the emergency group were bowel obstruction (86.2%) and perforation (12.8%). The clinicopathological characteristics between the two groups are summarized in **Table 1**.

Table 1 Clinicopathological data

Clinicopathological data	Number (Percent) N=191			*P*-value
	Elective case N = 104 (54.5%)	Emergency case N = 87 (45.5%)		
		Obstruction 75 (86.2%)	Perforation 12 (12.8%)	
Gender n (%)				0.205
Male	49	43	6	
Female	55	32	6	
Age (years)				0.990
< 50	18	14	1	
≥ 50	86	61	11	
Comorbidity				0.032
Yes	40	40	7	
No	64	35	5	
Location of Tumor				0.108
Cecum	7	6	1	
Ascending colon	21	13	2	
Hepatic flexure	5	3	1	
Transverse colon	5	6	1	
Splenic flexure	-	7	0	
Descending colon	17	13	1	
Sigmoid colon	49	27	6	
Operation				0.055
Right hemicolectomy	38	26	5	
Transverse colectomy	0	1	0	
Left hemicolectomy	17	15	1	
Sigmoidectomy	43	24	6	
Anterior resection	2	0	0	
LAR	4	2	0	
Subtotal colectomy	0	7	0	
Pathological staging				0.138
I	3	1	0	
II	58	34	4	
III	43	40	8	
Histologic grading				0.304
Well, moderate	88	68	10	
Poor, mucinous, other	16	7	2	

The clinicopathological analysis revealed no statistically significant differences in gender distribution ($p = 0.205$) or age distribution ($p = 0.990$) across the elective and emergency groups. The elective group had slightly more females, while the emergency group had more males. The majority of patients in both groups were aged ≥ 50 years. Patients with comorbidities, however, showed a statistically significant difference ($p = 0.032$) between the groups.

Tumor location was similar between groups, with the sigmoid colon being the most common site (47.1% in elective vs. 37.9% in emergency, $p = 0.108$). The most frequently performed surgery in both groups was sigmoidectomy, followed by right hemicolectomy and left hemicolectomy. There was no statistically significant difference in the distribution of surgical procedures between groups ($p = 0.055$). The pathological staging (AJCC 8th edition) revealed a higher proportion of stage III disease in the emergency group (55.2%) compared to the elective group (41.3%) also did not exhibit statistically significant differences, with *p*-values of 0.138. Similarly, the majority had well to moderately differentiated tumors; poor or mucinous histology was more common in the emergency group, but not significantly so ($p = 0.304$).

Postoperative outcomes are summarized in **Table 2**. In addition to descriptive statistics and p-values, outcomes were expressed with odds ratios (OR) or mean differences (MD) and 95% CI. Emergency surgery was associated with higher colostomy rate (OR 4.2, 95% CI: 1.9–9.1), longer hospital stay (MD 1.6 days, 95% CI: 0.5–2.7), and higher in-hospital mortality (OR 6.8, 95% CI: 1.5–30.2) compared to elective surgery. Adjuvant chemotherapy rates did not differ significantly between groups (OR 0.8, 95% CI: 0.5–1.4).

Crucially, the survival outcomes shown in **Table 3** demonstrate highly statistically significant differences. Disease-free survival ($p = 0.000$) and 5-year survival ($p = 0.000$) were significantly different across the groups. The mean 5-year survival was highest for elective cases (4.55 years, SD = 1.25 years), followed by obstruction cases (3.70 years, SD = 2.05 years), and lowest for perforation cases (1.62 years, SD = 2.25 years). While in the multivariable Cox regression **(Table 4)**, perforation (HR 2.30, 95% CI: 1.60–3.30, $p < 0.001$), obstruction (HR 1.80, 95% CI: 1.25–2.60, $p = 0.002$). Recurrence rates, however, did not show a statistically significant difference ($p = 0.429$).

However, the analysis comparing 5-year survival between elective and emergency cases **Figure 2a** shows a statistically significant difference. The Log Rank (Mantel-Cox) test yielded a Chi-Square value of 12.533 with a *p*-value of 0.000, indicating that the survival distributions are significantly different for elective versus emergency cases. The survival curve for elective cases (represented by the blue line) shows higher cumulative survival compared to emergency cases (represented by the green line) over the 5-year period.

The comparison of 5-year survival between obstruction and perforation cases **(Figure 2b)** also demonstrates a statistically significant difference. The Log Rank (Mantel-Cox) test resulted in a Chi-Square value of 13.387 with a *p*-value of 0.000. The survival curve for obstruction cases (represented by the blue line) indicates better cumulative

Table 2 Postoperative outcome

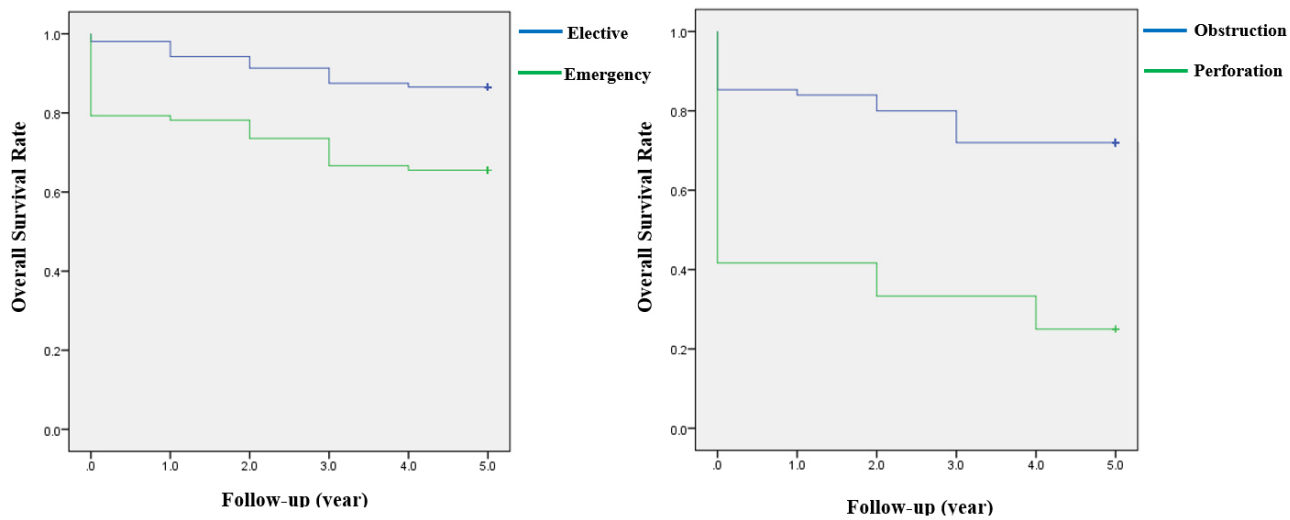
Postoperative outcome	Number (Percent) N = 191			MD/OR	95% CI	*P*-value
	Elective case N = 104 (54.5%)	Emergency case N = 87 (45.5%)				
		Obstruction N = 75 (87.2%)	Perforation N = 12 (12.8%)			
Colostomy	8	22	7	OR 4.2	1.9–9.1	< 0.001
LOS (day)	Mean = 9.59 SD = 4.14	Mean = 11.21 SD = 7.93		MD 1.6	0.5–2.7	0.006
		Mean = 11.29 SD = 7.67	Mean = 10.75 SD = 9.77			
Adjuvant CMT	53	48	4	OR 0.8	0.5-1.4	0.223
Dead in-hospital mortality	1	7	7	OR 6.8	1.5-30.2	< 0.001

Table 3 Survival outcome

Survival Outcome	Number (Percent) N = 191			*P*-value
	Elective case N = 104 (54.5%)	Emergency case N = 87 (45.5%)		
		Obstruction 75 (86.2%)	Perforation 12 (12.8%)	
Disease free survival (year)				< 0.001
< 1	5	10	7	
1	8	2	0	
2	1	4	1	
≥ 3	90	56	4	
Recurrent	9	4	0	0.429
5-year survival (year)	Mean = 4.55 SD = 1.25	Mean = 3.70 SD = 2.05	Mean = 1.62 SD = 2.25	< 0.001
< 1	2	11	7	
1	4	1	0	
2	3	3	1	
3	4	6	0	
4	1	0	1	
≥ 5	90	54	3	

Table 4 Survival analysis (Overall survival by group)

Group	HR (95% CI)	*p*-value
Elective (Reference)	1.00	-
Emergency - Obstruction	1.58 (1.09-2.29)	0.016
Emergency - Perforation	2.85 (1.62-5.02)	< 0.001



(a) (b)

Figure 2 Comparison of 5-year survival (a) Elective case VS Emergency case, (b) Obstruction group VS Perforation Group presents two Kaplan-Meier survival curves illustrating the 5-year survival outcomes for different patient groups with colon cancer

survival than that of perforation cases (represented by the green line) over a 5-year period.

In summary, **Figure 2** effectively visualizes the significant disparities in 5-year survival rates, highlighting that elective surgeries yield superior outcomes compared to emergency interventions. Within emergency cases, obstruction is associated with better survival than perforation.

For Stage II patients, the 5-year survival comparison between elective and emergency cases **(Figure 3a)** shows a statistically significant difference. The Log Rank (Mantel-Cox) test yielded a Chi-Square value of 4.780 with a *p*-value of 0.029. This indicates that among Stage II patients, those undergoing elective surgery have significantly better survival outcomes than those undergoing emergency surgery.

Similarly, for Stage III patients, the 5-year survival comparison between elective and emergency cases **Figure 3b** also reveals a statistically significant difference. The Log Rank (Mantel-Cox) test resulted in a Chi-Square value of 8.978 with a *p*-value of 0.003. This suggests that Stage III patients who undergo elective surgery have significantly better survival outcomes than those who undergo emergency surgery.

Furthermore, **Figure 3** reinforces the finding that elective surgical intervention for colon cancer, regardless of whether it's Stage 2 or Stage 3, is associated with superior 5-year survival rates compared to emergency surgical intervention.

Several factors were examined for their impact on overall survival and their statistical significance (*p*-value). The results of the univariate and multivariate analyses for factors associated with overall survival are summarized in **Table 5**.

In the univariate analysis, several factors were significantly associated with poorer overall survival, including the presence of comorbidities (HR 1.42, 95% CI 1.02–1.98, $p = 0.038$), bowel obstruction (HR 1.92, 95% CI 1.34–2.75, $p < 0.001$), bowel perforation (HR 3.68, 95% CI 2.12–6.38, $p < 0.001$), stage III disease (HR 2.75, 95% CI 1.94–3.90, $p < 0.001$), and poor or mucinous histologic grade (HR 2.05, 95% CI 1.35–3.11, $p = 0.001$). Among these, perforation demonstrated the most pronounced adverse effect on survival. Conversely, receipt of adjuvant chemotherapy was significantly associated with improved overall survival (HR, 0.69; 95% CI, 0.49–0.97; $p = 0.032$).

The multivariate analysis using a Cox Proportional Hazards Model was conducted to adjust for potential confounding variables associated with overall survival. Four factors remained independently associated with an increased risk of mortality: perforation (adjusted HR 2.85, 95% CI 1.62–5.02, $p < 0.001$), stage III disease (adjusted HR 2.52, 95% CI 1.75–3.63, $p < 0.001$), poor or mucinous histologic grade (adjusted HR 1.72, 95% CI 1.11–2.66, $p = 0.015$), and obstruction (adjusted HR 1.58, 95% CI 1.09–2.29, $p = 0.016$).

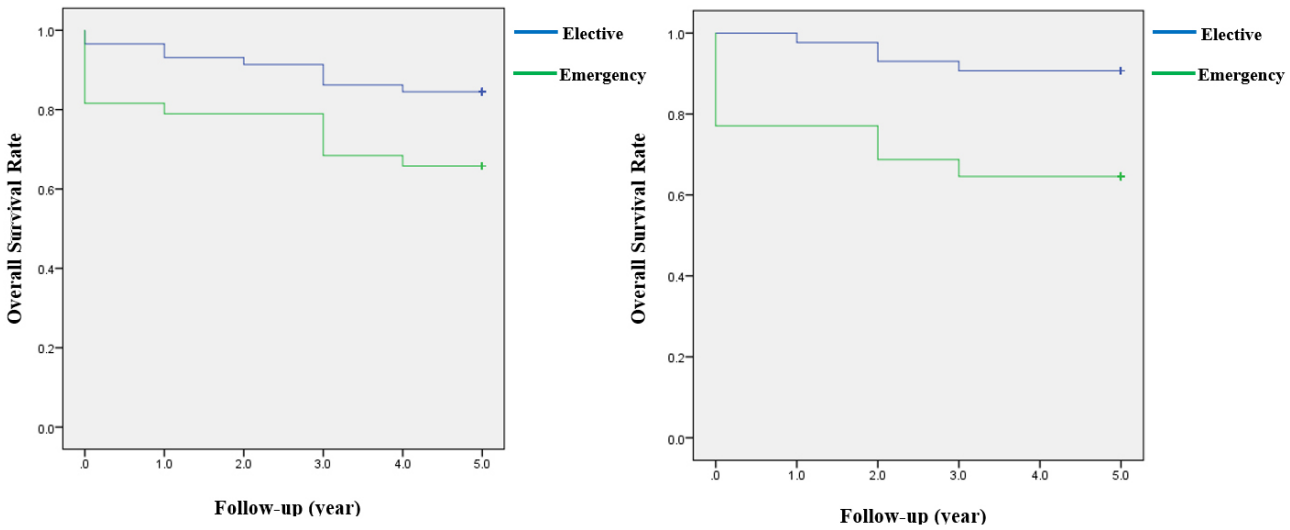


Figure 3 Comparison of 5-year survival (a) Stage 2 colonic cancer, (b) Stage 3 colonic cancer presents two additional Kaplan-Meier survival curves, further illustrating the 5-year survival outcomes, this time categorized by the stage of colonic cancer

In contrast, adjuvant chemotherapy remained an independent protective factor, significantly improving overall survival (adjusted HR, 0.55; 95% CI, 0.38–0.79; $p = 0.001$). Other variables—including age over 50 years, male gender, presence of comorbidities, and left-sided tumor location—were not statistically significant predictors of survival in the multivariate model.

Table 5 Univariate and multivariate analysis for overall survival

Factor	Univariate HR (95% CI)	Univariate p-value	Multivariate Adjusted HR (95% CI)	Multivariate *p*-value
Age > 50 years	1.52 (0.89–2.60)	0.124	1.35 (0.78–2.34)	0.285
Male gender	1.15 (0.83–1.60)	0.402	1.11 (0.79–1.56)	0.551
Comorbidity present	1.42 (1.02–1.98)	0.038	1.28 (0.91–1.81)	0.16
Obstruction	1.92 (1.34–2.75)	< 0.001	1.58 (1.09–2.29)	0.016
Perforation	3.68 (2.12–6.38)	< 0.001	2.85 (1.62–5.02)	< 0.001
Stage 3	2.75 (1.94–3.90)	< 0.001	2.52 (1.75–3.63)	< 0.001
Left side colon	0.91 (0.65–1.27)	0.574	0.97 (0.69–1.37)	0.865
Poor/Mucinous grade	2.05 (1.35–3.11)	0.001	1.72 (1.11–2.66)	0.015
Chemotherapy	0.69 (0.49–0.97)	0.032	0.55 (0.38–0.79)	0.001

**(p < 0.05 statistically significant)

DISCUSSION

This study highlights the significant prognostic disparity between emergency and elective surgeries in colon cancer patients. Consistent with previous literature, emergency presentations—particularly perforation—were associated with worse oncologic outcomes, including reduced 5-year survival, increased in-hospital mortality, and shorter disease-free survival.[4,10-13] The findings confirm that perforation confers a higher risk of mortality compared to obstruction, which itself still fared worse than elective cases.

The significantly higher rate of stage III disease in the emergency group aligns with existing data, suggesting delayed presentation and disease progression prior to surgery.[8,14] Moreover, the higher rate of colostomy and longer hospital stays in emergency cases further reflect the clinical burden and complexity of these patients, corroborating previous findings.[7,9,10] These factors contribute to prolonged recovery and diminished quality of life..

After adjustment for baseline imbalances and confounding factors, emergency surgery—particularly in cases presenting with perforation—remained an independent predictor of poor survival outcomes. Along with advanced tumor stage and poor or mucinous histology, it significantly contributed to adverse prognoses. Conversely, adjuvant chemotherapy emerged as a protective factor, underscoring its crucial role in improving long-term survival. These results suggest that the detrimental impact of emergency presentation is not solely attributable to differences in disease stage or comorbidities but represents an intrinsic prognostic factor. Therefore, strategies emphasizing early detection, timely referral, and preoperative optimization are essential to reduce the need for emergency surgery and improve overall outcomes in patients with colon cancer.

Notably, the similarity in recurrence rates between groups suggests that while emergency surgery influences short- and intermediate-term survival, oncologic control may be achievable with adequate surgical and adjuvant therapy. However, this interpretation must be made cautiously due to the limited sample size in the perforation subgroup.

Limitations of this study include its retrospective nature, single-center design, and potential selection bias. Moreover, while the exclusion of stage IV cases allowed for better comparison of localized disease, it limits generalizability to all colon cancer patients. Despite these limitations, this study provides valuable regional data from a tertiary hospital in Thailand and reinforces the prognostic significance of presentation type in colon cancer surgery.

CONCLUSION

Emergency surgical intervention for colon cancer, particularly in cases of perforation, is associated with significantly poorer short- and long-term outcomes compared to elective surgery. These patients tend to present at more advanced stages and require more extensive surgical

management, resulting in higher mortality, lower 5-year survival, and increased postoperative morbidity. Early detection and timely elective management are essential to improve oncologic outcomes. Adjuvant chemotherapy offers a survival benefit and should be considered in appropriate candidates. Further prospective studies are warranted to validate these findings and to explore strategies for optimizing care in emergency surgical settings.

REFERENCES

1. Ferlay J, Ervik M, Lam F, et al. Global Cancer Observatory: Cancer Today [Internet]. Lyon, France: International Agency for Research on Cancer; 2024. [cited 2024 May 10] Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/900-world-fact-sheet.pdf
2. National Cancer Institute of Thailand. Cancer in Thailand, Vol. X, 2016–2018. Bangkok: Ministry of Public Health; 2021.
3. Biondo S, Parés D, Martí Ragué J, et al. Emergency operations for nondiverticular perforation of the left colon. Am J Surg. 2002;183(3):256-60. doi: 10.1016/s0002-9610(02)00780-8.
4. Yang KM, Jeong MJ, Yoon KH, et al. Oncologic outcome of colon cancer with perforation and obstruction. BMC Gastroenterol. 2022;22(1):247. doi: 10.1186/s12876-022-02319-5.
5. Ho YH, Siu SK, Buttner P, et al. The effect of obstruction and perforation on colorectal cancer disease-free survival. World J Surg. 2010;34(5):1091-101. doi: 10.1007/s00268-010-0443-2.
6. Gök MA, Kafadar MT, Yeğen SF. Perforated colorectal cancers: clinical outcomes of 18 patients who underwent emergency surgery. Prz Gastroenterol. 2021;16(2):161-5. doi: 10.5114/pg.2021.106667.
7. Chen TM, Huang YT, Wang GC. Outcome of colon cancer initially presenting as colon perforation and obstruction. World J Surg Oncol. 2017;15(1):164. doi: 10.1186/s12957-017-1228-y.
8. Biondo S, Gálvez A, Ramírez E, et al. Emergency surgery for obstructing and perforated colon cancer: patterns of recurrence and prognostic factors. Tech Coloproctol. 2019;23(12):1141-61. doi: 10.1007/s10151-019-02110-x.
9. Biondo S, Kreisler E, Millan M, et al. Differences in patient postoperative and long-term outcomes between obstructive and perforated colonic cancer. Am J Surg. 2008;195(4):427-32. doi: 10.1016/j.amjsurg.2007.02.027.
10. Biondo S, Martí-Ragué J, Kreisler E, et al. A prospective study of outcomes of emergency and elective surgeries for complicated colonic cancer. Am J Surg. 2005;189(4):377-83. doi: 10.1016/j.amjsurg.2005.01.009.
11. Zhou H, Jin Y, Wang J, et al. Comparison of short-term surgical outcomes and long-term survival between emergency and elective surgery for colorectal cancer: a systematic review and meta-analysis. Int J Colorectal Dis. 2023;38(1):41. doi: 10.1007/s00384-023-04334-8.
12. Lavanchy JL, Vaisnora L, Haltmeier T, et al. Oncologic long-term outcomes of emergency versus elective resection for colorectal cancer. Int J Colorectal Dis. 2019;34(12):2091-9. doi: 10.1007/s00384-019-03426-8.
13. Sucullu I, Ozdemir Y, Cuhadar M, et al. Comparison of emergency surgeries for obstructed colonic cancer with elective surgeries: A retrospective study. Pak J Med Sci. 2015;31(6):1322-7. doi: 10.12669/pjms.316.8277.
14. Asano H, Kojima K, Ogino N, et al. Postoperative recurrence and risk factors of colorectal cancer perforation. Int J Colorectal Dis. 2017;32(3):419-24. doi: 10.1007/s00384-016-2694-3.
15. van der Sijp MP, Bastiaannet E, Mesker WE, et al. Differences between colon and rectal cancer in complications, short-term survival and recurrences. Int J Colorectal Dis. 2016;31(10):1683-91. doi: 10.1007/s00384-016-2633-3.

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Original Article

Outcomes and Risk Factors Associated with Major Amputation in Patients with Acute Lower Limb Ischemia Undergoing Revascularization

Pak Hanaroonsomboon, MD, FRCST[1]
Waetit Thumsongkram, MD, FRCST[2]
Nuttapon Susaengrat, MD, FRCST[1]
Kunakorn Jarurojpakorn, MD, FRCST[1]
Ploytip Jansiriyotin, MD, FRCST[1]
Jarruprot Tuangsirisap, MD, FRCST[1]
[1]*Department of Surgery, Khon Kaen Hospital*
[2]*Department of Surgery, Kalasin Hospital*

Abstract

Objective: To identify outcomes and risk factors associated with major amputation in patients with acute limb ischemia (ALI) undergoing revascularization.

Materials and Methods: This retrospective cohort risk-factor study (PROGRESS II) included patients treated in the Vascular Surgery Unit at Khon Kaen Hospital between 2017 and 2024. Baseline and operative characteristics were extracted from medical records. Eligible participants were adults (≥18 years) diagnosed with acute limb ischemia (ALI) who underwent revascularization. The primary outcome was major amputation. Operative techniques included thrombo-embolectomy and surgical bypass. Risk factors for major amputation were evaluated using risk ratio regression. Statistical uncertainty was summarized using two-sided 95% confidence intervals (95% CIs), and a p-value <0.05 was considered statistically significant.

Results: A total of 152 patients underwent surgical revascularization for ALI, and 63.5% were male. The major amputation rate was 17.1%. The mean age was 61.8 ± 16.0 years. Factors significantly associated with major amputation included longer symptom onset-to-treatment time, sepsis, and acute kidney injury (AKI). In multivariable analysis, hypertension (HT, mRR 3.27, p-value 0.047), chronic kidney disease (CKD, mRR 2.23, p-value 0.006), reperfusion injury (mRR 6.35, p-value 0.016), chronic heart failure (CHF, mRR 4.68, p-value 0.009), sepsis (mRR 4.68, p-value 0.009), and late onset > 24 h (mRR 2.11, p-value 0.009) were significant risk factors for major amputation among patients with ALI who underwent revascularization.

Conclusion: This high-volume retrospective cohort study demonstrated a substantial rate of major limb loss and identified several potentially modifiable prognostic factors. Fasciotomy may help improve limb salvage in selected patients. In addition, improving public awareness and health literacy may encourage earlier hospital presentation among patients with ALI.

Keywords: Acute limb ischemia, Revascularization, Thrombo-embolectomy, Bypass, Risk factors

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Corresponding author: Pak Hanaroonsomboon, MD, Department of Surgery, Khon Kaen Hospital; E-mail: pak44375.han@gmail.com; Phone number: +6689 171 6751

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INTRODUCTION

Acute limb ischemia (ALI) is defined as a sudden decrease in blood flow to a limb,[1] with onset ranging from a few hours to up to 14 days.[2] It is associated with substantial morbidity, including limb loss, acute kidney injury (AKI), and a mortality rate of 15 – 20%.[3] Common etiologies include atrial fibrillation (AF) with emboli formation, atherosclerotic plaque rupture, hypercoagulable states, trauma, and aortic dissection (AD).[4] The management strategies are guided by the Rutherford classification severity – I, IIA, IIB, and III.[5] Conservative treatment is generally used for class I, while primary amputation is often required for class III. For class II disease, revascularization, either catheter-based or open surgical, is the treatment of choice.[6] The selection between approaches depends on the duration and severity of ischemia, as well as the surgeon's preferences.[7]

Despite the increasing use of endovascular techniques in ALI management,[8] open surgical revascularization remains the standard treatment in many settings.[9] Surgical options include thrombo-embolectomy, surgical bypass, endovascular, and hybrid approaches. However, even with timely and appropriate treatment, complications from revascularization can be fatal, for example, ischemic-reperfusion injury. In severe cases, surgeons may resort to limb amputation as a life-saving measure. The reported rate of major amputation within 30 days after revascularization ranges from 10% to 30%.[10,11] Various prognostic factors were identified: age, emergent revascularization,[12] chronic kidney disease (CKD),[13] diabetes, and preexisting cerebrovascular disease.

The majority of the studies are in a chronic limb ischemia setting. There are very few findings on ALI. Furthermore, most prior Thai studies[10,14,15] have had small sample sizes (n < 100), and few have evaluated risk factors for major amputation. This study aims to identify outcomes and risk factors for major limb amputation in patients with ALI who underwent surgical revascularization in a tertiary care referral hospital in northeastern Thailand.

MATERIALS AND METHODS

Study design

This retrospective cohort prognostic (PROGRESS II) study was conducted at a tertiary care referral hospital in northeastern Thailand. The data were obtained from the electronic medical records (EMRs) of the vascular surgery unit in the Department of Surgery between 1st January 2017 and 31st December 2024. Eligible participants were patients aged 18 years or older who were diagnosed with ALI of the lower extremities and underwent primary surgical revascularization. ALI patients with Rutherford classification of I or III were automatically excluded, in accordance with the disease characteristics and international management guidelines[5]. Patient data were collected from disease onset until hospital discharge or in-hospital death. Multiple occlusion sites would be recorded as the most proximal occluded one. All patients received surgical revascularization and standard perioperative care. Baseline characteristics included sex, age, body mass index (BMI), comorbidities, clinical characteristics, and laboratory findings. Additional variables included disease severity and classification, time of onset, operative techniques, outcomes, and complications. The study was ethically approved by the Institutional Review Board (IRB) of the hospital (approval number: KEXP68018). The primary outcome was major amputation. Study size estimation was based on a prior institutional study, which reported a major amputation rate of 16.9%. Using onset proportions of 0.36 and 0.64, with 80% power, a significance level (alpha) of 0.05, and a 5:1 ratio, the required study size is estimated at 174 patients.

Surgical revascularization techniques

Two revascularization techniques were employed at the authors' institution: thrombo-embolectomy and surgical bypass.

Patients were diagnosed by preoperative computed tomography angiography of the lower extremities with distal run-off (CTA). Standard preparation included intravenous heparinization, hydration, oxygen supplementation, and analgesia. All procedures were performed under general anesthesia (GA). The lower abdomen, groin, and both legs were prepared and draped in a sterile fashion. The standard approach was exposure of the common femoral artery (CFA) at the bifurcation; exposure of the popliteal artery below the knee was occasionally required.

After induction of GA, the CFA was exposed at the groin under ultrasound guidance. The CFA, superficial femoral artery (SFA), and profunda femoris were identified and encircled with vascular loops, and proximal and distal control was ensured. A transverse arteriotomy was performed 1-2 centimeters above the bifurcation. Thrombus extraction was performed using appropriately sized Fogarty balloon catheters until balloon retrieval showed no residual thrombus and satisfactory antegrade and retrograde flow were achieved. A completion angiogram was performed to confirm clearance. The arteriotomy was closed. When concomitant atherosclerotic lesions or focal dissections impeded distal flow, trans-arterial bal-

loon angioplasty and stenting were performed following thrombus removal.

Surgical bypass was selected based on preoperative CTA findings or intraoperative failure of thrombo-embolectomy and/or angioplasty. Proximal and distal target vessels were exposed and controlled, and a polytetrafluoroethylene (PTFE) conduit or an autologous vein was used. Patency was confirmed with a completion angiogram. Fasciotomy was considered for patients with compartment syndrome or when clinical findings were equivocal. Technical success was defined as restoration of lower-limb blood flow confirmed by intraoperative angiography, Doppler ultrasonography, and palpable pedal pulses. Postoperatively, patients were admitted to either the intensive care unit (ICU) or the vascular surgery ward for routine monitoring. Continuous intravenous heparin infusion was maintained until the underlying etiology of ALI was identified and definitively managed.

When patients progressed to irreversible limb damage, amputation was performed. In this study, major amputation was defined as an amputation at or above the ankle. Minor amputation was defined as an amputation below the ankle.

Statistical analysis

Categorical variables were summarized as frequencies and percentages and compared using the exact probability test. Normally distributed continuous variables were summarized as means and standard deviations (mean ± SD) and compared using independent t-tests. Non-normally distributed continuous variables were summarized as medians and interquartile ranges (IQRs). Statistical uncertainty was expressed as 95% two-sided confidence intervals (95% CI). A p-value < 0.05 was considered statistically significant.

Risk factors for major amputation among patients with ALI who underwent surgical revascularization were evaluated using risk ratio regression. Variables for univariable analysis were selected based on clinical rationale and prior evidence. All potential variables were then entered into a multivariable model. All statistical analyses were performed using STATA version 18 (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC)

RESULTS

Patient characteristics

Among 152 patients who underwent surgical revascularization for ALI, 63.5% were male. The mean age was 61.8 ± 16.0 years. The most common comorbidities were hypertension (53.9%), dyslipidemia (50.0%), and AF (40.8%). Dyslipidemia was not significantly more prevalent in the major amputation group, whereas AF was significantly more prevalent in the limb salvage group. Alcohol use (32.9%) and intracardiac thrombus (11.2%) were also significantly more common in the limb salvage group. CKD was more frequent among patients who underwent major amputation. There were no significant between-group differences in BMI, smoking status, DM, cerebrovascular diseases, ischemic heart disease, or AAA, as shown in **Table 1**.

Table 1 Baseline characteristics of the patients who underwent surgical revascularization for ALI

Baseline characteristics, n (%)	All, n = 152 (%)	Limb salvage n = 126, (82.9%)	Major amputation n = 26, (17.1%)	*p*-value
Male sex	96 (63.2)	80 (63.5)	16 (61.5)	0.828
Age, years (mean ± SD)	61.8 ± 16.0	61.1 ± 16.1	65.6 ± 15.5	0.192
BMI, kg/m2 (mean ± SD)	23.2 ± 5.0	23.5 ± 5.2	21.5 ± 3.6	0.061
Smoking	42 (27.6)	35 (27.8)	7 (26.9)	1.000
Alcohol use	50 (32.9)	47 (37.3)	3 (11.5)	0.011
Underlying diseases				
Hypertension	82 (53.9)	63 (50.0)	19 (73.1)	0.050
DM	37 (24.3)	31 (24.6)	6 (23.1)	1.000
Dyslipidemia	76 (50.0)	59 (46.8)	17 (65.4)	0.131
Presence of intracardiac thrombus	17 (11.2)	17 (13.5)	0 (0.0)	0.045
CKD stage ≥ 3	11 (7.2)	6 (4.8)	5 (19.2)	0.022
AF	62 (40.8)	56 (44.4)	6 (23.1)	0.050
Cerebrovascular disease	24 (15.8)	21 (16.7)	3 (11.5)	0.768
IHD	16 (10.5)	15 (11.9)	1 (3.8)	0.309
AAA	4 (2.6)	4 (3.2)	0 (0.0)	1.000

ALI = acute limb ischemia; SD = standard deviation; BMI = body mass index; kg = kilograms; m = meters; DM = diabetic mellitus; CKD = chronic kidney disease; AF = atrial fibrillation; IHD = ischemic heart disease; AAA = abdominal aortic aneurysm

Clinical characteristics

All patients had lower-extremity ALI. Overall, 26 of 152 (17.1%) underwent major amputation. Rutherford class 2B predominated (87.5%), followed by class 2A (12.5%), with no significant between-group difference. Patients in the major amputation group presented after a significantly longer symptom duration; 50% presented more than 72 hours from onset. The anatomic level of occlusion varied across the aorta, iliac, femoral, popliteal, and tibioperoneal segments, with no significant differences between groups. Surgical revascularization consisted primarily of thromboembolectomy (141 of 152 patients); the remaining 11 patients underwent bypass surgery. The median length of stay was 6 [4, 10] days. The data were shown in **Table 2**.

Risk factors associated with major amputation

In univariable analysis, alcohol use was associated with a lower risk of major amputation (uRR 0.27, 95% CI 0.08 – 0.84, *p*-value = 0.025). Factors associated with a higher risk included hypertension (uRR 2.32, 95% CI 1.04 – 5.19, *p*-value = 0.041), CKD (uRR 3.05, 95% CI 1.43 – 6.51, *p*-value = 0.004), AKI (uRR 2.74, 95% CI 1.31 – 5.75, *p*-value = 0.008), sepsis (uRR 4.65, 95% CI 2.52 – 8.63, *p*-value < 0.001), and symptom onset more than 24 hours (uRR 2.39, 95% CI 1.16 – 4.19, *p*-value = 0.018). The multivariable risk ratio regression, protective factors were male sex (mRR 0.85, 95% CI 0.85 – 0.85, *p*-value < 0.001), alcohol use (mRR 0.14, 95% CI 0.03 – 0.73, *p*-value = 0.020), DM (mRR 0.48, 95% CI 0.27 – 0.85, *p*-value = 0.011), AF (mRR 0.14, 95% CI 0.04 – 0.54, *p*-value = 0.005), and fasciotomy performed (mRR 0.09, 95% CI 0.02 – 0.50, *p*-value = 0.005). Risk factors included hypertension (mRR 3.27, 95% CI 1.02 – 10.52, *p*-value = 0.047), CKD (mRR 2.23, 95% CI 1.26 – 3.91, *p*-value = 0.006), reperfusion injury (mRR 6.35, 95% CI 1.42 – 28.45, *p*-value = 0.016), CHF (mRR 4.68, 95% CI 1.48 – 14.80, *p*-value = 0.009), sepsis (mRR 2.11, 95% CI 1.21 – 3.70, *p*-value = 0.009), and symptom onset more than 24 hours (mRR 2.11, 95% CI 1.21 – 3.0, *p*-value = 0.009). The details were also shown in **Table 4**.

Table 2 Clinical characteristics of the patients diagnosed with ALI who underwent surgical revascularization

Clinical characteristics	all, n = 152 (%)	Limb salvage n = 126 (82.9%)	Major amputation n = 26 (17.1%)	*p*-value
Rutherford classification				
2A	19 (12.5)	17 (13.5)	2 (7.7)	0.532
2B	133 (87.5)	109 (86.5)	24 (92.3)	
Onset (hours)				
< 6	38 (25.0)	38 (30.2)	0 (0.0)	< 0.001
6 – 24	53 (34.9)	43 (34.1)	10 (38.5)	
24 – 72	29 (19.1)	26 (20.6)	3 (11.5)	
> 72	32 (21.1)	19 (15.1)	13 (50.0)	
Occlusion site				
Aortoiliac	13 (8.6)	13 (10.3)	0 (0.0)	0.303
Iliofemoral	34 (22.4)	30 (23.8)	4 (15.4)	
Femoropopliteal	59 (38.8)	47 (37.3)	12 (46.2)	
Popliteal bifurcation	40 (26.3)	31 (24.6)	9 (34.6)	
Tibioperoneal	6 (3.9)	5 (4.0)	1 (3.8)	
Revascularization technique				
Thrombo-embolectomy	141 (92.8)	116 (92.1)	25 (96.2)	0.691
Surgical bypass	11 (7.2)	10 (7.9)	1 (3.8)	
LOS, days [median, IQR]	6 [4, 10]	6 [4, 9]	7 [4, 13]	0.132

ALI = acute limb ischemia; IQR = interquartile range, LOS = length of stay

Outcomes and complications

No patient who underwent a major amputation also underwent a minor amputation. Fasciotomy was performed more frequently in the limb salvage group, but the difference was not statistically significant. AKI and sepsis occurred significantly more often in the major amputation group. In-hospital mortality was 11.2% overall and higher in the major amputation group (19.2%), although this difference did not reach statistical significance. The details were presented in **Table 3**.

Table 3 Outcomes and complications of the patients diagnosed with ALI who underwent surgical revascularization

Complications, n (%)	all, n = 152 (%)	Limb salvage n = 126 (82.9%)	Major amputation n = 26 (17.1%)	*p*-value
Minor amputation	9 (5.9%)	9 (7.1%)	0 (0.0%)	0.359
Fasciotomy	14 (9.2%)	13 (10.3%)	1 (3.8%)	0.466
Reperfusion injury	19 (12.5%)	13 (10.3%)	6 (23.1%)	0.099
Postoperative MI	13 (8.6%)	11 (8.7%)	2 (7.7%)	1.000
AKI	15 (9.9%)	9 (7.1%)	6 (23.1%)	0.024
Postoperative stroke	10 (6.6%)	8 (6.3%)	2 (7.7%)	0.681
CHF	22 (14.5%)	16 (12.7%)	6 (23.1%)	0.217
Sepsis	18 (11.8%)	8 (6.3%)	10 (38.5%)	< 0.001
in-hospital dead	17 (11.2%)	12 (9.5%)	5 (19.2%)	0.173

ALI = acute limb ischemia; MI = myocardial infarction; AKI = acute kidney injury; CHF = congestive heart failure

Table 4 Risk factors associated with major amputation

Risk factors	uRR	Lower 95% CI	Upper 95% CI	*p*-value	mRR	Lower 95% CI	Upper 95% CI	*p*-value
Male sex	0.93	0.46	1.91	0.851	0.85	0.85	0.85	< 0.001
Age > 75 years	1.54	0.74	3.23	0.251	1.05	0.73	1.51	0.775
BMI < 18.5 kg/m²	1.25	0.48	3.24	0.641	1.38	0.41	4.59	0.603
Smoking	0.96	0.44	2.13	0.929	2.02	0.56	7.24	0.282
Alcohol	0.27	0.08	0.84	0.025	0.14	0.03	0.73	0.020
DM	0.93	0.41	2.15	0.869	0.48	0.27	0.85	0.011
Hypertension	2.32	1.04	5.19	0.041	3.27	1.02	10.52	0.047
Dyslipidemia	1.89	0.90	3.97	0.093	1.91	0.53	6.96	0.325
AF	0.44	0.19	1.02	0.056	0.14	0.04	0.54	0.005
CKD	3.05	1.43	6.51	0.004	2.23	1.26	3.91	0.006
IHD	0.34	0.05	2.34	0.273	0.26	0.03	1.90	0.182
Aortoiliac occlusion	0.41	0.15	1.11	0.080	0.37	0.11	1.27	0.115
Fasciotomies perform	0.39	0.06	2.69	0.343	0.09	0.02	0.50	0.005
Reperfusion injury	2.10	0.97	4.56	0.061	6.35	1.42	28.45	0.016
MI	0.89	0.24	3.35	0.865	0.30	0.05	1.94	0.207
Acute kidney injury	2.74	1.31	5.75	0.008	0.63	0.21	1.85	0.396
Stroke	1.18	0.33	4.31	0.798	13.33	0.42	418.86	0.141
CHF	1.77	0.80	3.92	0.157	4.68	1.48	14.80	0.009
Sepsis	4.65	2.51	8.63	< 0.001	2.11	1.21	3.70	0.009
Embolectomy	1.95	0.29	13.07	0.491	1.60	0.18	14.30	0.673
Rutherford 2B	1.71	0.44	6.68	0.437	3.99	0.15	105.96	0.408
Onset > 24 h	2.39	1.16	4.91	0.018	2.11	1.21	3.70	0.009

uRR = univariable risk ratio; CI = confident interval; mRR = multivariable risk ratio; BMI = body mass index; kg = kilograms; m = meters; DM = diabetic mellitus; AF = atrial fibrillation; CKD = chronic kidney disease; IHD = ischemic heart disease; CHF = congestive heart failure; h = hours

DISCUSSION

ALI is a common vascular emergency. In the United States, the incidence is estimated at 4.16 – 7.16 per 100,000 persons per year.[16] Management strategies of ALI vary by occlusion type, etiology, Rutherford classification, ischemic duration, and available resources.[17,18] Endovascular therapies can be adopted in high-volume centers with sufficient capacity[19] and are associated with fewer in-hospital cardiopulmonary complications,[20] albeit with a moderate increase in hospital costs.[21] Nevertheless, open surgical revascularization remains crucial in patients with threatened limbs and prolonged ischemia.[17]

Major adverse cardiac and limb events (MACE and MALE, respectively) may occur after emergent or urgent revascularization for ALI. Hospitalization for MALE occurs in approximately in 1 in 10 patients within one year after peripheral revascularization.[22] Previously reported risk factors for limb loss included patient sex, etiology, including aneurysmal diseases and trauma, and hemodynamic instability.[23] Thai studies have also identified predictors such as clinical severity, symptom onset, and anatomic location; SFA occlusion has been associated with major limb loss.[11] Poor tibial runoff on completion angiography also gave a worse prognosis.[23]

In our cohort, hypertension, CKD, reperfusion injury, CHF, sepsis, and delayed presentation (more than 24 hours from onset) were associated with a higher major amputation rate. Hypertension, via arterial stiffness[24] Atherosclerosis likely increases the technical difficulty of revascularization due to pre-existing occlusions, calcification, and stenosis. These lesions can impede Fogarty catheter passage and often necessitate adjunct angioplasty to prevent re-occlusion. CKD, frequently coexisting with hypertension, confers both systemic and local vulnerabilities.[25] Patients with CKD have a higher prevalence of PAD, and revascularization in the setting of pre-existing PAD and CKD is associated with poorer outcomes.[22,26] Reperfusion injury after revascularization carries substantial morbidity, including AKI and hyperkalemia, and can be fatal.[27] These complications may precipitate the need for life-saving amputation. The associations observed with CHF and sepsis likely reflect systemic compromise that further jeopardizes limb viability. The effect of delayed presentation is intuitive; longer ischemic time intensifies ischemia-reperfusion injury and worsens tissue viability after revascularization.

Conversely, male sex, alcohol use, DM, AF, and performance of fasciotomy were identified as protective factors in multivariable analysis. The direction of association were lower probability of outcome occurring. Sex-related differences in arterial stiffness and vascular biology have been proposed,[27] but the direction of effect in our study contrasts with much of the literature and may be influenced by study size and residual confounding. The apparent protective association of diabetes and alcohol use also contradict most reports that identify diabetes and alcohol use as the risk factors for limb loss after ALI revascularization.[28,29] The limited power of the study size may explain this finding. In our institute, we did not select ALI management strategies based on underlying diseases. So, the confounding by indication was methodologically eliminated. AF is a common cause of ALI.[30] It often produces embolic occlusions in otherwise healthy arteries. Such patients tend to present earlier because of severe pain, the thrombus is typically fresh, and thrombo-embolectomy is often sufficient without the need for adjunct angioplasty or bypass, all of which may favor limb salvage. In our study, adjunctive angioplasty was occasionally required after thromboembolectomy in patients with thrombotic occlusion associated with pre-existing chronic stenotic lesions. Angioplasty was also performed to treat residual dissection following thromboembolectomy or to correct residual tibial vessel disease in order to improve distal runoff after either thromboembolectomy or bypass procedures. If angioplasty failed, patients subsequently underwent surgical bypass when adequate distal runoff was present. Finally, early or prophylactic fasciotomy can mitigate reperfusion-related edema and prevent compartment syndrome[31], thereby reducing the risk of limb loss, although prior evidence on outcome differences is mixed[32]. Delayed fasciotomy was also discussed in previous evidence. It is associated with a higher major amputation risk in patients with ALI[33]. Furthermore, because of the retrospective design, the indication and timing of fasciotomy were not consistently documented; therefore, we could not distinguish between prophylactic and therapeutic fasciotomy. This limitation may affect the interpretation of the observed association between fasciotomy and major amputation. Notably, recent studies have reported similar amputation-free survival between prophylactic and therapeutic fasciotomy in selected patients with acute limb ischemia, although these findings should be interpreted in the context of patient selection and ischemia severity[34].

This study has limitations inherent to its retrospective design. Including potential unmeasured confounding, especially on surgeon preferences and intraoperative decision-making. Recall bias is possible, particularly in symptom-onset time. The definition and diagnostic classification of reperfusion injury, sepsis, and acute kidney injury were not always clearly defined and depended on the treating surgeon's clinical judgment at the time of care. The achieved sample size was smaller than the prespecified estimate, reducing the statistical power to detect clinically meaningful associations. As a result, effect estimates, particularly in multivariable models and potential subgroup analyses, may be unstable with wide confidence intervals, and some true associations may have been missed (type II error). Future studies with larger study sizes are warranted. Furthermore, due to data-collection limitations, the etiology of ALI was not clearly documented, resulting in missing data for this variable. However, a preliminary review of the available records suggested that the etiologies were mixed. Despite these constraints, this work is among the first reports from Thailand to examine risk factors for major amputation after surgical revascularization for ALI, using a relatively large single-center cohort.

Our findings underscore the importance of timely presentation and aggressive management of systemic comorbidities (hypertension, CKD, CHF, sepsis) to optimize limb outcomes after ALI. The protective associations observed for AF and fasciotomy highlight potentially modifiable aspects of care (rapid diagnosis in suspected embolic ALI and selective early fasciotomy) that warrant further prospective evaluation.

CONCLUSION

ALI remains a common and clinically significant emergency. In this high-volume, single-center retrospective cohort, we observed a substantial rate of major limb loss. Several prognostic factors, such as Hypertension, CKD, reperfusion injury, CHF, sepsis, alcohol use, diabetes, and AF, some of which are potentially modifiable, were identified. Early or prophylactic fasciotomy may aid limb salvage in selected patients. Enhancing public and provider health literacy to promote earlier recognition and hospital presentation for ALI could reduce ischemic time and improve outcomes. Prospective studies are warranted to validate these findings and guide targeted interventions.

REFERENCES

1. Obara H, Matsubara K, Kitagawa Y. Acute Limb Ischemia. Ann Vasc Dis. 11(4):443-8. doi: 10.3400/avd.ra.18-00074. PMID: 30636997; PMCID: PMC6326052.
2. Gornik HL, Aronow HD, Goodney PP, et al. 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 149(24):e1313-e410. doi: 10.1161/CIR.0000000000001251.
3. Norgren L, Hiatt WR, Dormandy JA, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg. 45 Suppl S: S5-67. doi: 10.1016/j.jvs.2006.12.037.
4. Natarajan B, Patel P, Mukherjee A. Acute Lower Limb Ischemia-Etiology, Pathology, and Management. Int J Angiol. 29(3):168-74. doi: 10.1055/s-0040-1713769.
5. Björck M, Earnshaw JJ, Acosta S, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Acute Limb Ischaemia. Eur J Vasc Endovasc Surg. 59(2):173-218. doi: 10.1016/j.ejvs.2019.09.006.
6. Utsunomiya M. Endovascular Therapy for Acute Limb Ischemia. J Atheroscler Thromb. 28(11):1126-7. doi: 10.5551/jat.ED161.
7. Lukasiewicz A. Contemporary Management of Acute Lower Limb Ischemia: Determinants of Treatment Choice. J Clin Med. 9(5):1501. doi: 10.3390/jcm9051501.
8. Inagaki E, Farber A, Kalish JA, et al. Outcomes of Peripheral Vascular Interventions in Select Patients With Lower Extremity Acute Limb Ischemia. J Am Heart Assoc. 7(8):e004782. doi: 10.1161/JAHA.116.004782.
9. Wang JC, Kim AH, Kashyap VS. Open surgical or endovascular revascularization for acute limb ischemia. J Vasc Surg. 63(1):270-8. doi: 10.1016/j.jvs.2015.09.055.
10. Suesawatee A, Kritayamaneerat K, Wannasiri T, et al. Clinical Outcomes Following Surgical Revascularization for Acute Lower Limb Ischemia. Thai J Surg. 45(2):36–42.
11. 11.Rungkhachonsak S, Sumnuan T, Vutisirinukool S, et al. Prognostic Factors of Major Amputations in Patients with Acute Limb Ischemia. Health Sci Clin Res. 37(1):22–32.
12. Li Q, Birmpili P, Atkins E, et al. Illness Trajectories After Revascularization in Patients With Peripheral Artery Disease: A Unified Approach to Understanding the Risk of Major Amputation and Death. Circulation. 150(4):261-71. doi: 10.1161/CIRCULATIONAHA.123.067687.
13. Torbjörnsson E, Fagerdahl AM, Blomgren L, et al. Risk factors for reamputations in patients amputated after revascularization for critical limb-threatening ischemia. J Vasc Surg. 73(1):258-66.e1. doi: 10.1016/j.jvs.2020.03.055.
14. Mutirangura P, Ruangsetakit C, Wongwanit C, et al. Clinical differentiation between acute arterial embolism and acute arterial thrombosis of the lower extremities. J Med Assoc Thai. 92(7):891-7.
15. Ruangsetakit C, Niyomnaitham V, Chinsakchai K, et al. Outcomes of Intra-operative Thrombolysis in Late Acute Arterial Embolism of the Lower Limb in a Cohort of Patients in Thailand.
16. Jarosinski MC, Kennedy JN, Iyer S, et al. Contemporary National Incidence and Outcomes of Acute Limb Ischemia. Ann Vasc Surg. 110(Pt B):224-35. doi: 10.1016/j.avsg.2024.06.032.
17. Olinic DM, Stanek A, Tătaru DA, et al. J Clin Med. 8(8):1215. doi: 10.3390/jcm8081215.

18. Desai U, Kharat A, Hess CN, et al. Healthcare resource utilization and costs of major atherothrombotic vascular events among patients with peripheral artery disease after revascularization. J Med Econ. 24(1):402-9. doi: 10.1080/13696998.2021.
19. Elbadawi A, Elgendy IY, Rai D, et al. Impact of Hospital Procedural Volume on Outcomes After Endovascular Revascularization for Critical Limb Ischemia. JACC Cardiovasc Interv. (17):1926-36. doi: 10.1016/j.jcin.2021.06.032.
20. Kolte D, Kennedy KF, Shishehbor MH, et al. Endovascular Versus Surgical Revascularization for Acute Limb Ischemia: A Propensity-Score Matched Analysis. Circ Cardiovasc Interv. 13(1):e008150. doi: 10.1161/CIRCINTERVENTIONS.119.008150.
21. Ouriel K, Shortell CK, DeWeese JA, et al. A comparison of thrombolytic therapy with operative revascularization in the initial treatment of acute peripheral arterial ischemia. J Vasc Surg. (6):1021-30. doi: 10.1016/s0741-5214(94)70214-4.
22. Hess CN, Rogers RK, Wang TY, et al. Major Adverse Limb Events and 1-Year Outcomes After Peripheral Artery Revascularization. J Am Coll Cardiol. 72(9):999-1011. doi: 10.1016/j.jacc.2018.06.041.
23. Juneja A, Garuthara M, Talathi S, et al. Predictors of poor outcomes after lower extremity revascularization for acute limb ischemia. Vascular. 32(3):632-9. doi: 10.1177/17085381231154290.
24. Boutouyrie P, Chowienczyk P, Humphrey JD, et al. Arterial Stiffness and Cardiovascular Risk in Hypertension. Circ Res. 128(7):864-86. doi: 10.1161/CIRCRESAHA.121.318061.
25. Rerkasem A, Mangklabruks A, Buranapin S, et al. Chronic Kidney Disease Predicts Adverse Major Cardiovascular Events and Adverse Limb Events in Patients With Diabetes and Peripheral Arterial Disease. Int J Low Extrem Wounds. 23(1):19-26. doi: 10.1177/15347346231211959.
26. Garimella PS, Hart PD, O'Hare A, et al. Peripheral artery disease and CKD: a focus on peripheral artery disease as a critical component of CKD care. Am J Kidney Dis. 60(4):641-54. doi: 10.1053/j.ajkd.2012.02.340.
27. Wu MY, Yiang GT, Liao WT, et al. Cell Physiol Biochem. 46(4):1650-67. doi: 10.1159/000489241.
28. Pernès JM, Auguste M, Borie H, et al. Infrapopliteal arterial recanalization: A true advance for limb salvage in diabetics. Diagn Interv Imaging. 96(5):423-34. doi: 10.1016/j.diii.2014.09.002.
29. Rungkhachonsak S, Sumnuan T, Vutisirinukool S, et al. Prognostic Factors of Major Amputations in Patients with Acute Limb Ischemia. Health Sci Clin Res. 37(1):22–32.
30. Hess CN, Huang Z, Patel MR, et al. Acute Limb Ischemia in Peripheral Artery Disease. Circulation. 140(7):556-65. doi: 10.1161/CIRCULATIONAHA.119.039773.
31. Natour AK, Shepard AD, Rteil A, et al. Ann Vasc Surg. 94:143-53. doi: 10.1016/j.avsg.2023.04.023.
32. Lin JH, Humphries MD, Hasegawa J, et al. Outcomes After Selective Fasciotomy for Revascularization of Nontraumatic Acute Lower Limb Ischemia. Vasc Endovascular Surg. 56(1):18-23. doi: 10.1177/15385744211045493.
33. Rothenberg KA, George EL, Trickey AW, et al. Ann Vasc Surg. 59:195-201. doi: 10.1016/j.avsg.2019.01.028.
34. Apichartpiyakul P, Khorana J, Rerkasem K, et al. 33(6):1360-1367. doi: 10.1177/17085381241307758.

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Original Article

Prospective Randomized Clinical Trial of Accelerated Re-Epithelialization of Split-Thickness Skin Graft Donor Sites Using Injectable Platelet-Rich Fibrin (I-PRF)

Premsak Sakarinpanichakul, MD[1]
Watchara Burapholkul, MD[1]
Pucharaporn Jiengjariyanont, MD[2]

[1]*Division of Plastic and Reconstructive Surgery, Department of Surgery, Buriram Hospital, Buri Ram, Thailand*
[2]*Department of Anatomical Pathology, Buriram Hospital, Buri Ram, Thailand*

Abstract

Background: Autologous platelet-rich fibrin (PRF) is a fraction of blood with a high concentration of platelets and multiple growth factors. Its application has shown promising results in wound care. However, it remains controversial whether applying PRF to donor site wounds of split-thickness skin grafts (STSGs) improves the epithelialization rate. This study aimed to determine the effect of injectable platelet-rich fibrin (I-PRF) on the epithelialization of donor-site wounds in STSG.

Materials and Methods: This randomized controlled clinical trial included 30 patients who underwent STSG procedures at Buriram Hospital between November 2023 and February 2025. The donor site wounds were divided into two groups for the study. The intervention group received an I-PRF and paraffin gauze, while the control group received paraffin gauze alone. The evaluation assessed the time required to re-epithelialize donor-site wounds and measured epithelial thickness after full re-epithelialization.

Results: The mean age of the patients was 50.7 ± 18.7 years, and 63.3% were male. Time to complete epithelialization of donor wounds did not differ significantly between I-PRF and control groups (11.9 ± 2.6 days vs 11.9 ± 2.7 days; p = 0.851). The mean epithelial thickness of the I-PRF group was higher than that of the control group, but the difference was not statistically significant (208 ± 110 mm vs 197 ± 118 mm; p = 0.698).

Conclusion: Compared to traditional therapy, a single application of injectable platelet-rich fibrin did not significantly influence the re-epithelialization of an STSG donor wound.

Keywords: Platelet-rich fibrin, Injectable platelet-rich fibrin, Epithelialization, Donor site

INTRODUCTION

Split-thickness skin grafts (STSGs) consist of varying dermal layers and are a commonly used reconstructive technique for closing defects that cannot be closed primarily. The donor site of the STSG generally heals (re-epithelializes) in 7-21 days.[1] Theoretically, an ideal donor site wound dressing should be easy to apply, promote rapid re-epithelialization without adhering to the wound bed, reduce inflammation, minimize disease transmission and host immune response, significantly decrease wound pain, and be cost-effective.[2,3] Numerous studies are using various materials or methods to improve the re-epithelialization of the donor site after STSG, such as modern dressings,[4,5] biological dressings,[6-9] drugs[10] and medical equipment.[11]

A platelet-rich product is a biological preparation containing a platelet concentration higher than the baseline of whole blood. Growth factors, such as platelet-derived growth factor (PDGF), transforming growth factor β (TGF-β), epidermal growth factor (EGF), fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), and insulin-like growth factor (IGF), are released

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Corresponding author: Premsak Sakarinpanichakul, MD, Division of Plastic and Reconstructive Surgery, Department of Surgery, Buriram Hospital, Buri Ram, Thailand; E-mail: tommy.premsak@gmail.com; Phone number: +6686 873 8737
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after platelet activation to enhance wound healing.[12,13] Platelet-rich products are classified into two main categories: platelet-rich plasma (PRP) and platelet-rich fibrin (PRF).[14] Numerous studies have utilized platelet-rich products to enhance the healing of both acute and chronic wounds.[15,16]

PRF is a second-generation platelet concentrate developed by Choukroun et al. in 2001 that does not use anticoagulation factors. There are two types of PRF: a solid form and a liquid form. The solid form is the original PRF formulation developed by Choukroun and colleagues. The injectable liquid form of PRF (I-PRF) was developed by reducing the centrifugation force to 700 rpm (revolutions per minute) and 60g RCF (Relative Centrifugal Force) for 3 minutes.[17] I-PRF has been used in various oral and maxillofacial procedures,[18,19] as well as in wound healing.[20,21] However, few studies have directly examined the relationship between I-PRF and the healing of donor-site wounds following STSG.[22-24]

This study aimed to assess the potential benefits of I-PRF on wound healing in donor-site STSG wounds compared to the established standard treatment at our hospital.

MATERIALS AND METHODS

Study Design

This study was a prospective, randomized, controlled trial comparing the effectiveness of a paraffin gauze dressing plus I-PRF with that of the paraffin gauze dressing alone. The study was approved by the Ethics Committee of Buriram Hospital (Protocol No. BR 0033.102.1/73) and registered with the Thai Clinical Trials Registry (TCTR). The TCTR identification number is TCTR20240704001.

Material (Dressings)

A standard dressing for STSG donor site in our institution is paraffin gauze containing 0.5% chlorhexidine acetate (Bactigras; Smith & Nephew Medical Ltd.). This antiseptic, low-adherent dressing soothes and protects the wound while helping reduce infection and inflammation. The paraffin gauze allows the free passage of viscous exudate through the grid into a secondary dressing while maintaining a moist wound bed.[25] We assigned the paraffin gauze (Bactigras) to the control group.

We prepared the I-PRF according to the low-speed centrifugation concept[17] and assigned the Bactigras plus I-PRF to the intervention group.

Preparation of I-PRF (Figure 1)

- After harvesting the STSG from the donor site, 20 ml of peripheral venous blood was collected into a sterile 10 ml plastic syringe without a plunger (Nipro). The syringe tip was covered with a cap, and the barrel was held with a sterile surgical drape. No anticoagulants were used during the procedure.
- Centrifugation was performed immediately at 700 rpm (revolutions per minute) for 3 minutes at room temperature (MRC Laboratory Equipment, Model: SCEN-206).
- After centrifugation, a yellow I-PRF formed at the top layer, while other components settled at the bottom.
- The yellow fluid at an upper level was extracted using a 16G needle, 2 inches.

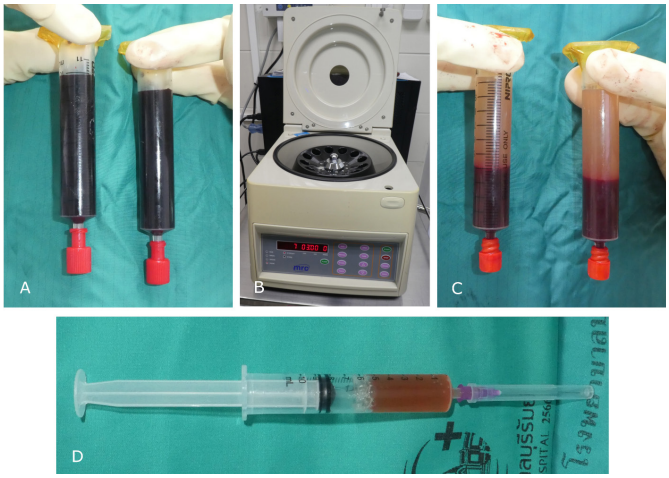


Figure 1 A) Collection of 20 ml (10 ml each × 2 tubes) of whole blood in sterile plastic syringes without a plunger, with the tip cap covering the syringe tip, and the barrel held with a sterile surgical plastic drape. B) A centrifuge was used to prepare I-PRF from blood samples. C) Appearance of I-PRF after centrifugation. D) I-PRF collection after extracting from the tubes.

Sample size

The required sample size was calculated using the formula for the difference between two correlated quantitative measurements (paired means):

$$n/group = \frac{2\left(Z_{\frac{\alpha}{2}} + Z_{\beta}\right)^2 \sigma^2(1-\rho)}{(\mu 1 - \mu 2)^2}$$

where $\alpha = 0.05$ ($Z_{\alpha/2} = 1.96$), $\beta = 0.10$ ($Z_{\beta} = 1.28$, power = 90%), and ρ is the correlation coefficient, estimat-

ed at 0.5 as a conservative value. The pooled variance$(\sigma)^2$ and mean values ($\mu1$, $\mu2$) were derived from a previous study by Senada et al.[22] which reported a mean epithelialization time of 11.55 ± 1.39 days in the experimental group and 13.45 ± 1.70 days in the control group. Substitution into the formula indicated a minimum requirement of 8 participants. After adjustment for an anticipated 30% attrition rate, the final required sample size was 12 participants. In practice, 30 participants per group were enrolled to increase statistical power, improve the precision of effect estimates, and better capture clinical variability.

Patients and randomization

Thirty patients with skin defects requiring partial-thickness skin grafting were enrolled in this study. The primary indications for STSG were reconstruction of defects following cancer excision (10 cases), trauma-related wounds (9 cases), burn injuries (6 cases), and post-debridement wounds from infection (5 cases). All patients provided written informed consent and were permitted to use their photos before enrollment. The donor sites were equally divided and randomized using one of two sealed envelope techniques for the intervention group. Both proximal and distal sides were labeled. Other officers allocated the wound dressing on the day of surgery before the procedure.

Outcome variables

The primary outcome was the time to complete donor-site healing (>90% re-epithelialization).[26] The secondary outcome was the epithelial thickness of the donor site after complete re-epithelialization.

Inclusion and exclusion criteria

The study included patients aged 18 and older who were hospitalized at Buriram Hospital and underwent STSG between November 2023 and February 2025.

The exclusion criteria were:

- Refusal to participate
- Patients with hematologic disorder
- Patients with a platelet count of less than 100,000 platelets per microliter or a history of platelet dysfunction
- Patients with severe cardiovascular, connective tissue disease, end-stage renal disease, liver cirrhosis or liver failure, cancer, septicemia, or other diseases that may affect wound healing
- Patients with severe malnutrition
- Pregnancy
- Patients with systemic steroids used within 2 weeks before surgery
- Patients with an immunocompromised host
- Patients with HIV infection
- Inflammation or infection of the donor site

Technique

The first author, a plastic surgeon (P.S), performed all operations under general anesthesia. The STSGs were taken from the thigh with the Air Zimmer Dermatome skin grafting system (Zimmer, Inc., Warsaw, US) at a depth of 0.175 mm. The donor site was divided into three zones: proximal, middle, and distal. The proximal and distal zones were split in half and randomly assigned to either the control or intervention group. To minimize contamination or bias, the middle zone was approximately 2 cm wide at the midline; it was defined as the border between the proximal and distal zones and was excluded from the evaluation (**Figure 2**). After harvesting STSG, the surgeon measured the wound length and width with a sterile ruler and photographed the donor site. The I-PRF was prepared, and the designated dressings were applied to the control and intervention groups (**Figure 3**). The assigned wound-dressing materials were then covered with sterile dry gauze and secured with an elastic bandage. To minimize the risk of cross-contamination during bandage application, each donor site zone was covered with individual sterile gauze before being secured with an elastic bandage, ensuring no fluid communication between the intervention and control sites.

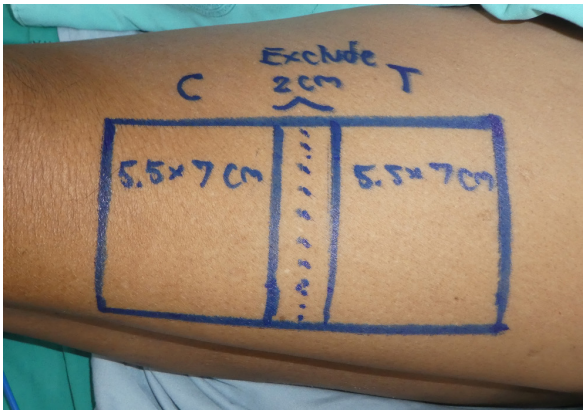


Figure 2 The area was divided into three zones (proximal, middle, and distal zones). The proximal and distal zones were randomly assigned to either the control or the intervention group. The middle zone was 2 cm wide at the midline. It was defined as the border between the proximal and distal zones and was not included in the evaluation.

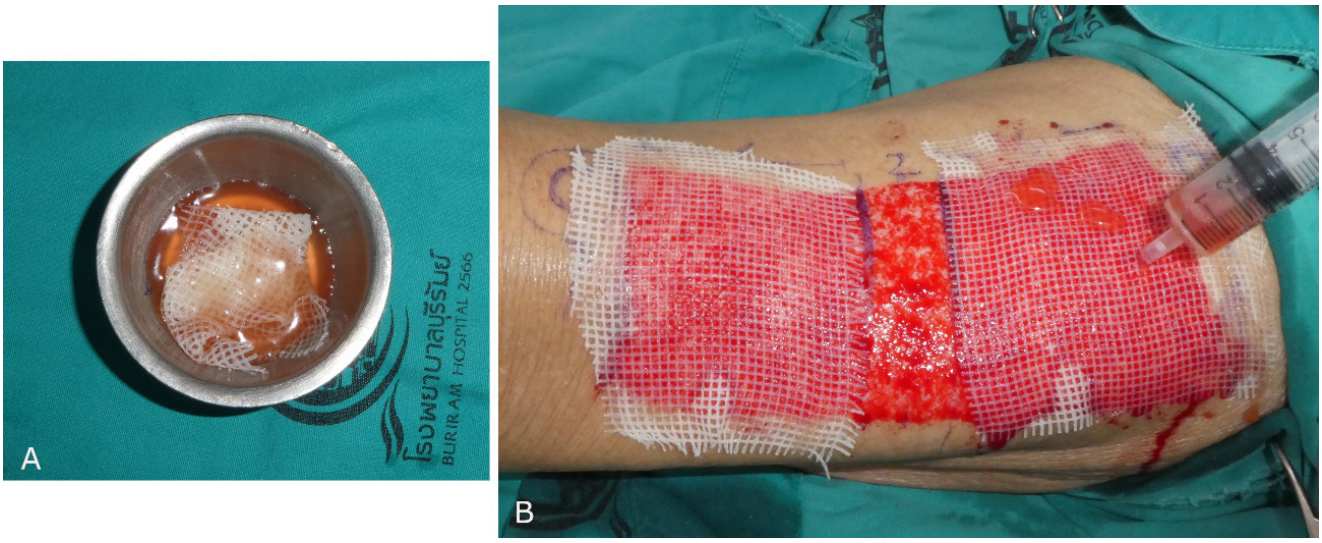


Figure 3 A) A paraffin gauze soaked in I-PRF preparation for the intervention side. B) A paraffin gauze dressing for the control side and a paraffin gauze soaked in I-PRF + I-PRF instillation for the intervention side are applied.

Postoperative management and follow-up

We evaluated wound-healing time, donor-site complications (signs of inflammation or infection), and microscopic epithelial thickness.

Wound healing was assessed visually by two independent plastic surgeons, experts in wound care, by measuring the re-epithelialization rate across the wound surface area. The initial dressing was changed on postoperative day 7. Subsequent dressings were altered based on the rate of re-epithelialization as follows: every 3 days if the rate was less than 50%, every 2 days if it was between 50% and 75%, and daily if it exceeded 75%. This process continued until the wound was fully healed. Photographs were taken during each dressing change. Complete healing of the donor site was defined as more than 90% re-epithelialization of the wound.[26]

After complete epithelialization, a 4-mm punch biopsy was performed on both the control and intervention sides using a KAI biopsy punch (KAI Industries Co., Ltd.), and the specimens were fixed in 10% natural formaldehyde for microscopic measurement of epithelial thickness. Paraffin-fixed specimens were stained with hematoxylin and eosin (H&E). The average epithelial thickness from 25 randomly selected microscopic fields from each H&E-stained specimen was then recorded by two independent, blinded pathologists. (**Figure 4**).[27]

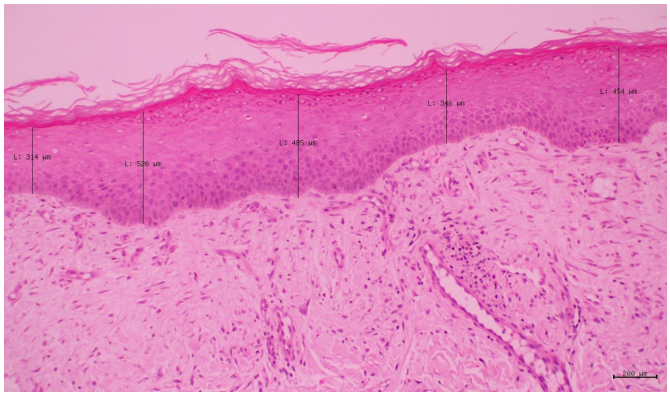


Figure 4. Specimen from the donor site after hematoxylin and eosin (H&E) staining. The section displays the epithelial thickness measurements from 25 randomly selected microscopic fields (see an example of 5 points in the image). × 10

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics. Inter-rater reliability for both the epithelialization rate and epithelial thickness was assessed using the Intraclass Correlation Coefficient (ICC). For the primary analysis, paired t-tests were performed to compare the mean epithelialization rate and epithelial thickness between the two groups. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Inter-rater reliability

Inter-rater reliability for both the epithelialization rate and epithelial thickness measurements was assessed using a two-way random-effects model with absolute agreement. The average measure, Intraclass Correlation Coefficient (ICC), for the epithelialization rate was 0.9 (95% CI: [0.7-1.0]), indicating excellent reliability. Similarly, the epithelial thickness measurement showed good reliability with an ICC of 0.9 (95% CI: [0.6-1.0]). Due to the high level of agreement between the two independent raters for both assessments, the average of their scores was used for all subsequent data analyses.

Epithelialization assessment

Thirty patients were included in the study, and all completed the follow-up period. **Table 1** shows the baseline data of the enrolled patients. The mean age of the participants was 50.7 ± 18.7 years.

Table 1 Demographic data of the patients

Characteristics	Mean ± SD or N (%)
No. of patients	30
Age, years	
Mean	50.7 ± 18.7
Range	18-84
Sex	
Male	19 (63.3%)
Female	11 (36.7%)
Site of STSG	
Right thigh	10 (33.3%)
Left thigh	20 (66.7%)

The mean area of donor-site wounds for evaluation was 49.4 cm2 (range: 20-96 cm^2) in both the control and I-PRF groups. The mean wound-healing time of donor-site wounds showed no statistically significant difference between the control and I-PRF groups ($p = 0.851$; **Table 2**).

Figure 5 compares the postoperative clinical outcomes of the I-PRF and control sides with respect to re-epithelialization of the donor area.

Table 2 Time to complete epithelialization

Groups	Mean ± SD (days)	95% CI for Mean Difference	*p* value*
Control (Bactigras)	11.9 ± 2.7		
Intervention (Bactigras + I-PRF)	11.9 ± 2.6		
Difference	0.0 ± 1.0	[-0.3, 0.4]	0.851

*Statistical analysis was performed using a paired t-test.

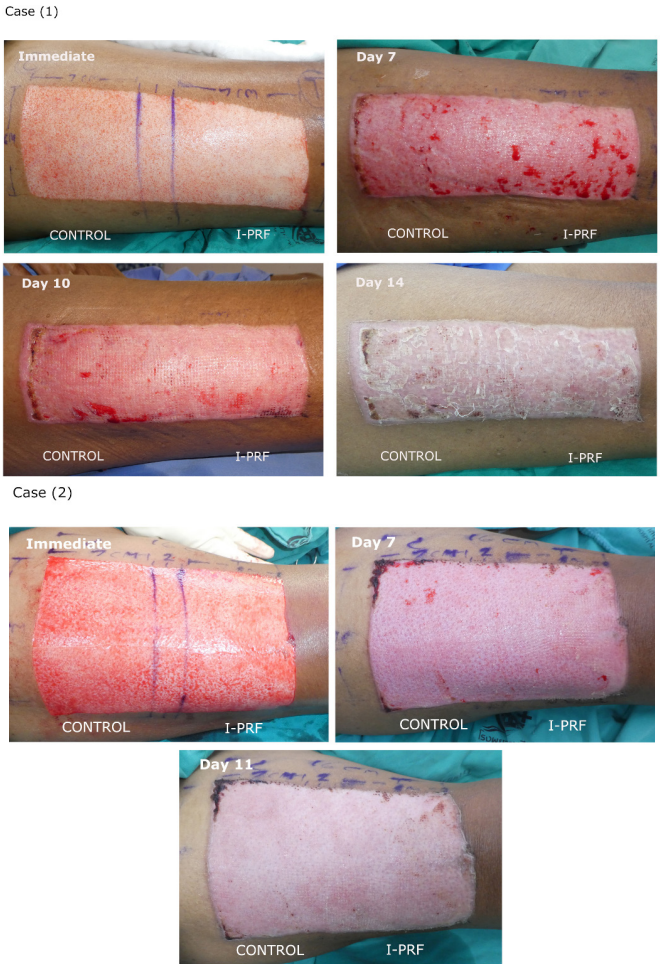


Figure 5 Postoperative results for two patients regarding re-epithelialization are presented. Case (1) includes images of the immediate donor-site wound, along with postoperative results on days 7, 10, and 14. Case (2) shows the immediate donor site wound and the postoperative results on days 7 and 11.

Epithelial thickness measurement

After complete epithelialization, a punch biopsy was performed. The average duration of the punch biopsy procedure was 15.6 ± 2.3 days, with a range of 11 to 21 days. In this study, the mean epidermal thickness after re-epithelialization was 197 ± 118 µm in the control group and 208 ± 110 µm in the I-PRF group. However, the two groups had no statistically significant difference ($p = 0.698$) (**Table 3**).

Figure 6 illustrates the histological results from H&E-stained sections: the epidermis on the I-PRF-treated side was slightly thicker than the control side.

Table 3 Epithelial thickness after re-epithelialization of the donor site

Groups	Mean ± SD (μm)	95% CI for Mean Difference	*p* value*
Control (Bactigras)	197 ± 118		
Intervention (Bactigras + I-PRF)	208 ± 110		
Difference	-11 ± 148	[-44.7, 65.9]	0.698

*Statistical analysis was performed using a paired t-test.

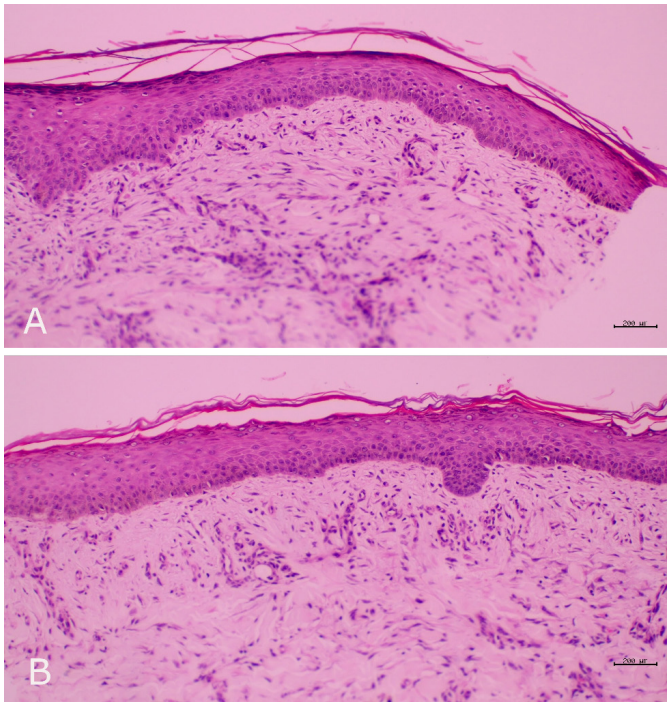


Figure 6 Specimens from the I-PRF and control sides after hematoxylin and eosin (H & E) staining showed that the epithelium was thicker on the I-PRF-treated side (A) than on the control side (B). × 10

DISCUSSION

The STSG procedure is commonly used for skin and soft tissue reconstruction.[1] There are various treatment options for the STSG donor site, but the best choice has yet to be determined. Innovative wound-dressing techniques and additional procedures are being developed to enhance epithelialization and accelerate healing at donor sites.[2,3] I-PRF has been used to improve wound healing across various wound types.[18-21] However, it remains unclear whether I-PRF can enhance epithelialization at the STSG donor site.[22-24] This study aimed to examine the effects of I-PRF on the epithelialization of donor-site STSG wounds.

Our study found no statistically significant difference in the time required for epithelialization between the I-PRF and control groups (see **Table 2**). This result aligns with a previous study conducted by Danielsen et al.,[24] which also reported no statistically significant differences in the macroscopic epithelialization of donor wounds or autografts between the platelet-rich fibrin and control groups on postoperative days 5 and 8.

In contrast to previous research, Senada et al.[22] Investigated the role of I-PRF in accelerating wound healing at donor sites following skin grafting in 20 burn patients. Their findings indicated that the healing time for donor sites injected with PRF was significantly shorter than that of the control sites, averaging 11.55 ± 1.39 days compared to 13.45 ± 1.70 days ($p < 0.001$). The differences between our findings and those of Senada et al. can be attributed to variations in study design and methodology. Their trial exclusively involved burn patients, whose altered physiology and systemic inflammatory responses may increase sensitivity to growth factor-based therapies such as PRF. In contrast, our study focused on a general surgical population. We standardized the donor site depth at 0.175 mm, while Senada et al. did not specify the wound depth, which could influence healing outcomes. The method of I-PRF administration may also be a critical factor. At the same time, Senada et al. utilized intradermal injections to deliver I-PRF directly into the tissue; our study employed topical application. This topical delivery might result in lower bioavailability of growth factors, as they could be partially sequestered by the primary dressing or fail to penetrate the wound bed as effectively as a direct injection. Additionally, their follow-up assessments were limited to days 10 and 14, whereas our study included more frequent evaluations starting as early as day 7 and continuing every 1 to 2 days thereafter. Such a rigorous assessment schedule may further account for the differences in observed epithelialization outcomes.

Similarly, Vaheb et al.[23] reported that the healing of donor sites was faster when treated with PRF in a study of 33 burn patients, showing significant differences on postoperative days 8 and 15 ($p < 0.001$). The differences between their findings and ours may be attributed to vari-

ations in study populations, postoperative care, and outcome assessments. Their trial specifically focused on deep burns, involved less frequent dressing changes, and had broader endpoints. In contrast, our study included a more diverse surgical cohort, utilized epithelialization-guided protocols, and measured the time to achieve more than 90% epithelialization.

Another consideration regarding our findings is the potential for local "diffusion" of various growth factors between the two adjacent study areas. In a split-body design on the same limb, bioactive molecules from the I-PRF site could diffuse through local tissue planes or systemic circulation to the control site, potentially narrowing the observable difference between groups. To ensure that no surface "contamination" occurred, we maintained a 2-cm bridge of intact skin. We used separate sterile dressings for each site, providing a physical barrier and preventing fluid communication between the proximal and distal zones.

In the histological evaluation, epithelial thickness at donor sites after re-epithelialization was assessed in both the control and I-PRF groups. Our study revealed no statistically significant difference in epithelial thickness between the I-PRF and control groups, with measurements of 208 ± 110 μm and 197 ± 118 μm, respectively (p = 0.698). However, our findings differ from those of Senada et al.,[22] who reported that the epidermis was significantly thicker on the PRF-treated side compared to the control side, with measurements of 195.79 ± 26.44 μm versus 113.55 ± 3.62 μm ($p < 0.001$). This discrepancy may be attributed to several factors, including differences in study design and the substantial variability observed in our measurements.

The high variability in epithelial thickness measurements, particularly the lack of a consistent trend between the control and intervention sides within individual patients, is a key finding of our study. This primarily reflects the inherent, substantial biological variability of the wound-healing process at the local level. While our intra-patient design optimally controls for systemic patient factors, it cannot account for micro-environmental differences within the wound. The absence of a clear directional treatment effect suggests that any potential benefit of I-PRF is minimal and likely overshadowed by this inherent biological noise. This underscores the challenge of demonstrating efficacy for interventions where the effect size is small and variable.

In our literature review and results, we observed significant variability in PRF's impact on wound-healing outcomes. No consensus exists regarding using PRF products to treat donor site wounds after STSGs. Regarding the mechanism of action, PRF contains a higher platelet concentration than whole blood and is rich in growth factors and cytokines.[12,13] The lack of a significant clinical difference in our study, despite these properties, suggests that further investigation into standardized preparation and delivery methods is required. Future research must explore the relationships among different PRF concentrations, preparation methods, and their effects on wound healing.

Limitations and strengths

The main limitations of our study were as follows: First, we did not quantitatively examine the concentrations of various cell populations, such as leukocytes and platelets, or specific growth factors in our I-PRF preparation. While we strictly followed the standard centrifugation protocols without modification, this remains a concern as inter-patient biological variability could still result in different concentrations of regenerative cytokines. Such variations, which were not laboratory-verified in this study, might have contributed to the lack of statistically significant differences observed. Second, we faced constraints preventing us from conducting extended patient follow-up periods.

On the positive side, our study's strengths included using the same patient, donor site area, and STSG donor wound thickness, which allowed us to effectively compare the efficacy of I-PRF. Lastly, we conducted a histological assessment, which was crucial for measuring the mean epidermal thickness after re-epithelialization in both groups.

CONCLUSION

This prospective, randomized, controlled intra-patient study found that the use of I-PRF did not significantly improve epithelialization rates or increase epithelial thickness in STSG donor sites compared to standard care. Consequently, the routine use of I-PRF for this specific purpose is not recommended. By omitting this unnecessary procedure, the surgical process can be streamlined, operative time reduced, and significant cost savings achieved, all without compromising patient outcomes. However, we acknowledge that further research is needed to fully assess its potential benefits in various clinical scenarios.

REFERENCES

1. Scherer-Pietramaggiori SS, Pietramaggiori G, Orgill DP. Chapter 17 Skin graft. In: Plastic surgery: Principle. 3rd ed. SAUNDERS ELSEVIER; 2012. p. 319–38.
2. Brown JE, Holloway SL. An evidence-based review of split-thickness skin graft donor site dressings. *Int Wound J*. 2018; 15: 1000–1009. https://doi.org/10.1111/iwj.12967
3. Schulz A, Depner C, Lefering R, et al. A prospective clinical trial comparing Biobrane® Dressilk® and PolyMem® dressings on partial-thickness skin graft donor sites. Burns. 2016 Mar 1;42(2):345–55.
4. Kazanavičius M, Cepas A, Kolaityte V, et al. The use of modern dressings in managing split-thickness skin graft donor sites: a single-centre randomised controlled trial. J Wound Care. 2017 Jun 2;26(6):281–91.
5. Dornseifer U, Lonic D, Gerstung TI, et al. The Ideal Split-Thickness Skin Graft Donor-Site Dressing: A Clinical Comparative Trial of a Modified Polyurethane Dressing and Aquacel. Plastic and Reconstructive Surgery 128(4): p 918-924, October 2011. | doi: 10.1097/PRS.0b013e3182268c02
6. Misirlioglu A, Eroglu S, Karacaoglan N, et al. Use of Honey as an Adjunct in the Healing of Split-Thickness Skin Graft Donor Site. Dermatol Surg. 2003;29(2):168–72.
7. Liang X, Zhou L, Yan J. Amniotic membrane for treating skin graft donor sites: A systematic review and meta-analysis. Burns. 2020 May 1;46(3):621–9.
8. Hu Z, Guo D, Liu P, et al. Randomized clinical trial of autologous skin cell suspension for accelerating re-epithelialization of split-thickness donor sites. Br J Surg. 2017 Jun 1;104(7):836–42.
9. ElSherbeny K, Elshahat A, Gad A. Effect of Nano Fat Graft on the Healing of Donor Site of Split Thickness Skin Graft. Egypt J Plast Reconstr Surg. 2023 Apr 1;47(2):79–88.
10. Abdel Razek HA, Badawy MS, Gad AM, et al. Impact of Local Insulin Injection on Split Thickness Skin Graft Donor Site Healing. Egypt J Plast Reconstr Surg [Internet]. 2022 Sep 5 [cited 2023 Aug 6];0. Available from: https://ejprs.journals.ekb.eg/article_257930.html
11. Ottomann C, Hartmann B, Tyler J, et al. Prospective Randomized Trial of Accelerated Re-epithelization of Skin Graft Donor Sites Using Extracorporeal Shock Wave Therapy. J Am Coll Surg. 2010 Sep 1;211(3):361–7.
12. Lacci KM, Dardik A. Platelet-Rich Plasma: Support for Its Use in Wound Healing. Yale J Biol Med. 2010 Mar;83(1):1–9.
13. Marck RE, Gardien KLM, Stekelenburg CM, et al. The application of platelet-rich plasma in the treatment of deep dermal burns: A randomized, double-blind, intra-patient controlled study. Wound Repair Regen. 2016;24(4):712–20.
14. Ehrenfest DMD, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol. 2009 Mar 1;27(3):158–67.
15. Brewer CF, Smith A, Miranda BH. The use of platelet-rich products for skin graft donor site healing: a systematic review and meta-analysis. J Plast Surg Hand Surg. 2021 Jun 1;55(3):133–40.
16. Yotsu RR, Hagiwara S, Okochi H, et al. Case series of patients with chronic foot ulcers treated with autologous platelet-rich plasma. J Dermatol. 2015;42(3):288–95.
17. Choukroun J, Aalam AA, Miron RJ. Platelet Rich Fibrin "PRF" and Regenerative Medicine: 'The Low-Speed Concept.' In: Tatullo M, editor. MSCs and Innovative Biomaterials in Dentistry [Internet]. Cham: Springer International Publishing; 2017 [cited 2023 Aug 6]. p. 21–42. (Stem Cell Biology and Regenerative Medicine). Available from: https://doi.org/10.1007/978-3-319-55645-1_2
18. Erdur EA, Karakaslı K, Oncu E, et al. Effect of injectable platelet-rich fibrin (i-PRF) on the rate of tooth movement: A randomized clinical trial. Angle Orthod. 2021 Jan 18;91(3):285–92.
19. İzol BS, Üner DD. A New Approach for Root Surface Biomodification Using Injectable Platelet-Rich Fibrin (I-PRF). Med Sci Monit Int Med J Exp Clin Res. 2019 Jun 26;25:4744–50.
20. Yu P, Zhai Z, Jin X, et al. Clinical Application of Platelet-Rich Fibrin in Plastic and Reconstructive Surgery: A Systematic Review. Aesthetic Plast Surg. 2018 Apr 1;42(2):511–9.
21. Miron RJ, Fujioka-Kobayashi M, Bishara M, et al. Platelet-Rich Fibrin and Soft Tissue Wound Healing: A Systematic Review. Tissue Eng Part B Rev. 2017 Feb;23(1):83–99.
22. Senada M, Adel Rahman S, Saleh M, et al. The Effect of Platelet-Rich Fibrin on Donor Site of Split Thickness Skin Graft in Burned Patients. Egypt J Plast Reconstr Surg. 2021 Oct 1;45(4):313–8.
23. Vaheb M, Karrabi M, Khajeh M, et al. Evaluation of the Effect of Platelet-Rich Fibrin on Wound Healing at Split-Thickness Skin Graft Donor Sites: A Randomized, Placebo-Controlled, Triple-Blind Study. Int J Low Extrem Wounds. 2021;20(1):29–36.
24. Danielsen P, Jørgensen B, Karlsmark T, et al. Effect of Topical Autologous Platelet-Rich Fibrin versus No Intervention on Epithelialization of Donor Sites and Meshed Split-Thickness Skin Autografts: A Randomized Clinical Trial. Plast Reconstr Surg. 2008 Nov;122(5):1431–40.
25. Muangman P, Nitimonton S, Aramwit P. Comparative Clinical Study of Bactigras and Telfa AMD for Skin Graft Donor-Site Dressing. Int J Mol Sci. 2011 Aug;12(8):5031–8.
26. Nouri M, Ebrahimi M, Bagheri T, et al. Healing Effects of Dried and Acellular Human Amniotic Membrane and Mepitelas for Coverage of Skin Graft Donor Areas; A Randomized Clinical Trial. Bull Emerg Trauma. 2018 Jul;6(3):195–200.
27. Kakudo N, Kushida S, Minakata T, et al. Platelet-rich plasma promotes epithelialization and angiogenesis in a splitthickness skin graft donor site. Med Mol Morphol. 2011 Dec 1;44(4):233–6.

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Original Article

Performance of APCS Risk Score and Fecal Immunochemical Test in Predicting Colorectal Cancer: A Retrospective Diagnostic Accuracy Study.

Peerapong Inlao, MD

General Surgery, Rattanaburi Hospital, Surin, Thailand

Abstract

Objective: To evaluate the diagnostic performance of APCS and FIT for predicting colorectal cancer (CRC), and to develop an enhanced predictive model incorporating clinical and laboratory parameters.

Methods: A retrospective study of 662 patients undergoing colonoscopy at Rattanaburi Hospital, Thailand (January 2022–April 2025). Clinical data, quantitative FIT, APCS scores, and histopathology were analyzed.

Results: Mean age was 61.3 years; 42.45% were male. Adenomas comprised 93.96% of lesions, and adenocarcinomas (CA) 2.87%. The subgroup with APCS ≥4 and positive FIT had the highest CA detection rate (6.29%). For predicting CA, FIT alone had an AUROC of 0.56 (sensitivity 68.4%, specificity 45.3%), while APCS ≥4 alone had an AUROC of 0.59 (sensitivity 68.4%, specificity 50.7%). Combining FIT and APCS ≥4 increased specificity to 79.0% (sensitivity 47.4%, AUROC 0.64). Multivariable regression identified FIT positivity (OR=7.66), APCS ≥4 (OR=4.54), diabetes mellitus (OR=8.84), and hematocrit (OR=0.70) as independent CA predictors ($p<0.01$ for all except APCS $p=0.01$). An enhanced model combining these variables significantly improved performance (AUROC 0.86).

Conclusion: Standalone APCS or FIT scores offer limited predictive accuracy (AUROC <0.65). However, incorporating diabetes and hematocrit into an enhanced model significantly improves diagnostic performance (AUROC 0.86), showing high potential for risk-based screening.

Keywords: APCS Risk Score, Fecal Immunochemical Test (FIT), Colorectal

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies found worldwide and remains a leading cause of cancer-related mortality. According to GLOBOCAN 2020, there were approximately 1.93 million new CRC cases and 935,000 deaths, accounting for about 10% of all cancer deaths.[1] The severity of CRC largely stems from the fact that many patients present with advanced stages when treatment outcomes are suboptimal. Nevertheless, CRC is a preventable disease through effective screening, since most cases develop from adenomatous polyps that undergo malignant transformation over several years. Early detection and removal of such polyps can significantly reduce both incidence and mortality.[2] Several CRC screening modalities are currently available, including the fecal immunochemical test (FIT), colonoscopy, flexible sigmoidoscopy, and CT colonography.[3] Among these, colonoscopy offers the highest sensitivity and specificity. However, its widespread implementation is constrained by resource availability, trained personnel, and cost, making its population-wide use impractical. Therefore, the tools that help to identify high-risk individuals for colonoscopy referral are of particular importance.

In Asia, the Asia-Pacific Colorectal Screening (APCS) score was developed using regional population data to estimate the risk of advanced colorectal neoplasia. This scoring system incorporates fundamental risk factors, such as age, sex, smoking status, and family history of CRC.[4] The APCS categorizes individuals into three risk groups: low risk (0–1 points), moderate risk (2–3 points), and high risk (≥ 4 points). In parallel, FIT is widely used as a simple, non-invasive, and low-cost screening tool

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Corresponding author: Peerapong Inlao, MD, General Surgery, Rattanaburi Hospital, 150 Rattanaburi District, Surin 32130, Thailand; E-mail: peerak999.ip@gmail.com

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that detects occult blood in stool, potentially arising from tumors or CRC, and is well-suited for large-scale population screening.[5] However, the diagnostic performance of FIT may vary across different populations and clinical contexts, and may be limited in non-bleeding lesions or small polyps, resulting in reduced sensitivity in certain real-world settings.

Previous studies have demonstrated that combining APCS with FIT improves screening accuracy compared with using either tool alone. Individuals with a high APCS score and positive FIT have been shown to have a substantially higher probability of advanced colorectal neoplasia than those with low-risk scores and negative FIT results.[6] For instance, a Thai study reported that APCS combined with FIT yielded markedly higher detection rates of advanced adenoma.[6] However, most prior studies primarily focused on advanced neoplasia rather than histologically confirmed colorectal cancer, and many were conducted under controlled research conditions. Therefore, their findings may not fully reflect the true performance of these tools in routine clinical service, particularly in opportunistic colonoscopy cohorts.

In this context, the present study aimed to evaluate the diagnostic performance of APCS and FIT for identifying individuals at risk of histologically confirmed colorectal cancer in a real-world opportunistic colonoscopy cohort. Rather than assuming superior performance, this study sought to objectively determine whether these tools provide adequate and clinically useful discrimination in routine practice. The ultimate goal is to inform the potential roles of APCS and FIT in supporting risk-based prioritization of colonoscopy in resource-limited healthcare settings.

RESEARCH OBJECTIVE

The objective of this study was to evaluate the diagnostic performance of the Asia-Pacific Colorectal Screening (APCS) score and the Fecal Immunochemical Test (FIT) in relation to histopathological findings of colorectal lesions, and to assess their ability to predict cancer.

MATERIALS AND METHODS

This was a retrospective diagnostic accuracy study. The study population represented a real-world opportunistic colonoscopy cohort at Rattanaburi Hospital. It consisted predominantly of asymptomatic individuals undergoing colorectal cancer screening, together with a smaller proportion of participants with mild, non-alarming gastrointestinal symptoms who were referred for early evaluation. This pattern reflects the routine CRC screening service model in district and provincial hospitals, rather than a strictly asymptomatic screening cohort.

All eligible individuals who underwent colonoscopy between January 2022 and April 2025 and had complete APCS, FIT, and histopathological results were included in the study. Clinical, colonoscopy, and pathology data were retrospectively retrieved from medical records.

Fecal immunochemical test (FIT) All participants underwent a quantitative fecal immunochemical test (FIT) before colonoscopy.FIT was performed using a quantitative immunoturbidimetric assay (Hangzhou AllTest Biotech Co., Ltd, Manufacturer, China). Results were reported in μg Hb/g of feces (cutoff 100 ng/ml). In accordance with the manufacturer's recommendation and institutional practice, FIT ≥ 10 μg Hb/g was defined as positive, and values below this threshold were considered negative. This predefined cut-off was consistently applied in all diagnostic and regression analyses.

APCS Risk Stratification The Asia-Pacific Colorectal Screening (APCS) score was calculated based on age, sex, smoking history, and family history of colorectal cancer. Participants were categorized into three risk groups: low risk (0–1 points), moderate risk (2–3 points), and high risk (≥ 4 points). For diagnostic and regression analyses, APCS was further dichotomized into high-risk (APCS ≥ 4) and non–high-risk (APCS < 4), consistent with previous APCS validation studies.

Endoscopic and histopathological classification In this retrospective analysis, we included only participants who had at least one biopsy or polypectomy specimen submitted for histopathological examination. As a result, individuals with completely normal colonoscopy findings and no biopsy were not captured in the analytic dataset. For each participant, endoscopic and histopathological findings were summarized per patient according to the most advanced lesion identified (adenocarcinoma > adenoma > colitis or other non-neoplastic lesions). Thus, the high proportion of adenomas observed in this cohort reflects an enriched subset of colonoscopy-and-biopsy cases rather than the adenoma detection rate in the entire screening-eligible population.

Outcomes

The primary outcome of interest was colorectal cancer (CRC), defined as histologically confirmed colorectal adenocarcinoma on biopsy or polypectomy specimens. For

descriptive purposes, histological findings were categorized into three groups: (1) colitis or other non-neoplastic inflammatory lesions; (2) adenoma (including tubular, tubulovillous, or villous adenomas without invasive carcinoma); and (3) adenocarcinoma (CRC).

Inclusion criteria

Participants were eligible if they had met the following criteria:

1. Age ≥ 18 years.
2. Underwent colonoscopy at Rattanaburi Hospital between January 2022 and April 2025 as part of colorectal cancer (CRC) screening or early evaluation of mild, non-alarming gastrointestinal symptoms (e.g., functional constipation or vague abdominal discomfort) in an outpatient setting.
3. Had an Asia-Pacific Colorectal Screening (APCS) score assessed before colonoscopy.
4. Underwent a quantitative fecal immunochemical test (FIT) prior to colonoscopy.
5. Had at least one biopsy or polypectomy specimen with available histopathological results.

Exclusion criteria

Participants were excluded if they met any of the following conditions:

1. Having a history or diagnosis of chronic inflammatory bowel disease (IBD), such as Crohn's disease or ulcerative colitis
2. Having received a previous diagnosis of colorectal cancer prior to the current screening
3. Having had incomplete or inadequate colonoscopies (e.g., poor bowel preparation, incomplete examination)
4. Presenting with alarm gastrointestinal features suggestive of a diagnostic rather than screening indication (e.g., overt gastrointestinal bleeding, suspected bowel obstruction, or severe unexplained anemia).

Sample size

The sample size for this study was determined using a single-proportion formula to estimate the predictive performance of each tool. Based on the study by Chiu et al. (2016).[8] which evaluated the effectiveness of an APCS combined with a FIT in a prospective international multi-center setting, the combination of APCS and FIT demonstrated the accurate identification of individuals requiring colonoscopy at an early stage, detecting up to 70.6% of those with advanced neoplasia (AN). Using the single-population proportion formula, the following parameters were applied:

$$n = \frac{Z^{2}_{\alpha/2} P(1-P)}{d^{2}}$$

Alpha (α)	=	0.05
Standard normal value (Z)	=	1.96
Prevalence (P)	=	0.70
Absolute precision (d)	=	0.035

95% confidence interval

The calculated sample size was 662 participants.

Ethic approval

The study was approved by the Ethics Committee for Human Research, Surin Provincial Public Health Office, Ministry of Public Health, Thailand (Ethics approval number: 85/2568). The review process was conducted under the expedited review category. The study adhered to the principles of the Declaration of Helsinki, the Belmont Report, CIOMS Guidelines, and the International Conference on Harmonization in Good Clinical Practice (ICH-GCP).

Data analysis and statistical methods

All data were processed and analyzed using STATA software.

1. Descriptive statistics: For the normally distributed data, the results were presented as means ± standard deviation (SD). For the non-normally distributed data, the results were reported as medians with interquartile ranges (IQRs), along with minimum and maximum values.
2. Comparisons of histopathological distribution between groups in Tables 3–5 were analyzed using the Chi-square test (or Fisher's exact test when expected cell counts were <5). A p-value <0.05 was considered statistically significant.
3. Diagnostic performance: Sensitivity, specificity, and accuracy of the individual and combined models were calculated.
4. Multivariable logistic regression was performed to identify factors associated with colorectal cancer (CRC). The dependent variable was defined as the presence of CRC, based on histologically confirmed colorectal adenocarcinoma (CRC = 1) versus all other histological

findings (CRC = 0). A total of 19 participants in the cohort had CRC, and this limited number of outcome events was explicitly considered when specifying the number of predictors included in the models to reduce the risk of overfitting. Results were presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs) and *p*-values. Model calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test and visually inspected using a calibration plot. Multicollinearity was evaluated using variance inflation factors (VIFs), with values >10 indicating substantial multicollinearity.

5. Model performance: Discriminative ability was assessed using the area under the receiver operating characteristic curve (AUROC) to evaluate the capacity for each model to distinguish between cancer and non-cancer cases.

RESULTS

Among 662 participants, 19 (2.87%) were diagnosed with histologically confirmed colorectal cancer (CRC), while 643 (97.13%) had non-CRC lesions. Univariable logistic regression analysis showed that age, diabetes mellitus, hematocrit, hemoglobin, neutrophil percentage, and lymphocyte percentage were significantly associated with CRC ($p < 0.05$). Sex, body mass index, smoking history, alcohol consumption, hypertension, dyslipidemia, family history of colorectal cancer, and platelet count were not significantly associated with CRC. (**Table 1**).

Colonoscopy findings revealed that 72.66% of participants were asymptomatic. Among those with symptoms, constipation was the most common (19.49%), followed by abdominal pain (6.80%). The most frequent diagnosis after colonoscopy was colonic polyps (93.81%), followed by colitis (3.02%) and colorectal cancer (2.42%). Histopathological examination confirmed that most lesions were adenomas (93.96%), which are precursor lesions of colorectal cancer, while adenocarcinoma accounted for 2.87% and colitis for 3.17% (**Table 2**).

Table 2 Colonoscopy findings, post-operative diagnoses, and histopathology results (n = 662)

Variables	Mean ± SD or n (%)
Clinical signs	
Bowel habit change	7 (1.06)
Constipation	129 (19.49)
Abdominal pain	45 (6.80)
No clinical signs	481 (72.66)
Post-operative diagnoses (Post-op Dx)	
Rectal polyp	2 (0.30)
Rectal cancer	3 (0.45)
Colitis	20 (3.02)
Colon cancer	16 (2.42)
Colonic polyp	621 (93.81)
Histopathology (Patho)	
Colitis	21 (3.17)
Adenocarcinoma	19 (2.87)
Adenoma	622 (93.96)

Table 1 The baseline characteristics of the participants (n = 662)

Variables	non-CRC (n=643)	CRC (n=19)	Total	OR (95%CI)	*p*-value
Age (years)	61.05±7.03	69.21±5.55	61.30 ± 7.12	1.17 (1.09-1.25)	<0.01
Male (%)	274(42.61)	7 (36.84)	281 (42.45)	1.27 (0.49-3.27)	0.61
Body mass index	24.45±7.55	22.60±4.46	24.40 ± 7.49	0.90 (0.80-1.01)	0.09
Smoking history	184(28.62)	8 (42.11)	192 (29.0)	1.81 (0.71-4.58)	0.20
Alcohol consumption	151(23.58)	6 (31.58)	157 (23.72)	1.50 (0.56-4.02)	0.41
Comorbidities					
HT	186(28.93)	9(47.37)	195 (29.46)	2.21(0.88-5.52)	0.09
DM	54 (8.40)	8 (42.11)	62 (9.37)	7.93 (3.06-20.56)	<0.01
DLP	37 (5.75)	3 (15.79)	40 (6.04)	3.07 (0.85-11.01)	0.08
Family history of colorectal cancer	190 (29.55)	9 (47.37)	199 (30.06)	2.15 (0.85-5.36)	0.10
Laboratory findings					
HCT (%)	38.24±4.44	33.94±3.43	38.12 ± 4.47	0.84 (0.77-0.91)	<0.01
HB (g/dL)	12.34±1.62	11.04±1.30	12.30 ± 1.63	0.65 (0.51-0.83)	<0.01
PLT (T/μL)	258388.8 ±69904	268473.7 ±106931	258,678.2 ± 71,136.09	1.00 (0.99-1.00)	0.54
Neutrophils%	58.29 ±10.22	67.57 ±8.27	58.56 ± 10.28	1.07 (1.03-1.12)	<0.01
Lympocytes%	31.22 ±9.11	23.0 ±6.93	30.98 ± 9.15	0.91 (0.86-0.95)	<0.01

When comparing the fecal immunochemical test (FIT) results with the histopathology, 297 participants had tested FIT−, of whom 92.26% had adenomas. Among 365 FIT+ participants, 95.34% had had adenomas. Adenocarcinoma was more common in the FIT+ group (3.56%) compared to the FIT− group (2.02%). Conversely, colitis had been more frequently detected in the FIT− group (5.72%) than in the FIT+ group (1.10%) (Table 3).

Table 3 A comparison between the FIT results and the histopathology findings

Histopathology	FIT- (n = 297)	FIT+ (n = 365)	*p*-value
Colitis	17 (5.72)	4 (1.10)	< 0.01
Adenocarcinoma	6 (2.02)	13 (3.56)	
Adenoma	274 (92.26)	348 (95.34)	

A comparison of histopathology by APCS score showed that participants with APCS ≥ 4 (the high-risk group) had a higher proportion of adenocarcinoma than those with APCS < 4 (3.94% vs. 1.81%). Adenomas were common in both groups but more frequent in the APCS < 4 group (95.18% vs. 92.73%). The prevalence of colitis was similar between the two groups (3.01% vs. 3.33%) (Table 4).

Table 4 A comparison between the APCS scores and the histopathology findings

Histopathology	APCS < 4 (n = 332)	APCS ≥ 4 (n = 330)	*p*-value
Colitis	10 (3.01)	11 (3.33)	0.24
Adenocarcinoma	6 (1.81)	13 (3.94)	
Adenoma	316 (95.18)	306 (92.73)	

When combining the APCS and FIT results, the highest proportion of adenocarcinoma was observed in the high-risk (APCS ≥ 4) + FIT+ group (6.29%), which was followed by APCS ≥ 4 + FIT− (2.14%). In contrast, groups with APCS < 4, regardless of their FIT statuses, had exhibited lower proportions (approximately 1.80-1.82%). Adenomas were highly prevalent across all groups, particularly in APCS < 4 + FIT+ (97.30%). Colitis, a non-cancerous lesion, was found to be more common in the FIT-groups (APCS < 4 + FIT−: 7.27%; APCS ≥ 4 + FIT−: 4.81%) compared with the FIT+ groups. These differences were determined to be statistically significant ($p < 0.01$) (Table 5).

Table 5 The distribution of histopathology findings according to APCS and quantitative Fecal Immunochemical Test (FIT) results

Histopathology	APCS ≥ 4 + FIT+	APCS ≥ 4 + FIT−	APCS < 4 + FIT+	APCS <4 + FIT−	*p*-value
Colitis	2 (1.40)	9 (4.81)	2 (0.90)	8 (7.27)	**< 0.01**
Adenocarcinoma	9 (6.29)	4 (2.14)	4 (1.80)	2 (1.82)	
Adenoma	132 (92.31)	174 (93.05)	216 (97.30)	100 (90.91)	

In evaluating the diagnostic performance of screening tools for predicting cancer, FIT alone had yielded a sensitivity of 68.4% but a low specificity (45.3%), with an AUROC of 0.56, indicating poor discriminative performance. Using APCS ≥ 4 alone, the same sensitivity (68.4%) was achieved, with a slightly higher specificity (50.7%) and an AUROC of 0.59. Combining FIT with APCS ≥ 4 increased specificity to 79.0% but reduced sensitivity to 47.4%. Nevertheless, the AUROC had improved to 0.64 (Table 6).

Table 6 The diagnostic performance for predicting colorectal cancer

	Sensitivity	Specificity	ROC areas
FIT positive	68.4 (43.4-87.4)	45.3 (41.4-49.2)	0.56 (0.45-0.67)
APCS ≥ 4	68.4 (43.4-87.4)	50.7 (46.8-54.6)	0.59 (0.48-0.70)
FIT positive and APCS ≥ 4	47.4 (24.4-71.1)	79. (75.8-82.2)	0.64 (0.51-0.74)

Multivariate analysis of the factors associated with colorectal cancer (CA) was performed using three models (Table 7). In Model 1, which included only FIT and APCS, FIT+ showed a non-significant trend toward increased risk (OR = 2.23, $p = 0.11$), while APCS ≥ 4 was determined to be borderline significant (OR = 2.66, $p = 0.05$). The AUROC was 0.64, indicating low accuracy. Model 2, which added risk behaviors (alcohol consumption) and comorbidities, identified diabetes mellitus as a strong independent predictor (OR = 7.62, $p < 0.01$). FIT+ also reached statistical significance (OR = 3.51, $p = 0.03$), with the AUROC increasing to 0.77. Model 3 achieved the highest AUROC of 0.86, demonstrating improved discriminative performance when FIT, APCS, diabetes mellitus, and HCT had been combined.

Table 7 A comparison of the multivariable logistic regression models for the predictors of colorectal cancer

Variables	Model 1		Model 2		Model 3	
	Adj.OR	*p*-value	Adj.OR	*p*-value	Adj.OR	*p*-value
FIT positive	2.23 (0.81-6.08)	0.11	3.51 (1.12-11.04)	0.03	7.66 (1.96-30.0)	< 0.01
APCS ≥ 4	2.66 (0.97-7.24)	0.05	2.70 (0.92-7.88)	0.06	4.54 (1.29-16.02)	0.01
Alcohol			1.80 (0.60-5.36)	0.28	0.83 (0.20-3.35)	0.80
Underlying						
HT			1.81 (0.67-4.86)	0.24	2.28 (0.74-7.04)	0.14
DM			7.62 (2.60-22.32)	< 0.01	8.84 (2.70-28.96)	< 0.01
DLP			2.19 (0.45-10.56)	0.32	3.66 (0.69-19.26)	0.12
LAB						
HCT (%)					0.70 (0.54-0.89)	< 0.01
HB (g/dL)					1.59 (0.85-2.99)	0.14
PL (T/μL)					1.00 (0.99-1.00)	0.33
Neutrophils (%)					1.01 (0.90-1.14)	0.74
Lympocytes (%)					0.93 (0.81-1.08)	0.38
ROC CURVE	0.64 (0.49-0.78)		0.77 (0.65-0.90)		0.86 (0.83-0.96)	

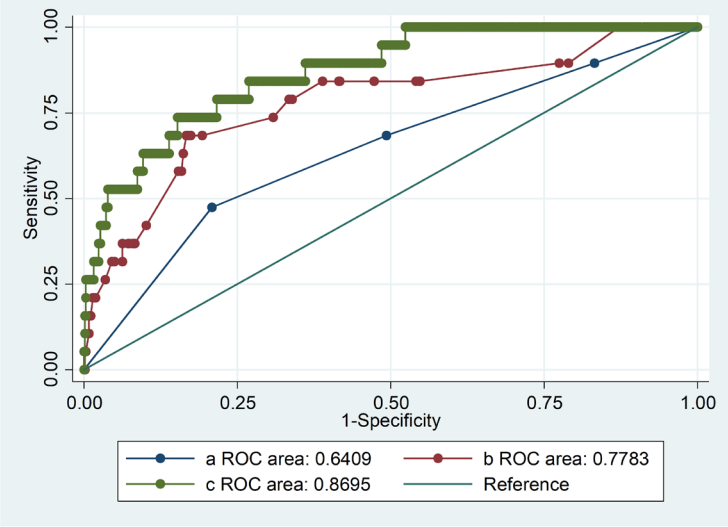


Figure 1 A comparison of the diagnostic performance for predicting colorectal cancer

DISCUSSION

This study aimed to evaluate the diagnostic performance of the Asia-Pacific Colorectal Screening (APCS) score and the Fecal Immunochemical Test (FIT), both individually and in combination, to predict colorectal cancer (CRC) using data from 662 participants who had undergone colonoscopy. Quantitative Fecal Immunochemical Test (FIT) results, APCS scores, and histopathological findings were analyzed retrospectively. Our analysis revealed that adenoma had been the most commonly detected lesion (93.96%), whereas adenocarcinoma was found in only 2.87% of cases. This finding indicated that the screening program had been more effective at detecting precursor lesions than advanced cancer, which is valuable for population-level prevention strategies. This aligned with Lieberman et al.[9] who followed 1,915 participants over 10 years and reported adenoma detection rates of 25–30% and advanced neoplasia (AN) rates of approximately 6%, which was comparable to the APCS ≥ 4 + FIT+ group in the present study.

Another important explanation for the modest diagnostic performance of FIT observed in this study is the very high proportion of adenomas in our cohort. Histopathological analysis revealed that 93.96% of lesions were adenomas, while only 2.87% were adenocarcinomas. Since FIT primarily detects occult gastrointestinal bleeding, its sensitivity is inherently lower in populations dominated by non-bleeding precursor lesions such as small

or non-advanced adenomas. Many adenomas do not bleed consistently and, therefore, may not produce detectable fecal hemoglobin, resulting in reduced FIT sensitivity and AUROC in this real-world screening cohort.

When considering FIT alone to predict CRC, sensitivity was 68.4%, specificity was 45.3%, and the AUROC was 0.56. The low specificity indicated a high false-positive rate. This contrasted with the meta-analysis by Anastasia Katsoula et al.,[10] which included 12 studies (n = 6,204) using colonoscopy as the reference standard and which reported a FIT sensitivity of 93% and a specificity of 91%. The discrepancy may be explained by our study population being asymptomatic, with a high prevalence of adenoma (93.96%) and a low prevalence of adenocarcinoma (2.87%). FIT is known to have limitations in detecting non-bleeding or small adenomas, which can lead to false negatives and reduce overall accuracy, unlike the high-risk or symptomatic populations analyzed by Katsoula et al.

For APCS ≥ 4 alone, the sensitivity was 68.4%, specificity was 50.7%, and the AUROC was 0.59, which was slightly lower than the meta-analysis by Mai Ngoc Luu et al.,[11] who reviewed 69,762 colonoscopy participants and reported an APCS sensitivity of 42% (95% CI: 40-44%) and a specificity of 86% (95% CI: 85–86%) for predicting advanced colorectal neoplasia (ACN), with a weighted AUROC of 0.642 (95% CI: 0.610–0.657). The difference may reflect the APCS score's limitations when applied to new, asymptomatic populations with low AN prevalence.

When combining FIT and APCS and specifically selecting the high-risk group (APCS ≥ 4 + FIT+), specificity increased significantly to 79.0%, while sensitivity decreased to 47.4%, with the AUROC rising to 0.64. This demonstrated improved discrimination between participants with and without CRC when using both tools together. This finding was consistent with Chiu et al. (8), who reported that combining APCS and FIT in a prospective multicenter study accurately identified participants who should undergo early colonoscopy, detecting 70.6% of those with advanced neoplasia. Although an AUROC value of 0.64 indicates fair discrimination (0.6–0.7), the combined use of APCS and FIT can improve the ability to distinguish participants with CRC, increase specificity, and reduce unnecessary colonoscopies in low-risk groups while still detecting a substantial proportion of advanced lesions.

Although combining a positive FIT result with a high APCS score (≥4) improved diagnostic performance compared with either tool alone, the AUROC of the combined strategy remained below 0.7. This modest discrimination is biologically and methodologically plausible. First, the APCS score was originally developed to predict advanced colorectal neoplasia rather than histologically confirmed colorectal cancer alone; therefore, its predictive ability is expected to decrease when CRC is used as the sole outcome. Second, the performance of FIT depends on

occult gastrointestinal bleeding, and many adenomas and some early cancers are non-bleeding lesions, which lowers sensitivity. Third, the relatively low CRC prevalence in this cohort (2.87%) may attenuate predictive performance due to spectrum and base-rate effects. In addition, our dataset was a colonoscopy-and-biopsy cohort enriched for neoplastic lesions rather than a true population screening cohort, and the number of CRC events was limited, which may contribute to modest AUROC estimates. These factors together likely explain why the combined approach, although superior to either tool alone, still demonstrated only poor discrimination.

Multivariable logistic regression analysis revealed that, in addition to FIT positivity (adjusted OR = 7.66) and APCS ≥ 4 (adjusted OR = 4.54), diabetes mellitus (DM) (adjusted OR = 8.84; 95% CI: 2.70–7.04) had been significantly associated with CRC risk, demonstrating a stronger predictive effect than FIT or APCS alone. Larsson et al.[12] analyzed 15 studies (6 case-control and 9 cohort, total n = 2,593,935) and found that DM had increased the risk of colorectal cancer compared with non-diabetic individuals (RR = 1.30, 95% CI: 1.20–1.40) and had been associated with higher CRC mortality (RR = 1.26, 95% CI: 1.05–1.50). Mechanistically, chronic hyperinsulinemia and insulin resistance may elevate IGF-1 levels, thereby stimulating abnormal cell proliferation, while chronic inflammation and oxidative stress in DM participants may promote DNA damage and tumorigenesis.

Laboratory parameters were also significant predictors. Hematocrit (HCT) showed an inverse association with CRC risk (adjusted OR = 0.70; 95% CI: 0.54–0.89), which is consistent with the clinical observation that anemia, especially in older adults, may be an early sign of CRC. HCT may be used in conjunction with other screening tools, such as FIT or APCS, to enhance the accuracy of risk assessment.

Limitations

1. This was a retrospective, single-center study, potentially introducing selection and recording bias and thereby limiting generalizability.

2. Most participants were asymptomatic, and the CRC prevalence was only 2.87%. These factors may have caused spectrum bias and reduced sensitivity/AUROC esti-

mates compared to studies with higher disease prevalence.

3. The AUROC for APCS + FIT may underestimate the true potential in settings with higher AN/CRC prevalence, optimized FIT cut-offs, population-specific APCS adjustments, and controlled colonoscopy quality and confounding factors.

4. Colonoscopy quality indicators such as CIR and ADR could not be fully assessed due to incomplete documentation, which may limit the interpretation of screening performance.

5. Formal internal and external validation of the predictive model was not performed in this study. The development of a validated prediction equation or nomogram will be addressed in future studies using independent datasets.

CONCLUSION

The combination of APCS ≥ 4 and a positive FIT result improves the identification of participants at risk for colorectal cancer (CRC) compared with either tool used alone. This combined approach substantially improved specificity (79.0%), suggesting its clinical utility in prioritizing colonoscopy among high-risk individuals. and had raised the AUROC to 0.64, representing fair discrimination. Whereas, FIT or APCS alone had yielded lower AUROC values of 0.56 and 0.59, respectively. Furthermore, a predictive model incorporating FIT, APCS ≥ 4, diabetes mellitus (DM), and hematocrit (HCT) demonstrated high performance (AUROC = 0.86), suggesting that adding comorbidity and laboratory indicators to the APCS + FIT screening strategy could enhance practical screening accuracy in both district-level and provincial-level hospitals.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49. doi: 10.3322/caac.21660.
2. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. N Engl J Med. 2012;366(8):687-96. doi: 10.1056/NEJMoa1100370.
3. US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. JAMA. 2021;325(19):1965-77. doi:10.1001/jama.2021.6238.
4. Yeoh KG, Ho KY, Chiu HM, et al. The Asia-Pacific Colorectal Screening score: a validated tool that stratifies risk for colorectal advanced neoplasia in asymptomatic Asian subjects. Gut. 2011;60(9):1236-41. doi: 10.1136/gut.2010.221168.
5. Lee JK, Liles EG, Bent S, et al. Accuracy of fecal immunochemical tests for colorectal cancer: systematic review and meta-analysis. Ann Intern Med. 2014;160(3):171. doi: 10.7326/M13-1484.
6. Aniwan S, Rerknimitr R, Kongkam P, et al. A combination of clinical risk stratification and fecal immunochemical test results to prioritize colonoscopy screening in asymptomatic participants. Gastrointest Endosc. 2015;81(3):719-27. doi: 10.1016/j.gie.2014.11.035.
7. Ze Y, Tu HM, Zhao YY, et al. Developing a Nomogram for Predicting Colorectal Cancer and Its Precancerous Lesions Based on Data from Three Non-Invasive Screening Tools, APCS, FIT, and sDNA. J Multidiscip Healthc. 2024;17:2891-2901. doi: 10.2147/JMDH.S465286.
8. Chiu HM, Ching JYL, Wu KC, et al. A Risk-scoring system combined with a fecal immunochemical test is effective in screening high-risk subjects for early colonoscopy to detect advanced colorectal neoplasms. Gastroenterology. 2016;150(3):617-625.e3. doi: 10.1053/j.gastro.2015.11.042.
9. Lieberman D, Sullivan BA, Hauser ER, et al. Baseline colonoscopy findings associated with 10-year outcomes in a screening cohort undergoing colonoscopy surveillance. Gastroenterology. 2020;158(4):862-874.e8. doi: 10.1053/j.gastro.2019.07.052.
10. Katsoula A, Paschos P, Haidich AB, et al. Diagnostic Accuracy of Fecal Immunochemical Test in Patients at Increased Risk for Colorectal Cancer: A Meta-analysis. JAMA Intern Med. 2017;177(8):1110-8. doi: 10.1001/jamainternmed.2017.2309.
11. Luu MN, Trinh NA, Tran TLT, et al. Performance of the Asia-Pacific colorectal screening score in stratifying the risk of advanced colorectal neoplasia: A meta-analysis and systematic review. J Gastroenterol Hepatol. 2024;39(6):1000-7. doi: 10.1111/jgh.16523.
12. Larsson SC, Orsini N, Wolk A. Diabetes mellitus and risk of colorectal cancer: a meta-analysis. J Natl Cancer Inst. 2005;97(22):1679-87. doi: 10.1093/jnci/dji375.

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Original Article

The Effect of Time-to-Surgery on Enteral Feeding Outcomes in Neonates with Uncomplicated Gastroschisis

Pattarin Lertnuwat, MD

Division of Pediatric Surgery, Department of Surgery, Lampang Regional Hospital

Abstract

Objectives: To evaluate the effect of time-to-surgery on enteral feeding outcomes in neonates with uncomplicated gastroschisis.

Materials and Methods: Retrospective review of NICU admissions for gastroschisis in Lampang Hospital, February 2014 – December 2024. The primary outcomes were the time to initiation of enteral feeding and the time to full enteral feeding (discontinuation of parenteral nutrition).

Results: Twenty-three patients with uncomplicated gastroschisis were analyzed in this study. Ten cases (43.5%) underwent surgery in less than 2 hours, 4 (17.4%) between 2–4 hours, 2 (8.7%) between 4–6 hours, 2 (8.7%) between 6–8 hours, and 5 (21.7%) between 8–10 hours. Primary fascial closure was performed in 5 cases (21.7%) and silo placement with staged closure in 18 cases (78.3%). The mean and median times to surgical intervention were 4.5 and 4 hours, respectively (range, 0.5–10 hours). The median time to start enteral feeding and achieve full enteral feeding was 15 days (IQR, 14.25–20.5) and 23.5 days (IQR, 21.0–28.0), respectively. One patient in the 8-10 hours group, managed with staged closure, died due to ventilator-associated pneumonia and sepsis. There were no statistically significant differences regarding the days to start enteral feeding, days to full enteral feeding, days to extubation, and length of stay. However, a clinical trend toward earlier enteral feeding and a shorter duration of total parenteral nutrition (TPN) was observed when surgery was performed earlier.

Conclusion: Although statistical significance was not reached, this study demonstrated that earlier surgical intervention may affect enteral feeding outcomes, specifically the time to start feeding and the duration of TPN in uncomplicated gastroschisis. Therefore, prenatal diagnosis and prompt in utero maternal transfer to a tertiary pediatric surgical center are advocated.

Keywords: Gastroschisis, Abdominal wall defects, Time-to-surgery, Abdominal wall closure method

INTRODUCTION

Gastroschisis is a congenital abdominal wall defect causing herniation of intra-abdominal organs into the amniotic cavity without a membrane covering.[1] The pathophysiology of bowel injury in gastroschisis is multifactorial. It is widely hypothesized that the degree of intestinal damage—often manifesting as bowel matting, peel formation, and atresia—is related to the duration of exposure to amniotic fluid and constriction at the abdominal ring defect.[2] The management of gastroschisis fundamentally revolves around two critical variables: the timing of intervention and the method of abdominal closure. Early surgical intervention soon after birth aims to restore gut circulation, reduce bowel edema, and cease heat and water loss.[3] Theoretically, minimizing the time between birth and surgical reduction should limit these inflammatory and ischemic processes, thereby preserving bowel function and reducing complications. In an effort to achieve earlier closure of the abdominal wall, delivery-room repair of gastroschisis has been reported.[3,4] However, the clinical benefit of immediate "emergency" repair remains a subject of debate, with conflicting evidence regarding whether shorter intervals truly translate to improved outcomes.[5]

The management of gastroschisis generally involves two surgical methods: primary fascial closure and staged closure. The selection of the appropriate method often depends on the severity of bowel edema, the size of the abdominal defect, and the neonate's hemodynamic stability.

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Corresponding author: Pattarin Lertnuwat, Department of Surgery, Lampang Regional Hospital, Lampang 52000, Thailand; E-mail: pattarin4407107@gmail.com; Phone number: +6654 237 400

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Primary fascial closure involves the immediate reduction of herniated viscera and suturing of the abdominal defect in a single procedure shortly after birth. This method is best suited for neonates with minimal bowel edema and the abdominal cavity capable of accommodating the organs without excessive intra-abdominal pressure. Staged closure, also known as silo reduction or delayed closure, is an alternative strategy employed when immediate reduction is precluded by severe bowel edema, viscero-abdominal disproportion, or hemodynamic instability. This technique is the use of a 'silo'—a temporary, sterile silicone receptacle designed to encase the eviscerated bowel. This device facilitates gradual reintroduction into the abdominal cavity via daily manual reduction, typically over 3 to 7 days. Once full reduction is achieved, the silo is removed, and definitive fascial closure is performed.[1,6,7] There are two primary types of silos utilized: the preformed spring-loaded silo and the surgically sutured silo. The preformed silo, widely considered the modern standard of care, features a flexible inner ring that secures the device within the abdominal wall without the need for sutures. In contrast, the surgically constructed silo involves suturing a silicone sheet directly to the fascia.[7]

A critical yet unresolved question is whether the time from delivery to surgery affects outcomes on an hour-by-hour basis. Identifying a specific 'optimal cutoff time' is essential for refining perinatal management protocols. If a distinct time-dependent correlation is established, it would scientifically justify the prioritization of prenatal maternal transfer to tertiary centers for fetuses with a prenatal diagnosis, ensuring immediate access to pediatric surgical care. Furthermore, for unexpected cases lacking prenatal detection, defining this timeframe would underscore the urgency of rapid referral, aiming to minimize the transport interval to achieve the best possible prognosis.

The main purpose of this study was to evaluate the effect of time from delivery to surgical repair on enteral feeding outcomes in neonates with uncomplicated gastroschisis. The primary outcomes were time to start enteral feeding and time to full enteral feeding (discontinuation of parenteral nutrition), while the secondary outcomes included ventilator days, postoperative complications, and length of stay.

MATERIALS AND METHODS

This study was a retrospective analysis approved by the Ethics Committee of Lampang Hospital. Our population comprised neonates with uncomplicated gastroschisis who were treated at Lampang Hospital from February 2014 to December 2024. The electronic database reviews included characteristic data, time-to-surgery (time from birth to first surgery is in hours), surgical method (primary closure or secondary closure), ventilator days, feeding data and postoperative complications. Patients were categorized based on the condition of the herniated bowel. Uncomplicated gastroschisis was defined as patients with an isolated defect and uncompromised bowel, whereas complicated gastroschisis was defined as cases presenting with associated bowel atresia, perforation, or volvulus. Consequently, the exclusion criteria were patients with complicated gastroschisis.

Upon admission to the neonatal intensive care unit (NICU), all neonates were placed under a radiant warmer to maintain normothermia. The eviscerated bowel was covered with sterile saline-soaked gauze, followed by an outer layer of dry gauze, to minimize heat and fluid loss.

A nasogastric tube was inserted for gastric decompression, and broad-spectrum antibiotics were administered. Intravenous fluid resuscitation was initiated immediately. The preoperative resuscitation targets included achieving hemodynamic stability (mean arterial pressure and heart rate within normal ranges for gestational age), ensuring adequate tissue perfusion (urine output > 1 mL/kg/hr), and maintaining a core body temperature between 36.5°C and 37.5°C.

The surgical procedure, primary closure or silo sac placement, was determined intraoperatively based on abdomino-visceral proportion and intra-abdominal pressure. A preformed silo was adapted from a wound protector as in laparoscopic surgery (**Figure 1**). The device was adapted by inserting the inner ring into the abdominal cavity and extending the plastic sheath upward to encase the eviscerated bowel. The distal end was then ligated to construct a temporary silo.

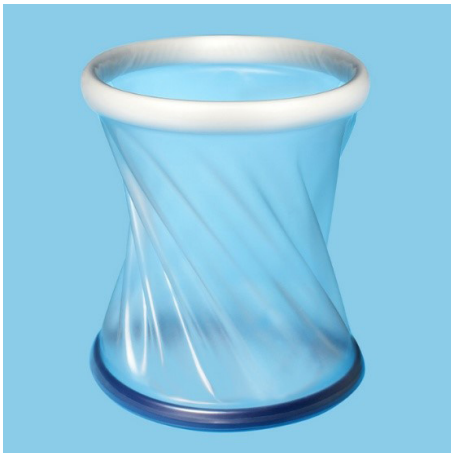


Figure 1 Silo

The reviewed feeding data were time to start enteral feeding (age at first enteral feeding) and time to full enteral feeding (age at full enteral feeding and discontinuation of parenteral nutrition). Enteral feeding was started once normal bowel function was established. The return of bowel function was assessed by the presence of normal bowel sounds, the resolution of bilious nasogastric drainage, and passage of stool. After enteral feeding was successful, parenteral nutrition was discontinued.

Statistical analyses included Student's t-test, Wilcoxon rank-sum test (Mann–Whitney U test), and Kruskal-Wallis test. A *p*-value less than 0.05 was considered statistically significant. A full parametric survival analysis with the Gompertz distribution was conducted and reported as a parametric failure curve.

RESULTS

Thirty-five cases of gastroschisis were treated at Lampang Hospital from February 2014 to December 2024. Twelve patients were excluded from the study: eight patients had incomplete data, and four patients had complicated gastroschisis. Twenty-three patients remained in the study (**Figure 2**). Among these, 6 patients (26.1%) were transferred from other hospitals. Fourteen cases (60.9%) were preterm neonates, and 9 (39.1%) were full-term. Nineteen cases (82.6%) had a low birth weight, 3 (13.0%) had a normal birth weight (> 2.5 kg), and 1 (4.3%) had a very low birth weight. There were no statistically significant differences in outcomes between patients born preterm and those born term, or between those with low birth weight and those with normal birth weight (**Table 1**).

A prenatal ultrasound successfully diagnosed gastroschisis in 15 cases (65.2%). Among these prenatally diagnosed cases, the mothers either received complete antenatal care and delivered at the study institution, were referred to other hospitals for in utero transfer prior to delivery, or delivered at other hospitals followed by a postnatal transfer of the neonate. Regarding neonatal comorbidities, respiratory and airway problems were the most commonly observed. Specifically, 5 patients (21.7%) developed respiratory distress syndrome (RDS), 2 patients (8.7%) had meconium aspiration syndrome (MAS), and 1 patient (4.3%) presented with subglottic stenosis. Additional concurrent anomalies in this cohort included atrial septal defect in 2 patients (8.7%), patent ductus arteriosus in 1 patient (4.3%), and septo-optic dysplasia in 1 patient (4.3%).

All surgical interventions took place following initial postnatal resuscitation. Primary fascial closure was performed in 5 cases (21.7%), and silo placement with staged closure was performed in 18 cases (78.3%). The data showed no statistically significant differences in feeding outcomes, ventilation days, and hospital stays between the two surgical groups (**Table 1**). The 23 patients were categorized into five groups based on their time-to-

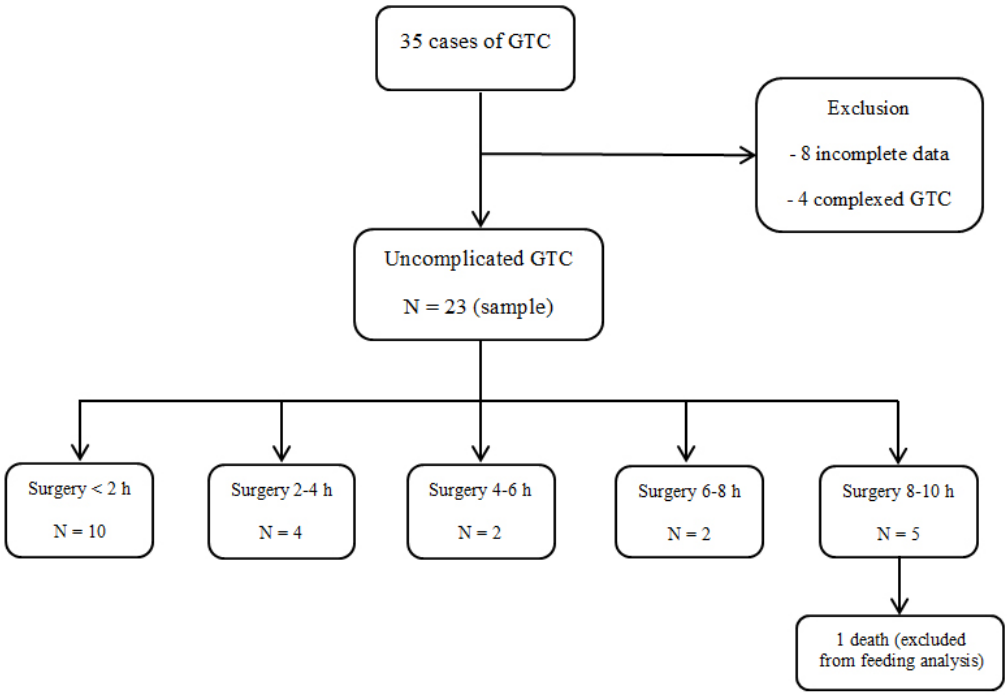


Figure 2 Classification of sample case according to time-to-surgery

Table 1 Outcome correlated to the gestational age, birth weight, abdominal wall closure method, and time-to-surgery

Characteristics	TTF (days)	TTFF (days)	Ven-Day	LOS (days)
GA	(mean ± sd)	(mean ± sd)	median (IQR)	median (IQR)
Term (n = 9)	16.1 ± 4.5	24.4 ± 6.0	3 (2-3)	24 (20-29)
Preterm (n = 13)	17.2 ± 3.9	25.8 ± 6.4	4 (3-7)	27 (25-29)
p value	0.570	0.631	0.060	0.226
Birth Weight	median (IQR)	median (IQR)	median (IQR)	median (IQR)
VLBW (n = 1)	16 (16-16)	23 (23-23)	10 (10-10)	27 (27-27)
LBW (n = 18)	15 (15-21)	24 (21-28)	3 (2-4)	26 (24-29)
NBW (n = 3)	13 (12-22)	19 (19-28)	2 (0-3)	20 (20-30)
p value	0.691	0.495	0.071	0.480
Sx method	(mean ± sd)	(mean ± sd)	median (IQR)	median (IQR)
Primary (n = 5)	17.4 ± 5.9	29.4 ± 7.1	3 (2-4)	32 (24-38)
Staged (n = 17)	16.5 ± 3.6	24.0 ± 5.5	3 (2-4)	25 (22-29)
p value	0.687	0.084	0.9034	0.237
Time-to-surgery	median (IQR)	median (IQR)	median (IQR)	median (IQR)
< 2 hr (n = 10)	15.5 (13-21)	22.5 (19-26)	2.5 (2-3)	25 (20-27)
2-4 hr (n = 4)	15 (12-17.5)	28 (26-32.5)	4 (2.5-6)	29 (27-33.5)
4-6 hr (n = 2)	19 (15-23)	26 (21-31)	5 (2-8)	27 (22-32)
6-8 hr (n = 2)	19.5 (15-24)	28 (21-35)	3.5 (3-4)	30.5 (22-39)
8-10 hr (n = 4)	15 (14.5-18.5)	22 (21-31.5)	3.5 (3-7)	26 (24.5-44.5)
p value	0.693	0.365	0.543	0.497

TTF: time to start enteral feeding (days) / TTFF: time to full enteral feeding (days) / Ven-Day: ventilation day / LOS: length of stay (days)

surgery: 10 cases (43.5%) underwent surgery in less than 2 hours, 4 (17.4%) between 2–4 hours, 2 (8.7%) between 4–6 hours, 2 (8.7%) between 6–8 hours, and 5 (21.7%) between 8–10 hours (**Figure 2**). The overall median time to surgery (n = 23) was 4 hours (range: 0.5–10 hours), with a mean of 4.5 hours. When stratified by surgical approach, the median time to surgery for the primary closure group was 6 hours (range: 4–9 hours). For the staged closure group, the median time to the first procedure was 2 hours (range: 0.5–10 hours), and the median time to the second procedure was 5 days (range: 3–7 days).

Post-operative complications included wound infection and wound dehiscence in 2 cases (8.7%), both of which were in the 2-4 hours time-to-surgery group and managed with staged closure. Necrotizing enterocolitis (NEC) developed in 2 cases (8.7%): one who had surgery within 4 hours with primary closure and the other at 10 hours with staged closure, which resulted in a prolonged time to full feeding period (37 and 40 days, respectively). The latter case also developed a catheter-related bloodstream infection (CRBSI). The neonate presented with respiratory distress syndrome (RDS) and, following initial surgery with a staged closure, subsequently died secondary to ventilator-associated pneumonia and sepsis at 6 days of life. Therefore, this patient was excluded from the statistical feeding analysis.

For the feeding analysis, the median time to start enteral feeding and full enteral feeding was 15 days (IQR, 14.25–20.5) and 23.5 days (IQR, 21.0–28.0), respectively. The outcomes showed no statistically significant differences regarding the number of days to start enteral feeding, days to full enteral feeding, days to extubation, and length of stay across the time-to-surgery groups (**Table 1**). However, a trend was observed associating earlier surgery with earlier initiation of enteral feeding (**Figure 3**) and a shorter duration to achieve full feeding (**Figure 4**).

DISCUSSION

Uncomplicated gastroschisis is currently characterized by low morbidity and gradually decreasing mortality.[8] However, clinical outcomes remain highly variable. To optimize patient care, various management strategies have been extensively evaluated in the literature, with particular attention paid to the interval between delivery and surgical intervention.[9,10] Theoretically, early primary closure performed within a few hours of birth offers benefits over staged closure by rapidly returning the intestines to their anatomical position. This minimizes the risk of vascular compromise arising from mesenteric compression at the ring defect[7] or mesenteric volvulus. Consequently, some studies advocate for immediate surgical repair following birth to maximize the likelihood of successful primary fascial closure.[4,11]

A study from Chiang Mai University (CMU) reported that several factors associated with successful early enteral

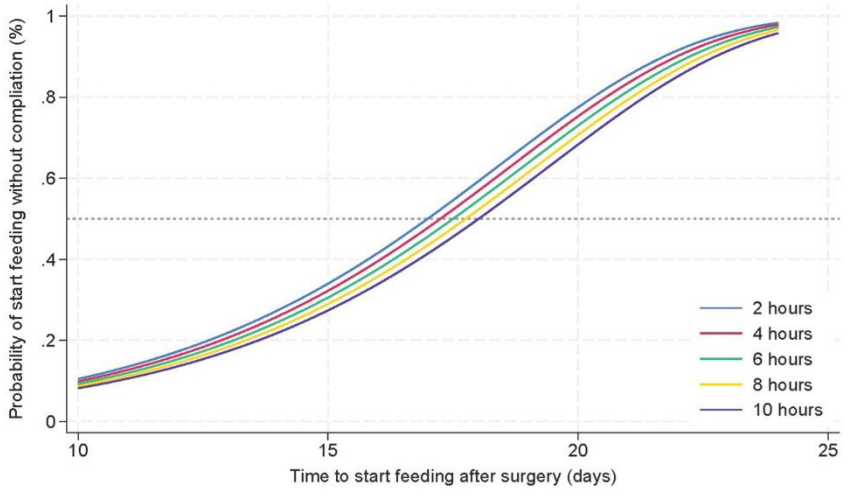


Figure 3 The probability of starting enteral feeding related to time-to-surgery

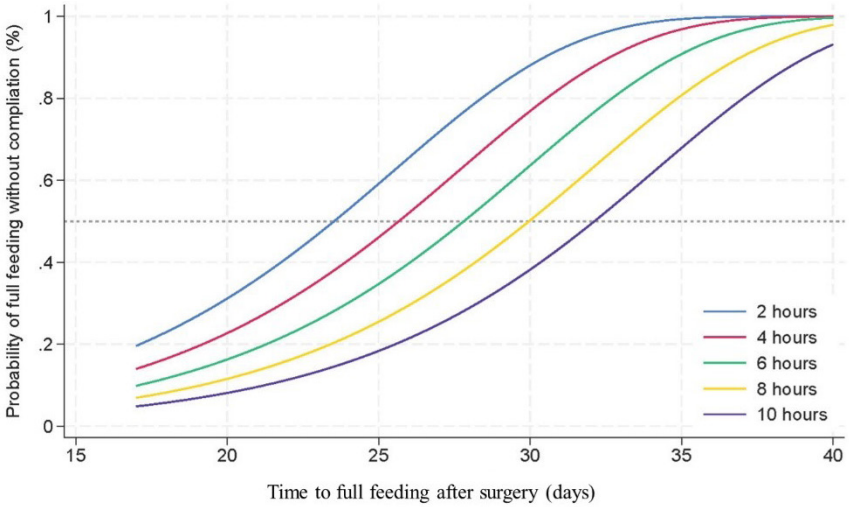


Figure 4 The probability of full feeding related to time-to-surgery

feeding were undergoing surgery within 10 hours, early postoperative extubation within 4 days, and initiating feeding before 10 days of life.[12] In the present study, all cases underwent the first surgical intervention within 10 hours after birth. Although there were no statistically significant differences regarding the effect of time-to-surgery on the days to start enteral feeding, days to full enteral feeding, and length of stay, a tendency was observed toward a higher probability of earlier enteral feeding and a shorter duration of TPN (full enteral feeding) when the surgery was performed earlier. A similar trend was reported by Tawil et al., where surgical intervention after 6 hours was associated with increased TPN duration and longer admission times, though their findings also did not reach statistical significance.[13] Singh et al. demonstrated that commencing feeds within 10 days is associated with significantly lower incidence of sepsis. This benefit is likely attributed to shorter TPN duration, reduced exposure to central venous catheters, and decreased length of stay.[9] Furthermore, minimizing TPN duration reduces the risk of parenteral nutrition-associated liver disease (PNALD). Consistent with these risks, the present cohort showed that the patient who developed NEC and required prolonged TPN subsequently developed a catheter-related bloodstream infection (CRBSI).

Regarding time to surgery, the median time from delivery to first documented operative intervention in this study was 4 hours, whereas Bucher et al. reported a shorter interval of approximately 2 hours.[14] However, these findings are consistent with a study from Chiang Mai University, which similarly reported prolonged time to surgery attributed to transportation time required for long-distance patient referrals.[12] While the median time

to start enteral feeding in the present cohort (15 days) was comparable to previous reports (18 days), the median time to full enteral feeding (23.5 days) was significantly shorter than the 44 days observed by Bucher et al.[14]

Most gastroschisis patients were preterm and had a low birth weight, which inherently predisposes them to respiratory distress syndrome (RDS). The presence of respiratory compromise significantly complicates initial stabilization. Consequently, the postnatal inter-hospital transport of these fragile, often intubated neonates carries a high risk of hypoxia due to suboptimal ventilatory support during transit. Therefore, early prenatal diagnosis, followed by in utero maternal transfer to a tertiary center, offers dual benefits: it significantly reduces time to surgery by eliminating postnatal transport delays and ensures immediate access to a specialized neonatal intensive care unit (NICU) for prompt ventilatory support. In this series, an overall prenatal diagnosis was achieved in 65.2% of the cases. Notably, over the last 7 years of the study period, the rate of prenatal diagnosis has improved to nearly 100%. However, it was noted that some prenatally diagnosed cases were still delivered at other hospitals, necessitating postnatal neonatal transfers.

The debate over the optimal location of delivery continues in the literature. Many studies have advocated for the benefits of maternal transfer during pregnancy to ensure delivery at a tertiary center. Quirk et al. reported that infants born at the surgical center benefited from earlier initiation of enteral feeds and a shorter length of stay compared with transferred neonates.[15] Conversely, recent studies from the United Kingdom suggest no significant advantage regarding the proximity of delivery to a pediatric surgical center,[10,16,] and Singh et al. recommended that adequate preoperative stabilization be prioritized over rapid surgical closure.[9] These latter findings align with the present study, which did not demonstrate a statistically significant effect of time-to-surgery on overall patient outcomes. Nevertheless, given the severe risks associated with transferring critically ill neonates and the widespread population distribution of Northern Thailand, the author advocates for the continuous improvement of the maternal referral system. Establishing a clear, standardized in utero transfer protocol for network hospitals is essential to facilitate prompt and standardized resuscitation, optimize preoperative conditions, and ultimately maximize patient safety.

The abdominal wall closure method appears to influence outcomes in uncomplicated gastroschisis, with primary closure generally superior to staged closure.[17,18] Specifically, staged closure is associated with prolonged durations of TPN, mechanical ventilation, and hospital stay compared to primary closure.[9] This comparison is prone to selection bias because primary closure is typically successful in patients with favorable bowel conditions and sufficient abdominal capacity. In contrast, neonates with compromised bowel conditions—such as severe edema or a shortened mesentery—are generally not amenable to primary reduction and undergo silo placement-staged closure, which is associated with a high rate of sepsis, delayed feeding, and other complications.[19] In this study, postoperative wound infection occurred in 2 cases (8.7%), both of which were in the staged closure group. This finding is consistent with the report by Sangkhathat et al., who observed a wound infection rate of 32.35% and similarly found a higher prevalence of infectious complications in patients undergoing staged reduction.[20] This predisposition may be attributed to the prolonged presence of the silo and the open nature of the abdominal defect during the reduction period. Despite this specific complication, there were no statistically significant differences in overall outcomes between primary closure and staged closure in this cohort. A possible explanation for this similarity could be the disparity in the number of cases between the two groups (5 primary vs. 17 staged closures). Nevertheless, primary closure remains the preferred surgical method when feasible.[21] Regardless of these findings, clinical decision-making must be tailored to each patient to avoid the risks of abdominal compartment syndrome[8] and respiratory distress.

Given the substantial proportion of patients requiring staged closure in this series, implementing routine bedside silo placement is a crucial future direction for our institution. Traditionally, silo construction at the center has been performed in the operating room, which inherently introduces delays related to surgical theater availability and transport. Conversely, the immediate bedside application of a preformed silo in the NICU offers profound physiological benefits. It significantly shortens the duration of bowel exposure, minimizes evaporative heat and fluid losses, and accelerates the initial resuscitation process. By completely bypassing the wait time for an operating room, bedside silo placement allows for earlier visceral protection and a more gradual reduction. This proactive approach may effectively mitigate bowel inflammation, thereby accelerating the recovery of physiological gut motility and ultimately improving enteral feeding out-

comes. Therefore, establishing a standardized bedside silo protocol is strongly recommended as a primary strategy to further optimize the management of gastroschisis in our regional network.

CONCLUSION

In conclusion, although statistical significance was not achieved due to sample size constraints, the present study demonstrated that earlier surgical intervention may affect enteral feeding outcomes in neonates with uncomplicated gastroschisis, specifically the probability of earlier feeding initiation and shorter TPN duration. To facilitate early and optimal surgical management, early prenatal diagnosis combined with prompt in utero maternal transfer to a tertiary pediatric surgical center is advocated. Furthermore, establishing standardized protocols for maternal transport and implementing routine bedside silo placement in the NICU are crucial next steps. These proactive strategies will minimize transport-related delays, accelerate initial resuscitation, and ultimately improve the overall quality of care for this vulnerable population.

REFERENCES

1. Holland AJ, Walker K, Badawi N. Gastroschisis: an update. Pediatr Surg Int. 26(9):871-8. doi: 10.1007/s00383-010-2679-1.
2. Langer JC, Longaker MT, Crombleholme TM, et al. Etiology of intestinal damage in gastroschisis. I: Effects of amniotic fluid exposure and bowel constriction in a fetal lamb model. J Pediatr Surg. 24(10):992-7. doi: 10.1016/s0022-3468(89)80200-3.
3. Saranrittichai S. Gastroschisis: delivery and immediate repair in the operating room. J Med Assoc Thai. 91(5):686-92.
4. Coughlin JP, Drucker DE, Jewell MR, et al. Delivery room repair of gastroschisis. Surgery. 114(4):822-6.
5. O'Shea K, Harwood R, O'Donnell S, et al. Does the time to the theater matter in simple gastroschisis? World J Pediatr Surg. 6(4):e000575. doi: 10.1136/wjps-2023-000575.
6. Klein MD. Congenital defects of the abdominal wall. In: Coran AG, editors. Pediatric Surgery. 7th ed. Philadelphia: Elsevier Saunders; 2012. p. 973-84. ISBN: 978-0323072557.
7. Skarsgard ED. Management of gastroschisis. Curr Opin Pediatr. 28(3):363-9. doi: 10.1097/MOP.0000000000000336.
8. Fraga MV, Laje P, Peranteau WH, et al. The influence of gestational age, mode of delivery, and abdominal wall closure method on the surgical outcome of neonates with uncomplicated gastroschisis. Pediatr Surg Int. 34(4):415-9. doi: 10.1007/s00383-018-4233-5.
9. Singh SJ, Fraser A, Leditschke JF, et al. Gastroschisis: determinants of neonatal outcome. Pediatr Surg Int. 19(4):260-5. doi: 10.1007/s00383-002-0886-0.
10. Nicholls G, Upadhyaya V, Gornall P, et al. Is specialist centre delivery of gastroschisis beneficial? Arch Dis Child. 69(1 Spec No):71-2. doi: 10.1136/adc.69.1_spec_no.71.
11. Swift RI, Singh MP, Ziderman DA, et al. A new regime in the management of gastroschisis. J Pediatr Surg. 27(1):61-3. doi: 10.1016/0022-3468(92)90106-h.
12. Pratheeppanyapat T, Tepmalai K, Singhavejsakul J, et al. The factors associated with successful early enteral feeding in gastroschisis. Pediatr Surg Int. 34(7):743-8. doi: 10.1007/s00383-018-4282-9.
13. Tawil KA, Gillam GL. Gastroschisis: 13 years' experience at RCH Melbourne. J Paediatr Child Health. 31(6):553-6. doi: 10.1111/j.1440-1754.1995.tb00883.x.
14. Bucher BT, Mazotas IG, Warner BW, et al. Effect of time to surgical evaluation on the outcomes of infants with gastroschisis. J Pediatr Surg. 47(6):1105-10. doi: 10.1016/j.jpedsurg.2012.03.016.
15. Quirk JG Jr, Fortney J, Collins HB 2nd, et al. Outcomes of newborns with gastroschisis: the effects of mode of delivery, site of delivery, and interval from birth to surgery. Am J Obstet Gynecol. 174(4):1134-8. doi: 10.1016/s0002-9378(96)70655-5.
16. Stoodley N, Sharma A, Noblett H, et al. Influence of place of delivery on outcome in babies with gastroschisis. Arch Dis Child. 68(3 Spec No):321-3. doi: 10.1136/adc.68.3_spec_no.321.
17. Luck SR, Sherman JO, Raffensperger JG, et al. Gastroschisis in 106 consecutive newborn infants. Surgery. 98(4):677-83.
18. Dore Reyes M, Triana Junco P, Barrena Delfa S, et al. Primary versus secondary closure: ventilatory and nutritional differences in patients with gastrosquisis (in Spanish). Cir Pediatr. 29(2):49-53.
19. Novotny DA, Klein RL, Boeckman CR. Gastroschisis: an 18-year review. J Pediatr Surg. 28(5):650-2. doi: 10.1016/0022-3468(93)90022-d.
20. Sangkhathat S, Patrapinyokul S, Chiengkriwate P, et al. Infectious complications in infants with gastroschisis: an 11-year review from a referral hospital in southern Thailand. J Pediatr Surg. 43(3):473-8. doi: 10.1016/j.jpedsurg.2007.10.026.
21. Alali JS, Tander B, Malleis J, et al. Factors affecting the outcome in patients with gastroschisis: how important is immediate repair? Eur J Pediatr Surg. 21(2):99-102. doi: 10.1055/s-0030-1267977.

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Case Report

Ileal Perforation and Cervical Nodal Metastasis in Small Bowel Adenocarcinoma: A Case Report

Huynh Loc Tran, MD[1,2]
Hoang Phuong Chung, MD[1]
My Tran Trinh, MD[1,3]

[1]*Department of Digestive Surgery, Nhan Dan Gia Dinh Hospital, Ho Chi Minh City, Viet Nam*
[2]*Department of General Surgery, School of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Viet Nam*
[3]*Department of General Surgery, Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Viet Nam*

Abstract Small bowel adenocarcinoma (SBA) is a rare malignancy that typically presents late and is difficult to diagnose, particularly when arising in the ileum. We report an exceptional case of SBA presenting simultaneously with ileal perforation and cervical lymph node metastasis - two manifestations that are individually uncommon and exceedingly rare in combination. A 69-year-old woman presented with an acute abdomen and a newly enlarged cervical lymph node; laparoscopy revealed a 2-mm ileal perforation with peritoneal nodules, and subsequent cervical node excision confirmed metastatic carcinoma. Histopathology and immunohistochemistry demonstrated CK7 and EMA positivity with CK20 negativity, supporting the diagnosis of SBA and excluding colorectal, neuroendocrine, and stromal neoplasms. This unusual presentation highlights the diagnostic challenges posed by ileal tumors, underscores the critical role of timely surgical exploration, and emphasizes the importance of immunohistochemistry in establishing tumor origin when clinical and radiologic findings are ambiguous.

Keywords: Adenocarcinoma, Bowel perforation, Small intestine neoplasms

INTRODUCTION

Small bowel adenocarcinoma (SBA) is a rare gastrointestinal malignancy, accounting for fewer than 5% of all gastrointestinal cancers despite the small intestine comprising nearly 90% of the bowel's mucosal surface.[1] Despite advances in diagnosis and treatment, the prognosis of small bowel adenocarcinoma remains poor, with reported 5-year overall survival rates of approximately 20%–30%.[2-4]

Small bowel neoplasms comprise a heterogeneous group of tumors, including adenocarcinomas, neuroendocrine tumors, gastrointestinal stromal tumors (GISTs), and lymphomas.[1-3] Its clinical course is frequently indolent, and early symptoms, such as vague abdominal discomfort, occult bleeding, or anemia, are nonspecific, leading to delay in diagnosis and resulting in presentation at more advanced stages.[2] Jejunal and ileal tumors are particularly difficult to detect because of their deep anatomical location and limited accessibility by standard endoscopic modalities.

While obstruction and bleeding are the most common initial manifestations, small bowel perforation is exceedingly uncommon, and cervical lymph node metastasis has been documented only rarely, even in large population-based cohorts.[3]

We report a case of SBA presenting simultaneously with ileal perforation and cervical lymph node involvement. This atypical and aggressive phenotype underscores the diagnostic challenges and biological heterogeneity of this already uncommon malignancy.

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Corresponding author: Huynh Loc Tran, Department of Digestive Surgery, Nhan Dan Gia Dinh Hospital, Ho Chi Minh City, Viet Nam; E-mail: thloc@ump.edu.vn; Phone number: +84 963468236
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CASE PRESENTATION

This case report was conducted in accordance with the Declaration of Helsinki. Written informed consent for publication of clinical details and images was obtained from the patient. All identifying information has been removed to preserve confidentiality.

A 69-year-old woman presented to the Emergency Department with 6 hours of progressively worsening right lower quadrant abdominal pain, accompanied by nausea without vomiting or fever. Her medical history was significant for well-controlled hypertension. On examination, the patient was hemodynamically stable. A firm, mobile, non-tender left cervical lymph node measuring approximately 1.5 cm was palpable at level III, while no supraclavicular lymph nodes were detected. The abdomen was non-distended, with localized tenderness in the lower abdomen. No other significant abnormalities were noted.

Laboratory investigations showed mild leukocytosis (WBC 11.5 k/μL) and elevated C-reactive protein (23.3 mg/L), while other parameters were within normal limits. Contrast-enhanced abdominal CT demonstrated an irregularly thickened segment of the small bowel in the right iliac fossa (approximately 12 mm in maximal wall thickness and 6 cm in length), with focal wall discontinuity, adjacent air bubbles, fat stranding, and a surrounding fluid collection, suggestive of a tumor-related small-bowel perforation. Several enlarged mesenteric lymph nodes were also observed. In addition, the CT scan revealed a suspicious lesion in the right lower lobe of the lung, suggestive of pulmonary metastasis. No CT imaging of the neck was performed at this stage.

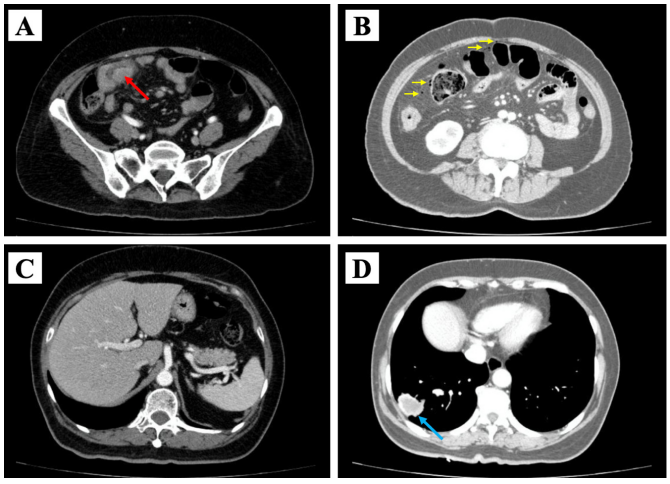


Figure 1 Preoperative contrast-enhanced abdominal CT scan showing: (A) Irregularly thickened small bowel segment (red arrow), (B) free intraperitoneal air bubbles (yellow arrows), (C) no evidence of hepatic metastasis, (D) a suspicious mass in the right lung suggestive of metastasis (blue arrow).

The patient was placed in the supine position. Laparoscopic access was established using three trocars: a 10-mm port at the umbilicus, a 5-mm port in the left iliac fossa, and a 5-mm port in the suprapubic region. Pneumoperitoneum was maintained at an intra-abdominal pressure of 12 mmHg. Initial exploration revealed a small amount of turbid fluid distributed around the liver, along the right paracolic gutter, and in the pouch of Douglas, while the left abdomen appeared clean. Fibrinous exudate was predominantly adherent to small bowel loops in the mid-abdomen. Multiple peritoneal nodules were identified in the right iliac fossa and lower abdomen; a representative nodule on the right lower abdominal wall was biopsied. Microbiological culture of the intraperitoneal fluid was performed, but showed no bacterial growth. The liver surface was smooth, with no visible metastases. A single inflamed ileal segment was identified, harboring a small perforation with enteric leakage, and no additional lesions were observed along the remaining small bowel, stomach, colon, or appendix (**Figure 1**).

The affected small-bowel segment was exteriorized via an approximately 5-cm extension of the umbilical port site, which was protected with a wound protector to minimize contamination. Intraoperative assessment confirmed a tumor-bearing ileal loop without evidence of mesenteric ischemia. Segmental resection was performed with proximal and distal margins of approximately 7 cm from the lesion. A functional end-to-end anastomosis was constructed using linear staplers, resulting in a well-perfused, widely patent anastomosis approximately 3 cm in diameter. The abdominal cavity was irrigated with approximately 2 L of normal saline, followed by thorough suction. After careful inspection and gauze-assisted drying, no drain was placed.

Gross examination of the surgical specimen revealed a 20-cm segment of small intestine. Approximately 7 cm from one resection margin, there was an ulcerated, indurated lesion measuring 4 × 4 × 1.5 cm, with a firm, whitish cut surface. The mesenteric adipose tissue adjacent to the lesion contained three firm nodules ranging from 0.5 to 0.7 cm in diameter. A separate peritoneal nodule, measuring 1 × 1 × 0.4 cm, was also identified.

A total of eight tissue blocks were submitted for Hematoxylin and Eosin staining. Microscopic evaluation showed atypical epithelial cells arranged in solid nests, sheets, and gland-like structures. The tumor cells exhibited enlarged pleomorphic nuclei, prominent nucleoli, abundant eosinophilic cytoplasm, and frequent mitotic figures,

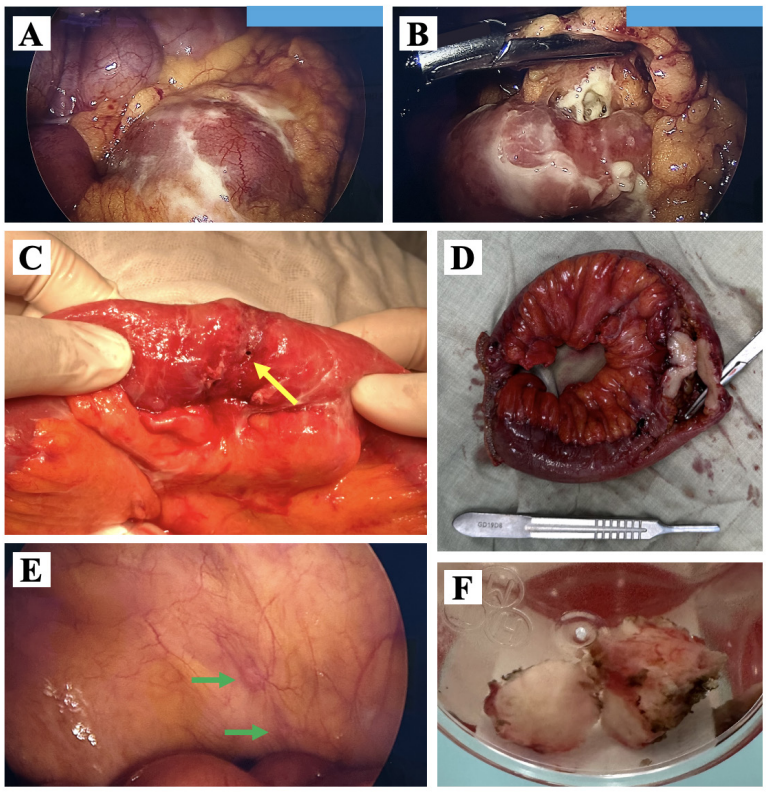


Figure 2 Intraoperative findings: (A) a mid-abdominal small bowel loop covered with fibrinous exudate; (B) a small bowel lesion walled off by the omentum; (C) tumor-associated small bowel perforation, with the yellow arrow indicating the perforation site; (D) resected small bowel segment containing the tumor; (E) peritoneal metastatic nodules on the lower anterior abdominal wall, with green arrows indicating peritoneal metastatic nodules; and (F) metastatic left level III cervical lymph node.

with focal areas of necrosis. The carcinoma infiltrated through the muscularis propria and extended into the surrounding mesenteric fat. Five metastatic lymph nodes were identified; however, the total number of examined lymph nodes was not reported. Both proximal and distal resection margins were free of tumor. The peritoneal nodule demonstrated histopathological features like those of the primary small bowel tumor; however, immunohistochemical staining was performed only on the primary lesion.

Based on the histomorphology, the differential diagnosis included poorly differentiated adenocarcinoma, gastrointestinal stromal tumor (GIST), neuroendocrine carcinoma, or a carcinoma of other origin. Given the deep mural invasion, peritoneal extension, and nodal metastases, an immunohistochemical panel was performed on the primary tumor, including CK7, CK20, EMA, Chromogranin, Synaptophysin, Ki-67, Vimentin, and CD117 (**Figure 3 and Table 1**). The Ki-67 index was approximately 30%, indicating moderate-to-high proliferative activity of tumor cells.

The tumor was staged as pT3N2M1c (Stage IVB). The T3 category indicates invasion through the muscularis propria into the mesenteric fat. The N2 classification reflects metastasis to three or more regional lymph nodes, with all five examined nodes involved. The M1c designation denotes peritoneal metastasis, supported by peritoneal nodules and further reinforced by metastatic disease in a cervical lymph node, indicating systemic dissemination. Collectively, these findings are consistent with advanced-stage disease characterized by deep local invasion, extensive nodal involvement, and distant metastasis.

After surgery, the patient remained stable, with no abdominal pain or fever. Oral intake was well tolerated, bowel movements were normal with yellow stool, and the surgical incision healed appropriately without signs of infection. The patient was discharged on postoperative day 5. During follow-up, the left cervical lymph node persisted after two weeks despite antibiotic therapy. Excisional biopsy of a level III lymph node, measuring ap-

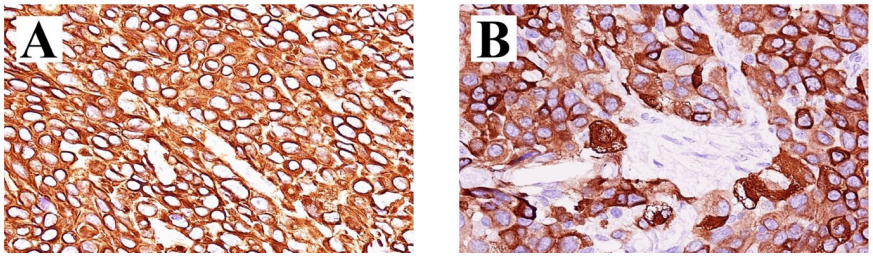


Figure 3 Postoperative histopathological examination with immunohistochemical staining. (A) CK7-positive immunostaining. (B) EMA-positive immunostaining.

proximately 1.5 cm with a firm consistency, well-defined capsule, whitish cut surface, and preserved mobility, was performed (**Figure 2F**). Histopathological examination using Hematoxylin and Eosin (H&E) staining revealed poorly differentiated carcinoma, consistent with metastatic disease; no immunohistochemical staining was performed on the cervical lymph node specimen.

The patient was later confirmed to have small bowel adenocarcinoma with carcinomatosis and was transferred to an oncology referral center for continuation of systemic chemotherapy. Postoperative CT evaluation of the chest and neck did not reveal any additional pulmonary lesions or cervical/supraclavicular lymphadenopathy.

DISCUSSION

The clinical presentation in this patient is remarkable for two scarce features: ileal perforation and concurrent cervical lymph node metastasis. Small bowel perforation is an exceedingly uncommon initial manifestation of SBA, as these tumors more frequently present with bowel obstruction or occult gastrointestinal bleeding.[2] Furthermore, cervical or supraclavicular lymph node involvement is also rarely documented even in large patient cohorts; SBA more typically metastasizes to mesenteric lymph nodes, the liver, lungs, and the peritoneum.[3] In this context, the present patient had small bowel cancer with carcinomatosis, indicating that the tumor had already disseminated systemically, with metastatic spread involving the lungs, peritoneum, and lymph nodes, including cervical lymph nodes. The coexistence of these rare features in a single patient suggests an unusually aggressive tumor phenotype and underscores the diagnostic challenges associated with this malignancy.

Furthermore, ileal tumors, such as in our patient, tend to be detected later than duodenal primaries due to their deeper anatomical position and the limited accessibility of this segment to conventional endoscopy.[4] Epidemiologic analyses demonstrate that jejunal and ileal tumors are more frequently associated with obstruction, bleeding, and peritoneal dissemination, findings which correlate closely with our intraoperative observations.[2]

Cross-sectional imaging, particularly contrast-enhanced CT, remains the cornerstone for evaluating suspected small bowel pathology in the emergency setting. Nevertheless, differentiating SBA from Crohn's disease or infectious enteritis can be challenging, leading to delayed or incorrect diagnoses in several reported cases.[2] In our patient, CT evidence of pneumoperitoneum and peritonitis mandated urgent surgical intervention, which remains the standard of care in perforated SBA.

Surgical resection is the primary therapeutic modality, with more than 80% of patients undergoing operative

Table 1 Immunohistochemical staining results.

Immunohistochemical staining	Result	Interpretation
CK7 and EMA	Strong and diffuse Positivity*	Confirming the epithelial nature and supporting a diagnosis of small bowel adenocarcinoma
Ki-67	30%	The tumor exhibited a proliferative index of approximately 30%
CK20	Negative	Differentiate this lesion from colorectal adenocarcinoma
Chromogranin and Synaptophysin	Negative	Effectively excluding neuroendocrine carcinoma
Vimentin and CD117	Negative	Ruling out sarcoma and gastrointestinal stromal tumor (GIST)

*Postoperative histopathological examination with immunohistochemical staining demonstrated CK7-positive and EMA-positive tumor cells, showing characteristic brown cytoplasmic and membranous staining.

management - often on an emergent basis rather than as a planned oncologic procedure.[3] Because SBA typically exhibits an infiltrative pattern of growth, segmental resection with margins of at least 5-10 cm is recommended to ensure oncologic safety, particularly when local inflammation or perforation obscures the true extent of disease.[2] The operative strategy in this case, involving emergency laparotomy with segmental resection and peritoneal lavage, aligns with established surgical principles.

The laparoscopic approach in this emergency setting provided both diagnostic and therapeutic advantages, allowing rapid identification of the perforation site and comprehensive assessment of intra-abdominal pathology with minimal invasiveness. In addition, it facilitated targeted biopsy of peritoneal nodules and guided appropriate surgical management. However, its application should be carefully selected, as certain conditions, such as hemodynamic instability, diffuse fecal peritonitis, or extensive intra-abdominal carcinomatosis, may compromise visualization and operative control, making open surgery a more appropriate option.

Adequate lymph node evaluation is essential for accurate staging of small bowel adenocarcinoma, with current evidence suggesting that examination of at least 8 lymph nodes is desirable to ensure reliable staging.[5] In the present case, the total number of examined lymph nodes was not documented, which limits the assessment of lymph node harvest adequacy. Nevertheless, five metastatic lymph nodes were identified, fulfilling the criteria for N2 disease and indicating a substantial nodal tumor burden. This finding reflects aggressive tumor biology despite incomplete nodal evaluation.

Histopathology and immunohistochemistry (IHC) remain essential for distinguishing SBA from mimickers such as lymphoma or Crohn-related carcinoma. Standard IHC markers, including CK7, CK20, and CDX2, aid in confirming the tumor's intestinal origin and guiding systemic therapy. Increasingly, molecular profiling plays a crucial role in treatment planning, as MSI-high or dMMR SBA, reported in approximately 1-16% of cases, may benefit from immune checkpoint inhibitors.[2] MSI-H/dMMR analysis could not be performed in our patient because this diagnostic modality was not available at the time of evaluation

Given the advanced stage of disease in this patient, systemic therapy remains the cornerstone of management. Fluoropyrimidine-based chemotherapy regimens, such as FOLFOX or CAPOX, are commonly used and are largely extrapolated from colorectal cancer treatment strategies.[2-5] In recent years, molecular profiling has become increasingly important, as tumors exhibiting microsatellite instability or mismatch repair deficiency may benefit from immune checkpoint inhibitors.[2-5] However, molecular testing was not performed in our case, representing a limitation. Despite ongoing advances, the prognosis of metastatic small bowel adenocarcinoma remains poor.[1-3,5]

Despite incremental advances in imaging, surgical technique, and systemic therapy, long-term outcomes for SBA remain poor. Contemporary estimates place the 5-year overall survival rate at roughly 30%, substantially worse than survival outcomes for colorectal cancer, even when stratified by stage.[1] Several factors contribute to this disparity: the disease's rarity, the paucity of prospective trials, the extrapolation of treatment paradigms from colorectal cancer, and persistent difficulties in achieving early diagnosis. Recent bibliometric analyses indicate that SBA remains an under-researched malignancy, despite a rapid increase in scientific output over the past decade.[6]

In summary, this case represents an exceptionally rare and biologically aggressive manifestation of SBA, marked by the combination of ileal perforation and cervical lymph node metastasis. These features highlight the importance of maintaining a high index of suspicion when evaluating acute abdomen with unexplained lymphadenopathy and underscore the necessity for multidisciplinary collaboration to optimize diagnostic accuracy and therapeutic decision-making in this challenging and understudied disease.

Given the limited data available in the current literature, certain atypical presentations of small bowel adenocarcinoma, such as perforation or distant lymph node involvement, may reflect a more advanced or biologically aggressive disease course. Although these features are individually uncommon, their presence should prompt careful evaluation for underlying malignancy. This case highlights the need for heightened clinical awareness when encountering such findings. Further studies may help to better clarify their clinical significance.

CONCLUSION

This case highlights an exceptionally aggressive form of small bowel adenocarcinoma, presenting with both ileal perforation and cervical nodal metastasis - a scarce combination. Clinicians should suspect SBA when an

acute abdomen is accompanied by unexplained lymphadenopathy. Importantly, immunohistochemistry remains essential for confirming intestinal origin and distinguishing SBA from colorectal carcinoma, neuroendocrine tumors, lymphoma, and GIST, thereby ensuring accurate diagnosis and appropriate oncologic management.

REFERENCES

1. Aparicio T, Zaanan A, Svrcek M, et al. Small bowel adenocarcinoma: Epidemiology, risk factors, diagnosis, and treatment. Dig Liver Dis. 2014;46:97-104. doi: 10.1016/j.dld.2013.04.013.
2. Khosla D, Dey T, Madan R, et al. Small bowel adenocarcinoma: an overview. World J Gastrointest Oncol. 2022;14:413-422. doi: 10.4251/wjgo.v14.i2.413.
3. Teufel A, Meindl-Beinker NM, Hösel P, et al. Characteristics and outcome of patients with small bowel adenocarcinoma (SBA). J Cancer Res Clin Oncol. 2023;149:4579-4590. doi: 10.1007/s00432-022-04344-z.
4. Sakae H, Kanzaki H, Nasu J, et al. The characteristics and outcomes of small bowel adenocarcinoma: A multicentre retrospective observational study. Br J Cancer. 2017;117:1607-1613. doi: 10.1038/bjc. 2017.338.
5. Benson AB, Venook AP, Al-Hawary MM, et al. Small Bowel Adenocarcinoma, Version 1.2020, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019;17(9):1109-1133. doi: 10.6004/jnccn. 2019.0043.
6. Li L, Zhang S, Fu G. Trending of small bowel adenocarcinoma research from 2000 to 2022: A bibliometric analysis. Medicine (Baltimore). 2024;103(15):e37795. doi: 10.1097/MD.0000000000037795.

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Review Article

Re-Evaluating the Role of Delayed Cholecystectomy: Safety and Timing in the Management of Acute Cholecystitis

Nan-ak Wiboonkhwan[1,2]

[1]*Department of Surgery, Songklanagarind Vejchavivat Hospital, Songkhla, Thailand*

[2]*Department of Surgery, Vachira Phuket Hospital, Phuket, Thailand*

Abstract

Background: Early laparoscopic cholecystectomy (LC) is the standard treatment for acute cholecystitis (AC) to reduce hospital stay and costs, but optimal timing remains debated due to severe complications like bile duct injury (BDI). Delayed LC (DLC) after conservative management or drainage provides a safer alternative with lower postoperative complications and BDI rates

Materials and Methods: This narrative review analyzed literature from PubMed and Embase (1990–October 2025). Surgical timing was categorized by inflammation phases: Early (<7 days), Intermediate (7 days to 6 weeks), and Delayed (>6 weeks). Evidence from RCTs, meta-analyses, and registries was evaluated, with a focus on BDI risks, surgeon experience, and hospital readiness. Limitations include potential selection bias and lack of formal quality assessment.

Results: Under optimal conditions, early LC reduced hospital stay and costs but was associated with higher postoperative complication rates (up to 26.7%). BDI rates peaked at 2.8% when operating between days 4–7, and open conversion rates reached 21%–28.6% in Grade I/II cases. Conversely, delayed LC after drainage mitigated these risks; one study reported zero conversions in the delayed group, and a meta-analysis showed a significantly higher BDI risk (HR 6.07) with early intervention.

Conclusion: Choosing between early and delayed LC must be individualized, prioritizing patient safety over economic benefits. While early LC is preferred under optimal conditions, it requires high expertise. In resource-variable settings, delayed LC serves as an essential, safer alternative that aligns with international guidelines.

Keywords: Acute cholecystitis, Cholecystectomy, Delayed cholecystectomy, Early cholecystectomy, Laparoscopic cholecystectomy, Safe cholecystectomy

INTRODUCTION

Currently, early laparoscopic cholecystectomy (LC) is the standard treatment for acute cholecystitis (AC) due to its proven ability to reduce total hospital stay and average costs.[1] However, the decision to proceed must weigh these benefits against the risk of bile duct injury (BDI), a critical complication that increases long-term mortality by 8.8%.[2] The key clinical dilemma lies in the gap between current guideline recommendations for early intervention and real-world clinical practice, where factors such as patient comorbidities, hospital readiness, and surgical expertise significantly influence outcomes.

MATERIALS AND METHODS

This study is a narrative review of the literature, identifying relevant articles through searches of PubMed and Embase for studies published from 1990 to October 2025. The search strategically combined terms such as "early versus delayed cholecystectomy" and "surgical outcomes of acute cholecystitis" to selectively review surgical outcomes, cost-effectiveness, and complication rates. Surgical timing was categorized into three distinct groups based on the underlying pathophysiologic evolution of gallbladder inflammation: The Early Phase (< 7 days), characterized by interstitial edema and easier dissection planes; the Intermediate Phase (7 days to 6 weeks), marked

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Corresponding author: Nan-ak Wiboonkhwan, MD, FRCST, Department of Surgery, Songklanagarind Vejchavivat Hospital, Hat Yai, Songkhla 90110, Thailand; E-mail: boatpsusurgery@gmail.com.

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by subacute fibroblastic proliferation and dense, vascularized adhesions; and the Delayed Phase (> 6 weeks), where inflammation has matured or resolved. Evidence from randomized controlled trials (RCTs), meta-analyses, and large-scale registry studies was interpreted with a focus on both statistical significance and clinical relevance, particularly regarding the risk of bile duct injury (BDI) and the impact of surgeon experience and hospital readiness. As a non-systematic narrative review, a key limitation of this study is the potential for selection bias and the lack of a formal quality assessment for all included evidence, which may influence the generalizability of the findings.

Bile duct injury and acute cholecystitis

Nuzzo et al.[3] reported the incidence of BDI following LC as 0.3%. They found that the incidence of BDI in the group with gallbladder inflammation was 0.56%, which was statistically significantly higher than in the group without inflammation. Furthermore, among the BDI group, 52.3% underwent LC for gallbladder inflammation, and 46.8% were described as easy surgeries.

Importance of the experience for LC in acute cholecystitis

Nuzzo et al.[3] found that, when comparing the incidence of BDI with the surgeon's experience in LC, fewer than 150 cases over three years were associated with a BDI incidence of 0.86%. This incidence decreased significantly to 0.19% when the surgeon had more than 250 cases over three years. From this study, the researchers concluded that gallbladder inflammation is an important risk factor for BDI; therefore, experience with more than 250 cases over three years is required to reduce the risk of BDI. However, the author found that the proportion of patients with gallbladder inflammation and BDI was higher when the surgeon had more than 250 cases in 3 years. The researchers therefore recommended performing the surgery with caution, even for surgeons with extensive experience.

Data from a Thai study by Noppakunsomboon et al.[4] investigated the outcomes of early LC in AC grade I versus grade II among surgeons with more than 50 LC cases per year. They found a minor BDI rate of 3.8% with no difference between grade I and II. The open conversion rate was 21%, attributable to dense intra-abdominal adhesions (63.6%), inflammation (50%), contamination (36.3%), and bleeding during surgery (22.7%).

While surgical volume serves as a useful proxy for experience, contemporary surgical standards emphasize that "high experience" must also incorporate individual outcome metrics and the mastery of safety protocols. Beyond achieving specific case volumes, a high-experience surgeon is defined by clinical judgment[5] and consistent proficiency in avoiding complications, particularly in maintaining low individual bile duct injury (BDI) rates. Although no standardized individual BDI rate is currently established in the literature to define high experience, the focus remains on the surgeon's ability to recognize when intraoperative difficulties[5]—such as dense adhesions, scarring, or bleeding—necessitate 'bailout' strategies[6,7], including open conversion or subtotal cholecystectomy, to prioritize patient safety over the goal of laparoscopic completion.

Role of delayed LC in acute cholecystitis

The definition of early LC in the Tokyo guideline 2018[1] and the World Society of Emergency Surgery 2020[8] refers to surgery performed within or equal to 7 days of hospital admission or within 10 days of symptom onset[8]. Delayed LC means surgery performed at least 6 weeks after the first day of symptoms (**Figure 1**). Surgery performed between 7 days and 6 weeks is considered intermediate LC based on the pathophysiology of inflammation and does not align with the definition of delayed LC in the aforementioned data.

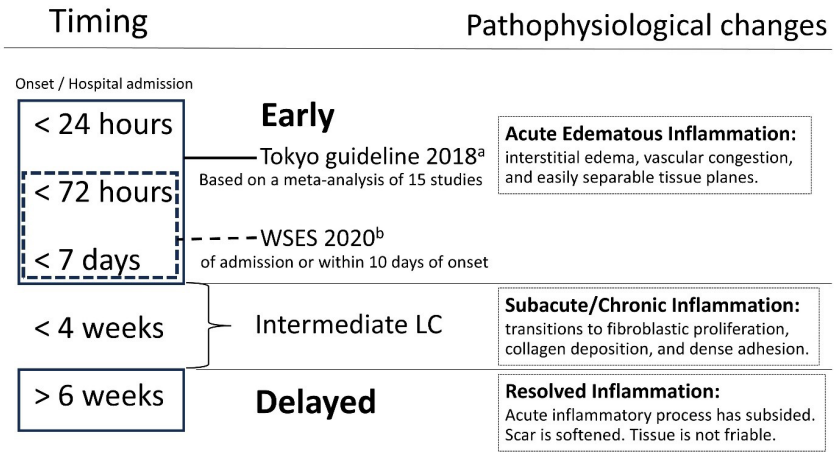


Figure 1 Definitions of early and delayed cholecystectomy

Note: a = Reference 1, b = Reference 8

Lo et al.[9] reported a prospective RCT in 1998 comparing early (< 72 hours) and delayed (8-12 weeks) LC in AC. They found that the early LC group had a statistically significantly shorter total hospital stay and recuperation period before returning to work compared to the delayed LC group. This included a lower complication rate in the early LC group than in the delayed LC group (13% vs. 29%; $p = 0.07$). However, the delayed group had a statistically significantly shorter postoperative hospital stay (4 and 3 days, respectively, $p = 0.04$) (**Table 1**). The researchers therefore concluded that early LC should be recommended within 72 hours of hospital admission and performed by an experienced surgeon, as it offers benefits in terms of both surgical outcomes and costs.

Table 1 Comparison of the outcomes of early LC and delayed LC[9]

	Early group	Delayed group	*p*-value
Postoperative pain score	2.3	2.7	0.275
Postoperative stay (days)	4	3	0.046
Total hospital stay (days)	6	11	< 0.001
Total recuperation period (days)	12	19	< 0.001
Duration of loss of working capacity (days)	15	26	0.017

Kolla et al.[10] reported a prospective RCT in 2004 comparing early (< 24 hours) and delayed (6-12 weeks) LC in AC. They found that the early LC group had a significantly greater blood loss. Furthermore, they had more complications, though this difference was not statistically significant. However, in the early LC group with complications, two out of four cases were due to BDI, while no BDI was found in the delayed LC group. The benefit of early LC reported by the authors in this study was a statistically significantly shorter total hospital stay in the early LC group compared to the delayed LC group (4.1 and 10.1 days, respectively) (**Table 2**). Nevertheless, the authors concluded that early LC is safe and should be recommended for AC patients, as it reduces hospital length of stay.

Ozkardes et al.[11] reported a prospective RCT in 2014 that compared early (< 24 hours) and delayed LC (6-8 weeks) in 60 AC patients. They found that the early LC group had a significantly higher rate of intraoperative and postoperative complications than the delayed LC group (26.7% vs 0%; $p = 0.002$). Of the eight patients with complications, two were due to BDI or bile leakage, and one was due to bleeding. However, the early LC group had a statistically significantly shorter total hospital stay than the delayed LC group (5.2 vs 7.8 days; $p = 0.04$). No difference was found in operative time or open conversion rate (**Table 3**). Based on the above data, the authors concluded that although early LC has more intraoperative and postoperative complications than delayed LC, early LC

Table 2 Outcomes of early LC and delayed LC from the study by Kolla et al.[10]

	Early group	Delayed group	*p*-value
Blood loss (mL)	228.5	114.5	0.006
Postoperative stay (days)	3.2	2.3	0.161
Total hospital stay (days)	4.1	10.1	0.023
Conversion rate (%)	25	25	0.540
Complications (%)	20	15	0.456

Table 3 Outcomes of early LC and delayed LC from the study by Ozkardes et al.[11]

	Early group	Delayed group	*p*-value
Operative time (min)	67.0	71.3	0.202
Hospitalization duration (days)	5.20	7.80	0.040
Intraoperative, postoperative complications (%)	26.70	0.00	0.002
Open conversion (%)	13.30	0.00	0.112
Cost (Turkish Lira)	2,500.97	3,713.47	0.030

should be recommended for AC due to the shorter hospital stay and lower costs in the early LC group.

From the aforementioned RCT data, early LC for AC is associated with a shorter total hospital stay than delayed LC across all studies, leading to reduced treatment costs. However, it cannot be concluded that early LC is safer, given the rate of intraoperative complications, particularly the higher incidence of BDI reported in some studies in the early LC group.[10,11]

Okamoto et al.[1] reported the results of a meta-analysis of 15 RCTs in AC to determine the optimal timing for LC. Four key factors were considered: (1) BDI; (2) operative time; (3) total hospital stay; and (4) medical costs.

(1) The comparison between early LC (< 72 hours) and a delayed LC of six weeks in BDI found that the early group had an odds ratio for BDI of 1.38 (95% CI: 0.21-8.95). Another comparison between early LC (< 1 week) and a delayed LC of six weeks found that the early LC group had an odds ratio for BDI of 0.77 (95% CI: 0.18-3.26). No statistically significant difference was found in either time period.

(2) The comparison between early LC (< 72 hours and one week) and delayed LC of six weeks found that the operative time in the early LC groups showed a tendency to be shorter than the delayed LC group with mean differences of 8.95, 95% CI: –3.17-19.18 and 6.92, 95% CI: –0.26-14.09, respectively. However, no statistically significant difference was found in either time period.

(3) The comparison between early LC (72 hours and one week) and delayed LC of six weeks found that the early LC groups had statistically significantly shorter total hospital stays than the delayed LC of six weeks with mean differences of –3.43, 95% CI: –4.97-1.89, and –3.31, 95% CI: –4.62-2.00, respectively.

(4) The comparison between early LC (< 72 hours) and delayed LC of six weeks found that the early LC group had a statistically significantly lower overall medical cost than the delayed LC group with a standard mean difference of –1.42, 95% CI: –2.32 to –0.52).

From a meta-analysis report by Pisano et al. In 2020,[8] the early LC group was found to have a shorter total hospital stay than the delayed LC group, with an average difference of 4 days, and to return to work an average of 9 days sooner. No difference was found in terms of the mortality rate or open conversion rate. However, two RCT studies that were not included in the 2018 meta-analysis by Okamoto et al. will be discussed next.

While some studies, such as the one by Mustafa et al.[12], report a statistically significant increase in bile duct injury (BDI) for early LC—finding a 10.5% rate compared to 0% in the delayed group ($p < 0.05$) (**Table 4**), these results are often viewed as outliers in the broader literature. For instance, a meta-analysis of 15 randomized controlled trials found no statistically significant difference in BDI rates between early and delayed approaches. However, a critical distinction must be made between statistical significance and clinical concern. While large-scale data may not always reach a p-value threshold for BDI due to the fortunately low frequency of the event, the devastating impact of a single injury on patient mortality and quality of life remains a primary clinical concern for the operating surgeon. Therefore, while high BDI rates in isolated studies such as Mustafa et al. may not reflect the standardized outcomes of high-volume centers, they serve as a cautionary "real-world" reminder of the risks associated with severe inflammation and variable surgical expertise.

Early LC has been widely accepted as the standard for AC due to its clear benefits, including a shorter total hospital stay and lower medical costs compared with delayed LC. The benchmark for the incidence of BDI is between 0.3% and 0.5%. RCTs with a high rate of BDI are often excluded from meta-analyses because the quality of surgery is considered below standard. Thus, the data on surgical complications are not sufficiently weighted to outweigh the benefits mentioned above.

Table 4 Outcomes of early LC and delayed LC from the study by Mustafa et al.[12]

	Early group	Delayed group	*p*-value
Operative time (min)	112.25	154.94	< 0.05
Blood loss (mL)	26	75	< 0.05
Bile duct injury (%)	10.50	0.00	< 0.05
Pain score (VAS)	2.98	2.43	0.67

VAS: visual analogue score

Limitations and safety of early LC in acute cholecystitis

The relationship between the timing of LC and the severity of acute cholecystitis (AC) is a critical factor in determining surgical success and patient safety. Endo et al.[13] reported an international, multicenter, retrospective observational study that was representative of real-world practice, as it was conducted in 155 hospitals across Japan and Taiwan. The study involved 5,329 AC patients who were divided into groups based on the treatment received: (A) primary cholecystectomy; (B) delayed LC after percutaneous gallbladder drainage (PTGBD); (C) PTGBD alone; and (D) medical treatment alone. The group with the highest mortality rate was the PTGBD alone at 9.8%, and the lowest was the delayed LC after PTGBD group at 0.6% (**Table 5**). However, a key finding was that the AC grade III group treated with primary cholecystectomy had a high mortality rate of 4.13%. After analyzing the factors that affected the mortality rate (multivariate analysis), they found that patients with any of the three negative predictive factors had a mortality rate increase from 0% to 9.3%. The negative predictive factors were jaundice, neurological dysfunction, and respiratory dysfunction. Although the study by Endo et al.[13] demonstrated that bile duct injury (BDI) rates were not significantly different between early LC and delayed LC after PTGBD, it is worth noting that the highest rate of BDI was found in the early LC group between days four and seven (2.8%) (**Table 6**). Notably, even though this study was conducted in training institutions where surgeries were performed exclusively by surgeons specializing in hepato-pancreato-biliary surgery, the peak BDI rate was still 2.8% in the early LC group during that specific four- to seven-day window. Their analysis further found that conversion rates to open surgery were 5.9% for primary cholecystectomy (Group A) and 8.3% for cholecystectomy after drainage (Group B). In addition, they observed a trend toward reduced operative time and blood loss in the early LC group, with the shortest operative times specifically recorded for patients undergoing surgery within zero to three days of admission

Conversely, other studies highlight that increased disease severity often leads to more challenging procedures and higher complication rates during the early phase. In a systematic review, Nassar et al.[14] reported that while early LC is preferred, it carries a higher risk of open conversion and BDI in cases of complicated AC, with overall conversion rates of 15.7% for early LC and 6.4% for delayed LC. This increased difficulty in moderate cases was echoed by Noppakunsomboon et al.[4], who observed that Grade II AC patients had a 28.6% conversion rate compared with 9.5% for Grade I, along with higher estimated blood loss. Furthermore, Bourgouin et al.[15] used a scoring system showing that, for high-risk patients, delayed LC significantly reduced serious operative events and resulted in a 0.0% conversion rate, compared with 16.7% with early intervention. However, database research by Altieri et al.[16] indicated that early LC (within 72 hours) is associated with a lower conversion rate of 7.5% compared to 13.8% for late interventions. These varied outcomes emphasize that while early surgery is optimal for many, patient-specific factors and disease severity must guide timing to avoid adverse outcomes.

AC patients planned for conservative treatment followed by delayed LC had a 6.8%[17] chance of failing conservative treatment. The management guidelines for this scenario were divided into emergency cholecystectomy

Table 5 Comparison of 30-day mortality rates stratified by treatment from a study by Endo et al.[13]

30-day mortality	1° cholecystectomy	DLC after PTGBD	PTGBD alone	Medical treatment alone
Grade I	0.25%	0.50%	4.76%	1.34%
Grade II	0.37%	0.00%	4.30%	1.68%
Grade III	**4.13%**	0.79%	13.46%	5.93%
Overall 90-day mortality	0.8%	**0.6%**	**9.8%**	3.4%

DLC: delayed laparoscopic cholecystectomy; PTGBD: percutaneous transhepatic gallbladder drainage

Table 6 Rate of bile duct injury stratified by the timing of cholecystectomy[13]

	Primary cholecystectomy						Delayed cholecystectomy after PTGBD				
Day	0-3	4-7	8-30	>31	Total	*p*-value	4-7	8-30	>31	Total	*p*-value
BDI (%)	1.1	**2.8**	1.5	0.7	1.2	0.199	0.8	0.8	2.1	1.3	0.405

BDI: bile duct injury; PTGBD: percutaneous transhepatic gallbladder drainage

and PTGBD, followed by delayed LC. A meta-analysis by Nassar et al.[14] in 2022 compared early LC with delayed LC after PTGBD in 216,926 patients from RCTs and observational studies. No difference in mortality rate was found between the two groups (hazard ratio [HR] = 1.3, 95% CI: 0.60-2.83). However, the postoperative complication rate in the early LC group was significantly higher than in the delayed LC group after PTGBD (HR = 2.88, 95% CI: 1.78-4.65). Importantly, the BDI rate in the early LC group was significantly higher than that in the delayed LC after PTGBD group (HR = 6.07, 95% CI: 1.67-21.99). The early LC group was also found to have a longer post-op hospital stay than delayed LC after PTGBD, with an average difference of 1 day. Nevertheless, the total hospital stay for the early LC group was statistically significantly shorter than that for the delayed LC group after PTGBD, with an average difference of 6.6 days, which aligns with data from all other studies.

While PTGBD is widely adopted in clinical practice, advanced endoscopic techniques—specifically endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) and endoscopic transpapillary gallbladder drainage (ETP-GBD)—have emerged as viable alternatives for high-risk surgical candidates. Systematic reviews indicate that EUS-GBD achieves technical and clinical success rates comparable to PTGBD. Notably, when using cautery-enhanced lumen-apposing metal stents (LAMS), EUS-GBD is superior to PTGBD in terms of safety and long-term efficacy.[18] Research shows EUS-LAMS significantly reduces adverse events (19.0% vs. 45.2%; p = 0.0006), recurrent cholecystitis (2.0% vs. 6.8%; p = 0.02), and hospital readmissions (7.3% vs. 37.1%; p = 0.03)[19] (**Table 7**). Conversely, ETP-GBD, while associated with lower mortality and reintervention rates than PT-GBD, typically yields lower technical success. Consequently, EUS-GBD with LAMS is increasingly preferred over percutaneous drainage in specialized centers for patients requiring definitive non-surgical management.

Considerations for translating the study data into clinical practice include these aspects. All studies were conducted in hospitals with high readiness in equipment, operating rooms, and postoperative intensive care units, or in training institutions where surgeries were performed by specialists in hepato-pancreato-biliary surgery or highly experienced laparoscopic surgeons.[1,8,13,20] Furthermore, patient selection and preparation were meticulous. The patient's clinical assessments, which included severity of inflammation, systemic organ failure, physical condition, and underlying diseases, were always considered. Thus, only when LC is performed strictly under all the above-mentioned conditions can a reduction in total hospital stay and medical cost be expected. There is no supporting data that postoperative complications or the BDI rate can be reduced. Moreover, the BDI rate in some reports is higher compared to delayed LC.[10,11,13,14]

Ultimately, the selection of surgical timing should not be based solely on predefined intervals but on a comprehensive synthesis of patient-specific risks, the local surgical environment, and the institutional support structure. While early LC remains the gold standard under optimal conditions, the transition from acute edema to dense fibrosis during the intermediate phase and the potential for catastrophic bile duct injury require a nuanced approach that prioritizes patient safety over economic benefits. To assist clinicians in navigating this complexity, particularly in resource-limited settings, we propose a practical decision-making framework. This framework, presented in **Table 8**, categorizes recommendations based on the severity of inflammation, the presence of negative predictive factors, and the level of available surgical expertise, thereby bridging the gap between international guidelines and real-world clinical practice.

Table 7 Summary of Outcomes EUS-GBD versus PTGBD[19]

Outcomes	EUS-GBD (LAMS)	PTGBD	*p*-value
Technical success	95.9 %	99.6 %	0.1
Clinical success	91.0 %	94.8 %	0.1
Adverse events	19.0 %	45.2 %	0.0006
Recurrent cholecystitis	2.0 %	6.9 %	0.02

EUS-GBD: endoscopic ultrasonography guided gallbladder drainage, LAMS: lumen apposing metallic stent, PTGBD: percutaneous transhepatic gallbladder drainage

Table 8 Proposed decision framework for surgical timing

Clinical Scenario	Recommended Timing	Supporting Rationale
Ideal Conditions (Grade I/II AC, high-volume center, expert HPB surgeon)	Early LC (< 72 hrs)	Maximizes cost-efficiency and reduces total hospital stay
High-Risk Patient (Grade III AC, multiple co-morbidities, jaundice/respiratory failure, ΔMS)	Initial PTGBD → Delayed LC	Significantly reduces mortality and postoperative complications compared to emergency surgery.
Limited Resources (Solo surgeon, no ICU backup, or lack of 24/7 laparoscopic equipment)	Delayed LC (6-12 weeks)	Prioritizes patient safety and avoids the high BDI rates seen in "standard" settings without expert support.
Failure of Conservative Treatment	Emergency LC vs. PTGBD	Requires immediate intervention; PTGBD is preferred if the surgical risk of BDI is deemed too high.

AC: acute cholecystitis, LC: laparoscopic cholecystectomy, ΔMS: mental status change, PTGBD: percutaneous transhepatic gallbladder drainage, ICU: intensive care unit, BDI: bile duct injury.

CONCLUSION

In light of the evidence reviewed, the decision between early and delayed LC for acute cholecystitis (AC) must be individualized and multifaceted. While our findings align with the Tokyo Guidelines 2018 (TG18) in recommending early LC as the preferred approach to reduce hospital stay and medical costs, this recommendation is predicated on "optimal conditions". These conditions include a highly experienced surgical team, adequate hospital infrastructure (such as 24/7 operating room availability and intensive care support), and a patient profile that lacks severe systemic negative predictive factors. In real-world clinical practice, where surgical expertise and institutional resources may vary, clinicians should utilize a practical decision-making framework to balance the clear economic benefits of the early approach against the potentially catastrophic risk of bile duct injury (BDI). Delayed LC following conservative management or PTGBD remains an essential and safer alternative for high-risk patients or in settings where "safe cholecystectomy" criteria cannot be strictly met. This stratified approach ensures that surgical timing prioritizes patient safety and the avoidance of postoperative complications without significantly increasing mortality rates.

REFERENCES

1. Okamoto K, Suzuki K, Takada T, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. J Hepatobiliary Pancreat Sci. 2018;25(1):55-72. doi: 10.1002/jhbp.516.
2. Halbert C, Altieri MS, Yang J, et al. Long-term outcomes of patients with common bile duct injury following laparoscopic cholecystectomy. Surg Endosc. 2016;30(10):4294-9. doi: 10.1007/s00464-016-4745-9.
3. Nuzzo G, Giuliante F, Giovannini I, et al. Bile duct injury during laparoscopic cholecystectomy: results of an Italian national survey on 56 591 cholecystectomies. Arch Surg. 2005;140(10):986-92. doi: 10.1001/archsurg.140.10.986.
4. Noppakunsomboon N, Swangsri J, Sirivatanauksorn Y, et al. Outcomes of an Early Laparoscopic Cholecystectomy in Acute Cholecystitis, Grades I and II. Siriraj Med J. 2022;74(8):495-501. doi: 10.33192/Smj.2022.59.
5. Strasberg SM. A three-step conceptual roadmap for avoiding bile duct injury in laparoscopic cholecystectomy: an invited perspective review. J Hepatobiliary Pancreat Sci. 2019;26(4):123-7. doi: 10.1002/jhbp.616.
6. Wakabayashi G, Iwashita Y, Hibi T, et al. Tokyo Guidelines 2018: surgical management of acute cholecystitis: safe steps in laparoscopic cholecystectomy for acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci. 2018;25(1):73-86. doi: 10.1002/jhbp.517.
7. Iwashita Y, Hibi T, Ohyama T, et al. Delphi consensus on bile duct injuries during laparoscopic cholecystectomy: an evolutionary cul-de-sac or the birth pangs of a new technical framework? J Hepatobiliary Pancreat Sci. 2017;24(11):591-602. doi: 10.1002/jhbp.503.
8. Pisano M, Allievi N, Gurusamy K, et al. 2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis. World J Emerg Surg. 2020;15(1):61. doi: 10.1186/s13017-020-00336-x.
9. Lo CM, Liu CL, Fan ST, et al. Prospective randomized study of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Ann Surg. 1998;227(4):461-7. doi: 10.1097/00000658-199804000-00001.
10. Kolla SB, Aggarwal S, Kumar A, et al. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective randomized trial. Surg Endosc. 2004;18(9):1323-7. doi: 10.1007/s00464-003-9230-6.
11. Ozkardeş AB, Tokaç M, Dumlu EG, et al. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective, randomized study. Int Surg. 2014;99(1):56-61. doi: 10.9738/INTSURG-D-13-00068.1.
12. Mustafa MIT, Mustafa AIT, Chaudhry SM, et al. Early vs delayed laparoscopic cholecystectomy in acute cholecystitis. Pak J Med Health Sci. 2016;10(2):371-3.
13. Endo I, Takada T, Hwang TL, et al. Optimal treatment strategy for acute cholecystitis based on predictive factors: Japan-Taiwan multicenter cohort study. J Hepatobiliary Pancreat Sci. 2017;24(6):346-61. doi: 10.1002/jhbp.456.
14. Nassar A, Elshahat I, Forsyth K, Shaikh S, Ghazanfar M. Outcome of early cholecystectomy compared to percutaneous drainage of gallbladder and delayed cholecystectomy for patients with acute cholecystitis: systematic review and meta-analysis. HPB (Oxford). 2022;24(10):1622-33. doi: 10.1016/j.hpb.2022.04.010.
15. Bourgouin S, Monchal T, Julien C, et al. Early versus delayed cholecystectomy for cholecystitis at high risk of operative difficulties: A propensity score-matching analysis. Am J Surg. 2021;221(5):1061-8. doi: 10.1016/j.amjsurg.2020.09.019.
16. Altieri MS, Brunt LM, Yang J, et al. Early cholecystectomy (<72 h) is associated with lower rate of complications and bile duct injury: a study of 109,862 cholecystectomies in the state of New York. Surg Endosc. 2020;34(7):3051-6. doi: 10.1007/s00464-019-07049-6.
17. Roulin D, Saadi A, Di Mare L, et al. Early versus delayed cholecystectomy for acute cholecystitis, are the 72 hours still the rule?: A randomized trial. Ann Surg. 2016;264(5):717-22. doi: 10.1097/SLA.0000000000001886.
18. Podboy A, Yuan J, Stave CD, et al. Comparison of EUS-guided endoscopic transpapillary and percutaneous gallbladder drainage for acute cholecystitis: a systematic review with network meta-analysis. Gastrointest Endosc. 2021;93(4):797-804.e1. doi: 10.1016/j.gie.2020.09.040.
19. Hemerly MC, de Moura DTH, do Monte Junior ES, et al. Endoscopic ultrasound (EUS)-guided cholecystostomy versus percutaneous cholecystostomy (PTC) in the management of acute cholecystitis in patients unfit for surgery: a systematic review and meta-analysis. Surg Endosc. 2023;37(4):2421-38. doi: 10.1007/s00464-022-09712-x.
20. Loozen CS, van Santvoort HC, van Duijvendijk P, et al. Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial. BMJ. 2018;363:k3965. doi: 10.1136/bmj.k3965.