

## ARTICLE INFO

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## Evaluation of Therapeutic Antibiotics After Laparoscopic Cholecystectomy: A Quasi-Experimental Study

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### Abstract

**Background:** The routine use of postoperative therapeutic antibiotics after laparoscopic cholecystectomy remains controversial due to limited evidence of clinical benefit and concerns over antimicrobial resistance. **Objective:** To evaluate the effect of postoperative therapeutic antibiotics on surgical site infections (SSI) and laboratory outcomes after laparoscopic cholecystectomy. **Methods:** A quasi-experimental, post-test-only study with a non-equivalent control group was conducted at RSUP Prof. Dr. I.G.N.G. Ngoerah (September 2023–March 2024). Fifty-six patients were divided into two groups: postoperative antibiotics (cefoperazone followed by cefixime) versus no antibiotics. SSI was assessed on postoperative days 7 and 30 using the ASEPSIS scoring system. Laboratory parameters (leukocytes, neutrophils, lymphocytes, hemoglobin, and platelet counts) were compared between groups. No SSI occurred in either group. Laboratory outcomes showed no statistically significant differences between the antibiotic and non-antibiotic groups ( $p > 0.05$ ). **Results:** The mean age of participants was  $45.2 \pm 15.1$  years, with female predominance. **Conclusion:** Postoperative therapeutic antibiotics did not reduce SSI rates or alter laboratory outcomes following laparoscopic cholecystectomy. Routine use is not supported in mild to moderate cases, and limiting unnecessary antibiotics may help reduce antimicrobial resistance.

**Keywords:** Antimicrobial resistance, Laparoscopic cholecystectomy, surgical site infection, Therapeutic antibiotics, Quasi-experimental study.

## Original Research Article

### INTRODUCTION

Cholelithiasis is one of the most prevalent gallbladder disorders worldwide, with its occurrence influenced by both geographic location and ethnic background (Chang et al., 2013; Littlefield & Lenahan, 2019). Laparoscopic cholecystectomy is currently the preferred surgical approach for managing symptomatic cholelithiasis. When performed electively, it is associated with a low risk of infection, typically ranging from 0.4% to 1.1%. Compared to open cholecystectomy, the laparoscopic technique is linked to a reduced rate of infectious complications (Azriyantha & Manjas, 2022; Passos & Portari-Filho, 2016).

A Surgical Site Infection (SSI) refers to an infection that develops at or near of a surgical site incision, typically within 30 until 90 days following the surgery, regardless of whether the wound is open or closed. These infections may affect superficial tissue, deeper layers, or even the organ or space involved in the surgery (Smith & Lee, 2025). SSIs are estimated to occur in 1% to 3.1% of all the procedures and 2% of the patients are death associated with healthcare-related infections. The incidence is notably higher in abdominal surgeries, (Azoury et al., 2015) with multiple prospective studies reporting SSI rates between 15% and 25%, depending on the level of surgical contamination (Blumetti et al., 2007; Diener et al., 2014; Mihaljevic et al., 2012; Pinkney et al., 2013).

Recent evidence increasingly questions the routine use of postoperative antibiotics following laparoscopic cholecystectomy. Large cohort and randomized studies suggest that the risk of surgical site infection (SSI) after this procedure is intrinsically low, especially in low-risk or elective cases. For instance, Wang (2025) demonstrated that prophylactic antibiotics offered no significant reduction in SSI compared with no antibiotics among patients undergoing laparoscopic cholecystectomy. Similarly, Verma et al. (2024) reported that most SSIs in elective laparoscopic cholecystectomy were unrelated to postoperative antibiotic use, underscoring that over-prescription may not provide additional benefit.

Meta-analyses further strengthen this position. La Regina et al. (2019) found no advantage in extended postoperative antibiotics for mild to moderate acute cholecystitis, emphasizing that shorter regimens or no postoperative treatment can be equally safe. A more recent trial-sequential meta-analysis by Wang et al. (2025) confirmed that prophylactic antibiotics do not significantly reduce postoperative infection risk in laparoscopic cholecystectomy, and routine use may contribute to antimicrobial resistance.

Other recent reviews also highlight the public health implications of unnecessary antibiotic use. Long et al. (2024) stressed that antimicrobial stewardship in surgery is essential, as indiscriminate use of perioperative antibiotics contributes to resistance without improving patient outcomes. In pediatric and low-risk populations, similar conclusions were reached by Briggs et al. (2022) and Graham et al. (2025), both reporting no clinically meaningful reduction in SSIs despite widespread prophylaxis.

Collectively, these findings position the present study within an ongoing debate: while some centers continue to prescribe antibiotics postoperatively, accumulating evidence from diverse settings increasingly supports limiting their use. By adopting a quasi-experimental approach, our study adds further insight into this global conversation, particularly in the context of Indonesian surgical practice, where standardized guidelines remain lacking.

The use of therapeutic antibiotics following surgery remains a subject of debate, particularly due to concerns that overprescription may contribute to the rise in bacterial resistance. In 2014, the World Health Organization identified antimicrobial resistance as a growing public health threat. It is escalating rapidly, with projections suggesting it could result in over 10 million deaths annually by 2050. One of the key drivers of this issue is the inappropriate use of antibiotics. According to the U.S. Centers for Disease Control and Prevention (CDC), antibiotic-resistant infections affect at least 2.8 million people each year in the United States, leading to approximately 35,000 deaths. In surgical settings, antibiotic resistance is associated with longer hospital stays, extended antibiotic treatment, increased mortality, a higher likelihood of surgical re-intervention, and the need for newer, potentially more toxic antibiotics. The financial burden of antibiotic resistance in countries such as the United States, Europe, and Australia is estimated at around USD 3.5 billion annually. Globally, the total cost is projected to exceed USD 100 trillion by 2050 (Menz et al., 2021). Consequently, current guidelines advise against the routine use of postoperative antibiotics in patients undergoing laparoscopic cholecystectomy for mild to moderate acute cholecystitis. Where antibiotics are necessary, treatment should be limited to a maximum of four days and potentially even shorter in cases of severe cholecystitis. (Colling et al., 2022) Despite this, the Guidelines for the Use of Prophylactic and Therapeutic Antibiotics (PPAB) at RSUP Prof. IGNG Ngoerah continue to recommend cefuroxime as prophylaxis for gallstone surgery. As of now, there is no standardized guideline for the choice of therapeutic antibiotics (Ngoerah, 2024).

This study aims to evaluate the impact of postoperative therapeutic antibiotic use on patient outcomes following laparoscopic cholecystectomy, with a focus on the incidence of surgical site

infections (SSI) and related laboratory findings. Despite the growing body of literature, important gaps remain. Most prior studies have primarily evaluated postoperative antibiotic effectiveness using SSI rates as the sole endpoint. However, SSI is a relatively rare outcome in elective laparoscopic cholecystectomy, which limits its utility in detecting clinically meaningful differences (La Regina et al., 2019; Wang et al., 2025). Laboratory parameters such as leukocyte count, C-reactive protein (CRP), and procalcitonin may provide early signals of infection, but they lack specificity and are insufficient to fully capture postoperative morbidity (Long et al., 2024). Moreover, few studies have systematically examined broader clinical outcomes (e.g., postoperative fever, wound complications, or reintervention), healthcare resource utilization (e.g., hospital stay, readmission, or antibiotic escalation), and cost-effectiveness of routine postoperative antibiotics.

The novelty of this study lies in its evaluation of both SSI and laboratory outcomes in a quasi-experimental design within the Indonesian healthcare setting, where standardized therapeutic antibiotic guidelines are absent. By situating the findings within the context of antimicrobial resistance concerns and limited regional data, this study provides new evidence to inform clinical practice in Southeast Asia. The rationale is to contribute locally relevant data to the global debate on antibiotic stewardship, with the ultimate aim of supporting safer, more cost-effective, and resistance-conscious surgical care.

## **MATERIALS AND METHOD**

This study employed a quasi-experimental design, specifically a post-test-only format with a non-equivalent control group. The control group consisted of patients who did not receive postoperative antibiotics. In this design, outcomes were evaluated solely after the surgical procedure. Primary data were collected through direct observation of patients on the 7th and 30th days following laparoscopic surgery, based on the criteria for surgical site infections (SSI). The research was conducted at RSUP Prof. Dr. I.G.N.G. Ngoerah in Denpasar, Bali. Data collection spanned a six-month period, from September 2023 to March 2024, and included all patients who underwent laparoscopic cholecystectomy at the hospital during that time.

The participants in this study were patients who underwent laparoscopic cholecystectomy at RSUP Prof. Dr. I.G.N.G. Ngoerah between 2023 and 2024 and met the specified inclusion and exclusion criteria. The inclusion criteria encompassed patients aged 18 years or older who were scheduled for laparoscopic cholecystectomy during the study period. Exclusion criteria included individuals requiring biliary drainage, those undergoing emergency operation due to severe infection, patients with clinical signs persisting for more than five days, biliary peritonitis, acute pancreatitis, cirrhosis, biliary malignancies, known antibiotic allergies, pregnant or breastfeeding women, and patients who declined to give informed consent. Patients who met the eligibility criteria were thoroughly briefed about the study and requested to provide written informed consent before taking part. The study used consecutive sampling to recruit participants. The estimated proportion of surgical site infections (SSI) was 3.3% in the group not receiving postoperative antibiotics and 6.7% in the antibiotic group. (de Santibañes et al., 2018) Based on these proportions, A minimum of 23 participants was determined to be necessary for each group. After accounting for a 10% potential dropout rate, the final minimum sample size per group was adjusted to 26 participants.

All laparoscopic cholecystectomy procedures were performed by three consultant surgeons from the Department of Surgery, each with more than ten years of operative experience in advanced laparoscopic techniques. To minimize operator-related variability, standardized operative protocols were strictly followed across all cases.

The inclusion criteria specified patients aged  $\geq 18$  years, and no upper age limit was applied. This approach ensured the inclusion of both younger and older adults, thereby reflecting the full spectrum of patients undergoing laparoscopic cholecystectomy in routine clinical practice.

Indications for laparoscopic cholecystectomy in this study included symptomatic cholelithiasis, biliary colic, chronic cholecystitis, and mild to moderate acute calculous cholecystitis (Tokyo Guidelines 2018 grade I–II). Patients with severe acute cholecystitis (grade III), gallbladder empyema, malignancy, or other contraindications to laparoscopic surgery were excluded.

A surgical site infection (SSI) was defined as an infection at the surgical site within 30 until 90 days following the procedure. (Smith & Lee, 2025) SSI assessment was conducted using the ASEPSIS scoring system, which evaluates factors such as Additional treatment, Serous discharge, skin redness, presence of pus, deep tissue separation, bacterial identification, and length of hospitalization. This system was employed to monitor the condition of the surgical wound and determine both the occurrence and severity of SSI. An ASEPSIS score exceeding 20 was considered indicative of an SSI. Evaluations were performed on postoperative days 7 and 30. (de Santibañes et al., 2018) Laparoscopic cholecystectomy was carried out with the patient in a supine position under general anesthesia using orotracheal intubation (GA OTT). The surgical site was disinfected with povidone-iodine and covered with sterile drapes to maintain a sterile field. Trocar incisions were made in the infraumbilical, epigastric, and right lumbar areas. The gallbladder was inspected for adhesions and wall thickening. The cystic duct and artery were identified and ligated using Hemolock clips. The gallbladder was detached from the liver bed, hemostasis was achieved, and the organ was extracted from the abdominal cavity. After the removal of three trocars, the incisions were closed in layers and covered with Bactigras and sterile gauze. Postoperative antibiotic therapy included cefoperazone 1 g intravenously every 12 hours for three days, followed by oral cefixime 200 mg twice daily for five days after discharge (Ngoerah, 2024). Laboratory parameters analyzed in this study included white blood cell count with other component like lymphocytes, neutrophils, platelets, and hemoglobin levels.

The Statistical analyze using SPSS version 25.0, with descriptive statistics employed to outline the demographic and clinical characteristics of the study participants. If the data followed a normal distribution, results were expressed as means and standard deviations; otherwise, medians and interquartile ranges were reported. To compare the incidence of surgical site infections (SSI) between patients who received postoperative antibiotics and those who did not, a chi-square test was applied. For laboratory parameters, comparisons between the two groups were made using either the independent t-test or the McNemar test, depending on the type and distribution of the data. Prior to these tests, a normality assessment was conducted to determine the appropriate statistical method. A p-value of less than 0.05 was considered statistically significant.

At the time of this study, the nosocomial infection rate at RSUP Prof. Dr. I.G.N.G. Ngoerah was approximately X% based on the hospital infection surveillance reports for 2023–2024. This background data provides an institutional benchmark for infection control practices and assists in interpreting the observed surgical outcomes within a broader epidemiological context. Laboratory analyses were performed using an automated hematology analyzer (Sysmex XN-1000™, Sysmex Corporation, Kobe, Japan) with routine internal quality control and calibration performed according to the manufacturer's recommendations. This ensured reliability and reproducibility of hematological measurements across all participants. All statistical analyses were conducted using SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA), accessed under an official institutional license provided through Udayana University.

## RESULT

The study included a total of 56 participants, with 28 individuals in the antibiotic group and 28 in the non-antibiotic group. Among them, 21 were male and 25 were female, with an average age of  $45.23 \pm 15.10$  years (Table 1). No cases of surgical site infection (SSI) were observed in either group. Laboratory findings across all participants showed a median leukocyte count of 9.23 (range: 4.66–19.62), neutrophil count of 5.60 (range: 2.49–16.92), mean lymphocyte level of  $2.46 \pm 0.64$ , platelet count of  $326.88 \pm 89.39$ , and hemoglobin level of  $13.02 \pm 1.03$ . The demographic comparison presented in Table 1 demonstrated no significant differences between the antibiotic and non-antibiotic groups in terms of age or sex distribution. While these results may appear statistically non-significant or “meaningless” at first glance, they are important for confirming baseline comparability between groups. Balanced demographic characteristics reduce the risk of confounding and strengthen the internal validity of the analysis, ensuring that any observed postoperative outcomes are less likely to be attributable to population differences.

**Table 1.** Characteristics of Study Subjects

	With Antibiotic (n=28)	Without Antibiotic (n=28)	p-value
<b>Sex <sup>a</sup></b>			
Male	9	12	0.41
Female	19	16	
<b>Age <sup>b</sup></b>	45.36±15.39	45.11±15.09	0.95

<sup>a</sup>Chi-Square; <sup>b</sup>Independent t-test

The additional analysis comparing patients who received postoperative therapeutic antibiotics with those who did not revealed no cases of surgical site infection (SSI) on either postoperative day 7 or day 30. Although this observation suggests that postoperative antibiotics did not influence SSI incidence in this cohort, the complete absence of SSI events restricts the ability to establish definitive conclusions about efficacy. This outcome likely reflects the inherently low baseline risk of SSI in elective laparoscopic cholecystectomy and underscores the influence of sample size and study power on the interpretation of results. These limitations should be considered when applying the findings to broader clinical contexts and in planning future research with larger populations. Furthermore, there were no considerable statistical disparities ( $p > 0.05$ ) between the two groups across all laboratory parameters (Table 2).

**Table 2.** Comparison of Hematological Parameters

	With Antibiotic (n=28)	Without Antibiotic (n=28)	p-value
<b>Lymphocyte <sup>b</sup></b>	2.53±0.68	2.38±0.59	0.38
<b>Platelet <sup>b</sup></b>	312.68±86.29	341.07±91.73	0.24
<b>Haemoglobin <sup>b</sup></b>	12.91±1.14	13.11±79.92	0.47
<b>Leucocyte <sup>c</sup></b>	9.68±4.09	8.79±1.69	0.98
<b>Neutrophil <sup>c</sup></b>	5.77±3.65	5.42±1.61	0.43

<sup>a</sup>Chi-Square; <sup>b</sup>Independent t-test; <sup>c</sup>Mann-Whitney

Table 2 compared hematological parameters between groups, showing no statistically significant differences. However, the panel of tests employed—including leukocyte, neutrophil, lymphocyte, platelet, and hemoglobin counts—is relatively non-specific for detecting surgical site infection or assessing the effectiveness of antibiotic therapy. Hemoglobin levels, in particular, primarily reflect perioperative blood loss rather than infection or inflammatory status. While leukocyte and neutrophil counts are acceptable secondary markers of postoperative inflammation, more specific biomarkers such as C-reactive protein (CRP), procalcitonin, and the neutrophil-to-lymphocyte ratio (NLR) have demonstrated greater diagnostic accuracy in identifying infection and antibiotic response in surgical patients (Long et al., 2024; Wang et al., 2025). Future research should incorporate these markers alongside standardized SSI definitions from CDC and ECDC guidelines to provide a more comprehensive and clinically meaningful assessment of postoperative antibiotic efficacy.

### DISCUSSION

This study evaluated the effect of postoperative therapeutic antibiotics on outcomes following laparoscopic cholecystectomy and found no cases of surgical site infection (SSI) in either treatment group, with no significant differences in hematological parameters. These findings suggest that routine postoperative antibiotic administration may not provide additional clinical benefit in low- to moderate-risk cases. Our results align with recent randomized trials and meta-analyses that demonstrated no reduction in SSI incidence with postoperative antibiotics in laparoscopic cholecystectomy (de Santibañes et al., 2018; Regimbeau et al., 2014; Wang et al., 2025). Current international guidelines, including those of the Surgical Infection Society and WHO, also recommend against prolonged or routine postoperative antibiotic use in uncomplicated cases (Colling et al., 2022). The consistency of our findings with this body of evidence strengthens their validity and clinical relevance. Biologically,

the absence of a measurable difference between groups can be explained by the inherently low baseline risk of infection in laparoscopic cholecystectomy. The minimally invasive approach is associated with reduced tissue trauma, lower bacterial contamination, and shorter hospital stays, which collectively diminish the likelihood of SSI. Furthermore, bile is typically sterile in the early stages of cholelithiasis, limiting the role of antibiotics in influencing infection risk. The participant profile also provides important context. The mean age was 45 years, with a predominance of female patients—consistent with known epidemiology of cholelithiasis. The absence of an upper age limit in recruitment enhanced external validity by including both younger and older adults, though the sample did not include many patients with advanced age or significant comorbidities. These demographic characteristics may have contributed to the low complication rate observed. Moreover, all procedures were performed in a tertiary care hospital with established infection control protocols and relatively low nosocomial infection rates, further reducing the risk of SSI in this cohort.

Although no significant differences were observed between the antibiotic and non-antibiotic groups in terms of SSI incidence or hematological outcomes, these results should be interpreted with caution. The absence of SSI events across both groups may reflect the intrinsically low baseline risk associated with elective laparoscopic cholecystectomy rather than a true lack of antibiotic effect. In addition, the relatively small sample size and limited statistical power restrict the ability to detect subtle or rare differences. These methodological constraints highlight the importance of avoiding overgeneralization and underscore the need for larger, multicenter studies with extended follow-up to more definitively assess the role of postoperative antibiotics in this surgical context. (Sajid et al., 2018) One retrospective study analyzed patients undergoing surgery for grade I or II acute cholecystitis. Antibiotic regimens included amoxicillin-clavulanic acid in 70% (127/182) of cases, third-generation cephalosporins with imidazole in 20% (36/182), and fluoroquinolone with imidazole in 10% (19/182). Among 283 patients, 64% received postoperative antibiotics, with only 19% continuing treatment beyond the first postoperative day. Perioperative outcomes were comparable between patients who received antibiotics after day one and those who did not. Interestingly, the median length of hospital stay was shorter for patients who did not receive postoperative antibiotics (4 days [range 1–20]) versus those who did (6 days [range 1–50];  $p > 0.001$ ) (Dembinski et al., 2020; Sajid et al., 2018). The CHART study (Cholecystectomy Antibiotic Randomized Trial), prospective, a single-center, double-blind randomized controlled trial, assigned patients with mild to moderate acute cholecystitis undergoing laparoscopic cholecystectomy to either a five-day course of amoxicillin/clavulanic acid or placebo. In the per-protocol analysis, postoperative infectious complications occurred in 5.8% (6/104) of the placebo group and 6.6% (6/91) of the antibiotic group, showing no significant difference (absolute difference 0.82; 95% CI, –5.96 to 7.61;  $P = .81$ ). The average hospital stay was 3 days, with no mortality reported and no differences in readmission or reoperation rates between groups (de Santibañes et al., 2018).

Another open-label, randomized noninferiority trial including 414 patients across 17 centers treated for grade I or II calculous acute cholecystitis compared outcomes between patients who received perioperative amoxicillin/clavulanic acid and those who did not receive postoperative antibiotics. The intention-to-treat analysis revealed postoperative infection rates of 17% (35/207) in the no-antibiotic group and 15% (31/207) in the antibiotic group (absolute difference 1.93%; 95% CI, –8.98% to 5.12%). Using a noninferiority margin of 11%, withholding postoperative antibiotics did not result in worse outcomes. Bile cultures were pathogen-free in 60.9% of cases. Both groups showed similar complication severity based on the Clavien-Dindo classification: in the no-antibiotic group, 94.2% (195 patients) scored 0 to I, and 0.97% (2 patients) scored III to V; in the antibiotic group, 87.8% (182 patients) scored 0 to I, and 1.93% (4 patients) scored III to V (Regimbeau et al., 2014).

Cholelithiasis is consistently associated with an inflammatory response, though it does not always involve infection. Gallbladder inflammation arises from bile stasis, which causes ischemia of the gallbladder wall and subsequent irritation. During the initial phase, bile is typically sterile. Normally, the bile ducts remain free of bacteria because bile contains antibacterial agents such as lipopolysaccharides and lipoteichoic acid, which damage bacterial cell walls. Moreover, the bile duct epithelium produces a mucus layer that facilitates the delivery of immunoglobulins to the ducts,

helping to maintain minimal bacterial contamination under normal conditions (Fico et al., 2024). This explains why no significant differences were observed in surgical site infection rates or laboratory results between the antibiotic and non-antibiotic groups. These findings further support the notion that postoperative antibiotic use following laparoscopic cholecystectomy may be unnecessary.

The study has some limitations, including a relatively narrow study group of 28 participants per group, which may restrict the broader applicability of the findings. The quasi-experimental design, lacking randomization, also poses a risk of selection bias. The follow-up duration was limited to 30 days after surgery, which may have overlooked late-onset complications. Additionally, as this research was carried out at a single center, the findings may not be applicable to broader populations or different clinical environments. Nevertheless, this study can serve as a foundational investigation for future research. It is recommended that subsequent studies incorporate larger sample sizes and utilize randomized designs to minimize bias. Future research could also consider including variables such as hospital length of stay to evaluate the impact on treatment costs.

The findings of this study carry several important implications. From a clinical perspective, the absence of benefit from postoperative therapeutic antibiotics supports the growing movement toward more judicious antibiotic use in elective laparoscopic cholecystectomy. Avoiding unnecessary antibiotic administration not only reduces the risk of antimicrobial resistance but also minimizes patient exposure to potential drug-related adverse effects and decreases treatment costs. For policymakers and hospital administrators, these results highlight the need to update institutional protocols and align local practices with international guidelines that discourage routine postoperative antibiotic use in low- to moderate-risk cases. For future research, larger multicenter randomized controlled trials are needed to confirm these findings and provide stronger causal evidence. Incorporating additional outcome measures—such as postoperative fever, wound complications, length of hospital stay, readmission, antibiotic escalation, and cost-effectiveness—would allow for a more comprehensive assessment of antibiotic efficacy. Furthermore, the inclusion of more specific biomarkers, such as C-reactive protein, procalcitonin, and the neutrophil-to-lymphocyte ratio, may provide earlier and more accurate indicators of postoperative infection risk. By addressing these gaps, subsequent studies can advance both the scientific evidence base and clinical decision-making, ultimately contributing to safer, more effective, and resource-conscious surgical care.

## CONCLUSION

This study evaluated the effect of postoperative therapeutic antibiotics on outcomes following laparoscopic cholecystectomy. No surgical site infections (SSI) were detected in either the antibiotic or non-antibiotic group, and no significant differences were observed in hematological parameters. The study contributes evidence from an Indonesian tertiary care center, reinforcing international findings that routine postoperative antibiotics may not provide additional benefit in low- to moderate-risk laparoscopic cholecystectomy. This supports the rationale for antibiotic stewardship and the avoidance of unnecessary prescribing in surgical practice. However, several limitations must be acknowledged, including the relatively small sample size, the quasi-experimental design without randomization, the absence of more specific infection biomarkers, and the single-center setting. These factors limit the generalizability and strength of the conclusions. Future research should involve larger, multicenter randomized trials that incorporate broader outcome measures such as postoperative fever, wound complications, reinterventions, length of stay, cost-effectiveness, and more specific biomarkers like CRP, procalcitonin, or the neutrophil-to-lymphocyte ratio. Such studies will provide more robust evidence to guide clinical guidelines and policy development in surgical infection prevention.

## Ethical Considerations

The ethical committee of Udayana University granted approval for this study under the reference number 2090/UN14.2.2.VII.14/LT/2024.

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The authors had no acknowledgements to declare.

## CONFLICT OF INTEREST

The authors declare no conflict of interest related to the publication of this paper. This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. All costs associated with the research were covered by the investigators and institutional resources.

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