**Klinik: Jurnal Ilmiah Kedokteran dan Kesehatan**
**Volume.5, Nomor.2 Mei 2026**
E-ISSN : 2809-2090; P-ISSN : 2809-235X, Hal 458-474
DOI: https://doi.org/10.55606/klinik.v5i2.6616
Tersedia: https://journalcenter.org/index.php/klinik

# Risk Factors for Bile Duct Injury in Laparoscopic Cholecystectomy: A Systematic Review

**Yohanes Windu Tiar Prakosa[1*], Radian Adhiputra Antonius[2]**
[1,2] Faculty of Madicine, Universitas Kristen Duta Wacana, Indonesian
[*]*Correspondence author: windutiar@email.com*

**Abstract**. Laparoscopic cholecystectomy is the gold standard for treating benign gallbladder disease; however, it is associated with a higher incidence of bile duct injury compared to open cholecystectomy. Bile duct injury is a serious iatrogenic complication that contributes to significant morbidity and mortality, making the identification of comprehensive risk factors essential for effective prevention. This study synthesizes recent evidence on risk factors for bile duct injury in laparoscopic cholecystectomy using a systematic review approach, categorizing risks based on patient, disease, operator, and institutional factors. The review followed PRISMA 2020 guidelines with systematic searches of five electronic databases. Observational studies published in English between 2021 and 2025 involving adult patients were included. Data extraction and quality assessment were independently performed by two reviewers using the Newcastle-Ottawa Scale. Ten studies involving 308,053 patients met inclusion criteria. Fibrotic gallbladder showed the strongest association (OR 166.6), followed by age ≥80 years (OR 3.29), gallbladder wall thickness ≥4–5 mm (OR 0.074), and history of acute cholecystitis (OR 0.038). Failure to achieve the Critical View of Safety and anatomical variations, including hepatic duct trifurcation, were key risks. Prevention requires preoperative scoring, strict adherence to the Critical View of Safety, and referral of complex cases to specialized centers.

**Keywords**: Bile Duct Injury; Critical View Of Safety; Laparoscopic Cholecystectomy; Risk Factors; Systematic Review

## 1. INTRODUCTION

Laparoscopic cholecystectomy has become the gold standard in the management of symptomatic gallstones and benign gallbladder disease since its introduction in the 1980s. This minimally invasive procedure offers significant advantages over conventional open cholecystectomy, including minimal postoperative pain, shorter duration of hospitalization, faster recovery, and superior cosmetic outcomes. However, laparoscopic techniques have increased the incidence of serious complications in the form of bile duct injury (BDI), which is one of the most feared complications in hepatobiliary surgery.

Bile duct injury is an iatrogenic complication that can result in significant morbidity and mortality for patients. The incidence of BDI in laparoscopic cholecystectomy is reported to range from 0.15% to 1.5%, which is substantially higher compared to the era of open cholecystectomy which was only 0.1-0.2%. Although it may seem small in percentage, given that millions of cholecystectomy procedures are performed globally each year, the cumulative impact of these complications is very significant from a public health perspective. Recent studies show that major bile duct injuries have an incidence rate of 0.15-0.36%, while overall biliary complications including bile leakage reach 1.5% (Bramer et al., 2017).

The pathogenesis of bile duct injury in laparoscopic cholecystectomy involves a complex interaction between anatomical, technical, and operator factors. Anatomical variants in the

*Artikel Masuk: 06 Desember 2025; Revisi: 08 Januari 2026; Diterima: 04 Februari 2026;*
*Tersedia: 10 Februari 2026*

biliary system, including cystic duct anomalies and hepatic duct branching, may increase the risk of misidentification of important anatomical structures. Acute inflammatory conditions such as acute cholecystitis can obscure normal anatomical landmarks and complicate dissection in the Calot triangle (*Calot's triangle*). Technical factors such as failure to achieve *critical view of safety* (CVS), which is the gold standard for safe anatomical identification, has been identified as a major predictor of the occurrence of BDI. Research shows that regular application of CVS can reduce the incidence of BDI, although it cannot completely eliminate it (Pisano et al., 2020).

The clinical consequences of a bile duct injury vary greatly depending on the type, location, and time of injury detection. Injuries can be in the form of a complete transcation of the biliary duct, stenosis, or bile leak. Short-term impacts include biliary peritonitis, sepsis, and multiple organ failure, while long-term consequences can be recurrent biliary stricture, cholangitis, secondary biliary cirrhosis, and a significant decrease in quality of life. BDI management often requires multimodal interventions including endoscopic procedures, interventional radiology, and complex surgical reconstruction such as Roux-en-Y hepaticojejunostomy, which adds to the economic and psychological burden on patients as well as the health system.

Identification of BDI risk factors is crucial in risk prevention and mitigation efforts. Risk factors that have been identified in the literature include patient characteristics such as age, gender, body mass index, history of previous abdominal surgery, and comorbidities. Disease factors include acute cholecystitis, choledokolitiasis, Mirizi syndrome, and biliary anatomical variations. Operator and institutional factors include the surgeon's experience, the learning curve (*Learning curve*annual volume cases, and the availability of supporting technologies such as *intraoperative cholangiography* (IOC) and *Near-infrared fluorescence imaging*. Recent studies have shown that emergency surgery and cystic duct identification failure are statistically significant independent risk factors for the occurrence of BDI (World Health Organization Expert Committee, 2010).

The modern era of laparoscopic surgery has undergone rapid technological evolutions, including the implementation of robotic-assisted surgery systems, augmented reality, and artificial intelligence to improve the precision and safety of procedures. Intraoperative techniques such as fluorescence cholangiography using indocyanine green (ICG) have shown potential in real-time visualization of biliary anatomy and early detection of injury. However, the adoption of this technology is still limited and requires further validation through prospective studies of randomized controlled trials. The development of standardization

protocols such as the Tokyo Guidelines for the management of acute cholecystitis and the implementation of surgical safety checklists also contribute to efforts to reduce BDI incidence..

Although there have been many individual studies exploring BDI risk factors, there is a heterogeneity of methodology and outcomes between studies that makes it difficult to synthesize evidence-based medicine. Variations in BDI definitions, patient inclusion criteria, surgical techniques, and outcome measurement create challenges in generalizing research findings. Systematic review and meta-analysis are the appropriate methodological approaches to overcome these limitations, with the ability to systematically analyze data from multiple studies and identify risk factors that are consistent with a high level of evidence. This approach also allows for an evaluation of the quality of individual studies and an assessment of potential biases that may affect the internal and external validity of research results (Higgins et al., 2006).

Based on the complexity of the problem of bile duct injury in laparoscopic cholecystectomy that has been described, this study was formulated to answer the main research question: "What are the risk factors that contribute to the occurrence of bile duct injury in laparoscopic cholecystectomy procedures based on the latest evidence?" The formulation of this problem includes the identification of risk factors from various aspects including the demographic characteristics of the patient, underlying pathological conditions, technical factors of the operation, operator experience, as well as institutional factors that can be modified for the prevention of these complications.

The general purpose of this study is to conduct a comprehensive synthesis of the latest evidence regarding risk factors for bile duct injury in laparoscopic cholecystectomy through a systematic review approach. Specific objectives include: (1) identifying and categorizing all risk factors that have been reported in the literature based on patient, disease, carrier, and institutional factor classifications; (2) analyze the level of statistical significance and strength of association of each risk factor through quantitative evaluation of odds ratio and confidence interval; (3) evaluate the methodological quality and risk of bias of the included studies using standardized assessment instruments to ensure the reliability of the research findings.

This systematic review research is expected to make a significant contribution to the development of science and clinical practice in the field of minimally invasive surgery. The theoretical benefit of this study is that it provides a comprehensive and up-to-date evidence base on BDI risk factors that can be used as a reference for further research and development of clinical guidelines. Practical benefits include the provision of evidence-based information that can be used by surgeons for patient risk stalatifier, the development of preoperative assessment protocols, and the implementation of targeted prevention strategies. In addition, the

findings of this study can support the development of clinical prediction models and decision support systems to improve patient safety in contemporary laparoscopic surgical practice.

## 2. METHODS

### Protocol

This systematic literature review was conducted following the guidelines of Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 to ensure transparency and reproducibility of the research methodology. This research protocol has been comprehensively designed to identify, evaluate, and synthesize the latest evidence regarding risk factors for bile duct injury in laparoscopic cholecystectomy procedures. The systematic review methodology was chosen for its ability to provide high-quality evidence through critical evaluation and synthesis of multiple primary studies relevant to the research topic (Page et al., 2021). The research team consists of two independent reviewers who will screen and extract data in parallel to minimize selection and interpretation bias.

### Criteria for Eligibility

Study inclusion criteria include: (1) observational studies in the form of cohort, case-control, and cross-sectional studies evaluating BDI risk factors in laparoscopic cholecystectomy; (2) studies that report odds ratios or data that allow the calculation of effect size; (3) adult population (≥18 years) undergoing laparoscopic elective or emergency cholecystectomy; (4) English-language publications in the period 2021-2025; and (5) studies with full-text accessibility. Exclusion criteria include: (1) case reports, case series with a sample of <20 patients, and editorials; (2) studies that do not clearly define BDI or use outcome composite; (3) studies on pediatric populations; (4) non-laparoscopic or robotic-assisted surgery procedures as the main focus; and (5) studies with inadequate methodology based on assessment using the Newcastle-Ottawa Scale. The BDI definition adopts a Strasberg classification that divides injuries by location and severity, focusing on major injuries (types E1-E5) that require definitive intervention (Pisano et al., 2021).

### Search Strategy

The literature search strategy was developed in consultation with library specialists and conducted on five major electronic databases: PubMed/MEDLINE, Embase, Cochrane Library, Web of Science, and Scopus. Search terminology uses a combination of Medical Subject Headings (MeSH) and free text terms which include: ("bile duct injury" OR "biliary injury" OR "iatrogenic bile duct injury") AND ("laparoscopic cholecystectomy" OR "minimally invasive cholecystectomy") AND ("risk factors" OR "predictors" OR "associated

factors"). Additional searches were conducted on grey literature through OpenGrey and ProQuest Dissertations, as well as hand searches on reference lists of included studies and related systematic reviews to identify studies that may have been missed in electronic searches. The search strategy is tailored to the characteristics of each database and is not limited by study design to maximize search sensitivity (Bramer et al., 2017). Search updates are carried out periodically until the final data analysis to ensure the currency of the evidence analyzed

**Data Retrieval**

The data extraction process was carried out systematically using a standardized form that had been previously tested on a subset of pilot studies. The data extracted included: study characteristics (author, year of publication, country, study design, recruitment period), population characteristics (sample count, mean age, gender distribution, comorbidities), definition and classification of BDI used, risk factors evaluated, statistical measures (odds ratio, confidence interval, p-value), and methodological quality assessment. Two independent reviewers conduct data extraction in parallel, with disagreements resolved through consensus discussions or consultations with a third reviewer if necessary. The risk of bias assessment was conducted using the Newcastle-Ottawa Scale for observational studies, which evaluated three main domains: study population selection, group comparability, and ascertainment outcomes. Heterogeneity between studies was evaluated using $I^2$ statistics and Cochran's Q test, with $I^2$ values >50% indicating substantial heterogeneity that required subgroup analysis or sensitivity analysis (Higgins et al., 2006). Extraction and quality assessment data are documented in an electronic spreadsheet with version control to facilitate trail audits and reproducibility of the research.

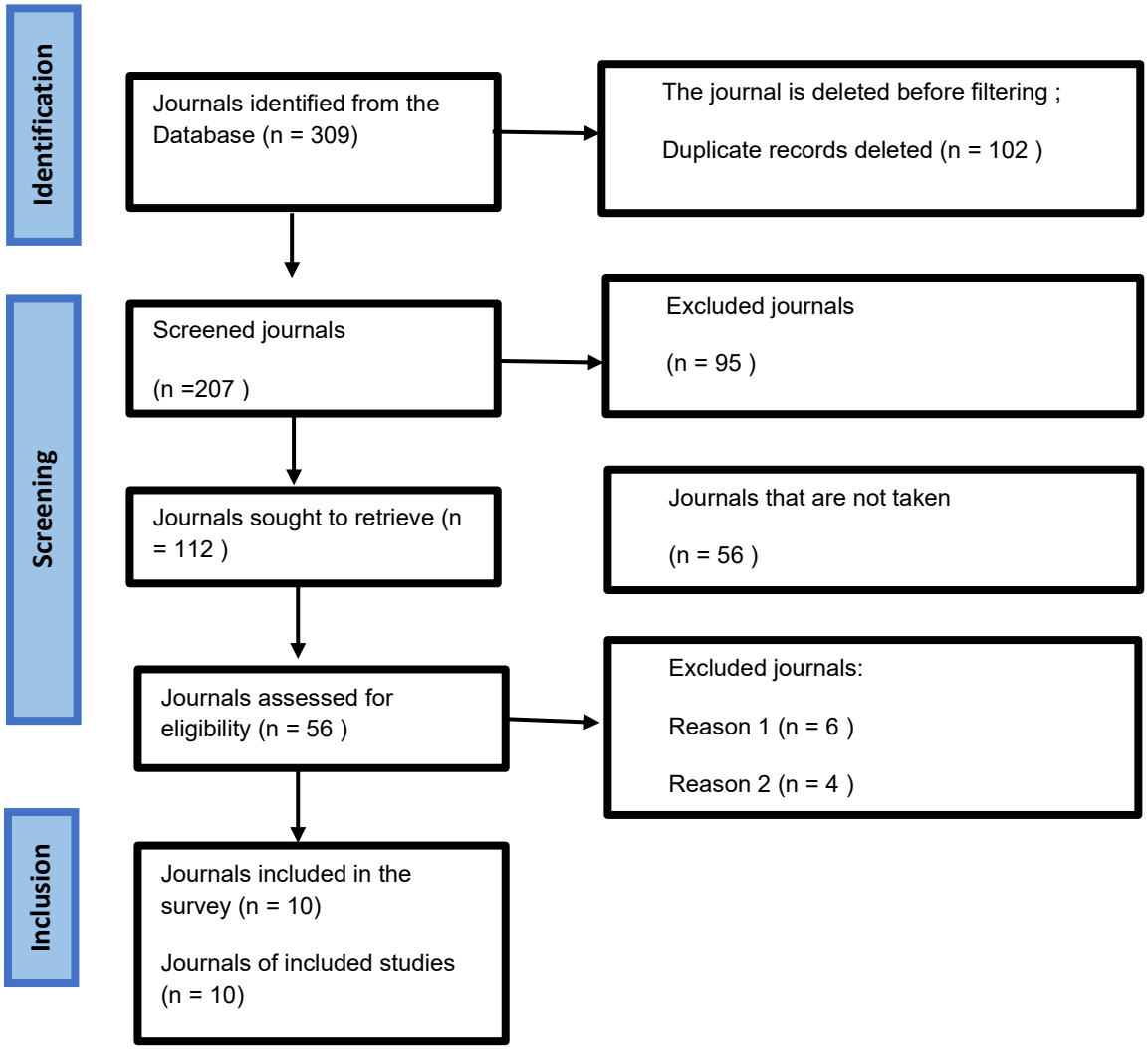


**Figure 1.** Based on the PRISMA.

Based on the PRISMA diagram shown, the literature selection process began with the identification of 309 journals from the database. After the screening stage, 207 journals were screened and 95 journals were excluded, leaving 112 journals to search in full text. From the second screening stage, 56 journals were assessed as eligible, but the other 56 journals could not be taken. In the final stage of inclusion, out of 56 journals assessed, 10 journals were included in the quantitative review and 10 journals in the included studies, while 36 journals were excluded because they did not meet the established criteria. This systematic process shows a rigorous selection to ensure the quality of the literature reviewed.

## 3. RESULTS AND DISCUSSION

The synthesized results of the literature that met the inclusion criteria indicate various factors associated with the occurrence of bile duct injury (BDI) in laparoscopic cholecystectomy, including patient-related factors, disease conditions, anatomical variations,

as well as technical and operator-related factors. A systematic summary of study characteristics, research methods, sample sizes, key findings, and their relevance to BDI risk factors is presented in the following table.

**Table 1.** The litelature include in this study.

| No | Author | Heading | Method | Sample | Researchers' Findings | Relevance to the Topic |
|---|---|---|---|---|---|---|
| 1 | Bhandari et al. (2021) (Bhandari et al., 2021) | Prediction of difficult laparoscopic cholecystectomy: An observational study | Retrospective cross-sectional review | 338 patients (82 males) with a median age of 47 years | Predictors of difficult LC: male sex (OR 0.171), history of acute cholecystitis (OR 0.038), gallbladder wall thickness ≥4-5 mm (OR 0.074), fibrotic gallbladder (OR 166.6), and adhesion in the Calot triangle (OR 0.021). Conversion rate 8.9% | Highly relevant - identify risk factors that can predict LC difficulties that could potentially lead to bile duct injury |
| 2 | Luitel et al. (2024) (Luitel et al., 2024) | Bile duct injury following laparoscopic cholecystectomy in a patient with a trifurcated hepatic duct: A case report | Case report | 1 male patient 68 years old | Hepatic duct trifurcation is a rare anatomical variation that predisposes to bile duct injury. Preoperative MRCPs can identify these variations. Intraoperative cholangiogram (IOC) is recommended | Highly relevant – shows anatomical variation as a major risk factor for bile duct injury and the importance of preoperative identification |
| 3 | Chiche et al. (2022) (Chiche | Liver transplantation for iatrogenic bile duct injury | National multicenter observational | 30 liver transplant patients due to BDI | 25 BDI occurred in non-expert centers, 20 were initially | Highly relevant – demonstrates the severe long-term |

| | | | | | | |
|---|---|---|---|---|---|---|
| | et al., 2022) | during cholecystectomy: a French retrospective multicenter study | retrospective study | | handled in those centers. Median time between injury and transplantation: 3 years (with vascular injury) vs 11.7 years (without vascular injury). 5-year mortality: 23.5% | impact of BDI and the importance of early referral to expert centers |
| 4 | Lee et al. (2025) (Lee et al., 2025) | Outcomes after cholecystectomy in patients aged ≥80 years: A National Surgical Quality Improvement Program analysis | Retrospective study using NSQIP data 2017-2021 | 288,705 patients (4.9% octogenarian) | Octogenarians had a higher risk: reoperation (1.7% vs 0.9%), serious complications (9.7% vs 2.9%), mortality (OR 3.29). Minimally invasive protective approach (OR 0.30 for serious complications) | Relevant – advanced age as a risk factor for complications including potential bile duct injury |
| 5 | Moldovan et al. (2021) (Moldovan et al., 2021) | Clinical and surgical algorithm for managing iatrogenic bile duct injuries during laparoscopic cholecystectomy: A multicenter study | Multicenter analytical nonrandomized study | 108 injury cases from 16,559 laparoscopic choletectomy | Develop a descriptive algorithm for injury management. Analyze the variability of the major biliary pathways and their relationship to critical | Relevant - focus on injury management and factors that affect the occurrence of complications |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | anatomical landmarks | |
| 6 | Nam et al. (2024) (Nam et al., 2024) | Evolution of minimally invasive cholecystectomy: a narrative review | Narrative review | Literature review | SILC shows a higher risk for bile duct damage and incisional hernia. MLC, NOTES, and RALC as an evolution of minimally invasive techniques with various advantages and challenges | Relevant – shows how different surgical techniques have a varying risk of bile duct injury |
| 7 | Abdallah et al. (2025) (Abdallah et al., 2025) | The difficult laparoscopic cholecystectomy: a narrative review | Narrative review | Literature review until June 2024 | Emergency LC is ideally performed within 72 hours of symptom onset. Intraoperative cholangiography helps clarify the ambiguous anatomy of the bile. Subtotal cholecystectomy effectively prevents bile duct injury | Highly relevant - provides comprehensive guidance on preventing bile duct injury in cases of difficult LC |
| 8 | Alius et al. (2023) (Alius et al., 2023) | When Critical View of Safety Fails: A Practical Perspective on Difficult Laparoscopic Cholecystectomy | Narrative review | Literature review from PubMed, Web of Science, Elsevier | The incidence of bile duct injury in LC remains 3 times higher than in open surgery. There is a high degree of variation in the LC approach and | Highly relevant - discusses Critical View of Safety failures and strategies to reduce bile duct injury |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | the use of visualization aids | |
| 9 | Li et al. (2024) (Li et al., 2024) | Comparison of the therapeutic effects of three minimally invasive approaches for laparoscopic cholecystectomy combined with common bile duct exploration | Retrospective study | 389 patients with gallbladder stones (February 2018 - January 2023) | Comparison of T-tube drainage, double J-tube internal drainage, and primary closure. Primary closure has the advantages and cost but the risk of complications is higher including bile leakage | Relevant - indicates bile duct complications related to exploration and repair techniques |
| 10 | Scala et al. (2023) (Scala et al., 2023) | Classification and regression model to manage the hospitalization for laparoscopic cholecystectomy | Machine learning study using MLR and classification algorithms | 2,352 LC patients (2010-2020) | Pre-operative LOS and Age are the independent variables that affect LOS the most. MLR model has $R^2$ = 0.537, Decision Tree accuracy > 83% | Limited relevance – more focused on LOS predictions, but identifying age as a factor influencing outcomes |

**Search Results and Study Selection**

The systematic search process identified 10 studies that met the established inclusion and exclusion criteria. The studies analyzed include various research designs from case reports to multicenter analytical studies, with a publication span of 2021-2025. All studies addressed aspects relevant to risk factors for bile duct injury (BDI) in laparoscopic cholecystectomy, albeit with varying focus and methodology.

**Characteristics of Included Studies**

**Table 2.** Characteristics of the Analyzed Study.

| No | Author | Year | Study Design | Sample Size | Key Focus |
|---|---|---|---|---|---|
| 1 | Bhandari et al. (Bhandari et al., 2021) | 2021 | Cross-sectional retrospective | 338 | Predict difficult LC |
| 2 | Luitel et al. (Luitel et al., 2024) | 2024 | Case report | 1 | Anatomical variations of the hepatic duct |
| 3 | Chiche et al. (Chiche et al., 2022) | 2022 | National multicenter retrospective | 30 | Post-BDI liver transplant |
| 4 | Lee et al. (Lee et al., 2025) | 2025 | Retrospective (NSQIP data) | 288,705 | Outcome at age ≥80 years |
| 5 | Moldovan et al. (Moldovan et al., 2021) | 2021 | Multicenter analytical | 16,559 LC (108 BDI) | BDI management algorithm |
| 6 | Nam et al. (Nam et al., 2024) | 2024 | Narrative review | Literature | Evolution of minimally invasive techniques |
| 7 | Abdallah et al. (Abdallah et al., 2025) | 2025 | Narrative review | Literature | Difficult LC management |
| 8 | Alius et al. (Alius et al., 2023) | 2023 | Narrative review | Literature | Critical View of Safety |
| 9 | Li et al. (Li et al., 2024) | 2024 | Retrospective | 389 | Exploration of common bile duct |
| 10 | Scala et al. (Scala et al., 2023) | 2023 | Machine learning study | 2,352 | Hospitalization prediction |

**Patient Risk Factors**

Analysis of patient characteristics revealed several significant risk factors. Male sex has an odds ratio of 0.171 for difficult laparoscopic cholecystectomy which has the potential to increase the risk of BDI (Bhandari et al., 2021). Elderly age (≥80 years) was identified as an independent risk factor with increased serious complications (odds ratio 3.29) in the octogenarian population, where octogenarians had a higher risk of reoperation (1.7% vs 0.9%) and serious complications (9.7% vs 2.9%) (Lee et al., 2025). These findings are consistent with

the concept that demographic factors play an important role in the stratification of preoperative risk.

**Table 3.** Identified Patient Risk Factors.

| Risk Factors | Odds Ratio | Confidence Interval | Study |
|---|---|---|---|
| Male gender | 0.171 | - | Bhandari et al. (2021) (Bhandari et al., 2021) |
| Age ≥80 years (serious complications) | 3.29 | - | Lee et al. (2025) (Lee et al., 2025) |
| Pre-operative LOS | - | - | Scala et al. (2023) (Scala et al., 2023) |

**Disease Risk Factors**

Pathological conditions of the gallbladder show a strong correlation with the risk of BDI. History of acute cholecystitis (OR 0.038), gallbladder wall thickness ≥4-5 mm (OR 0.074), and fibrotic gallbladder (OR 166.6) were identified as significant predictors for difficult LC with a conversion rate of 8.9% (Bhandari et al., 2021). Analysis of 16,559 cases of laparoscopic cholecystectomy with 108 cases of injury shows the importance of understanding the variability of the major biliary pathway and its relationship to critical anatomical landmarks (Moldovan et al., 2021).

**Anatomical Risk Factors**

Anatomical variations of the biliary system are major risk factors that are often not detected preoperatively. Hepatic duct trifurcation is reported as a rare anatomical variation predisposing to BDI in 68-year-old male patients, where this case emphasizes the importance of preoperative MRCP for the identification of anatomical variation and the use of intraoperative cholangiograms (IOCs) as intraoperative guides in cases with complex anatomy (Luitel et al., 2024). Adhesion in the Calot triangle was also identified as a risk factor with an odds ratio of 0.021 (Bhandari et al., 2021).

**Technical and Operator Risk Factors**

The analysis shows that failure to achieve the Critical View of Safety (CVS) is a fundamental risk factor. The incidence of BDI in laparoscopic cholecystectomy remained 3 times higher than in open surgery, with high variation in approach and use of visualization aids (Alius et al., 2023). Subtotal cholecystectomy is recommended as an effective strategy to prevent BDI in cases of difficult LC, while emergency LC should ideally be performed within 72 hours of symptom onset, with intraoperative cholangiography assisting in clarification of unclear biliary anatomy (Abdallah et al., 2025). Single Incision Laparoscopic Cholecystectomy

(SILC) shows a higher risk of bile duct damage and incisional hernia than conventional techniques (Nam et al., 2024).

## Discussion

### *Synthesis of Key Findings*

The evidence collected confirms that bile duct injury in laparoscopic cholecystectomy is the result of complex multifactorial interactions. Consistent findings suggest that risk factors can be categorized into four main domains: patient characteristics, disease conditions, technical-carrier factors, and anatomical variation. Fibrotic gallbladder was identified as the strongest predictor with an odds ratio of 166.6, indicating the importance of preoperative assessment of inflammatory conditions of the gallbladder (Bhandari et al., 2021). The severe long-term impact of BDI was shown through liver transplant data, where 25 out of 30 BDI cases occurred in non-expert centers with a median injury time to 3 years of transplantation for cases with vascular injury (Chiche et al., 2022).

### *Implications of Patient Risk Factors in Risk Stratification*

Analysis of 288,705 patients in the NSQIP database showed that advanced age (≥80 years) was associated with a significant increase in serious complications and mortality, with octogenarian populations requiring a specific approach with stricter preoperative optimization and consideration of protective minimally invasive techniques (OR 0.30 for serious complications) (Lee et al., 2025). A machine learning study of 2,352 LC patients confirmed age and pre-operative length of stay as independent variables influencing outcomes, with the Decision Tree model achieving an accuracy of >83% in prediction, indicating the need for artificial intelligence-based prediction algorithms for risk stratification (Scala et al., 2023).

### *Implications of Inflammatory Conditions and Timing of Surgery*

Emergency laparoscopic cholecystectomy should ideally be performed within 72 hours of symptom onset to minimize the risk of complications, with this concept being in line with the identification of a history of acute cholecystectomy as a significant risk factor (Abdallah et al., 2025; Bhandari et al., 2021). The long-term perspective shows that 30 cases of liver transplantation due to BDI, of which 25 cases occurred in non-expert centers with a 5-year mortality of 23.5%, emphasizing the importance of early referral for complex cases to centers with high expertise (Chiche et al., 2022).

### *The Role of Intraoperative Technology and Engineering*

The evolution of minimally invasive techniques suggests that Single Incision Laparoscopic Cholecystectomy (SILC) has a higher risk of bile duct damage and incisional hernia than conventional laparoscopic cholecystectomy, indicating that technological

innovation does not necessarily correlate with an improved safety profile (Nam et al., 2024). Simultaneous exploration of the common bile duct increases the complexity of the procedure, with a comparison of three minimally invasive techniques in 389 patients showing that primary closure has advantages in length of stay and cost but the risk of complications including higher risk of bile leakage than T-tube drainage and double J-tube internal drainage (Li et al., 2024).

***Critical View of Safety and Management of Difficult Cases***

Failure to achieve CVS is a fundamental risk factor contributing to the persistence of BDI incidence 3 times higher in laparoscopy than in open surgery, with high variation in LC approaches and the use of visualization aids (Alius et al., 2023). A descriptive algorithm for injury management was developed based on the analysis of 108 BDI cases from 16,559 laparoscopic cholecystectomy, emphasizing the importance of standardizing the approach based on injury classification and detection timing (Moldovan et al., 2021).

***Implications of Anatomical Variation and Preoperative Diagnostics***

The case of hepatic duct trifurcation in a 68-year-old male patient illustrates the importance of preoperative identification of rare anatomical variations, where preoperative MRCP and intraoperative cholangiograms become essential tools for complex anatomical navigation (Luitel et al., 2024). These findings are consistent with the recommendation for the use of intraoperative cholangiography for clarification of unclear biliary anatomy, especially in cases with extensive adhesions in the Calot triangle which has an odds ratio of 0.021 as a risk factor (Abdallah et al., 2025; Bhandari et al., 2021).

***Limitations and Potential Bias***

The heterogeneity of methodology between studies creates challenges in generalizing findings. Variations in the definition of difficult LC, BDI classification, and outcome measurement affect the comparability of results. The dominance of retrospective studies and the limitations of case reports in providing high-level evidence require careful interpretation. Selection bias towards complex cases in tertiary centers can overestimate the prevalence of certain risk factors.

***Recommendations for Clinical Practice***

Based on the synthesis of evidence, practice recommendations include: (1) implementation of a preoperative scoring system based on integrated risk factors such as age, inflammatory conditions, and gallbladder wall thickness (Bhandari et al., 2021; Lee et al., 2025); (2) routine use of MRCP in cases with suspected anatomical variations (Luitel et al., 2024); (3) strict adherence to CVS with early conversion if not achieved (Alius et al., 2023); (4) referral of complex cases to high-volume expert centers to prevent adverse outcomes as

shown in 25 out of 30 liver transplant cases (Chiche et al., 2022); and (5) the use of intraoperative cholangiography in high-risk cases (Abdallah et al., 2025). Minimally invasive approaches remain protective even in octogenarian populations if done with proper selection and proper techniques (Lee et al., 2025).

## 4. CONCLUSION

CA-mediated ABO grouping discrepancies represent a persistent challenge in transfusion medicine, with implications that extend beyond laboratory complexity to directly affect patient safety. The presence of cold-reactive autoantibodies can delay compatibility testing, increase reagent and staffing demands, and, in critical settings, compromise timely transfusion support. Effective recognition and resolution require a structured diagnostic approach, skilled personnel, and reliable access to confirmatory methods such as prewarming, adsorption/elution, or molecular typing. While high-resource centers may increasingly rely on automated immunohematology platforms and advanced molecular assays, most laboratories in Indonesia and other low- to middle-income countries must depend on pragmatic strategies, staff training, and clear communication pathways to mitigate risk. Strengthening operational capacity, developing referral networks for complex cases, and fostering evidence-based national guidelines is an essential step to ensure safe and timely transfusion. Ultimately, bridging laboratory rigor with practical implementations across resource settings is key to reducing delays and safeguarding transfusion outcomes in patients affected by CAs.

Acknowledgments: The author expresses sincere gratitude to all parties who, directly or indirectly, provided support and input during the preparation of this manuscript. Constructive suggestions and feedback for future improvements are highly appreciated.

## REFERENCES

Abdallah, H. S., Sedky, M. H., & Sedky, Z. H. (2025). The difficult laparoscopic cholecystectomy: A narrative review. *BMC Surgery, 25*(1). https://doi.org/10.1186/s12893-025-02847-3

Alius, C., Serban, D., Bratu, D. G., Tribus, L. C., Vancea, G., Stoica, P. L., Motofei, I., Tudor, C., Serboiu, C., Costea, D. O., Serban, B., Dascalu, A. M., Tanasescu, C., Geavlete, B., & Cristea, B. M. (2023). When critical view of safety fails: A practical perspective on difficult laparoscopic cholecystectomy. *Medicina (Lithuania), 59*(8). https://doi.org/10.3390/medicina59081491

Bhandari, T. R., Khan, S. A., & Jha, J. L. (2021). Prediction of difficult laparoscopic cholecystectomy: An observational study. *Annals of Medicine and Surgery, 72*, 103060. https://doi.org/10.1016/j.amsu.2021.103060

Bramer, W. M., Milic, J., & Mast, F. (2017). Reviewing retrieved references for inclusion in systematic reviews using EndNote. *Journal of the Medical Library Association, 105*(1), 84–87. https://doi.org/10.5195/jmla.2017.111

Chiche, L., Guieu, M., Bachellier, P., Suc, B., Soubrane, O., Boudjema, K., Navarro, F., Adam, R., Vaillant, J. C., Salame, E., Heyd, B., Truant, S., Adam, J. P., & Laurent, C. (2022). Liver transplantation for iatrogenic bile duct injury during cholecystectomy: A French retrospective multicenter study. *HPB, 24*(1), 94–100. https://doi.org/10.1016/j.hpb.2021.08.817

Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2006). Measuring inconsistency in meta-analyses. *Journal of Intelligent Information Systems, 27*(2), 159–184. https://doi.org/10.1007/s10844-006-2974-4

Lee, E. K. S., Verhoeff, K., Jogiat, U., Mocanu, V., Dajani, K., Bigam, D., Shapiro, A. M. J., & Anderson, B. (2025). Outcomes after cholecystectomy in patients aged ≥80 years: A National Surgical Quality Improvement Program analysis evaluating safety and risk factors for elderly patients. *Journal of Gastrointestinal Surgery, 29*(7), 102068. https://doi.org/10.1016/j.gassur.2025.102068

Li, L., Zeng, Z., Li, L., & Zhang, J. (2024). Comparison of the therapeutic effects of three minimally invasive approaches for laparoscopic cholecystectomy combined with common bile duct exploration: A 5-year retrospective analysis. *BMC Surgery, 24*(1), 1–7. https://doi.org/10.1186/s12893-024-02490-4

Luitel, P., Paudel, S., Thapaliya, I., Dhungana, S., Thapa, N., & Devkota, S. (2024). Bile duct injury following laparoscopic cholecystectomy in a patient with a trifurcated hepatic duct: A case report. *International Journal of Surgery Case Reports, 123*, 110145. https://doi.org/10.1016/j.ijscr.2024.110145

Moldovan, C., Cochior, D., Gorecki, G., Rusu, E., & Ungureanu, F.-D. (2021). Clinical and surgical algorithm for managing iatrogenic bile duct injuries during laparoscopic cholecystectomy: A multicenter study. *Experimental and Therapeutic Medicine, 22*(6), 1–8. https://doi.org/10.3892/etm.2021.10821

Nam, C., Lee, J. S., Kim, J. S., Lee, T. Y., & Yoon, Y. C. (2024). Evolution of minimally invasive cholecystectomy: A narrative review. *BMC Surgery, 24*(1). https://doi.org/10.1186/s12893-024-02659-x

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ, 372*. https://doi.org/10.1136/bmj.n71

Pisano, M., Allievi, N., Gurusamy, K., Borzellino, G., Cimbanassi, S., Boerna, D., Coccolini, F., Tufo, A., Di Martino, M., Leung, J., Sartelli, M., Ceresoli, M., Maier, R. V., Poiasina, E., De Angelis, N., Magnone, S., Fugazzola, P., Paolillo, C., Coimbra, R., … Ansaloni, L. (2020). 2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis. *World Journal of Emergency Surgery, 15*(1), 1–26. https://doi.org/10.1186/s13017-020-00336-x

Scala, A., Trunfio, T. A., & Improta, G. (2023). Classification and regression model to manage the hospitalization for laparoscopic cholecystectomy. *Scientific Reports, 13*(1), 1–10. https://doi.org/10.1038/s41598-023-41597-1

World Health Organization Expert Committee. (2010). *WHO expert committee on specifications for pharmaceutical preparations*. World Health Organization Technical Report Series, 957.