

Ultrasonographic Gallbladder Wall Thickness as a Pathophysiological Predictor of Surgical Outcome in Laparoscopic Cholecystectomy: A Prospective Study

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ABSTRACT

Background: Laparoscopic cholecystectomy (LC) is the gold standard treatment for symptomatic gallstone disease. Gallbladder wall thickness (GBWT) is a well-established pathophysiological marker reflecting the degree of mural inflammation and fibrosis, and is an important preoperative predictor of surgical difficulty. Thickened gallbladder walls are frequently associated with higher rates of intraoperative complications and prolonged hospital stays.

Objectives: To assess the relationship between preoperative ultrasonographic GBWT and the pathophysiological and clinical challenges encountered during laparoscopic cholecystectomy.

Patients and Methods: A prospective study conducted on 144 patients who underwent LC at the Surgical Department of Al-Hussain Teaching Hospital and Al-Nassiriya Teaching Hospital, Nasiriyah, Iraq, from January 2023 to July 2024. GBWT was classified by ultrasonography as normal, mild, moderate, or severe. LC difficulty was assessed based on operative time, intraoperative complications, and the ability to achieve the critical view of safety (CVS).

Results: LC was classified as easy in 58.33% and difficult in 41.67% of cases. Difficult LC was significantly associated with male sex (21.67% vs. 3.57%, $p=0.001$), higher BMI (30.29 ± 3.08 vs. 28.71 ± 3.95 , $p=0.011$), elevated WBC count ($p=0.001$), pericholecystic fluid (35% vs. 7.14%, $p<0.001$), and moderate/severe GBWT ($p<0.001$). Moderate/severe GBWT was present in 18% of cases and was significantly associated with older age (48.19 ± 13.36 vs. 41.62 ± 11.45 years, $p=0.011$), male sex ($p=0.032$), hypertension ($p=0.002$), leukocytosis ($p=0.016$), pericholecystic fluid ($p<0.001$), prolonged operative time ($p<0.001$), adhesions ($p<0.001$), hemorrhage ($p=0.045$), and postoperative collection ($p=0.010$).

Conclusions: GBWT is a significant preoperative pathophysiological predictor of LC difficulty. Moderate to severe GBWT is associated with higher rates of intraoperative and postoperative complications. Preoperative identification of GBWT by ultrasonography enables better patient counselling and surgical planning.

Keywords: laparoscopic cholecystectomy; gallbladder wall thickness; difficult cholecystectomy; intraoperative complications; ultrasonography; pathophysiology.

1. Introduction

Laparoscopic cholecystectomy (LC) is the gold standard for the surgical management of symptomatic gallstone disease, having replaced open cholecystectomy since the early 1990s due to its well-established

advantages: shorter hospital stay, earlier return to normal activity, improved cosmesis, and significantly reduced postoperative pain [1]. Gallbladder wall thickness (GBWT), as measured preoperatively by abdominal ultrasonography, has emerged as an independent predictor of LC outcome. Most investigators use a threshold of GBWT >3 mm or >4 mm as indicative of increased surgical risk [2], while a GBWT \geq 5 mm has been specifically associated with a substantially higher likelihood of postoperative complications and prolonged operative time [3]. GBWT is not merely a technical measurement; it reflects the underlying pathophysiological state of the gallbladder wall, representing the degree of acute or chronic inflammation, mural ischemia, fibrosis, and subserosal oedema [4].

The normal gallbladder wall consists of four distinct histological layers: mucosa, lamina propria, an irregular muscular layer, and a serosa of loose connective tissue. On ultrasound, it appears as a thin echogenic line measuring no more than 3 mm in a fasting, adequately distended gallbladder.[8] On computed tomography (CT), the normal wall is visible as a thin rim of soft tissue density with homogeneous contrast enhancement.[4] Mural thickening is defined sonographically as a transverse wall measurement \geq 4 mm and may present with a layered or "sandwich-like" configuration on CT, reflecting subserosal oedema between the enhancing mucosal and serosal layers.[6] Differentiating subserosal oedema from pericholecystic fluid, and distinguishing inflammatory from neoplastic thickening, often requires a multimodality imaging approach [4],[7].

Diffuse GBWT (\geq 3 mm by ultrasound) arises from a wide spectrum of conditions. Primary inflammatory causes include acute calculous cholecystitis, acalculous cholecystitis, and chronic cholecystitis; the last of these is characterised by recurrent cycles of obstruction, inflammation, and fibrosis resulting in a permanently thickened, contracted gallbladder [9],[11].

Secondary causes include adjacent inflammatory processes such as acute pancreatitis and hepatitis, as well as systemic conditions including cardiac failure, hepatic cirrhosis with portal hypertension, renal failure, and sepsis [7],[13]. Neoplastic causes, notably gallbladder adenocarcinoma, account for approximately 90% of malignant gallbladder tumours and may present as asymmetric or irregular focal wall thickening exceeding 10 mm.[15,16] Focal thickening has a narrower differential including adenomatous polyps, focal adenomyomatosis, and xanthogranulomatous cholecystitis, the latter being a rare pseudotumoral form of chronic calculous cholecystitis associated with bile leakage into the gallbladder wall [18,20].

The clinical relevance of GBWT as a predictor of intraoperative difficulty has been demonstrated in multiple studies. Kania demonstrated that sonographic GBWT was directly associated with the rate of conversion from laparoscopic to open cholecystectomy [21]. A meta-analysis by Yang et al. on 14,545 laparoscopic cholecystectomies confirmed that preoperative GBWT was a significant predictor of conversion [22]. Kokoroskos et al. conducted a prospective study of 1,089 patients and showed that histopathological wall thickness exceeding 7 mm was strongly linked to intraoperative complications, including surgical drain placement, conversion to open surgery, bile spillage, major haemorrhage, and common bile duct injury; both moderate and severe wall thickening independently predicted hospital stay exceeding four days [25].

Khan et al. further quantified the impact of GBWT severity on operative outcomes and demonstrated a stepwise increase in complications with increasing wall thickness.[23] The pathophysiological mechanism underlying these associations is the progression from recurrent cholecystitis to pericholecystic adhesion formation and obliteration of Calot's triangle, which renders the critical view of safety (CVS) difficult or impossible to achieve [24].

Despite this accumulating evidence, prospective data from Iraq documenting the relationship between ultrasonographic GBWT and LC outcomes remain scarce, particularly from the southern provinces. The present study was therefore conducted to prospectively assess the relationship between preoperative

GBWT, classified by ultrasonography, and the intraoperative and postoperative challenges of laparoscopic cholecystectomy in a cohort of patients from Nasiriyah, southern Iraq.

2. PATIENTS AND METHODS

2.1. Study Design and Setting

This prospective cohort study was conducted at the Surgical Departments of Al-Hussain Teaching Hospital and Al-Nassiriya Teaching Hospital, Nasiriyah, Dhi Qar, Iraq, from January 2023 to July 2024. Ethical approval was obtained from the Iraqi Council of Medical Specialization. Written informed consent was obtained from all participants.

2.2. Study Population

A total of 144 patients who underwent LC for gallbladder disease (calculous cholecystitis, cholelithiasis, or other inflammatory gallbladder conditions requiring surgery) were enrolled. Patients with a prior history of multiple abdominal surgeries or those unable to tolerate pneumoperitoneum due to cardiopulmonary disorders were excluded [26].

2.3. Preoperative Assessment and GBWT Classification

All patients underwent preoperative abdominal ultrasonography. GBWT was measured at the anterior gallbladder wall in a fasting patient and classified as: normal (≤ 3 mm), mild (>3 – 4 mm), moderate (>4 – 5 mm), or severe (>5 mm). Demographic data, comorbidities, body mass index (BMI), white blood cell (WBC) count, haemoglobin level, and presence of pericholecystic fluid were recorded.

2.4. Operative Technique and Difficulty Classification

All operations were performed by consultant general surgeons using the standard four-port laparoscopic technique. LC was classified as difficult if any of the following criteria were present: inability to achieve the critical view of safety (CVS), operative time ≥ 60 minutes, bile spillage, significant haemorrhage, iatrogenic bile duct injury, or conversion to open surgery[1,25].

2.5. Statistical Analysis

Data were analysed using SPSS version 25.0. Continuous variables were expressed as mean \pm standard deviation (SD) and compared using the independent samples t-test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test where appropriate. A p-value < 0.05 was considered statistically significant.

3. RESULTS

3.1 Patient Characteristics

Of the 144 patients, 124 (86.11%) were female and 20 (13.89%) were male, with a mean age of 42.79 ± 12.0 years (range: 18–85). The mean BMI was 29.37 ± 3.67 kg/m². Comorbidities included hypertension (HTN) in 22 (15.28%), diabetes mellitus (DM) in 9 (6.25%), and ischaemic heart disease (IHD) in 2 (1.39%). The mean Hb was 12.5 ± 1.33 g/dL and mean WBC was $8.96 \pm 3.11 \times 10^9$ /L. Pericholecystic fluid was present in 27 patients (18.75%). Mean operative time was 59.8 ± 16.72 minutes.

3.2 GBWT Distribution

Mean GBWT was 2.85 ± 1.66 mm (range: 1.0–7.0 mm). GBWT was classified as normal in 79 (54.86%), mild in 39 (27.08%), moderate in 18 (12.5%), and severe in 8 (5.56%) patients. Thus, 26 patients (18.06%) had moderate or severe GBWT.

3.3 LC Difficulty and Associated Factors

LC was classified as easy in 84 patients (58.33%) and difficult in 60 patients (41.67%). The most frequent intraoperative finding was adhesion (57 patients, 39.58%), followed by unclear CVS (32 patients, 22.22%), and haemorrhage (13 patients, 9.03%). Bile spillage occurred in 9 (6.25%), conversion to open surgery in 5 (3.47%), and iatrogenic injury in 3 (2.08%) patients [27]. Postoperatively, bile collection was recorded in 6 patients (4.17%) and jaundice in 2 (1.39%).

Table 1 presents comparisons of clinical and operative variables between easy and difficult LC groups. Male sex (21.67% vs. 3.57%, $p=0.001$), higher BMI (30.29 ± 3.08 vs. 28.71 ± 3.95 kg/m², $p=0.011$), elevated WBC count (9.92 ± 3.70 vs. $8.27\pm 2.41 \times 10^9/L$, $p=0.001$), pericholecystic fluid (35.0% vs. 7.14%, $p<0.001$), and moderate/severe GBWT (35.0% vs. 5.95%, $p<0.001$) were all significantly more common in the difficult LC group.

Table 1. Clinical and operative variables associated with LC difficulty

Variable	Easy LC (n=84)	Difficult LC (n=60)	p-value
Age, years (Mean±SD)	41.57±13.0	44.53±10.21	0.143
Male sex, n (%)	3 (3.57%)	13 (21.67%)	0.001
BMI, kg/m ² (Mean±SD)	28.71±3.95	30.29±3.08	0.011
WBC $\times 10^9/L$ (Mean±SD)	8.27±2.41	9.92±3.70	0.001
Pericholecystic fluid, n (%)	6 (7.14%)	21 (35.0%)	<0.001
Moderate/severe GBWT, n (%)	5 (5.95%)	21 (35.0%)	<0.001
Operative time, min (Mean±SD)	50.37±5.21	73.0±18.3	<0.001

Table 2 summarises intraoperative and postoperative complications stratified by LC difficulty. Adhesion (63.33% vs. 22.62%, $p<0.001$), haemorrhage (16.67% vs. 3.57%, $p=0.015$), conversion to open surgery (8.33% vs. 0%, $p=0.015$), and postoperative collection (10.0% vs. 0%, $p=0.004$) were all significantly more frequent in difficult LC cases.

Table 2. Intraoperative and postoperative complications according to LC difficulty

Complication	Easy LC (n=84)	Difficult LC (n=60)	p-value
Adhesion	19 (22.62%)	38 (63.33%)	<0.001
Hemorrhage	3 (3.57%)	10 (16.67%)	0.015
Bile spillage	2 (2.38%)	7 (11.67%)	0.308

Conversion to open surgery	0 (0%)	5 (8.33%)	0.015
Postoperative collection	0 (0%)	6 (10.0%)	0.004

3.3 Association of GBWT with Outcomes

Patients with moderate/severe GBWT were significantly older (48.19±13.36 vs. 41.62±11.45 years, p=0.011), more frequently male (23.08% vs. 8.47%, p=0.032), and more frequently hypertensive (34.62% vs. 11.02%, p=0.002). They also had significantly higher rates of leukocytosis (WBC >10×10⁹/L: 46.15% vs. 22.88%, p=0.016), pericholecystic fluid (38.46% vs. 14.41%, p<0.001), prolonged operative time ≥60 min (80.77% vs. 32.2%, p<0.001), adhesion (76.92% vs. 31.36%, p<0.001), haemorrhage (19.23% vs. 6.78%, p=0.045), and postoperative collection (15.38% vs. 1.69%, p=0.010). These data are summarised in Table 3.

Table 3. Association of demographic, clinical, and operative variables with GBWT severity

Variable	Normal/Mild (n=118)	Moderate/Severe (n=26)	p-value
Age, years (Mean±SD)	41.62±11.45	48.19±13.36	0.011
Male sex, n (%)	10 (8.47%)	6 (23.08%)	0.032
Hypertension, n (%)	13 (11.02%)	9 (34.62%)	0.002
Pericholecystic fluid, n (%)	17 (14.41%)	10 (38.46%)	<0.001
WBC >10×10 ⁹ /L, n (%)	27 (22.88%)	12 (46.15%)	0.016
Operative time ≥60 min, n (%)	38 (32.2%)	21 (80.77%)	<0.001
Adhesion, n (%)	37 (31.36%)	20 (76.92%)	<0.001
Hemorrhage, n (%)	8 (6.78%)	5 (19.23%)	0.045
Postoperative collection, n (%)	2 (1.69%)	4 (15.38%)	0.010

4. DISCUSSION

This prospective study evaluated the relationship between preoperative ultrasonographic GBWT and intraoperative difficulty and postoperative outcomes in 144 patients undergoing LC at two teaching hospitals in southern Iraq. Difficult LC was encountered in 41.67% of patients, a rate consistent with previously reported figures ranging from 14.5% to over 50% [38-40]. The wide variation in reported rates across the literature largely reflects differences in the definition of “difficult” LC and the case-mix of included patients.

Male sex and elevated BMI were identified as significant independent predictors of difficult LC in the present study. These findings are consistent with multiple published series. Bhandari et al. from Nepal [41], Philip Rothman et al. in a systematic review and meta-analysis [42], and Gupta and Jain from India [43] all identified male sex as an independent predictor of difficult LC. The predominance of female patients in LC series worldwide, combined with the greater degree of inflammatory change observed in males, likely underlies this association. In obese patients, increased abdominal wall thickness, excess

preperitoneal and omental fat, and fatty infiltration of the hepatoduodenal ligament significantly impair peritoneal entry, pneumoperitoneum establishment, and safe exposure of Calot's triangle, all of which contribute to higher conversion rates [46].

Elevated WBC count, a surrogate marker of active or advanced gallbladder inflammation, was significantly associated with difficult LC in the present study. Leukocytosis reflects the severity of the inflammatory response and, in advanced cases, may signal gallbladder wall ischaemia, gangrenous change, or incipient perforation, all of which render dissection technically hazardous [50]. Pericholecystic fluid, present in 35% of difficult versus only 7.14% of easy LC cases ($p < 0.001$), was also a strong predictor of difficulty, consistent with Di Buono et al [47], and Hassan et al. [45]. Pericholecystic fluid reflects active inflammation extending beyond the gallbladder wall and is associated with dense adhesion formation in Calot's triangle [28,29].

The present study confirms that GBWT is a key pathophysiological predictor of LC difficulty. Moderate and severe GBWT were present in 35.0% of difficult versus only 5.95% of easy LC cases ($p < 0.001$). This is consistent with Kokoroskos et al. [25], Yang et al. [22], and Kania [21], who all demonstrated an incremental relationship between GBWT and adverse surgical outcomes. The pathophysiological basis for this association is the progression from acute or chronic cholecystitis to irreversible fibrosis of the gallbladder wall and pericholecystic tissues. This process obliterates the anatomical planes of Calot's triangle, prevents achievement of the CVS, prolongs operative time, and increases the risk of haemorrhage and biliary injury [28-30]. Adhesion formation in Calot's triangle and at the gallbladder bed is the principal operative challenge, as confirmed in the present study where adhesions occurred in 63.33% of difficult versus 22.62% of easy LC cases.

With respect to the pathophysiological determinants of moderate/severe GBWT, older age, male sex, and comorbid hypertension were significantly associated in the present study. The association with older age likely reflects the accumulation of repeated inflammatory episodes over time and greater comorbidity burden [51]. Alotaibi similarly reported that GBWT was associated with both older age and male sex in a Saudi Arabian cohort [2]. The association with hypertension is biologically plausible: elevated leptin levels – consistently documented in hypertensive individuals – directly stimulate leptin receptors on the gallbladder wall, inducing localised inflammation, reducing gallbladder contractility, promoting bile stasis, and ultimately favouring gallstone formation and mural thickening [52-56]. These findings suggest that GBWT is not merely a structural measurement but a reflection of a complex systemic and local pathophysiological milieu.

The significantly higher rate of postoperative bile collection in patients with moderate/severe GBWT (15.38% vs. 1.69%, $p = 0.010$) supports a direct mechanistic link between mural pathology, intraoperative difficulty, and postoperative morbidity. Khan et al. reported that conversion to open surgery was more frequent in the thicker wall group, primarily due to dense inflammatory adhesions secondary to cholecystitis or gallbladder empyema making safe dissection impossible [23].

Salah and Yahia similarly found that GBWT was a significant predictor of LC difficulties in an East African cohort [56].

This study has several limitations. The sample size is modest and the study was confined to a single region of Iraq, which may limit generalisability. The classification of LC difficulty was based on a composite criterion set rather than a validated intraoperative scoring system such as the Parkland Grading Scale or the WSES intraoperative score [29]. Future prospective multicentre studies using standardised validated grading systems are warranted to confirm these findings.

5. CONCLUSIONS

Gallbladder wall thickness, as measured by preoperative ultrasonography, is a readily available and non-invasive pathophysiological predictor of laparoscopic cholecystectomy difficulty. Moderate to severe GBWT occurs in approximately 18% of patients and is independently associated with older age, male sex, hypertension, and elevated inflammatory markers. It is significantly linked to higher rates of intraoperative adhesions, haemorrhage, conversion to open surgery, and postoperative bile collection. Routine preoperative assessment and reporting of GBWT should be incorporated into patient counselling, consent, and surgical planning for all patients undergoing laparoscopic cholecystectomy.

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