Journal of Research in Applied and Basic Medical Sciences 2025; 11(2): 186-192

Original Article

Urmia University of Medical Sciences

RABMS Journal of Research in Applied and Basic Medical Sciences

De novo ECG changes in patients without a history of heart problems presenting with acute cholecystitis: etiology and clinical importance

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Abstract

***Background & Aims*:** Acute cholecystitis, primarily an inflammatory condition of the gallbladder, has been associated with electrocardiographic (ECG) changes that mimic cardiac pathology. While laparoscopic cholecystectomy is a well-established treatment for acute cholecystitis, its potential impact on postoperative ECG changes in patients without pre-existing cardiovascular disease remains unclear. This study aims to investigate the incidence and nature of ECG alterations following laparoscopic cholecystectomy in patients without prior cardiac disease.

***Materials & Methods*:** In this single-arm cohort study, we reviewed 75 patients who underwent laparoscopic cholecystectomy for acute cholecystitis at Firouzabadi General Hospital between March 2020 and March 2021. Patients with pre-existing cardiac conditions or abnormal preoperative ECGs were excluded. A 12-lead ECG was performed within 48 hours before and 24 hours after surgery. ECGs were analyzed by a cardiologist and an internist, and discrepancies were resolved through consensus. The difference in the incidence of postoperative ECG changes was assessed using McNemar's Chi-Square test.

***Results*:** Among the 75 patients included (mean age: 47.38 ± 13.16 years, 74.7% female), four patients (5.3%) had benign T-wave inversions before surgery. Following surgery, 13 patients (17.3%) exhibited new ECG changes, including T-wave inversions (precordial: 5, limb leads: 5) and ST-segment depressions (precordial: 1, limb leads: 2). McNemar's Chi-Square test indicated a statistically significant increase in ECG changes postoperatively ($p = 0.012$). All patients were discharged without persistent ECG abnormalities or major postoperative complications.

***Conclusion*:** This study suggests a potential association between laparoscopic cholecystectomy and transient ECG alterations in patients without prior cardiac disease. Proposed mechanisms include gallbladder manipulation, sympathetic adrenergic stimulation, and laparoscopy-induced hemodynamic stress. Future studies with larger cohorts and control groups undergoing non-biliary laparoscopic surgeries are needed to delineate the effects of cholecystectomy from those of laparoscopy itself on cardiac electrophysiology.

***Keywords*:** Acute cholecystitis, Electrocardiographic changes, Laparoscopic cholecystectomy, Postoperative cardiac monitoring, Sympathetic stimulation

Received 10 February 2025; accepted for publication 25 March 2025

Introduction

Acute cholecystitis, characterized by gallbladder inflammation, manifests abruptly with severe upper abdominal pain, fever, nausea, and potential complications such as infections or gallbladder perforation. Surgical excision is the treatment of choice and ECG is an inseparable part of the preoperative anesthesiology assessment (1, 2). While the electrocardiogram (ECG) is a vital tool for detecting cardiac ischemia or arrhythmias, acute abdominal conditions such as acute cholecystitis, pancreatitis, gastric distension, and intestinal dilation have the potential to trigger dynamic ECG changes (3, 4). These alterations could potentially stem from sympathetic adrenergic activation, decreased intracellular potassium levels, or stimulation of proteolytic enzyme systems (5).

ECG changes in acute cholecystitis may resemble cardiac ischemia, presenting as ST-segment depression or T-wave inversions. (6-10) Additionally, biliary colic can lead to pronounced yet reversible reflexive slowing of the heart rate (known as Cope's sign), and in severe cases, may even result in complete heart block (11, 12).

However, several studies have reported patients who experienced ECG changes within a day of laparoscopic cholecystectomy, rather than before the surgery. It is unclear whether there is a correlation between ECG changes and laparoscopic cholecystectomy itself in patients without a history of cardiovascular diseases (13-15).

This study aims to elucidate the association between laparoscopic cholecystectomy and ischemic ECG changes by excluding patients with preoperative ECG changes or a history of cardiac diseases. It would aid clinicians in the appropriate management of *de novo* ECG changes in post-operative care.

Materials & Methods

Ethical Considerations

After obtaining approval (approval number: IR.IUMS.REC.1399.434) from the Iran University of Medical Sciences Ethical Board, we reviewed patients who underwent cholecystectomy for acute cholecystitis at Firoozabadi General Hospital between March 2020 and March 2021.

Study Design

We studied a single-arm cohort of patients with acute cholecystitis without any history of cardiac disease, who underwent cholecystectomy. A pre-specified checklist of risk factors was completed for all patients. Patients were required to be reviewed by a cardiologist for history and physical examination, specifically documenting the presence of ischemic heart diseases such as myocardial infarction (MI), coronary syndromes, heart failure, or hypertension. Complete blood count (CBC), creatinine, urea, electrolytes, chest X-ray, and a 12-lead ECG were obtained within 48 hours before surgery. Exclusion criteria included lack of consent, any history of established cardiac disease, or abnormal ECG findings suggestive of arrhythmia or ischemia based on the definitions by the AHA Standardization and Interpretation of the Electrocardiogram guidelines, adjudicated by a cardiologist. (16) Whether T-wave inversions were benign was judged based on the cardiac and social history (17, 18). All patients underwent standard laparoscopic cholecystectomy without any other concomitant procedures. Our primary goal was to detect any electrophysiological changes in heart activity, within 48 hours before and 24 hours after cholecystectomy. ECGs were reviewed separately by a cardiologist and an internist, and discrepancies were resolved through discussion. Results were reported according to the AHA standards document for ischemia/infarction. (16)

Statistical Analysis

Descriptive statistics were presented as mean and standard deviation for continuous data and frequencies with percentages for categorical data. McNemar’s Chi-square test was used to assess the change in the incidence of ECG findings before and after surgery. All statistical analyses were performed using SPSS statistical software version 26 (IBM). A two-sided $P < 0.05$ was considered statistically significant. Data were analyzed from March 20th, 2020, through March 20th, 2021.

Results

Overall, 502 patients underwent cholecystectomy due to acute cholecystitis from March 2020 to March 2021; 75 of them met the eligibility criteria for our study. The average age of the participants was 47.38 (± 13.16). Our population consisted mostly of women (74.7%). Table 1 presents our patients' demographics.

Table 1. Demographics and baseline characteristics

Characteristics	Mean (SD)/N (%)
N	75
Age	47.38 (13.16)
Sex (female)	56 (74.7)
Weight (kg)	64.6 (7.6)
Height (cm)	164.8 (6.9)
BMI	23.7 (1.61)
Smoking	11 (14.7)
Pain location	
- Epigastric	- 24 (32)
- Right Upper Quadrant	- 51 (68)
Nausea	56 (74.7)
Fever	9 (12)

Patients with arrhythmia or ischemic ECG changes were excluded from our study. Four patients had precordial T-wave inversion preoperatively. In the absence of clinical findings or a remarkable cardiac history, these were deemed benign and did not reappear in post-operative ECGs.

As shown in Table 2, after the surgery, 10 patients developed new T-wave inversions in contiguous leads. Additionally, three patients developed ST-segment depressions. Follow-up of patients did not show any unresolved ECG changes at the time of discharge. All patients were successfully discharged within 2 to 5 days, without significant post-operative complications.

Table 2. Distribution of leads and types of ECG change before and after cholecystectomy

ECG change	Type of ECG change	Frequency (N)	Total
Before surgery	T-wave inversion (Precordial)	4	4.75 (5.3%)
	ST-Depression (Precordial)	0	
	T-wave inversion (Limb)	0	
	ST-Depression (Limb)	0	
After surgery	T-wave inversion (Precordial)	5	13.75 (17.3%)
	ST-Depression (Precordial)	1	
	T-wave inversion (Limb)	5	
	ST-Depression (Limb)	2	

Table 3 presents McNemar's Chi-square test of these paired observations, which suggests a significant difference before and after cholecystectomy in patients with previously unremarkable ECG changes.

Table 3. McNemar's Chi-Square test on before vs. after cholecystectomy ECG changes

ECG changes	Condition	N	%	*P-value*
Before surgery	Yes	4	5.3	0.012*
	No	71	94.7	
After surgery	Yes	13	17.3	
	No	62	82.7	

*$P < 0.05$

Discussion

Our single-arm cohort of acute cholecystitis patients suggests that laparoscopic cholecystectomy may correlate with new ECG changes in individuals without a history of cardiac disease. Three potential mechanisms are hypothesized for this observation:

1. Acute cholecystitis: Previous research has documented instances where acute cholecystitis induced ECG changes that mimicked cardiac ischemia (19-22). These studies have emphasized the need for careful evaluation to differentiate abdominal from cardiac etiology in patients presenting with concurrent ECG changes, such as Wellens' type A (biphasic T wave in leads V2 and V3) (23, 24) and T-wave inversions (20, 25-27), or even transient elevations in cardiac enzymes pre-operatively (20). Animal studies on the other hand, have shown that gallbladder distension, could potentially decrease blood flow to the heart, elevate heart rate, and raise arterial blood pressure, causing myocardial ischemia and subsequently, ECG changes in the ST segment (28, 29).
2. Laparoscopic cholecystectomy: Fillippou et al. conducted a large prospective cohort study of 500 laparoscopic cholecystectomy patients with per-existing cardiac disorders in 2004 and observed a 3% rate of ECG changes, namely LV strain, AF, RBBB, and ST-depression, regardless of the amount of insufflated gas, history of cardiovascular disease, or intra-abdominal pressure (13). Other observations, however, are on a much smaller scale. O'Leary et al. observed ECG changes in one of a 16- patient cholecystectomy series without any cardiac history, in the form of ST-depression (15). Conversely, two other observational studies of laparoscopic cholecystectomy patients did not report any ECG changes in patients without prior cardiac problems, with sample sizes of 50 and 15 patients, respectively (30, 31). Finally, a comparative study by Chopra et al. between elective laparoscopic and open cholecystectomy in 60 randomized patients did not report any ECG changes in either group (32). This may be due to the small sample size of 60 patients.
3. Abdominal laparoscopy: It is noteworthy that abdominal laparoscopy itself might cause transient ECG changes regardless of the procedure site. Todesco et al. found that in a cohort of 63 patients undergoing laparoscopy for liver disease, 24 patients experienced T-wave flattening or inversion and four more had ST-depressions (44.4% in total). After deflation, ECG changes were reduced to 17 and one case, respectively (28.6%). Nonetheless, only four (6%) cases had contiguous T-wave inversions (33). Kim et al. also reported a prolonged QTc interval in a series of 28 laparoscopic gastrectomy patients without previous cardiac problems, attributing this to prolonged sympathetic stimulation due to extended pneumoperitoneum and intra-abdominal pressure required for robotic gastrectomy (14).

As literature suggests, transient arrhythmias are common during laparoscopic procedures. Therefore, there may be an overlap of effects between cholecystectomy and laparoscopy, with over-stimulation of the sympathetic system being a common factor.

Future studies could aim to differentiate the effects of cholecystectomy from laparoscopy in general regarding post-operative *de novo* ECG changes. Several improvements could be made to this study:

First, the addition of a control laparoscopic arm, such as gynecologic or bariatric surgery, would help assess the effect of laparoscopy as a surgical method on cardiac electrophysiology.

Second, measurement of high-sensitivity troponin—which correlates with cardiac strain—along with quantified CRP levels to stratify for inflammation. Correlations could then be investigated, and subgroup analysis based on these two markers would allow for the calculation of a dose-response incidence rate.

Conclusion

Our study suggests that laparoscopic cholecystectomy may be linked with new ECG changes. Stretching of the gallbladder muscles, surgical manipulation of the gallbladder, and over-stimulation of the sympathetic system due to insufflation in the laparoscopic method are some of the proposed mechanisms for the observed phenomenon. It would be wise to interpret post-cholecystectomy ECGs with caution and avoid their routine use, as transient ischemia-mimicking changes are likely to be present.

Acknowledgments

We would like to kindly thank the personnel of Firoozabadi General Hospital for their efforts.

Ethical statement

This study was conducted in accordance with the Declaration of Helsinki guidelines. Ethical clearance was obtained from the Ethical Committee of Iran University of Medical Sciences (Approval No.: IR.IUMS.REC.1399.434). Prior to enrollment, all participants provided written informed consent.

Data availability

The data supporting this study's findings are available from the corresponding author upon request. Due to the confidential nature of certain information, some restrictions may apply.

Conflict of interest

The authors affirm that they have no competing interests associated with this research.

Funding/support

This study did not receive any external financial support from governmental, commercial, or non-profit organizations.

Author contributions

Mohammad Amin Abbasi and Shahin Keshtkar Rajabi enrolled the patients and reviewed their ECGs before and after surgery. Nogol Motamed-Gorji, Nima Azh, and Shadab Dalirani collected post-operative patient data. Nima Azh analyzed the data. Shadab Dalirani and Nima Azh prepared the manuscript.

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