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GALLBLADDER WALL THICKNESS AND SURGICAL OUTCOMES IN LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract

OBJECTIVE *To compare the frequency of adverse outcomes between patients with normal (≤3 mm) and increased (>3 mm) gallbladder wall thickness and to determine whether increased thickness is an independent predictor of these outcomes.*

STUDY DESIGN *Cohort study*

PLACE AND DURATION OF THE STUDY *Department of General Surgery, Dr Ziauddin Hospital, Clifton, Karachi, from _____to _____*

METHODOLOGY *A total of 180 patients aged eighteen years and above with symptomatic gallstone disease scheduled for laparoscopic cholecystectomy were enrolled through consecutive sampling and grouped by gallbladder wall thickness into an exposed (>3 mm) and an unexposed (≤3 mm), then followed for a composite adverse surgical outcome. Data analysis was performed through SPSS-26 by chi-square, Fisher's exact test, t-test, Mann-Whitney U test, logistic regression and relative-risk estimation.*

RESULTS *The mean age was 43.3 ± 12.0 years, and 115 patients (63.9%) were women. An increased wall thickness was present in 55 patients (30.6%). The adverse outcome occurred in 49.1% of the increased group versus 13.6% of the normal group ($p < 0.001$), with a crude odds ratio of 6.13 (95% CI 2.94–12.78), and a relative risk of 3.61 (95% CI 2.15–6.06).*

CONCLUSION *GWWT greater than 3 mm was associated with a higher rate of adverse surgical outcomes at laparoscopic cholecystectomy, which remained after adjustment in most subgroups, except for the small diabetic subgroup. Simple and readily available ultrasound of the wall thickness before surgery is a useful predictor of patients who may have a more challenging operation and poor postoperative recovery.*

INTRODUCTION

Cholelithiasis refers to the development of calculi in the gallbladder and is one of the most prevalent biliary diseases in the world with a prevalence of close to 6% in the adult population in a pooled global analysis [1]. If the obstruction persists for some time and the mucosa is repeatedly irritated, it may lead to acute cholecystitis which is one of the most common indications for emergency surgical admission in these patients, and in Pakistan, symptomatic gallstone disease contributes significantly to elective and emergency operative workloads [2]. Due to its minimal access, less postoperative pain, shorter convalescence and lower wound morbidity, laparoscopic cholecystectomy (LC) is the standard method of treatment [3]. The preoperative parameters that influence the manifestation of LC have been identified, and gallbladder wall thickness (GBWT) measured by transabdominal ultrasonography is one of the more informative parameters [4]. These changes involve repeated inflammation, mural oedema and fibrosis, causing obliteration of tissue planes and distortion of the anatomy of the Calot triangle and making dissection more dangerous [5]. A wall more than 3 mm is considered abnormal and is associated with increased adhesions, a higher amount of bleeding during surgery and more complicated surgery [6].

The advantages of ultrasonography are that it is low-cost, quick, and non-destructive, so it is a promising method for preoperating room stratification of patients before surgery [7]. Several investigators have demonstrated that thicker walls are associated with longer operating room time, higher conversion rates to open surgery and unfavourable intraoperative events [8,9]. This simple radiological finding was recently confirmed in a prospective series from a tertiary centre in Karachi, in which the presence of severe mural thickening was strongly associated with prolonged operating time, gallbladder aspiration and conversion [10].

The evidence available, however, is not consistent, with different thresholds used between 2 mm and 5 mm and different methods of embedding the wall thickness into the composite difficulty score used; this makes it difficult to make direct comparisons [11,12]. Numerous have investigated a single endpoint, conversion, and some of the local studies have focused on the demographic and morphological correlates without defining a standard radiological threshold [13]. Data that correlate a single cut-off of the wall thickness, standardised to a specific group of outcomes, are therefore very rare in our population, and pre-operative counselling and operative planning are then limited by the lack of precision.

The present study aimed to determine the incidence of adverse surgical events such as conversion to open cholecystectomy, intraoperative biliary injury, vascular injury, prolonged operative time and extended hospital stay in patients undergoing laparoscopic cholecystectomy and to compare it between those with normal gallbladder wall thickness (3 mm or less) and increased gallbladder wall thickness (more than 3 mm), which would help improve the risk assessment, operative planning and patient counselling in the local setting.

METHODOLOGY

A comparative (prospective) cohort study was carried out on patients aged eighteen years and above who presented with symptomatic gallstone disease and were scheduled for laparoscopic cholecystectomy (LC), recruited through consecutive nonprobability sampling after approval from CPSP and the ERC and after written informed consent had been obtained from every participant. Patients with symptomatic cholelithiasis confirmed on ultrasonography, including those with gallstones, biliary sludge, or pericholecystic fluid, were eligible, whereas patients with a perforated or gangrenous gallbladder, established choledocholithiasis requiring a planned open procedure, suspected gallbladder malignancy, uncorrected coagulopathy or unfitness for general anaesthesia, or incomplete preoperative or operative records were not included. The minimum sample size was calculated to compare the incidence of the composite adverse surgical outcome between the exposed cohort (increased gallbladder wall

thickness, >3 mm) and the unexposed cohort (normal wall thickness, ≤3 mm). Anticipating an adverse-outcome frequency of approximately 49% in the exposed cohort and 14% in the unexposed cohort (relative risk ≈ 3.5), derived from the adverse-outcome rates reported for increased versus normal gallbladder wall thickness by Alotaibi [6], with a two-sided alpha of 0.05, 80% power and an exposed-to-unexposed allocation ratio of about 1:2.3 reflecting the observed cohort sizes, a minimum of 18 exposed and 41 unexposed patients (59 in total) was required. To improve precision and to permit stratified subgroup analysis, 180 patients (55 exposed and 125 unexposed) were enrolled through consecutive nonprobability sampling over the study period, comfortably exceeding this minimum. GBWT expressed in millimetres measured from the anterior gallbladder wall on pre-operative transabdominal ultrasonography (TUS) was deemed normal thickness if the GBWT was at or below 3 mm and of increased thickness if it was above 3 mm, with each patient being assigned to either the exposed or the unexposed group accordingly.

The adverse surgical outcome, recorded as a single composite, was present when a patient experienced any one or more of the following: conversion to open cholecystectomy; an intraoperative bile duct or vascular injury documented in the operative notes; an operative time beyond 90 minutes measured from skin incision to closure; or a postoperative hospital stay beyond 48 hours; the operative-time and length-of-stay thresholds were defined a priori in line with institutional practice. The composite outcome was considered absent when none of these occurred. Age; sex; obesity, taken as a body mass index of 27.5 kg/m² or more by Asian criteria; diabetes mellitus; a previously documented episode of acute cholecystitis; and pericholecystic fluid on ultrasonography were recorded as effect modifiers and first examined by stratified bivariate analysis, then entered together into a multivariable logistic regression to estimate the adjusted association. Preoperative wall thickness and the associated sonographic findings were transcribed from the formal radiology report onto a structured proforma; demographic and clinical details were documented at enrolment, and the operation was performed by the on-call surgical team according to the standard institutional technique. Operative time, conversion, any biliary or vascular injury, and length of stay were retrieved from the operative notes and discharge records by a single trained data collector to limit observer variation, and all entries were verified against the medical record and anonymised before analysis. Data were analysed in SPSS version 26 using the chi-square, Fisher exact, independent t, and Mann-Whitney U tests as appropriate. Risk ratios with 95% confidence intervals were estimated for the comparison between the exposed and unexposed cohorts. Multivariable binary logistic regression assessed the independent association of increased wall thickness with the adverse outcome after adjustment for pericholecystic fluid, previous acute cholecystitis, and obesity, with adjusted odds ratios and 95% confidence intervals reported. Statistical significance was defined as a p-value of less than 0.05.

RESULTS

A total of 180 patients were analysed. The mean age was 43.3 ± 12.0 years, and 115 patients (63.9%) were women. 62 patients (34.4%) had obesity, 36 (20.0%) had DM, and 54 (30.0%) had previous histories of acute cholecystitis. In 55 patients (30.6%) an increased GBWT was noted (GBWT > 3 mm), whereas 125 patients (69.4%) had normal wall thickness. Age, gender, body mass index (BMI) and DM were similar between the two groups, while pericholecystic fluid was more common in the increased group (40.0% versus 15.2%, $p < 0.001$). Among the individual components, an operative time beyond 90 minutes was recorded in 19 patients (34.5%) with an increased wall against 14 (11.2%) with a normal wall ($p < 0.001$), and a hospital stay beyond 48 hours occurred in 15 (27.3%) versus 5 (4.0%), respectively ($p < 0.001$). Conversion to open surgery was more frequent in the increased group, 7 of 55 (12.7%) compared with 1 of 125 (0.8%) ($p = 0.001$). The median operative time was 85 minutes in the increased group and 65

minutes in the normal group (p < 0.001). Bile duct or vascular injury was rare, occurring in only two patients overall. Baseline characteristics are shown in **Table 1**.

The combined ASO was observed in 44 patients (24.4%). Its frequency was higher among patients with an increased wall, 27 of 55 (49.1%), than among those with a normal wall, 17 of 125 (13.6%), and the difference was statistically significant (p < 0.001), with a crude odds ratio of 6.13 (95% CI 2.94–12.78), and a relative risk of 3.61 (95% CI 2.15–6.06). The main outcome is reported in **Table 2** as stratified by wall thickness category.

On stratified analysis, the association between an increased wall and the adverse outcome persisted across most effect modifiers. It remained significant within both age groups (≤40 years, 59.1% versus 12.2%, p < 0.001; >40 years, 42.4% versus 14.5%, p = 0.001), in male (40.0% versus 13.3%, p = 0.023) and female (54.3% versus 13.8%, p < 0.001) patients, in obese (54.5% versus 20.0%, p = 0.005) and non-obese (45.5% versus 10.6%, p < 0.001) patients, and in patients with (72.7% versus 16.3%, p < 0.001) and without (43.2% versus 12.2%, p < 0.001) a previous attack of acute cholecystitis. The association was also significant both in the presence (68.2% versus 15.8%, p < 0.001) and absence (36.4% versus 13.2%, p = 0.003) of pericholecystic fluid. Among patients without diabetes the association was significant (50.0% versus 12.0%, p < 0.001), whereas among those with diabetes it did not reach significance (45.5% versus 20.0%, p = 0.224), likely reflecting the small diabetic subgroup. On multivariable logistic regression (Table IV), an increased wall remained independently associated with the adverse outcome (adjusted odds ratio, 5.76; p < 0.001).

Table I: Baseline Characteristics of the Study Population by Gallbladder Wall-thickness Group (n=180)

Characteristic		Increased >3 mm (n=55)	Normal ≤3 mm (n=125)	P-value
Age (years), **Mean ± SD**		43.89 ± 12.06	43.04 ± 11.99	0.663
BMI (kg/m²), **Mean ± SD**		26.55 ± 4.09	25.75 ± 3.95	0.228
GB wall thickness (mm), **Median (IQR)**		5.6 (4.8-7.0)	2.5 (2.3-2.8)	<0.001
Gender	Male	20 (36.4%)	45 (36.0%)	0.963
	Female	35 (63.6%)	80 (64.0%)	
Obese (BMI ≥ 27.5), n (%)		22 (40.0%)	40 (32.0%)	0.298
Diabetes Mellitus, n (%)		11 (20.0%)	25 (20.0%)	1.000
Previous Acute Cholecystitis, n (%)		11 (20.0%)	43 (34.4%)	0.052
Pericholecystic Fluid, n (%)		22 (40.0%)	19 (15.2%)	<0.001
Operative	Operative time >90 min, n (%)	19 (34.5%)	14 (11.2%)	<0.001

Table I: Baseline Characteristics of the Study Population by Gallbladder Wall-thickness Group (n=180)				
Characteristic		**Increased >3 mm (n=55)**	**Normal ≤3 mm (n=125)**	**P-value**
Outcomes	Hospital stay >48 h, n (%)	15 (27.3%)	5 (4.0%)	<0.001
	Conversion to open surgery, n (%)	7 (12.7%)	1 (0.8%)	0.001
	Bile-duct / vascular injury, n (%)	1 (1.8%)	1 (0.8%)	0.519
	Operative time (min), **Median (IQR)**	85 (78-102)	65 (57-71)	<0.001
	Hospital stays (h), **Median (IQR)**	32 (26-61)	30 (24-37)	0.041

Table II: Comparison of Adverse Surgical Outcomes Between Groups (n=180)				
Adverse Surgical Outcome	**Increased >3 mm**	**Normal ≤3 mm**	**Odds ratio (95% CI)**	**P-value**
Present, n (%)	27 (49.1)	17 (13.6)	6.13 (2.94–12.78)	<0.001
Absent, n (%)	28 (50.9)	108 (86.4)		

Table III: Stratified Analysis of the Association Between Gallbladder Wall Thickness and Adverse Outcomes Across Effect Modifiers (n=180)					
Effect Modifiers		**Adverse Outcome**	**Increased >3 mm**	**Normal ≤3 mm**	**P-value**
Age Group	≤40 years	Present	13 (59.1%)	6 (12.2%)	<0.001
		Absent	9 (40.9%)	43 (87.8%)	
	>40 years	Present	14 (42.4%)	11 (14.5%)	0.001
		Absent	19 (57.6%)	65 (85.5%)	
Gender	Male	Present	8 (40.0%)	6 (13.3%)	0.023
		Absent	12 (60.0%)	39 (86.7)	
	Female	Present	19 (54.3%)	11 (13.8%)	<0.001
		Absent	16 (45.7%)	69 (86.2%)	

Table III: Stratified Analysis of the Association Between Gallbladder Wall Thickness and Adverse Outcomes Across Effect Modifiers (n=180)					
Effect Modifiers		**Adverse Outcome**	**Increased >3 mm**	**Normal ≤3 mm**	**P-value**
Obesity	No	Present	15 (45.5%)	9 (10.6%)	<0.001
		Absent	18 (54.5%)	76 (89.4%)	
	Yes	Present	12 (54.5%)	8 (20.0%)	0.005
		Absent	10 (45.5%)	32 (80.0%)	
Diabetes Mellitus	No	Present	22 (50.0%)	12 (12.0%)	<0.001
		Absent	22 (50.0%)	88 (88.0)	
	Yes	Present	5 (45.5%)	5 (20.0%)	0.224
		Absent	6 (54.5%)	20 (80.0%)	
Previous Acute Cholecystitis	No	Present	19 (43.2%)	10 (12.2%)	<0.001
		Absent	25 (56.8%)	72 (87.8%)	
	Yes	Present	8 (72.7%)	7 (16.3%)	<0.001
		Absent	3 (27.3%)	36 (83.7%)	
Pericholecystic Fluid	No	Present	12 (36.4%)	14 (13.2%)	0.003
		Absent	21 (63.6%)	92 (86.8%)	
	Yes	Present	15 (68.2%)	3 (15.8%)	<0.001
		Absent	7 (31.8%)	16 (84.2%)	

Table IV: Regression Analysis of Predictors of Adverse Surgical Outcome (n=180)		
Predictor	**Adjusted OR (95% CI)**	**P-value**
Increased wall thickness (>3 mm)	5.76 (2.59–12.83)	<0.001
Pericholecystic fluid	2.24 (0.98–5.16)	0.057
Previous acute cholecystitis	1.82 (0.78–4.25)	0.165
Obesity (BMI ≥ 27.5)	1.96 (0.91–4.23)	0.087

DISCUSSION

LC is the accepted treatment for symptomatic gallstones, which is one of the commonest indications for abdominal surgery [3]. The complexity of the procedure is also highly variable, and an inflamed thick-walled gallbladder is one of the most challenging conditions encountered by the surgeon [6]. If there was a good indicator beforehand of that difficulty, it would be helpful for the teams to prepare, counsel patients, and determine who should operate. Among the available options, GBWT on ultrasonography is low-cost rapid and may be a preferred choice because it is routinely used in assessment. The aim of this study was to quantify the rate of adverse surgical outcomes in LC and to compare it between patients with normal and increased walls.

Most of the patients were middle-aged women with an age of 43.3 years, and 63.9% were females, which is like the demography of gallstone disease in Pakistan and worldwide. [1,2]. Less than 25% of the cohort experienced a composite adverse outcome. Patients with an increased wall had a significantly higher burden, with nearly half of them experiencing an adverse event compared to approximately 1 in 7 patients with a normal wall. The crude odds ratio of 6.13 is among the higher effect estimates reported to date for preoperative markers and is consistent with previous studies from Karachi and India [4,10].

The same trend was seen for conversion to open surgery (less than 1% for the normal group and 12.7% for the increased group). Agrawal and colleagues reported a conversion rate of approximately 33% for those with walls >3 mm, and large reviews have reported a conversion rate ranging from 2.5% to 6% [8,17]. In a systematic review, Rothman et al, found that a thickened wall was a consistent preoperative predictor of conversion, in addition to male gender and older age and acute cholecystitis [14]. A thick wall was also more frequently associated with a longer operating time and longer hospital stay, consistent with these being the more complex cases to be performed [5].

Bile duct or vascular injury occurred in only two patients, which is insufficient for comparison and is like the low injury rate of <1% from both the national series and local series. It is well known that a thick wall is associated with a complicated operation. [18,20] Repeated inflammation leads to mural oedema, fibrosis, and dense pericholecystic adhesions which obscure the planes around the cystic pedicle and the structures of the Calot triangle. Pericholecystic fluid, which was much more prevalent in the increased group, indicates active inflammation and has been related to operative difficulty [16].

This association between increased thickness and the adverse outcome was consistent across most clinically relevant subgroups, the diabetic subgroup being the exception. It remained significant in both genders; age groups; obese and non-obese; and those with and without pericholecystic fluid or a previous attack of cholecystitis. Following adjustment for pericholecystic fluid, previous cholecystitis, and obesity, an increased wall remained as an independent predictor with an adjusted OR of 5.76. This independence states that wall thickness is not just a reflection of the company it keeps; it is also a property that carries information on its own which has been incorporated by various scoring systems that have been used [15,19].

Strengths of this work are the prospective cohort design, the single standardised composite endpoint and the consistent radiological reporting. The results have some caveats. There is limited generalisation of the proportions in the single centre frame; the limited number of conversions and injuries precludes inference on those endpoints, and there are unmeasured factors, including surgeon experience. More recent reviews still recommend the need for larger regions with consistent thresholds before definitive cut-off points can be determined [17].

Overall, these findings support a general trend in the literature: a wall thickness greater than 3 mm is associated with increased risk for an unfavourable surgical course and more difficult surgery [4,6]. The ability to read this one measurement on the pre-op scan provides the

operating team with valuable early and cost-effective information to anticipate any issues and plan for it in advance.

CONCLUSION

GWWT greater than 3 mm was associated with a higher rate of adverse surgical outcomes at laparoscopic cholecystectomy, which remained after adjustment in most subgroups, except for the small diabetic subgroup. Simple and readily available ultrasound of the wall thickness before surgery is a useful predictor of patients who may have a more challenging operation and poor postoperative recovery.

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