## ORIGINAL ARTICLE

# **Does the Difficulty of Laparoscopic Cholecystectomy Differ Between Genders?**

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Abstract Some studies have shown that severe fibrosis and anatomical anomalies are more common in men, and subsequently, laparoscopic cholecystectomy is more difficult in male than female patients. We aimed to evaluate the effect of gender in patients who underwent laparoscopic cholecystectomy, with regard to the conversion rate, the differences in histological inflammation severity, and anatomical difficulty. We reviewed retrospectively 915 patients with symptomatic cholelithiasis who underwent laparoscopic cholecystectomy in the First Department of General Surgery at Vakif Gureba Training and Research Hospital. Patients were divided into male (group 1) and female (group 2) groups. Both groups were compared with demographic criteria, the type of inflammation found on resected gallbladder, anatomical difficulty, gallbladder perforation during the operation, length of operation time, conversion rate, and omental and organ adhesions to the gallbladder. Of the 915 patients, 173 patients (19%) were males (group 1), and 742 (81 %) were females (group 2). Mean age was  $53\pm12$ (range 22 to 80)years in group 1 and 49±13 (range 17 to 85) years in group 2. The average duration of surgery was  $71\pm33$  min (range 20 to 160) in group 1 and  $58\pm27$  min (range 15 to 135) in group 2 (p < 0.001). The conversion rate between

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G. Sahin Department of Surgery, Private Ethica Hospital, Istanbul, Turkey groups was significantly different (p < 0.05). Inflammatory findings (acute or chronic) in resected gallbladder between groups 1 and 2 were significantly different (p < 0.0001 and p < 0.05, respectively). The frequency of adhesions between the gallbladder and omentum and other organs was higher in male (p=0.003 and p=0.0006, respectively). Anatomical difficulty was more prominent in male patients (p < 0.0001). The findings of higher scores of anatomical difficulty in operation and inflammation in cholecystectomy specimens, as well as higher rates of conversion in males, suggested that laparoscopic gallbladder surgery is more difficult in men.

Keywords Laparoscopic cholecystectomy  $\cdot$  Gender  $\cdot$  Operation time  $\cdot$  Conversion

#### Introduction

Laparoscopic cholecystectomy (LC) is the gold standard for treatment of cholecystitis due to short hospital stay, decreased postoperative pain, and improved cosmesis. Apart from many technological advances and experiences, conversion to laparotomy during LC to minimize the complications is still encountered. The conversion rate is reported between 3 and 24 %, and acute cholecystitis, severe fibrosis, male gender, obesity, older age, and technical difficulties are the most common associated risk factors [1-5]. The most important factor affecting the decision to convert open surgery is the anatomical "changes" like adhesions and distortions due to the severe fibrosis induced by inflammation. Although true anatomical anomalies in biliary and vascular system (i.e., aberrant biliary channels, duct of Luschka, and aberrant or accessory cystic artery) are rather rare, many reported variations in biliovascular tree may also lead to conversion to avoid the injury [6]. Male patients have increased risk for the severity of cholecystitis [7]. In fact, severe fibrosis and anatomical

changes due to the inflammation are more common in men, and hence, LC is more difficult in these patients [7–9]. Whereas some series reported that male gender carried an increased risk for conversion [10–12], there are still others who claimed inconclusive effect of gender on conversion [13, 14]. Here, we studied the effect of gender on inflammation severity of gallbladder, anatomical strains imposed by inflammation, subsequent conversion rate, and morbidity in patients who underwent LC.

#### **Materials and Methods**

We studied 915 patients with symptomatic gallstones, who underwent LC between July 1997 and May 2005, in the First Department of General Surgery at Vakif Gureba Training and Research Hospital. The spectrum of study group included the patients with biliary colic and cholecystitis except the acute flare of inflammation since we had adopted a policy of conservative treatment (i.e., bowel rest, antibiotics, and IV therapy) to relieve the acute phase of cholecystitis during the indicated period. Two months later, the patients were re-admitted for LC. The patients with acute cholecystitis requiring urgent operations, such as with perforations and gangrenous cholecystitis with peritoneal findings confirmed by clinical, laboratory, and radiological examinations, were excluded from the study. Moreover, patients with malignancy, other surgical pathologies detected at the exploration, and with common bile duct exploration were also excluded.

Preoperative evaluation of patients included routine blood tests, electrocardiogram, posteroanterior chest X-ray, and abdominal ultrasonography. White blood cell (WBC) count; total, direct, and indirect bilirubin; aspartate aminotransferase (AST); alanine aminotransferase (ALT); gamma-guanosine triphosphate (GGT); lactate dehydrogenase (LDH); and amylase values were all noted. Computed tomography, magnetic resonance imaging, and endoscopic retrograde cholangiopancreatography were used only when indicated. Antibiotic prophylaxis was not used routinely. The standard LC with four ports was performed in patients with pneumoperitoneum. The surgical team consisted of six consultant surgeons and four residents. The residents performed the operation under the supervision of a consultant surgeon. All surgeons had already fulfilled their learning curve of 50 LC by the time the study was conducted. The team used a standard definition of operative findings such as adhesions, the severity of inflammation, anatomical strain, etc., agreed upon for the operation records. The decision to conversion was left to the operating surgeon. The routine postoperative care was assigned for all patients. The demographic data, intraoperative records, and final pathology reports were retrieved from patient's medical files. The intraoperative records were used to retrieve information about the operative findings, complications during surgery like perforation of the gallbladder, length of operation, and conversion to open surgery. The adhesion scoring was performed using the operative records defined earlier. Patients were divided into two groups according to the gender: male (group 1) and female (group 2) groups. Both groups were compared in terms of age, the severity of gallbladder inflammation, anatomical difficulty, gallbladder perforation during the operation, length of operation time, conversion rate, and omental and organ adhesions to the gallbladder. Anatomical difficulty was defined and classified as either normal (including normal anatomic structures even in the presence of inflammation and adhesion) or abnormal (including the anatomical structural changes with adhesions and distortions of normal structures due to the inflammation, as well as true biliary and vascular anomalies). All resected specimens were evaluated by a single experienced pathologist retrospectively, and histological inflammation was scored according to the Sakuramoto et al. [15, 16] (Table 1).

Statistical analysis was carried out by SPSS 11.0 for Windows program. Continuous data were compared by Student's t test. Categorical data were analyzed by Mann– Whitney U test, chi-square (Yates' correction), or Fisher's exact test where appropriate. Statistical significance was indicated by a p value less than 0.05.

#### Results

Of the 915 patients who underwent LC, 173 patients (19 %) were male (group 1), and 742 patients (81 %) were female (group 2). Mean age was  $53\pm12$  (range 22–80)years in group 1 and  $49\pm13$  (range 17–85)years in group 2. The difference between the two groups was significant (p<0.001). Two groups did not differ in terms of laboratory values such as WBC count; total, direct, and indirect bilirubin; AST; ALT; GGT; LDH; and amylase levels (p>0.05).

The average duration of surgery was different between groups 1 and 2 (71±33 min (range 20–160 min) and 58±27 min (range 15–135 min) (p<0.001)). The frequency of adhesions between the gallbladder and omentum and the other organs was significantly higher in male patients (p=0.003 and p=0.0006, respectively). There was no difference between the groups for gallbladder perforation during the operation (Table 2). However, the conversion rate was significantly different ( $\chi^2$ =3.83, p<0.05). A total of 43 patients (4.7 %) underwent conversion to open cholecystectomy. However, the percentage of conversion in group 1 (8 %) doubled than that in group 2 (4 %) (n, 14 patients in group 1 to 29 patients in group 2).

The distribution of anatomical structures classified according to the anatomical difficulty in 173 males was as follows: 49.7 % patients had normal anatomical structure, whereas 50.3 % had abnormalities mainly due to the

 Table 1
 Histological findings for the resected gallbladder (Sakuramoto classification)

Acute cholecystitis findings	
None (0)	Those free of acute findings.
Slight (1)	Those with only inflammatory cell invasion, such as slight neutrophil infiltration.
Moderate (2)	Those with inflammatory cell invasions, such as moderate neutrophil infiltration, edema of mucosal layers, epithelaxia, and erosion formation.
Severe (3)	Those with inflammatory cell invasions, such as severe neutrophil, visible abscess formation, hyperemia, bleeding, and mucosal ulceration.
Chronic cholecystitis finding	58
None (0)	Those free of chronic findings.
Slight (1)	Those with lymph follicle formation and slight chronic inflammatory cell invasion.
Moderate (2)	Those with lymph follicle formation, chronic inflammatory cell invasion, and fibrosis to muscular or subserosal layer.
Severe (3)	Those with fibrosis in complete layers and destruction of mucosal layer.

Histological findings for the resected gallbladder

inflammation. However, the anatomy of biliovascular tree in operative field of 742 female patients was considered normal in 70.6 %, whereas 29.4 % had abnormalities. The difference carried statistical significance between male and female patients (p < 0.0001).

The rate of acute and chronic inflammation in gallbladder specimen between groups 1 and 2 differed significantly (p=0.001 and p=0.001, respectively). On the basis of the four stages of scoring for inflammation where acute and chronic inflammation was quantified to give a total of between 0 and 3, the mean  $\pm$  standard deviation for the acute cholecystitis finding of male was  $1.02\pm1.27$ , and the mean for chronic cholecystitis findings was  $1.33\pm0.92$ . The mean  $\pm$  standard deviation of acute finding of female was  $0.45\pm0.92$ , whereas the mean for chronic finding was  $1.18\pm0.77$ . The mean for the total of acute and chronic inflammation was  $1.63\pm0.96$  in females, whereas  $2.35\pm1.20$  in males. There was a statistical significance for acute, chronic, and total inflammation scoring between male and female patients (Table 2).

### Discussion

LC is the preferred technique for the treatment of cholecystitis. Many conditions related with patients such as severe fibrosis, anatomical anomalies, presence of severe inflammation, intraoperative complications (bleeding, bile duct, or visceral injuries), age over 65 and previous abdominal surgery, and instrument failure might result in conversion from LC to open surgery [8]. Shea et al. reported that the most important factors for conversion include severe adhesions and inflammation [17]. Although some controversy still exists, it recently has become apparent that males have more surgical difficulties and increased conversion rates than females [5, 7, 10, 13, 14, 18, 19]. In our study, both the conversion rate and the duration of surgery were increased in men, an indirect clue indicating the more pronounced surgical difficulty in men. In conjunction with our findings, Fried et al. published a study stating that the most significant predictors of conversion included male sex, increased age, obesity, thickened gallbladder wall detected in preoperative biliary ultrasound, and acute cholecystitis [20]. A multivariate analysis by Lipman et al. suggested a scoring system where it predicted conversion accurately with independent factors such as male gender, elevated WBC count, low serum albumin level, presence of pericholecystic fluid in US, diabetes mellitus, and elevated total bilirubin [21]. Moreover, many reports have shown that LC is more difficult in males than in females [2-5, 7-9].

The severe inflammation and anatomical anomalies are the most important reasons for the anticipated difficulty [7-10]. We observed that both acute and chronic inflammatory changes were more prominent in cholecystectomy specimens of male than female patients. Furthermore, more omental and organ adhesions were observed in men than women during surgical exploration. Although we excluded the patients with acute cholecystitis from the study, the pathological detection of acute inflammatory changes in the resected specimen might have several explanations. First, the patients who were scheduled LC in 2 months after their initial attack might have had still persisting acute inflammatory changes. Second, patients might have acute flare of cholecystitis during the waiting period for the operation. Alternatively, the patients had unnoticed acute attack of cholecystitis that induced inflammatory changes yet neglected by the patient. The increased rate of inflammatory changes in gallbladder specimens of males might depend on many factors. First, men are more negligent about their health, and they seek medical attention late. In case of cholecystitis, male patients have been shown to apply medical help after several attacks of inflammation, resulting in chronic changes that make operation more difficult [8]. Second, the differential effect of sex hormones might play an important role in wound healing. Frazier-Jessen et al. studied the effect of exogenous administration of low and high doses of estradiol to ophorectomized rats on peritoneal fibrosis. They found that low doses of estradiol suppressed connective tissue formation by 29 %, whereas high doses by 65 %. They concluded that estradiol appears to prevent connective tissue formation in peritoneal injuries with a dose-

Table 2 Comparison between male and female groups regarding inflammatory finding, anatomical difficulty, gallbladder perforation, omental and organ adhesions, age, length of operation time, and conversion

		Gender			
		Male ( <i>n</i> =173)	Female $(n=742)$	Total ( <i>n</i> =915)	р
Acute inflammation <sup>a</sup>	0	99 (57.2 %)	586 (79.0 %)	685	0.001
	1	8 (4.7 %)	17 (2.3 %)	25	
	2	29 (16.8 %)	97 (13.1 %)	126	
	3	37 (21.3 %)	42 (5.6 %)	79	
Chronic inflammation <sup>a</sup>	0 1	36 (20.8 %) 58 (33.5 %)	76 (10.2 %) 344 (46.4 %)	112 402	0.001
	2	63 (36.4 %)	267 (36.0 %)	330	
	3	16 (9.2 %)	55 (7.4 %)	71	
Acute cholecystitis findings <sup>a</sup>		$1.02 \pm 1.27$	$0.45 {\pm} 0.92$		< 0.0001
Chronic cholecystitis findings <sup>a</sup>		$1.33 \pm 0.92$	$1.18 {\pm} 0.77$		< 0.05
Acute and chronic cholecystitis findings <sup>a</sup>		$2.35 \pm 1.20$	$1.63 {\pm} 0.96$		0.0001
Anatomical difficulty	Normal Abnormal	86 (49.7 %) 87 (50.3 %)	524 (70.6 %) 218 (29.4 %)	610 305	< 0.0001
Gallbladder perforation	Yes No	45 (26 %) 128 (74 %)	156 (21 %) 586 (79 %)	201 714	NS
Omental adhesion	Yes No	63 (15 %) 110 (64 %)	185 (25 %) 557 (75 %)	248 667	0.003
Organ adhesion	Yes No	26 (15 %) 147 (85 %)	52 (7 %) 690 (93 %)	78 837	0.0006
Age	53±12		49±13		< 0.001
Operation time	71±33		58±27		< 0.001
Conversion	14 (8 %)		29 (4 %)	43	< 0.050

The anatomical difficulty was classified as followed: normal, normal anatomical findings in the surgery; abnormal, anatomical structural changes including adhesions, distortions due to the inflammation or true abnormalities, and variations in biliovascular tree according to the findings in operation room

NS nonsignificant

<sup>a</sup> Defined after the pathological examination of the specimen

dependent fashion [22]. It was suggested that estrogen may suppress the macrophage activation or impede their accumulation in the wound, thereby inhibiting the development of adhesion [8, 22]. Although the administration of exogenous testosterone had no effect on either castrated or noncastrated mice, on collagen deposition [23], Yol et al. found higher levels of collagen and hydroxyproline in cholecystectomy samples from male patients, suggesting a difference in cellular processes of inflammation [24]. They suggested an explanation for the difficulty in dissections during LC and a higher rate of conversion to open surgery in male patients based on this difference. In our study, beside the higher rate of inflammation in males, intra-abdominal organ adherence was more prominent in men. Although gallbladder perforation rates during surgery showed no differences between genders, the conversion rate to open surgery was higher in male patients. We think that the higher rate of conversion to open surgery in males might be due to the repeated attacks of inflammation resulting in excessive fibrosis and chronic inflammatory changes, thereby making the dissection more difficult and rendering anatomical structures vulnerable to injury. To avoid inadvertent injury in LC, surgeons prefer the conversion to open surgery as similar to the study performed by Zisman et al. We also found a high rate of anatomical difficulty in men [9]. The anatomical difficulty described in our study might represent anatomical changes induced by severe inflammation rather than true anomalies in either vascular or biliary system. It might be speculated that high muscle proportion and narrow chest circumference may facilitate the adherence of adjacent organs to the gallbladder. Delay in seeking medical care and high recurrence rate of the attacks also may contribute to the difficulty [8]. The longer duration of surgery found in our male patients reflects the summation and higher anatomical changes.

In conclusion, the findings of higher scores of anatomical difficulty in operation and inflammation in cholecystectomy specimens, as well as higher rates of conversion in males, suggested that laparoscopic gallbladder surgery is more difficult in men. Therefore, necessary precautions such as experienced operative team and the prompt information to the patients about the risks and conversion to the open surgery must be undertaken before the operation.

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