



# Algerian Cholecystectomy Outcomes and Determinants Study (AL-CODS): Protocol for a prospective multicentre observational study

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## Abstract

**Introduction:** Cholecystectomy is common, yet outcomes vary with case-mix, technique, and system capacity. Algeria lacks contemporary national data. The AL-CODS study will estimate 30-day outcomes after cholecystectomy and identify determinants relevant to the Algerian context.

**Methods:** AL-CODS is a prospective, multicentre observational cohort across public and private hospitals in Algeria (1 January–30 June 2025). Consecutive adults undergoing cholecystectomy for presumed benign disease will be enrolled via a secure electronic case report form. Primary outcomes are 30-day morbidity (Clavien-Dindo) and all-cause mortality. Secondary outcomes include bile duct injury (Strasberg classification), incidental gallbladder cancer on histology, and key practice patterns (operative approach, cholangiography, drains, antibiotics, day-case surgery, timing, use of extraction devices, length of stay). A minimum sample of 526 cases provides precise estimation of rare events (e.g., bile duct injury  $\approx 0.8\%$ ) with  $\pm 1\%$  margin of error at 99% confidence. Prespecified analyses will use descriptive statistics and multivariable logistic regression; model building will consider clinical plausibility, multicollinearity, and standard diagnostics, reporting adjusted odds ratios with 95% confidence intervals.

**Ethics and governance:** Ethical approval has been granted by EHU 1er Novembre 1954 (EHU-2024-éthique-01). Written informed consent is required. Data are stored on a password-protected platform with investigator-restricted access. The study is registered at ClinicalTrials.gov (NCT-64810007) and will follow STROBE guidance.

**Expected impact:** AL-CODS will deliver the first national estimates of cholecystectomy outcomes in Algeria, define context-specific risk factors to inform training and peri-operative decision-making, quantify the incidence of bile duct injury and incidental gallbladder cancer, and provide benchmarks for quality improvement. Results will support guideline development and contribute evidence from a lower-middle-income setting to the international literature.

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## Introduction

Cholecystectomy, the surgical removal of the gallbladder, is one of the most commonly performed procedures worldwide due to its effectiveness in treating symptomatic gallstones and other gallbladder-related conditions. In Algeria, as in many regions, cholecystectomy is a frequently performed surgery. In the United States, more than 300,000 cholecystectomies are performed annually<sup>1</sup>. Despite being considered a routine procedure, it carries

risks and is associated with varying levels of morbidity and mortality across different countries<sup>2</sup>. Although routinely performed, the outcomes and determinants of cholecystectomy can vary significantly depending on several factors, including patient demographics, general health status, comorbidities, surgical techniques, and healthcare systems. Understanding these variations is essential to improving patient outcomes and optimizing surgical practices<sup>2,3</sup>.

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Previous studies have highlighted the importance of regional and demographic factors in surgical outcomes. Research has shown that results may be influenced by variables such as patient age, sex, comorbidities, and surgical techniques<sup>4,5</sup>. Moreover, differences in postoperative complications and recovery times have been documented across various healthcare systems, underscoring the need for region-specific studies to tailor practices and recommendations<sup>6</sup>. A survey conducted in 2017 by our team reported interesting data regarding surgical practices for cholecystectomy in Algeria. These practices varied depending on the surgeon's years of experience, the surgical approach used, and the type of healthcare institution (university hospital, public health facility, or private practice)<sup>7</sup>.

However, data on the outcomes and risk factors of cholecystectomy specific to the Algerian context remain limited. The Algerian cholecystectomy outcomes and determinant study aims to address this gap by providing a comprehensive analysis of cholecystectomy results and identifying the main risk factors influencing these outcomes within the Algerian population. By analysing data from a prospective multicenter study of patients who have undergone cholecystectomy in Algeria, this study aims to contribute to the advancement of knowledge in the field and to identify best practices that can be taught to surgeons, ultimately improving patient care in Algeria.

## Methods

### *Ethical approval*

This study has been approved by the Ethics Committee of EHU 1er Novembre 1954 on 4 November 2024 under reference EHU-2024-éthique-01. No further local ethical approvals will be required at participating institutions under Algerian regulations. The law requires signed informed consent from all participants, as detailed in Appendix 1. All data will be recorded in a secure, password-protected electronic database using the DZ-ECRF application, accessible only to registered investigators. The study will adhere to STROBE reporting guidelines. This study is registered on ClinicalTrials.gov under the identifier NCT-64810007.

### *Study objectives*

The primary objectives will be to assess 30-day postoperative mortality and morbidity following

cholecystectomy for presumed benign gallbladder disease in Algeria, and to identify factors associated with these 30-day outcomes. Secondary objectives will be to estimate the incidence of incidental gallbladder cancer diagnosed on cholecystectomy specimens within 30 days postoperatively, to estimate the incidence of bile duct injury within 30 days following cholecystectomy for benign disease, and to evaluate surgical practices related to cholecystectomy across Algerian centres.

### *Recruitment of participating surgeons*

Surgeons will be invited to participate after registration via an electronic form distributed through the mailing lists of the Algerian Society of Surgery and the Algerian Society of Visceral and Endocrine Surgery. Regional investigator leads will be appointed in each Wilaya to verify surgeon credentials and to ensure data quality and consistency across participating centres.

### *Sample size calculation*

The minimum required sample size will be calculated using the standard formula  $n_0 = (Z^2 \times p \times (1-p)) / E^2$ . Assuming a complication rate  $p$  of 0.8%, a margin of error  $E$  of  $\pm 1\%$ , and a 99% confidence level  $Z = 2.576$ , the minimum sample size required will be 526 cholecystectomy cases. Given an anticipated bile duct injury rate of about 0.8%, the goal will be to estimate this rate with high precision using a  $\pm 1\%$  margin of error at a 99% confidence level.

### *Inclusion period*

Patients undergoing cholecystectomy between 1 January 2025 and 30 June 2025 will be eligible. Participating surgeons will consecutively include all eligible patients during this window without selection. Each centre will ensure complete case capture by reviewing theatre logs, operating room schedules, surgical registries, or the DEM-DZ (Dossier Electronique Médical DZ) to minimise selection bias.

### *Inclusion criteria*

Eligible patients will be aged 18 years or older and undergoing cholecystectomy for presumed benign gallbladder disease in any Algerian healthcare facility, public or private, even if postoperative histology subsequently reveals malignancy. Procedures may include or exclude exploration of the common bile duct.



Cases with an intraoperative diagnosis of gallbladder cancer will remain eligible provided malignancy was not suspected preoperatively.

### *Exclusion criteria*

Patients will be excluded if they are younger than 18 years, decline to participate, are operated outside the inclusion period, undergo cholecystectomy combined with another major operation such as pancreatoduodenectomy, bariatric surgery, or gastrectomy, or have missing or incomplete data.

### *Definitions of key variables*

Morbidity will be defined as any postoperative complication classified using the Clavien–Dindo system. Bile duct injury will be defined as any iatrogenic injury to the biliary tree diagnosed during or within 30 days of cholecystectomy and classified according to the Strasberg bile duct injury classification. Postoperative mortality will be defined as death from any cause within 30 days of surgery.

### *Outcomes*

The primary outcome will be the 30-day postoperative complication rate, defined and graded according to the Clavien–Dindo classification system<sup>8</sup>. Secondary outcomes will include the incidence of bile duct injury classified by Strasberg<sup>9,10</sup>, 30-day all-cause postoperative mortality<sup>11</sup>, the incidence of incidental gallbladder cancer on histology<sup>12,13</sup>, and the rate of laparoscopic (minimally invasive) versus open surgery as a marker of access to minimally invasive surgery. Surgeon practices will also be evaluated, including approach (laparoscopic, open, conversion), use of intraoperative cholangiography, use of drains, antibiotic prophylaxis, timing as elective versus emergency surgery, performance of ambulatory surgery, use of extraction devices in laparoscopic surgery, and postoperative length of stay. All patients will be followed for 30 days postoperatively, either through in-person clinic visits or telephone contact, to ascertain outcomes.

### *Data collection*

All participating surgeons will register on the study website at [www.al-cods.org](http://www.al-cods.org). Each surgeon will be assigned a secure account and will consecutively include all eligible patients. Data will be entered into a secure electronic

case report form; surgeons will have access only to their own cases. Prior to inclusion, informed consent will be obtained using a standardised form available in Arabic and French. Personal health data will be protected and will not be shared with third parties. Collected data will include surgeon identifiers, patient demographics, comorbidities, cholecystitis severity, surgical technique, intraoperative and postoperative events, and histopathology results. Data entry and validation will be completed by 31 August 2025, and only fully completed records will be included in the final analysis. Clear instructions will be provided to ensure reporting of all cases, whether straightforward or complicated. The case report form used for data collection is provided in Appendix 2.

### *Data analysis*

A comprehensive approach will be applied. The database will be reviewed for accuracy and completeness, and missing data will be addressed using appropriate methods such as imputation or case exclusion. Descriptive statistics will summarise demographic and clinical characteristics using means, medians, standard deviations, and frequencies. Binary logistic regression will identify independent predictors of 30-day postoperative complications and mortality. Candidate variables for multivariable models will be selected on clinical grounds and prior literature rather than on univariate p-values alone. Model building will be iterative, accounting for multicollinearity and optimising fit and parsimony with criteria such as the Akaike Information Criterion and Bayesian Information Criterion. Statistical significance in the final multivariable model will be set at  $p < 0.05$ . All analyses will be conducted using SPSS version 24. Results will be presented with odds ratios, 95% confidence intervals, and p-values, with subgroup analyses undertaken where clinically relevant. This analytical framework will support robust conclusions regarding outcomes and determinants of cholecystectomy in the Algerian context.

### *Expected outcomes and impact*

The study will identify key risk factors for 30-day mortality and morbidity to improve risk stratification for patients undergoing cholecystectomy in Algeria. It will estimate the national incidence of incidental gallbladder cancer, which is expected to be higher than in France, where a rate of 0.3% has been reported. It will also provide national



estimates of bile duct injury during cholecystectomy and support the development of targeted training and quality-improvement programmes to promote best practice and reduce complications.

### *Dissemination of results*

Authorship will follow the recommendations of the Global Surgery Research Unit to ensure fair recognition based on contribution. Results will be published under the collective authorship of the AL-CODS Collaborative Study, which will also be used for all scientific communications and presentations related to the study<sup>14</sup>.

### *Study bias and mitigation*

Centre-to-centre variability is a recognised source of bias. Despite shared protocols, surgeons may differ in patient selection and technique. To address this, data will be collected on surgeon profiles, healthcare settings (university hospitals, public health institutions, or private practices) and surgical approaches, enabling stratified analyses to reduce confounding from practice variability<sup>15</sup>.

## **Discussion**

Cholecystectomy remains one of the most frequently performed surgical procedures worldwide, primarily for symptomatic cholelithiasis and benign biliary conditions. Despite being considered a routine operation, significant disparities in postoperative outcomes have been documented, particularly between high-income and low- and middle-income countries (LMICs), largely due to variations in surgical expertise, patient comorbidities, and healthcare infrastructure<sup>16,17</sup>. This study aims to address the lack of national data in Algeria by prospectively analysing outcomes and their determinants across diverse hospital settings.

Our primary objective is to evaluate 30-day morbidity and mortality after cholecystectomy. In global literature, 30-day mortality rates range from 0.1% to 0.5%, while morbidity rates can vary from 5% to 15% depending on surgical indications, timing (elective vs. emergency), and patient risk profiles<sup>18,19</sup>. Through detailed data collection on demographics, disease severity, and perioperative details, this study will offer Algeria-specific estimates, crucial for clinical benchmarking and future quality improvement initiatives.

Identifying predictors of complications and mortality is another major goal. Previous studies have established risk factors such as advanced age, male sex, high BMI, ASA classification, acute cholecystitis, and conversion to open surgery<sup>20,21</sup>. Institutional factors, including surgical volume and the experience level of the operating surgeon, also influence outcomes<sup>22</sup>. By using multivariate logistic regression, this study will determine which of these variables hold prognostic value in the Algerian context.

Another important focus is the incidence of incidental gallbladder cancer (IGBC), a rare but potentially aggressive malignancy. IGBC is typically discovered on routine histopathologic analysis of cholecystectomy specimens and is often unsuspected preoperatively. Western studies report an incidence of 0.2% to 0.3% , but higher rates have been observed in certain endemic regions such as India, Chile, and Korea<sup>23,24</sup>. Algeria is believed to have a higher burden of gallbladder cancer, although no large-scale epidemiologic data currently exist. This study will fill that knowledge gap and may guide future screening and pathology guidelines.

Bile duct injury (BDI) is another critical outcome being measured. BDI has devastating consequences for patients and is associated with significant morbidity, mortality, and litigation. The global incidence is approximately 0.2–0.8%, with higher rates in emergency settings or in surgeries performed by inexperienced surgeons<sup>25</sup>. This study will allow for a more accurate estimation of the incidence of this complication and will serve as a valuable source of documentation. It may also lead to training reforms in surgical education and promote active awareness of this complication in Algeria.

A notable strength of this study will be its prospective, multicentre design. The inclusion of both public and private institutions, along with regional coordination through designated investigators, ensures diverse representation. The standardized data collection through electronic case report forms (eCRFs) and mandatory inclusion of all consecutive cases will minimize selection and reporting bias. However, the study has certain limitations. Inter-institutional variability in practice, surgical technique and decision-making may impact the consistency of reported outcomes. Moreover, the 30-day follow-up period may underestimate long-term complications or delayed diagnoses of events.



The results of this research could guide national surgical audits, inform preoperative risk stratification models, and enhance patient safety by identifying modifiable risk factors. Furthermore, national incidence data on IGBC and BDI could influence routine protocols, raise awareness among surgeons, and inform public health policies. Ultimately, this project aligns with broader efforts to strengthen surgical systems and improve perioperative outcomes in LMICs.

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**GAIT statement for Generative AI use<sup>26</sup>:** Generative AI was used to adjust the grammar of the manuscript and to edit it, however no AI was used in terms of data analysis, instead we would like to acknowledge our colleague efforts for the data analysis.

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