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# Is the Male Gender an Independent Risk Factor for Complication in Patients Undergoing Laparoscopic Cholecystectomy for Acute Cholecystitis?

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**This paper was designed to investigate the gender dependent risk of complication in patients undergoing laparoscopic cholecystectomy for acute cholecystitis. Laparoscopic cholecystectomy is the standard procedure for benign gallbladder disorders. The role of gender as an independent risk factor for complicated laparoscopic cholecystectomy remains unclear. A retrospective single-center analysis of laparoscopic cholecystectomies performed for acute cholecystitis over a 5-year period in a community hospital was performed. Within the period of examination, 1884 laparoscopic cholecystectomies were performed. The diagnosis was acute cholecystitis in 779 cases (462 female, 317 male). The male group was significantly older ($P = 0.001$). Surgery lasted significantly longer in the male group ($P = 0.008$). Conversion was done in 35 cases (4.5%). There was no significant difference in the rate of conversion between both groups. However the rate of conversion was significantly higher in male patients $>$ 65 years ($P = 0.006$). The length of postoperative hospital stay was significantly longer in the male group ($P = 0.007$), in the group $>$ 65 years ($P = 0.001$) and following conversion to open surgery ($P = 0.001$). The male gender was identified as an independent risk factor for prolonged laparoscopic cholecystectomy on multivariate analysis. The male gender could be an independent risk factor for complicated or challenging surgery in patients undergoing laparoscopic cholecystectomy for acute cholecystitis.**

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Gallbladder disorders represent common medical problems for which surgery is usually indicated. With about 1 million procedures performed worldwide per year and close to 170,000 in Germany alone, laparoscopic cholecystectomy (LC) belongs to one of the most commonly performed surgical procedures.[1] Over the last decades this procedure has grown to be the standard procedure for the management of benign gallbladder disease.[2–4] The surgical challenges in LC, especially converting from laparoscopic to open surgery has been a matter of concern.[5–9] The gender-associated risk of complication in laparoscopic cholecystectomy has not been clearly defined.[2,10–11]

The aim of this study was to investigate whether the male gender is an independent risk factor for complication in patients undergoing laparoscopic cholecystectomy for acute cholecystitis (AC).

## Patients and Methods

A retrospective review of the charts of patients undergoing LC in a primary care center was performed. Demographic data including sex, age, body mass index (BMI) and comorbidities as defined by the American Association of Anesthesiologists (ASA) was collected for each patient.

Acute cholecystitis was suspected from the medical history, physical examination, and the results of blood chemistry (leukocytosis, elevated C-reactive protein, and liver enzymes). The suspected diagnosis was verified using an abdominal ultrasound and the severity of AC was graded as recommended in the Tokyo guidelines.[12] The diagnosis was evident during surgery and was finally confirmed by histopathology.

Surgery was performed either by 1 of 5 attending surgeons with experience in laparoscopic surgery or by 1 of 8 surgical residents under direct supervision. A 4-incision LC was performed in all patients. Pneumoperitoneum was installed via a Veress needle placed in the left upper quadrant, with a maximum intra-abdominal pressure of 12 mmHg. Since our departmental standard required all patients with acute cholecystitis to be put on intravenous antibiotics, single-shot antibiotics were given depending on the time interval between the last antibiotic dose and surgery. Surgery was performed either by an attending surgeon (>250 LC) or by a surgical resident under direct supervision. The duration of surgery was recorded as the time from the placement of the Veress needle to suture in minutes. Surgeon's notes, surgical documentation sheets, and anesthesiology protocols were reviewed for information on the course of surgery and intraoperative blood loss. Postoperative complications and the length of hospital stay were retrieved from discharge notes.

Data analysis was done with the Statistical Package for Social Science (SPSS), IBM (Armonk, New York), version 21. A Kolmogorov–Smirnov test was significant for all the variables investigated.[13] Therefore a normal distribution was not probable. Thus the study population was statistically described using absolute number of cases, percentages, medians, and ranges. Significances were calculated using the Mann-Whitney *U* Test with levels of significance at $P > 0.05$.[14] Furthermore, a multivariate analysis was used to examine if the male gender was an independent risk.

Primary endpoints included the duration of surgery in minutes and the rate of conversion. Secondary endpoints included intraoperative blood loss, length of postoperative hospital stay, and postoperative complications.

## Results

In the period from January 1, 2005 to December 31, 2010, 1884 laparoscopic gallbladder procedures were recorded. The diagnosis at surgery was AC 853 cases. After excluding 53 cases due to incomplete charts and 21 cases of open cholecystectomy, 779 cases (462 female, 317 male) were included for analysis (Fig. 1). The baseline characteristics of the study population are presented in Table 1. High blood pressure was the most common concomitant disease in patients with ASA 1–2. Besides high blood pressure, diabetes, arrhythmia, and chronic renal failure were frequently seen in patients with ASA 3–4. Surgery was performed in 84.7% of cases by experienced surgical attendings.

### *Indication for surgery*

The indication for surgery was AC with cholecystolithiasis in 572 cases (73.4%), acalculous AC was seen in 134 cases (17.2%), and AC with bile duct

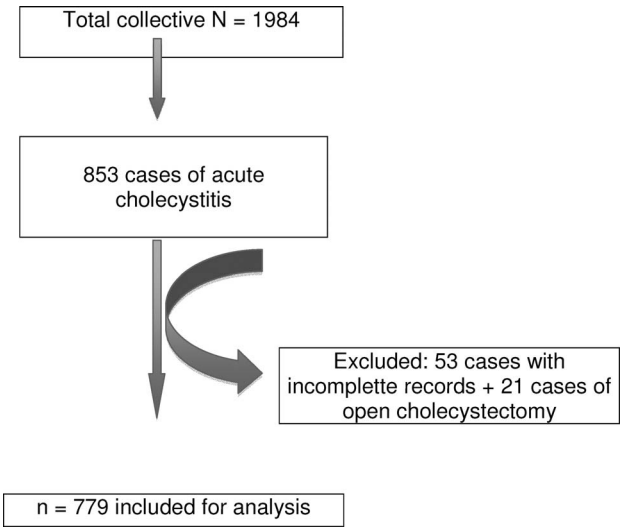


**Fig. 1** Distribution of the study population. A total of 1984 cases of laparoscopic cholecystectomy, including 853 cases with acute cholecystitis, were reviewed; 779 cases were included for analysis.

obstruction was diagnosed in 73 cases (9.4%). Calculous AC was present in 346 female patients (44.4%) and in 226 male patients (29.0%). Acalculous AC was found in 72 female patients (9.2%) and 62 patients in the male group (8.0%), while AC with bile duct stones was present in 44 female (5.6%) and 29 male (3.7%) patients respectively. There was no significant difference amongst both groups in terms of diagnoses ($P = 0.352$). Equally, there was no significant difference among both groups with respect to disease severity, Table 2.

*Table 1 Baseline characteristics of the study population. The male group was significantly older at the time of surgery. There was no significant difference among both groups with respect to BMI and ASA*

| Characteristics | Female cohort | Male cohort | *P* value |
|---|---|---|---|
| Median age (range) yrs | 56 yrs (15–93 yrs) | 62 yrs (15–92 yrs) | 0.001 |
| ASA | | | |
| 1–2 | 515 | 278 | >0.05 |
| 3–4 | 47 | 39 | |
| Mean BMI (kg/m$^2$) | 27.6 ± 11.4 | 25.1 ± 10.5 | >0.05 |

*Table 2 Disease severity. Severity grading of the study population according to the Tokio guidelines.[12] There was no significant difference among both groups with respect to disease severity*

| Severity grade | Female group | Male group | *P* value |
|---|---|---|---|
| I | 367 | 213 | >0.05 |
| II | 59 | 77 | >0.05 |
| III | 36 | 27 | >0.05 |

### *Age at surgery*

The median age at surgery for the entire collective was 59 years (15–93 years). The corresponding values were 56 years (12–93 years) and 62 years (16–92 years) for the female and male group, respectively. The male group was significantly older at the time of surgery ($P = 0.001$). To further characterize the effect of age, the study population was divided into 2 groups (≤65 years and >65 years). At the time of surgery 275 (148 female, 127 male) patients were >65 years. The male patients in this group were significantly older ($P = 0.021$).

### *Time interval between admission and surgery*

The median interval from admission to surgery in the study was 1 day (0–30 days). The corresponding values were 1 day (0–30 days) and 2 days (0–29 days) for the female and male group, respectively. The vast majority of patients (624 cases, 80.1%) underwent surgery within 3 days (early LC). Intermediate LC was defined as LC between the fourth and seventh day following admission and was performed in 118 cases (15.1%). Delayed LC was performed >7 days after admission in 37 cases (4.7%). There was no significant difference among these groups ($P = 0.183$).

### *Duration of surgery*

The median duration of surgery for this study was 37 minutes (11–22) minutes. The corresponding values were 36 minutes (11–221) minutes and 39 minutes (12–159) minutes for the female and male group, respectively. Surgery lasted significantly longer in the male group ($P = 0.008$). This trend was confirmed on multivariate analysis ($P = 0.012$). There was no significant difference in the duration of surgery between patients ≤65 years and those >65 years ($P = 0.191$). Similarly there was no significant relationship between the length of surgery and the time interval between admission and surgery ($P = 0.785$; Fig. 2).

### *Rate of conversion*

Thirty-five cases (4.5%) were converted from laparoscopic to open cholecystectomy. The rates of conversion were 4.11% (19/462) and 5.04% (16/317) in the female and male group, respectively. This difference was not statistically significant ($P = 0.363$). However, the rate of conversion was signif-

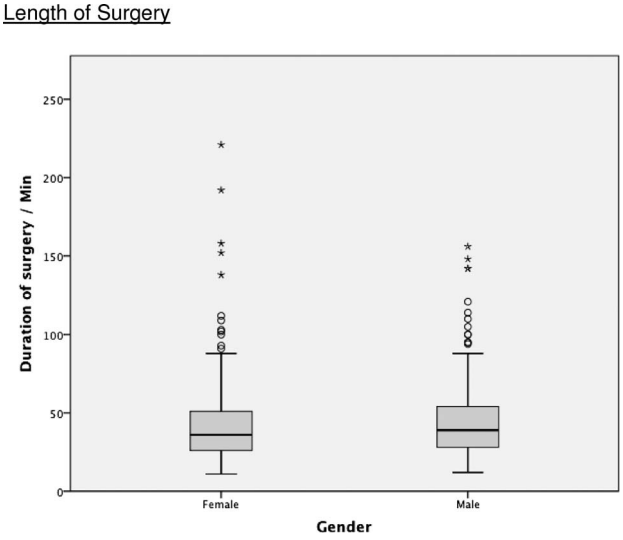


**Fig. 2** Duration of surgery. Laparoscopic cholecystectomy lasted significantly longer in the male group ($P = 0.001$).

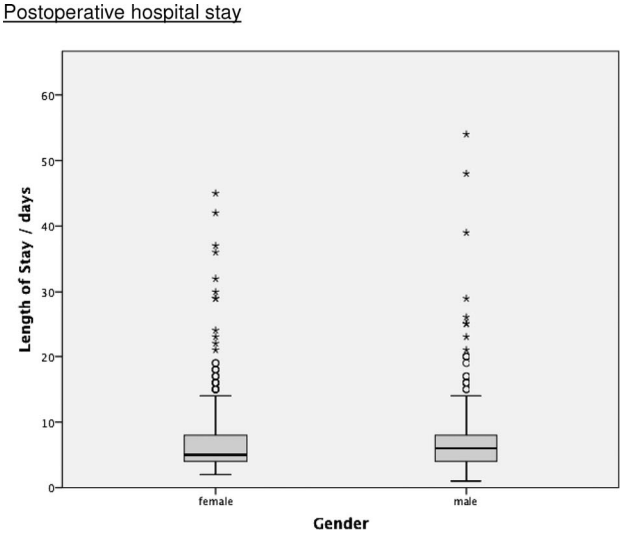


**Fig. 3** Length of postoperative hospital stay. There was no significant difference among both groups with respect to the length of postoperative hospital stay ($P = 0.201$).

icantly higher in male patients >65 years compared to female patients of the same age group ($P = 0.006$). The rate of conversion was also significantly higher in patients undergoing delayed LC ($P = 0.020$). Conversion was performed due to the inability to clearly identify the structures within the triangle of calot.

*Length of hospital stay*

The median length of postoperative hospital stay in the study population was 5 days (1–54 days). The corresponding values for the female and male group were 5 days (2–42 days) and 6 days (1–54 days) respectively. This difference was statistically significant ($P = 0.007$). Hospital stay was significantly longer patients >65 years ($P = 0.001$). This was independent of the gender ($P = 0.227$). Conversion from laparoscopic to open surgery was associated with a significant prolongation of hospital stay ($P = 0.001$; Fig. 3).

*Complications*

Postoperative complications included 18 cases of urinary tract infection, 7 cases of pneumonia in patients following conversion, and wound infection in 21 cases. Five of the 9 male patients with wound infection developed an infection of the subcostal incision following conversion to open surgery. In the female group, 7 patients developed an infection of the subcostal incision after conversion to open surgery. All of these cases were management conservatively after wound opening. There was no significant difference amongst both groups with respect to postoperative complications (Table 3). There was no mortality in this series.

## Discussion

Laparoscopic cholecystectomy is the standard procedure for benign gallbladder disorders. Initially LC was widely employed to treat symptomatic cholecystolithiasis. With increasing experience, LC has been increasingly employed to manage acute cholecystitis. Over the last decades many authors have sort to characterize predictive factors for a challenging or complicated laparoscopic cholecystectomy.[2,15–19]

This study aimed at analyzing the gender associated surgical challenge in patients undergoing LC for AC. Surgical challenge was defined by the duration of surgery in minutes and the rate of conversion. The duration of surgery was defined as the time from incision (for the Veress needle) to suture in minutes. Furthermore, the length of postoperative hospital stay and postoperative complications were analyzed and compared for both groups.

Donkervoort *et al*[6] and Lee *et al*[20] have described the male gender as a risk factor for complication in patients undergoing LC. According to Van der Steeg *et al*,[21] the male gender, age (>65 years), acute

*Table 3 Perioperative morbidity*

| Complications | Female group | Male group | *P* value |
|---|---|---|---|
| Urinary tract infection | 11 | 7 | >0.05 |
| Pneumonia | 3 | 4 | >0.05 |
| Wound infection | 11 | 9 | >0.05 |
| Intraoperative blood loss | 115 ± 55 ml | 123 ± 64 ml | >0.05 |

cholecystitis and recent obstructive jaundice represent independent predictive factors for conversion in patients undergoing LC. Al-Mulhim,[10] on the other hand, did not find any difference between both genders after reviewing 391 cases of LC. Therefore, it is still not clear whether or not the male gender is an independent risk factor for complicated LC.

The male group in this study was significantly older ($P = 0.001$) compared to the female group at the time of LC. About one-third of the study population was >65 years at the time of surgery. Male patients in the group >65 years were significantly older than their female counterparts. This is in accordance with existing data.[6]

Timing of LC for AC has been controversially discussed.[22–23] In the past, many authors argued that early LC for AC is associated with a high risk of complications. In 1992, Frazee *et al*[17] declared AC as a contraindication for LC. Early LC, defined as surgery within 72 hours, was performed in over 80% of the study population. In fact, more than half of the patients were operated upon within 24 hours of admission. Over 93% of the study population underwent surgery within 7 days. Delayed LC (>7 days after admission) was carried out in 7% of the study population. These patients either underwent an endoscopic retrograde cholangiopancreatography (ERCP) or we treated for concomitant diseases prior to surgery. In these cases, LC was performed mainly due to failure to recover under treatment with antibiotics. There was no significant difference between the timing of surgery and the duration of surgery. However, the rate of conversion was significantly higher in patients undergoing delayed LC. This contradicts the trend reported in a meta-analysis by Siddiqui et al[24] and the recently-published ACDC study.[25] A possible explanation could be the relatively small number of patients (32/779) undergoing delayed LC in our study.

Close to 75% of the collective had gallbladder stones. There was no significant difference in the duration of surgery and the rate of conversion in patients presenting with calculous and acalculous cholecystitis. As expected, surgery lasted longer in patients with bile duct stones. This, however, was not significant.

Surgery lasted significantly longer in the male group compared to the female group. A multivariate analysis confirmed the male gender as an independent risk factor for prolonged surgery. In all patients above the age of 65 years, there was no significant difference in the duration of surgery between the male and the female group.

The rate of conversion in this study was 4.5%. This is comparable to the rates reported in other series.[8–9,26] The rate of conversion was higher in the male cohort (5% versus 4%). This difference, however, was not statistically significant. The rate of conversion was significantly higher in male patients >65 years. Delayed LC was also seen to be associated with a significant increase in the rate of conversion. A similar trend was reported by Peng and colleagues.[27]

Postoperative hospital stay was significantly longer in the male cohort. This trend was also observed patients >65 years. As expected, conversion to open surgery was associated with a significant prolongation of hospital stay.

Our results suggest that the male gender is an independent risk factor for a challenging or complicated LC in patients with AC.

There are two possible explanations for this gender associated trend. First, it is thinkable that male patients do have a higher threshold for pain and therefore seek medical attention later than their female counterpart. In this case, surgery is performed in the most unsuitable time. Second, it is possible that male patients may have had a series of undiagnosed subacute inflammations. This could have led to changes in anatomic layers of the gallbladder thus making surgical dissection difficult.

## Conclusion

The male gender is an independent risk factor for complication in patients undergoing laparoscopic cholecystectomy for acute cholecystitis. Endoscopic surgeons should be informed about this gender-associated risk of complication.

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## References


1. Litwin DE, Cahan MA. Laparoscopic cholecystectomy. *Surg Clin North Am* 2008;**88**(6):1295–1313
2. Ambe P, Esfahani BJ, Tasci I, Christ H, Köhler L. Is laparoscopic cholecystectomy more challenging in male patients? *Surg Endosc* 2011;**25**(7):2236–2240
3. Cuschieri A, Dubois F, Mouiel J, Mouret P, Becker H, Buess G *et al*. The European experience with laparoscopic cholecystectomy. *Am J Surg* 1991;**161**(3):385–387
4. Schirmer BD, Edge SB, Dix J, Hyser MJ, Hanks JB, Jones RS. Laparoscopic cholecystectomy. Treatment of choice for symptomatic cholelithiasis. *Ann Surg* 1991;**213**(6):665–676; discussion 677
5. Costantini R, Caldaralo F, Palmieri C, Napolitano L, Aceto L, Cellini C *et al*. Risk factors for conversion of laparoscopic cholecystectomy. *Ann Ital Chir* 2012;**83**(3):245–252
6. Donkervoort SC, Dijksman LM, de Nes LC, Versluis PG, Derksen J, Gerhards MF. Outcome of laparoscopic cholecystectomy conversion: is the surgeon's selection needed? *Surg Endosc* 2012;**26**(8):2360–2366
7. Gouma DJ. Conversion from laparoscopic to open cholecystectomy. *Br J Surg* 2006;**93**(8):905–906
8. Spatariu A, Nicolau AE, Beuran M, Tudor C, Oprescu C. Conversion in laparoscopic cholecystectomy for acute cholecystitis [in Romanian]. *Chirurgia (Bucur)* 2010;**105**(4):469–472
9. Zehetner J, Leidl S, Wuttke ME, Wayand G, Shamiyeh A. Conversion in laparoscopic cholecystectomy in low versus high-volume hospitals: is there a difference? *Surg Laparosc Endosc Percutan Tech* 2010;**20**(3):173–176
10. Al-Mulhim AA. Male gender is not a risk factor for the outcome of laparoscopic cholecystectomy: a single surgeon experience. *Saudi J Gastroenterol* 2008;**14**(2):73–79
11. Yol S, Kartal A, Vatansev C, Aksoy F, Toy H. Sex as a factor in conversion from laparoscopic cholecystectomy to open surgery. *JSLS* 2006;**10**(3):359–363
12. Kiriyama S, Takada T, Strasberg SM et al. New diagnostic criteria and severity assessment of acute cholangitis in revised Tokyo Guidelines. *J Hepatobiliary Pancreat Sci* 2012;**19**(5):548–556
13. Lilliefo HW. On the Kolmogorov-Smirnov test for normality with mean and variance unknown. *J Am Stat Assoc* 1967;**62**:399
14. Rosner B, Grove D. Use of the Mann-Whitney U-test for clustered data. *Stat Med* 1999;**18**(11):1387–1400
15. Botaitis S, Polychronidis A, Pitiakoudis M, Perente S, Simopoulos C. Does gender affect laparoscopic cholecystectomy? *Surg Laparosc Endosc Percutan Tech* 2008;**18**(2):157–161
16. Chandio A, Timmons S, Majeed A, Twomey A, Aftab F. Factors influencing the successful completion of laparoscopic cholecystectomy. *JSLS* 2009;**13**(4):581–586
17. Frazee RC, Roberts JW, Symmonds R, Snyder SK, Hendricks J, Smith R *et al*. What are the contraindications for laparoscopic cholecystectomy? *Am J Surg* 1992;**164**(5):491–494; discussion 494–495
18. Giger UF, Michel JM, Opitz I, Inderbitzin D, Kocher T, Krähenbühl L. Risk factors for perioperative complications in patients undergoing laparoscopic cholecystectomy: analysis of 22,953 consecutive cases from the Swiss Association of Laparoscopic and Thoracoscopic Surgery database. *J Am Coll Surg* 2006;**203**(5):723–728
19. Lipman JM, Claridge JA, Haridas M, Martin MD, Yao DC, Grimes KL *et al*. Preoperative findings predict conversion from laparoscopic to open cholecystectomy. *Surgery* 2007;**142**(4):556–563; discussion 563–555
20. Lee NW, Collins J, Britt R, Britt LD. Evaluation of preoperative risk factors for converting laparoscopic to open cholecystectomy. *Am Surg* 2012;**78**(8):831–833
21. van der Steeg HJ, Alexander S, Houterman S, Slooter GD, Roumen RM. Risk factors for conversion during laparoscopic cholecystectomy - experiences from a general teaching hospital. *Scand J Surg* 2011;**100**(3):169–173
22. Kolla SB, Aggarwal S, Kumar A, Kumar R, Chumber S, Parshad R *et al*. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective randomized trial. *Surg Endosc* 2004;**18**(9):1323–1327
23. Lau H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis. *Surg Endosc* 2006;**20**(1):82–87
24. Siddiqui T, MacDonald A, Chong PS, Jenkins JT. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis of randomized clinical trials. *Am J Surg* 2008;**195**(1):40–47
25. Gutt CN, Encke J, Köninger J, Harnoss JC, Weigand K, Kipfmüller *et al*. Acute cholecystitis: early versus delayed cholecystectomy, a multicenter randomized trial (ACDC study, NCT 00447304). *Ann Surg* 2013;**258**(3):385–393
26. Ghnnam W, Malek J, Shebl E, Elbeshry T, Ibrahim A. Rate of conversion and complications of laparoscopic cholecystectomy in a tertiary care center in Saudi Arabia. *Ann Saudi Med* 2010;**30**(2):145–148
27. Peng WK, Sheikh Z, Nixon SJ, Paterson-Brown S. Role of laparoscopic cholecystectomy in the early management of acute gallbladder disease. *Br J Surg* 2005;**92**(5):586–591