

Factors influencing delayed discharge after day-surgery laparoscopic cholecystectomy: the DeDiLaCo study protocol

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Abstract. – OBJECTIVE: Laparoscopic cholecystectomy (LC) is the gold standard for most benign gallbladder diseases. Early discharge (<24 hours) has the same outcomes as longer (>24 hours) hospital stay. Nevertheless, the rate of delayed discharge >24 hours range from 4.6% to 37%. The primary endpoint of this Italian nationwide study is to analyze the prevalence of patients undergoing elective LC who experienced a delayed discharge >24 hours and identify potential limiting factors of early discharge. Results from these analyses will be used to select patients who can be safely discharged on the same day after surgery. Secondary endpoints will be to evaluate the patient's quality of life (QoL), assess the direct health costs associated with late discharge, and quantify the patient's involvement in the treatment process.

PATIENTS AND METHODS: This prospective, observational study was conducted following a resident-led model and the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines. All patients were treated according to the local hospital protocol and received routine care as standard therapy.

RESULTS: We expected to obtain the enrollment of at least 500 patients based on an assumed difference in discharge delay between the reference and the recruitable population of 6% and the identification of factors related to discharge failure within 24 h. Early discharge after LC leads to advantages both in terms of clinical outcomes and quality of life of the patient, and it is highly effective in terms of health costs and shortening the waiting list. However, clinical reality differs from the results of randomized studies by a complex series of non-objectionable real-world data influencing treatment plans. Therefore, we expected

to identify independent predictors and factors of failure of early discharge.

CONCLUSIONS: Clinical reality often differs from randomized trial results. In Italy, the vast majority of delayed discharges after LC may not be related to surgery and can be prevented both with logistical reorganization and with a readjustment of the trust reimbursement policies.

Key Words:

Laparoscopic cholecystectomy, Early discharge, Delayed discharge, Outcomes, Predictive factors, Multicenter study.

Introduction

Laparoscopic cholecystectomy (LC) was first performed by Erich Muhe in 1985¹ and has now become the gold standard procedure for most benign gallbladder diseases, such as symptomatic gallstones and acute cholecystitis. As surgeons' experience improved, LC has become common even in patients with severe inflammation, such as acute cholecystitis (AC)^{2,3}. Due to surgeons' sufficient experience in laparoscopic surgery, the remarkable development of various laparoscopic surgical equipment, and new anesthesiology and analgesic techniques, the safety and feasibility of an early discharge (≤ 24 hours) after LC are now well-established⁴⁻¹². Over the last two decades, outpatient LC has become standard practice in the USA and UK⁷⁻⁸. However, despite its acceptance in several European and non-European countries, early discharge after LC has not been

widely adopted in Italy (Figure 1). Early discharge seems to have the same clinical outcomes as procedures performed on patients with a conventional hospital stay in regard to complications and hospital readmission⁶⁻¹¹. Nevertheless, the incidence of delayed discharge >24 hours still range from 4.6% to 37% in different series¹⁰⁻¹⁴. Studies¹²⁻¹⁴ suggest that shared decision-making, communication, surgeon's skill, nursing care, and patient and surgeon relation are critical influencers for a discharge within 24 hours. As far as we know, the reasons for a delayed discharge include psychosocial issues, postoperative nausea and pain, placement of abdominal drainage at the end of the procedure, postoperative complications, conversion to open surgery, and residual choledocholithiasis. Moreover, many studies¹⁰⁻¹⁴ have shown that the advanced age of the patient, prolonged operating time, presence of abdominal adhesions, and complexity of surgical dissection can affect the early discharge rate. In the wake of this scenario, a careful selection of patients is needed to have good outcomes for early discharge after LC. A large multicenter study investigating the reasons for delayed discharge >24 hours of LC in our country might enhance the selection process and outcomes of patients undergoing LC. This study aims to analyze the prevalence of patients undergoing elective LC with delayed discharge >24 hours in an extensive Italian national database and identify potential limiting factors of early discharge after LC. Results from these analyses could be used to select patients who can be safely discharged on the same day or within 24 hours after surgery and help enhance organizational pathways for early discharge after LC.

Patients and Methods

Study Protocol

Objectives

- The primary endpoint of this Italian nationwide study is to assess the prevalence of patients with delayed (or late) discharge (>24 h) after elective LC.
- Secondary endpoints aim to evaluate the patient's quality of life (QoL), assess the direct health costs associated with late discharge, and quantify the patient's involvement in the treatment process.

Study Design and Participating Sites

This prospective, observational study was conducted following a resident-led model, similar to what has been described by Bhangu et al¹⁵ and according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines¹⁶. Briefly, teams of medical students and surgical residents under senior staff surgeon oversight have been collecting data on patients across Italy for 12 months. The Data Coordination Center (DCC) is the UOC Chirurgia Generale, Ospedale SS. Trinità Cagliari, Italy. The study director was responsible for the selection of the study sites. Any center performing elective LC could participate in this study. The centers included academic medical centers, teaching hospitals, tertiary referral centers, and community hospitals. Single patient data will not be published and stored separately for further analyses. All patients were treated according to the local hospital protocol and received routine care as standard therapy.

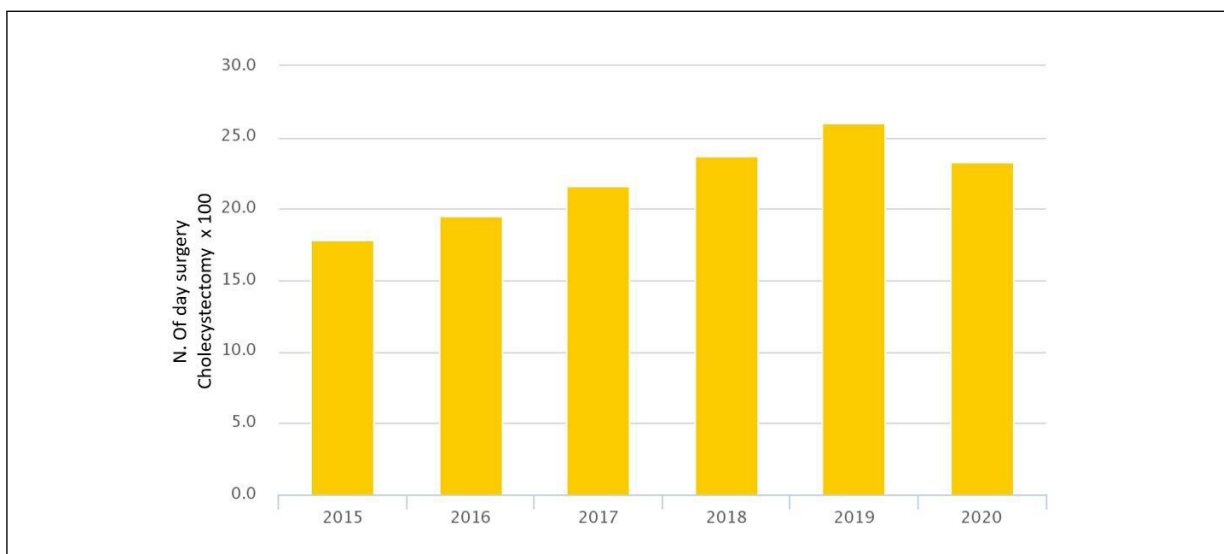


Figure 1. Laparoscopic cholecystectomy: day surgery admissions.

The main strength of this project is the multi-center, prospective, contemporary methodology with independent data validation. This produces high-quality data on LC carried out for elective benign gallbladder cases and on outcomes throughout Italy from a wide range of hospital types.

As for the anesthesiologic aspects and pain treatment, we have drawn up a protocol to limit the pain factor as conditioning for delayed discharge. We added it as supplement material ([Appendix 2](#)). We took into consideration 24 hours, as the standard of care because, in the National Results Plan (PNE), cholecystectomy in day surgery is defined as “all admissions, in day hospital/day surgery regimen and ordinary patients between 0 and 1 day”.

Eligibility and Enrollment

Inclusion criteria for early discharge

- All patients over the age of 18 years old.
- All patients submitted to elective LC for the following diseases: symptomatic cholelithiasis, gallbladder polyposis, gallbladder adenomyosis, dyskinesia of the gallbladder, chronic cholecystitis, previous cholecystitis, previous biliary pancreatitis, previous choledocholithiasis.
- Presence of a family member or trusted person available to assist the patient during the postoperative period for at least 24 hours.
- American Society of Anesthesiologists (ASA) score I, II, and/or III.
- Possibility of direct telephone contact between the patient and the hospital.
- Possibility to reach the hospital within an hour in case of need.

The type of surgical approach included LC: LC is defined and coded (51.23) according to the ninth revision of the International Classification of Disease Clinical Modification (ICD-9-CM).

Exclusion criteria for early discharge

- Body mass index (BMI) >40.
- Acute cholecystitis.
- Open first or conversion to open cholecystectomy.
- Absolute contraindications to laparoscopy according to the 1994 European Association for Endoscopic Surgery (EAES) consensus conference: diffuse peritonitis, cholangitis, septic shock, severe acute pancreatitis, liver cirrhosis with portal hypertension, severe coagulopathy, choledochoduodenal fistula.
- Pregnancy or lactation.
- Lack of informed consent or non-compliant patients.
- Allergy to analgesic drugs included in the pro-

- tocol (ketorolac, paracetamol, ketoprofen).
- Patients already hospitalized and scheduled for the same procedure, or participation in another trial.

Outcome Measures

The study’s primary outcome is the discharge rate within 24 hours of surgery.

Secondary outcomes are:

- Assessment of the patient’s quality of life.
- Assessment of the direct health costs associated with late discharge.
- Assessment of patient involvement in the treatment path.
- Unscheduled ambulatory visit/hospital readmission.

Criteria for a Safe Discharge Within the First 24 Hours

- Length of surgery (LOS) <120 minutes.
- Absence of intraoperative complications.
- Well-controlled postoperative pain [Numerical Rating Scale (NRS) <4] only with oral analgesics (using NRS scale).
- No other contraindication to oral feeding after the surgical procedure.

Data Collection, Validation, and Management

In each participating hospital, one local investigator (usually a surgical resident and/or student) was responsible for data collection and uploading data into a central password-protected electronic spreadsheet specifically constructed with predefined data fields. There are three categories, demographics, perioperative data, and postoperative data (collected within one week from the discharge) (Table I). Patient details were recorded and anonymized using the code center, an ID number, and a unique alphanumeric code for any further integration. The enrolling center provided the anonymization procedure. If possible, patient data were collected daily; preoperative and intraoperative data were processed after surgery, and the postoperative outcomes were noted at the time of discharge and the end of follow-up. Data were obtained from the electronic patient database, admission charts, and operative reports or directly from the surgeon who operated when details were unclear or missing. Consent for participation and personal data management and transfer was obtained from the patient at admission. The Ethics Committee of the Azienda Tutela Salute (ATS) Sardegna approved the study protocol on October 20, 2020, with protocol number 271/2020/CE. There is no minimum

Table I. Data spreadsheet fields.

Form	Field	Options (definitions)
Demographics	ID	Progressive number
	ID center	Number
	ID code	Alphanumeric (center choice)
	Age	In years
	Sex	Male/Female
	Numbers of procedures/centers	<100, 100-200, >200
	BMI	BMI in kg/m ²
	Risk of SSIs	M-1-2-3-4
	Diabetes	Yes/No
	Scores	Apfel, ASA, CCI
	Pre-operative diagnosis	Symptomatic cholelithiasis, Polyposis, Adenomyosis, Biliary dyskinesia, Chronic cholecystitis, Previous lithiasis cholecystitis, Previous lithiasis pancreatitis, Previous choledocholithiasis
	Pre-operative ERCP	Yes/No
	If YES	Operative/non-operative
	Complete the questionnaire	Italian version of the Patient Activation Measure 13 (PAM13-I)
Perioperative data	Antibiotic Prophylaxis	Yes/No
	Peritoneal adhesions	Yes/No
	Biliary tract anatomical abnormalities	Yes/No
	Vascular anatomical abnormalities	Yes/No
	Time of Surgery	Minutes
	Conversion to open surgery	Yes/No
	If YES, reason for conversion	Bleeding, Presence of anatomical abnormalities, Adhesion, Others
	Use of surgical drainage	Yes/No
	Use of hemostatic agents	Yes/No
	Intraoperative complications	Yes/No
Postoperative data	VAS pain score at discharge	From 1 to 10
	Nausea	Yes/No
	Vomit	Yes/No
	Fever (>38C°)	Yes/No
	Early post discharge hospital within 24hrs readmission	Yes/No
	Reason for a delayed discharge (>24hrs)	Altered blood test, Fever, Pain, Conversion to open surgery, Cholangitis, SSIs, Bleeding, Residual choledocholithiasis, Biliary leakage, Abscess, Medical choice not supported by objective elements, Psychosocial issues, Healthcare cost issue, Other
	Total length of stay	Days
	Outpatient visit one week after admission	Free text
	Unplanned need/access to healthcare within 7 days from discharge	Yes/No
	Complications 30 days postoperatively	Yes/No
	Surgical site infection	Yes/No
	Complication grade (Clavien-Dindo classification)	I, II, IIIa, IIIb, Iva, IVb,V
	Hospital readmission within 7 days from discharge	Yes/No

ID: identifier, BMI: body mass index, ERCP: endoscopic retrograde cholangiopancreatography, SSI: surgical site infection, ASA: American Society of Anesthesiologists index, CCI: Charlson comorbidity index.

number of patients per center. Only datasets with >95% data completeness were accepted for pooled national analysis after data collection. The local leaders at the selected site identified an

independent assessor to validate all data, with a target of >98% accuracy. Overall, at least 5% of the datasets were independently validated. Outcome data were not explicitly analyzed for each center.

Data were submitted monthly via e-mail or included in an online module. Once in the Data Coordination Centre (DCC) pooled warehouse, records were reviewed and edited and, whenever necessary, transformed to comply with the DeDiLaCo data dictionary (see Table I for further information). The study director and coordinator then identified unacceptable data entries using custom software queries to detect missing, impossible, and improbable values and logical inconsistencies between data fields and across the forms. The DCC then asked local investigators to check for incomplete data, and once the sites had resolved the data queries, the DCC updated the patient records. The data were collected from each center according to the current Italian Law regarding privacy policy (Legislative Decree No. 196/2003 “RIGHT TO PERSONAL DATA PROTECTION CODE”). It was the responsibility of the local investigators to ensure that the local data would be protected and held according to the privacy policy and in line with what has been approved by the Ethics Board. No patients were involved in setting the research questions or the outcome measures, nor were they involved in the design and implementation of the study. There were no plans to involve patients in the dissemination of results.

Study Timeline

The following timeline has been outlined to define specific stages of the study:

- October 20, 2020 – study protocol was approved by the Ethics Committee of the ATS Sardegna with protocol number 271/2020/CE.
- November 1, 2020 – invitations have been sent to Italian centers to participate.
- January 1, 2021 – starting of the center recruitment period.
- January 1, 2021 – December 31, 2021: main data collection period.
- January 1, 2022 – February 28, 2022: study completion for the last potential follow-up.
- March 1, 2022 – May 31, 2022: “interim analysis” of complete data.
- June 1, 2022 – September 31, 2022: definitive statistical analysis.

Statistical Analysis

The report of this study was prepared following guidelines set by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational studies¹⁷. Statistical analysis was performed either with SPSS software [Released 2020, Version 27.0 (IBM Corp., Armonk, NY, USA)] for MacOSX or Sta-

taCorp2019 STATA Statistical Software: release 16 (StataCorp LLC, College Station, Texas, USA). First, data normality was tested using the Shapiro-Wilk test or Kolmogorov-Smirnov test. Dichotomous data and counts were presented in frequencies, whereas continuous data were presented as mean values±standard deviations (SD) and/or median with a 25-75 Interquartile Range (IQR) and minimum-maximum range. The 95% confidence interval was reported where appropriate. Differences between means were compared using the independent sample Student’s *t*-test, the pairwise comparison Student’s *t*-test, the Mann-Whitney U test, the Kruskal-Wallis’ test, or other analysis of variance (ANOVA) tests. Differences between medians were compared using the Kolmogorov-Smirnov test or a special application of the Pearson’s Chi-square test by using the median as a cut-off. To compare differences in frequencies, Fisher’s exact test or χ^2 test, with or without Yates correction, was performed. Receiver operating characteristic (ROC) curve analysis was performed to estimate the sensitivity and specificity of each score. If necessary, the linear correlation was assessed by Pearson’s or Spearman’s test. Multivariate analyses were performed using logistic regression models considering mortality and morbidity as dependent variables. A *p*-value <0.05 was considered statistically significant.

Results

Sample Size Assessment

Enrollment of at least 504 patients based on an assumed difference in discharge delay between the reference and the recruitable population of 6% (Δ 24-30%), considering a statistical power of 80% and an alpha error of 5%.

Expected Results

Identification of independent predictors of failure of early discharge within 24 hours after LC.

Ethical Aspects and Ethics Committee

The study was conducted following the Declaration of Helsinki and respecting the guidelines on good clinical practice. The study protocol was included in the “iFAIR program”: a project finalized for the dissemination of Findability, Accessibility, Interoperability, and Reuse of digital assets (FAIR) best practices among the clinical researchers in Sardinia (Italy). Before the data entry period, the study steering committee informed

the local investigators of the participating centers of the study, methodology, and aims¹⁸.

iFAIR project

This study is linked to the iFAIR project, aimed at setting up a virtual register, i.e., a “container” with metadata and research data, called the Regional Register for Biomedical Research (RRRB). The RRRB is a virtual platform that collects, processes, catalogs, conserves, and distributes metadata (labels) from scientific research. Researchers participating in this project had the opportunity to directly submit metadata, which represented the descriptive elements of multiple data sets, to the RRRB. The choice to share this type of element allows not to disperse the data already collected but not entirely used for research purposes and translates into the possibility of preventing other patients from being involved in new research and undergoing procedures of investigation, even minimally invasive or in any case burdensome due to the commitment they require¹⁸.

Privacy Policies

Each center collected data anonymously according to the current privacy regulations (Annex/Art. 13 of Legislative Decree 196/2003 “CODE REGARDING THE PROTECTION OF PERSONAL DATA”), use a progressive identification number and a unique code for any patient. All data collection forms were sent to a non-medical collaborator who accumulated them in a single general database, ensuring the anonymity of the patients and the center that sent them. The data and their processing phase were managed by the center promoting the study but at the disposal of the Principal Investigator of each center.

Publication Policy and Communication of Results

The results of the DeDiLaCo Study were disseminated through national and international conference presentations. Furthermore, additional studies and publications were performed to analyze specific aspects of the data that were presented. We are committed to ensuring that appropriate recognition is given to everyone who works on the study.

Discussion

Early discharge after LC leads to advantages both in terms of clinical outcomes and quality of life of the patient, and it is highly effective in terms of health costs and shortening the waiting list. In particular,

this is an essential topic after years of restriction due to the COVID-19 pandemic¹⁹⁻²³. However, clinical reality differs from the results of randomized studies by a complex series of non-objectionable real-world data influencing treatment plans. Therefore, defining which patients are suitable for early discharge is pivotal²⁴⁻²⁶. This study will contribute to the identification of possible clinical-pathological features, pathways, and psychosocial factors related to the failure of early discharge plans. Early discharge strategies after LC are currently practiced in many countries worldwide with varying penetration rates. In the UK, daytime LC, despite initial difficulties in establishing it as a standard practice, is now considered routine¹². The British Association of Day Case Surgery²⁷ recommends that at least 60% of LCs are performed as day cases to achieve optimal patient outcomes and cost-effectiveness. Increasing the number of elective LCs performed as day-cases to 75% was a crucial objective in the National Health System (NHS) plan issued by the UK Department of Health in 2015²⁸. Following these recommendations, data²⁹⁻³¹ from the UK show that 70 to 85% of patients undergoing LC are discharged home on the day of surgery. Equivalent results have also been achieved in other countries, such as the US³², after implementing same-day discharge protocols for LC. In Italy, since its introduction, the PNE has defined postoperative hospitalization less than three days after LC as a tool to assess the performances of the surgical units³³. This goal, reached in 2016 in 72.71% of cases, currently appears anachronistic and not stimulating for achieving new goals in the rest of the world.

Conclusions

In Italy, the vast majority of delayed discharges >24 hours after LC may not be related to surgical factors. We believe they can be prevented with a logistical reorganization and readjustment of the trust reimbursement policies. Many elements can contribute to reducing the length of hospitalization, in particular: acting with a reform of the reimbursement systems and educating patients and health professionals on the benefits and feasibility of early discharge after LC. In our opinion, the results of this study will help demonstrate that discharge ≤24 hours represents a valid therapeutic option for patients requiring LC, but this can only be achieved by creating an adequate performance indicator for surgeons and hospital managers and by educating patients before and after surgery with adequate discharge instructions.

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Ethics Approval

The Ethics Committee of the Azienda Tutela Salute (ATS) Sardegna approved the study protocol on 20 October 2020 with protocol number 271/2020/CE.

Informed Consent

Informed consent for participation and personal data management and transfer was obtained from the patients at admission.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

Authors have no competing interests to declare.

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Authors' Contributions

Nicola Cillara: Conception and design of the DeDiLaCo project and the DeDiLaCo study; Acted as study principal investigator and guarantor of the integrity and precision of the manuscript with the other co-authors; Acquisition, analysis, and interpretation of data for the study. Pietro Fransvea, Raffaele Sechi, Enrico Cicalò, Amedea Agnes, Giovanni Sotgiu, Maria Provenzano, Gaetano Poillucci, Mauro Podda: Review of the study critically for important intellectual contents; Final approval of the protocol version.

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