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original article

Laparoscopic cholecystectomy for acute cholecystitis: are intended operative approach, timing and outcome affected by BMI? A multicenter retrospective study

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SUMMARY: **Laparoscopic cholecystectomy for acute cholecystitis: are intended operative approach, timing and outcome affected by BMI? A multicenter retrospective study.**

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Background. *Laparoscopy is the gold-standard for cholecystectomy after acute cholecystitis, but the issue is controversial in obese subjects.*

Patients and methods. *We reviewed 464 patients operated for acute cholecystitis (59 open and 405 laparoscopic) over the last five years at St Orsola University Hospital-Bologna and Umberto I University Hospital-Rome, comparing retrospectively: 1) BMI < 30 (397 patients) and BMI =/> 30 (67 patients) and moreover 2) BMI < 25 (207 patients) and BMI =/> 25 (257 patients).*

Results. *In the* first comparison*, obese patients showed higher cardiovascular co-morbidity (61.1% vs 44.5%, p=0.01), worse symptoms (Murphy's sign positive in 92.5% vs 80.8%, p=0.02; fever >38.5°C in 88.0% vs 76.0 %, p=0.02) and significant radiologic imaging (95.5% vs 85.1%, p=0.01) of acute cholecystitis. Laparoscopy was used in 83.6% of obese patients vs 87.9% without any difference, and operative time or conversion rate were similar. According to Tokyo Guidelines 2013, the number of patients who underwent surgery within 3 days or after 6 weeks was similar without statistical difference between the two groups. Hospital stay, morbidity and mortality were similar. Complications were seen in 25.4% of obese patients vs 15.9% (p= 0.03), mainly represented by wound infections. The* second comparison *did show no difference between two groups BMI =/>25 and BMI < 25.*

Conclusions. *Our retrospective multicenter study showed no difference related to intended operative approach, timing and outcome in higher BMI versus lower BMI patients operated for acute cholecystitis.*

KEY WORDS: Cholecystitis - Laparoscopy - Outcome - BMI - Timing.

Introduction

With a prevalence of 10-15% in adults (1), gallstone disease is one of most expensive to treat and most common digestive disorders in Europe and USA that need admission to hospital. Every year in USA more than one million people are newly diagnosed with gallstones (1), there are >800 000 hospitalizations (2-5), and about 700 000 individuals have cholecystectomies (1). In the United States, cholesterol stones account for ~80% of the gallstones removed from patients (2). Obesity is a national health problem that affects 35% of adults in the United States (6): a recent analysis (6) found that 75% of patients who underwent cholecystectomy were overweight or obese, and >20% of all cholecystectomies were for acute cholecystitis. Therefore, surgeons are increasingly likely to encounter a growing number of obese patients who require a cholecystectomy for symptomatic cholelithiasis (7). First laparoscopic cholecystectomies were performed in 1985 by Mühe (8) and in 1987 by Mouret (9), which is today the treatment of choice for symptomatic gallstones. Since its first performance in Europe and its subsequent introduction to the United States in 1988, the overall use of the laparoscopic approach to perform cholecystectomy has steadily increased from 0% in 1987 to 93% in

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2005 (10). It is currently estimated that more than 700,000 laparoscopic cholecystectomies are performed annually in the United States, accounting for approximately 90% of all cholecystectomies (10) because the procedure decreases postoperative pain, allows earlier oral intake, shortens hospital stay, enhances earlier return to normal activity, and improves cosmesis over open cholecystectomy (11). The overall morbidity and mortality rate, reported in international literature (7), is 5-10% and 0.1% respectively. Reduction in postoperative disability has transformed the conduct (12) of one of the most frequently performed general surgical operations because, as experience with the operation grew, its indications expanded to progressively more complex and high risk patients. It has been reported (13) that the risk of possible perioperative complications can be estimated based on patient characteristics (gender, age, ASA score, body weight), clinical findings (acute versus chronic cholecystitis), and the surgeon's own clinical practice with laparoscopic cholecystectomy. Traditionally, obesity has been considered a relative contraindication (7) to laparoscopic cholecystectomy, as the technical difficulties associated with the procedure in these patients were thought to be associated with higher morbidity and mortality as well as increased open conversion rates. However, with increasing experience in laparoscopic surgery and the development of better instruments, the practice in obese patients is growing (7). While most recent studies (14) have noted a complication rate comparable to non-obese patients, few reports have noted an increased rate of wound infection (14), longer operative time (7) and higher conversion to open surgery together with increased BMI (14). On the other hand (6), an open operation is associated most strongly with an increased rate of complications after cholecystectomy among obese patients. The findings of this last study (6) suggest that the current practice in which high-BMI patients are less likely to undergo laparoscopic cholecystectomy than patients of a normal BMI may be suboptimal in selected patients in whom a laparoscopic approach may be feasible. The issue is still controversial and, in order to explore the ways in which the type of cholecystectomy approach , timing of procedure from acute episode and its outcomes are associated with BMI class, we performed a retrospective cohort study of laparoscopic cholecystectomy for acute cholecystitis registered in a validated, common database shared by two Italian institutions (St. Orsola University Hospital-Bologna and Umberto I University Hospital-Rome), evaluating the impact of BMI on surgeons (intended operative approach and timing) and patients (outcome).

Patients and methods

We reviewed the charts of 464 patients operated for acute cholecystitis (59 open and 405 laparoscopic) over the last five years (2013-2017) at St Orsola University Hospital-Bologna and Umberto I University Hospital-Rome. In order to analyze the importance of BMI on surgeons and patients, we compared retrospectively two different groups of patients, featured by obesity or overweight: *1*) BMI < 30 (397 patients) and BMI =/> 30 (67 patients) and moreover *2*) BMI < 25 (207 patients) and BMI =/> 25 (257 patients). Results were expressed as median (range) unless otherwise stated. Comparisons between categorical variables were determined using the chi-square or Fisher's exact test, as appropriate. Continuous variables were assessed with the Mann–Whitney U-test. Logistic backward regression was undertaken to determine factors independently associated with mortality, morbidity and discharge at home including all factors where the P-value was less than 0.05 on univariate analysis. A statistical software package (SPSS Version XX.0; IBM Co, Armonk, NY, USA) was used for the analysis, with $p < 0.05$ considered statistically significant.

Results

In the *first comparison* (Table 1) age was similar in both groups: obese patients showed higher ASA score and cardiovascular co-morbidity (61.1% vs 44.5%, p=0.01), worse symptoms (Murphy's sign positive in 92.5% vs 80.8%, p=0.02; fever >38.5°C in 88.0% vs 76.0 %, p=0.02) and significant radiologic imaging (95.5% vs 85.1%, p=0.01) of acute cholecystitis. Laparoscopic approach was used in 83.6% of obese patients versus 87.9% without any difference, and operative time or conversion rate were similar. According to Tokyo Guidelines 2013 (15), the number of patients who underwent surgery within 3 days or after 6 weeks was similar without statistical difference between the two groups. Hospital stay, morbidity and mortality were similar. Complications were seen in 25.4% of obese patients versus 8.8% (p= <0.05), but most of the complications were represented by wound infections. The *second study* (Table 2) compared overweight patients (BMI =/>25) versus normal weight subjects (BMI < 25)

TABLE 1 - BMI≥30 *VERSUS* BMI<30.

	BMI≥30	BMI<30	P-value
NUMBER of patients	67	397	-
AGE (years)	57.0±16.7	59.7±17.6	0.95
MALE gender	24	207	**0.01**
ASA score (I-II / III-IV)	41/26	286/111	**<0.01**
COMORBIDITY (CardioVascular/Diabetes/COPD/CRF)	41/8/6/3	177/41/39/19	**0.01**/0.66/1.00/1.00
Murphy's sign positive	62	321	**0.02**
Fever (T>38.5° C)	59	302	**0.02**
Positive imaging findings	64	338	**0.01**
PROCEDURE (Open/Laparoscopic/Conversion to open)	11/56/8	48/349/43	0.32/0.66
OPERATIVE TIMING (Within 72h / 3 days or beyond / 6 weeks)	15/31/21	78/167/152	0.62/0.59/0.33
NO COMPLICATIONS	49	360	**<0.01**
WOUND INFECTION	6	16	0.76
COMPLICATIONS according CLAVIEN-DINDO classification (I-II /III-IV)	11/6	23/12	1.00
MORTALITY	1	2	0.37
HOSPITAL STAY (days)	6.8±11.5	4.6±6.8	0.89

and did show no difference among all analyzed parameters between two groups: even in this case, intended operative approach, timing and outcome were similar.

Discussion

We analyzed the impact of BMI class on surgeons and patients during laparoscopic cholecystectomy for acute cholecystitis, evaluating the surgeon's point of view on the intended operative approach, conversion rate and operative timing from acute episode, together with the outcome of patients. Regarding "*intended operation type*", data on international literature (6) regarding 9.666 obese patients who underwent cholecystectomy for acute cholecystitis showed that > 80% had a laparoscopic operation and < 6% of these patients required conversion to an open approach, reporting an independent association between super obesity (body mass index 50+) and an intended open operation (p =0.01). To put our findings in perspective, our series showed that overweight did not affect the surgeon's decision to approach laparoscopically the acute gallbladder disease in two different Italian institutions (Bologna and Rome) , analyzing 257 patients with BMI =/> 25 versus 207 patients with BMI <25. We could not make the same statement regarding obesity: in fact, the number of operated obese patients (67 patients with BMI =/>30) in our series was remarkably lower than the one of non-obese (397 patients with BMI <30) and we should have collected a higher number of obese subjects in order to draw definitively similar conclusions. Notwithstanding, our *conversion rate* was not affected by BMI in both comparisons, showing that also surgeon's decision during procedure was not driven by weight. In international literature (12, 16-18) there is an approximately 5% to 10% conversion rate. The major risk factors for conversion include male sex, obesity, and cholecystitis. A study (11) evaluated patients with acute cholecystitis: only a body mass index > 30 predicted conversion. For patients undergoing elective cholecystecto-

TABLE 2 - BMI≥25 *VERSUS* BMI<25.

	BMI≥25	BMI<25	P-value
NUMBER of patients	257	207	-
AGE (years)	59.1±16.8	59.6±18.4	0.98
MALE gender	134	97	0.26
ASA score (I-II / III-IV)	182/75	145/62	0.92
COMORBIDITY (CardioVascular/Diabetes/COPD/CRF)	128/29/27/13	90/20/18/9	0.19/0.64/0.37/0.83
PROCEDURE (Open/Laparoscopic/Conversion to open)	28/201/28	30/154/23	0.26/0.26/0.88
OPERATIVE TIMING (Within 72h / 3 days or beyond / 6 weeks)	52/119/86	42/78/87	1.00/0.07/0.62
COMPLICATIONS according CLAVIEN-DINDO classification (I-II /III-IV /V)	14/8/1	20/10/2	0.10/0.35/0.58
HOSPITAL STAY (days)	4.9±7.8	5.0±7.5	0.99

my, a body mass index >40 and a wall thickness >0.4 cm predicted conversion (11). It has been shown an association between male gender, body weight, and the severity of gallbladder inflammation (11): 62% ($p < 0.001$) of empyema and gallbladder perforations were found in male patients with body weights > 70 kg. These results confirm that male patients with an increased body weight have the highest risk of undergoing a "difficult cholecystectomy", so male sex and obesity are two very common risk factors for conversion (12). Patients with an increased body weight have been reported (13) to be especially prone to more severe inflammation or fibrosis of the gallbladder, which makes dissection more difficult. Other series (11) have reported that obesity independently predicted conversion to open cholecystectomy in those patients with acute cholecystitis: these series identified obese patients with acute cholecystitis undergoing laparoscopic cholecystectomy as having an increased chance of conversion and, in an elective laparoscopic cholecystectomy, morbidly obese patients with chronic cholecystitis and a thickened gallbladder wall were more likely to require conversion. Analyzing the "*timing of procedure*" from acute episodes of cholecystitis, it did not affect surgeon's choice: in both series (St. Orsola and Umberto I University Hospitals), there was no difference on the number of patients operated within 3 days or after 6 weeks as reported by Tokyo 2013 guidelines (15), and the outcome was similar among patients with different operative timings. This finding should be carefully evaluated in view of the heterogeneity and retrospective nature of our data collected in two different institutions, and it should be prospectively validated in a multicenter study. Finally, few studies (14, 19-26) have addressed the relationship between obesity and "*outcome*" of laparoscopic cholecystectomy: some studies have found a positive correlation between obesity and adverse outcomes while others have not. In general these studies have used variable definition of obesity, using both body weight and variable cutoffs of BMI. A recent study (14) matched 13.780 obese and 1.410 super-obese patients to non-obese patients : obese patients were more likely to present with chronic rather than acute cholecystitis , and Clavien 4 complications (27) were significantly increased among super-obese patients especially with acute cholecystitis ,where rate of open surgery was significantly higher. Another study (7) analyzed 629 patients with BMI >26 among a total of 799, reporting no statistically significant differences in the peri-operative complication rates, open conversions or bile duct injuries among the BMI groups. It has been described (13) that higher perioperative "local" complications occur in patients with body weights > 90 kg, but on the other hand "systemic" complications do not correlate with body weight. In our series, outcome was no different among laparoscopic patients, independently by overweight and obesity:

there was only a tendency to have more wound infections in the obese population.

Conclusions

Our multicenter study from two different Institutions showed no difference related to intended operative approach, conversion rate , operative timing from acute episode and results in higher BMI versus lower BMI among subjects operated for acute cholecystitis: overweight did not impact on surgeon's decision or on patient's outcome. A prospective study will allow a more systematic collection of data such as the operative timing and number of obese patients, which would validate our retrospective findings and provide useful information for clinical practice.

Conflict of interest/Financial support and sponsorship
None.

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