**Title:** INCREASED RATE OF CHOLECYSTECTOMIES PERFORMED WITH DOUBTFUL OR NO INDICATIONS AFTER LAPAROSCOPY INTRODUCTION: A SINGLE CENTER EXPERIENCE

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ABSTRACT

Background. During recent years laparoscopic cholecystectomy has dramatically increased, sometimes resulting in overtreatment. Aim of this work was to retrospectively analyze all laparoscopic cholecystectomies performed in a single center in order to find the percentage of patients whose surgical treatment may be explained with this general trend, and to speculate about the possible causes.

Methods. 831 patients who underwent a laparoscopic cholecystectomy from 1999 to 2008 were retrospectively analyzed.

Results. At discharge 73.05% patients were diagnosed as having cholelithiasis. 37.79% were operated on because of at least one previous episode of biliary colic; 12.52% were operated on because of an increase in white blood cell count and in bilirubin level, or both; and 1.56% was operated on because of a previous episode of jaundice. By excluding these patients, 21.18% were operated on without indication.

Conclusions. The broadening of indications for laparoscopic cholecystectomy is undisputed and can be considered a consequence of new technologies that have been introduced, increased demand from patients, and the need for practice by inexperienced surgeons. If not prevented, this trend could continue indefinitely.

KEY WORDS: Laparoscopic Cholecystectomy; Open Cholecystectomy; Gallbladder Stones; Surgical Indications; Laparoscopy.
BACKGROUND

Gallstones are a very common disease affecting up to 15% of the general population in the US and Europe [1], with a higher prevalence in women [2]. About 50 to 70% of patients with gallstones are asymptomatic [1] and nearly 1 in 10 individuals with asymptomatic gallstones may be expected to develop symptoms or complications that require treatment within five years [2].

Since its first introduction in the late 1980s, laparoscopic cholecystectomy has been extensively adopted as the treatment of choice in patients with gallstones and other less frequent benign gallbladder diseases [3] due to its undeniable advantages, such as the reduction of postoperative pain, faster recovery, and improved cosmesis [4]. Nevertheless, the undeniable advantages related to this procedure compared to the traditional open approach have resulted in a broadening of indications in performing such an operation, sometimes resulting in expensive and unnecessary overtreatment [4,5].

The aim of this work was to retrospectively analyze all patients who underwent a laparoscopic cholecystectomy in our department in order to find the percentage of patients whose surgical treatment may be explained with the general trend of increase in laparoscopy utilization, and to speculate about the possible causes.
MATERIAL AND METHODS

All patients who underwent a laparoscopic cholecystectomy at the Department of Surgical Sciences, Organ Transplantation and Advanced Technologies of University of Catania - Cannizzaro Hospital from 1999 to 2008 were retrospectively analyzed after approval of hospital ethics committee. Data were collected from medical records and patients were analyzed depending on the symptoms at admission and diagnosis at discharge in order to find the percentage of patients admitted and subsequently operated on with no indication. Patients operated with open technique and those who experienced a conversion to laparotomy were not considered for the present study.

Patient preoperative assessment was performed according the standard of care in our practice by routine laboratory tests and ultrasound (US). Computed tomography (CT) scan was performed only in cases of unclear diagnosis.

All patients admitted for trauma underwent focused assessment with sonography for trauma (FAST) performed in the trauma room, in order to timely diagnose potentially life-threatening hemorrhage and to help determine the need to transfer the patient to the operating room. Patients who were diagnosed for gallstones at FAST and subsequently operated on at the resolution of the main cause of admission were also included in the present study.

Diagnosis of acute cholecystitis was based on the presence of right upper quadrant pain with or without fever and with evidence of raised WBC count, ultrasonographic evidence of gallstones, or pericholecystic fluid collection.

According to the evidences in literature [6-11], conditions that were considered correct indications for surgery were the following: acute cholecystitis, acute biliary pancreatitis, gallbladder adenomas, cholangitis with evidence of gallstones, biliodigestive fistula, lithiasis of the biliary ducts with or without jaundice, and recurrent episodes of biliary colic or
recurrent jaundice. Conversely, medical records of patients who were admitted only because of the general diagnosis of abdominal pain with gallstones, or patients without symptoms in which diagnosis was performed incidentally during FAST exam for trauma were further analyzed in order to find the percentage of patients operated on without indication.

The following parameters were considered: sex, age, presence of comorbidities (diabetes mellitus, hepatic cirrhosis, and immunosuppression), pre-and postoperative stay, length of hospitalization, history of previous biliary colic or jaundice, symptoms referred at the admission, diagnostic imaging performed, white blood cell count and bilirubin levels at the admission.

Patients with gallstones and vague abdominal pain with atypical localization or characteristics, who underwent an operation for gallbladder stones without previous episodes of pain, jaundice, increase in WBC count or bilirubin were considered as operated on without indication. These patients were subsequently contacted by telephone and an oral questionnaire was administered in order to assess the percentage of those who experienced early (within 30 days) or delayed recurrence of symptoms, as well as those who had no improvement in symptoms despite the operation.
RESULTS

From 1999 to 2008, 987 patients underwent a cholecystectomy. Among these, 105 patients (10.64%) underwent a primary open operation and 51 patients (5.17%) experienced a conversion to laparotomy after a laparoscopic attempt, so these 156 patients were excluded from the study. Among the remaining 831 patients, 491 (59.57%) were female. The main characteristics of these patients are shown in Table 1. Twenty-nine (3.49%) patients were diabetic and 20 (2.41%) were cirrhotic. The median age (25-75th percentile) was 57 years (43-68).

The operative trend during the nine-year period with regard to the approaches performed is shown in Figure 1 and Table 2, which compare the number of laparoscopic cholecystectomies performed with open cholecystectomies and conversions to laparotomy. The study started when the laparoscopic cholecystectomy had already become the standard of care in our practice, replacing the open approach in most uncomplicated patients. At the beginning of 1999, the percentage of open cholecystectomy was higher, as a residual of the previous trend.

Median time (25-75th percentile) from admission to operation was 2 (1-5) days, and median (25-75th percentile) postoperative stay was 2 (1-3) days with a median (25-75th percentile) overall hospital stay of 4 (2-8) days.

The main causes of admission followed by surgery were: abdominal pain, jaundice, acute pancreatitis and abdominal trauma.

At discharge, all patients were diagnosed as follows (Figure 2): 607 (73.05%) as having cholelithiasis; 84 (10.11%) as having acute cholecystitis; 51 (6.14%) as having associated choledocholithiasis; 36 (4.33%) as having chronic cholecystitis; 29 (3.49%), as having acute biliary pancreatitis; 8 (0.96%) as having gallbladder carcinoma (diagnosed post-operatively at pathologic exam); 6 (0.72%) as having gallbladder adenomas; 6 (0.72%) as having
cholangitis; 3 (0.36%) as having biliodigestive fistula; and 1 (0.12 %) as having acalculous cholecystitis.

Further analysis of medical records of 607 patients (Figure 2) operated on strictly because of cholelithiasis showed that 314 patients (37.79%) were operated on because of at least one previous episode of biliary colic before the one at admission; 13 patients (1.56%) were operated on because of a previous episode of jaundice; 33 patients (3.97%) were operated on because of pain with increase in WBC count without fever, jaundice or pericholecystic collection; 45 patients (5.42%) were operated on because of an increase in bilirubin level; and 26 patients (3.13%) were operated on because of an increase of both WBC count and bilirubin. By excluding these 431 patients, 176 patients (21.18% including 78 patients admitted only for gallstones presence diagnosed incidentally at FAST) were operated on without indication for vague symptoms not related to gallstones or for request of the patients.

The main characteristics of this subpopulation of 176 patients are reported in Table 3. Most of these patients (64.77%) were female, with a median age (25-75th percentile) of 54 (44-65) years.

At follow-up, 150 of 176 patients (85.23%) were contacted by telephone (19 were unavailable and 7 died for causes unrelated to gallbladder disease) and an oral questionnaire was administered with the following results: 6 patients (4%) experienced early recurrence of pain within 30 days after the cholecystectomy; 34 patients (22.66%) experienced late recurrence of pain (30 days after operation); 107 patients (71.33%) referred no improvement in symptoms after operation, with persistence of the same preoperative vague pain whose source required further exams (e.g. gastroscopy, computed tomography, magnetic resonance imaging) to be identified. Only 3 patients (2%) referred complete disappearance of pain after operation. In conclusion, for 147 patients (98%) included in follow-up, cholecystectomy determined no
early or late improvement in symptoms, confirming that these symptoms were not related to
gallstones and the operation should have been avoided.
DISCUSSION

The classic approach to gallbladder disease involves access to the abdominal cavity through a wide incision that is associated with a long postoperative stay with related pain and disability [12]. Laparoscopic introduction has been responsible of the reduction of the most important consequences related to laparotomy [13]. These benefits during the last two decades have resulted in increased adoption of this approach, which has rapidly become the gold standard in management of gallbladder diseases [13]. Nevertheless, immediately following the introduction of laparoscopic cholecystectomy, many authors have detected a dramatic increase in the amount of cholecystectomies performed in general hospitals. From 1990 to 1993, for instance, this increase has been approximately 30% in New York [4]. Another paper reports the same remarkable trend during the years 1990-2001, with a peak between 1994-1998 and a subsequent stabilization through 2001 [5]. Many reasons have been proposed to explain this growth trend. Initially, it was speculated that the increase was due to a high number of patients who put off having the operation for fear of the consequences of the laparotomic approach, but then decided to be operated on given the favorable outcome related to laparoscopy [4]. However, if true, the increase of laparoscopic cholecystectomies should have been temporary and would have been extinguished in a few years concurrent with the decrease in the procrastinating patients [4]. Conversely, the increase in laparoscopic cholecystectomies has been maintained; therefore, the explanation of this trend could be only the broadening of indications for performing such an operation. In a very extensive review of cholecystectomies performed over time in the state of Maryland, involving more than 54 institutions, between 1985 and 1992, the annual cholecystectomy rate had risen from 1.69 per 1000 to 2.17 per 1000, representing a 28-percent increase. This increase was related to the introduction of laparoscopic technique, in which younger patients, less likely to have acute cholecystitis and/or have common bile duct stones, had acquiesced to have surgery. The
gained benefit was a reduction in the overall mortality of this operation from 0.84 percent in 1989 to 0.56 percent in 1992 (a 33% reduction), at the expense of an increased rate, for more benign and lesser symptomatic cases, including possible doubtful indications [14].

General indications and contraindication for performing laparoscopic cholecystectomy are well established [6]. Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) guidelines for the clinical application of laparoscopic biliary tract surgery [7] indicate that conditions requiring cholecystectomy include but are not limited to cholelithiasis (when symptomatic), choledocholithiasis, biliary dyskinesia, acute cholecystitis and pancreatitis related to common bile duct stones. Asymptomatic gallstones are not included among the indications for laparoscopic cholecystectomy (level II, Grade A) [7].

Nevertheless, laparoscopy is not suitable in every situation. Many limitations have been described, such as multiple previous abdominal surgery, diffuse peritonitis, or severe complications, such as empyema or gallbladder necrosis [15]. Especially in cases of confusion of the anatomy of Calot’s triangle, open cholecystectomy is strongly recommended to obtain direct control of every structure and avoid lesions of the biliary tract [16]. According to SAGES guidelines [7], relative contraindications are: untreated coagulopathy, lack of equipment, lack of surgeon expertise, hostile abdomen, advanced cirrhosis or liver failure, and suspected gallbladder cancer (Level II, Grade A).

Concerning the difference of access, SAGES guidelines report no demonstrable difference in the safety of open versus closed techniques: decisions are left to the surgeon and should be based on individual training, skill and case assessment (Level I, Grade A) [7]. However, the safety of laparoscopic cholecystectomy requires correct identification of relevant anatomy (Level I, Grade A) [7].
For acute cholecystitis, Tokyo guidelines [8] report that laparoscopic cholecystectomy is preferable to open cholecystectomy (recommendation A) whenever it is performed early after admission.

By comparing the outcomes of laparoscopic versus open cholecystectomies, in 1996 Shea and colleagues [9] reported a MEDLINE search regarding more than 100,000 patients from many different studies. According to this paper, laparoscopic cholecystectomy appears to be as safe as open cholecystectomy, with a higher common bile duct injury rate in patients who undergo laparoscopic approach. Later in 1998, Targarona et al. [10] reported that laparoscopic cholecystectomy carries a similar postoperative morbidity and mortality to open approach and that Incidence of bile duct injuries in converted cases increases significantly. In 2001, Kama and colleagues [11] assessed the main factors responsible of conversion to laparotomy, reporting that the most common reason for conversion was inability to define anatomy in patients with inflamed gallbladder. Male gender, previous abdominal surgery, acute cholecystitis, thickened gallbladder wall on preoperative ultrasonography, and suspicion of common bile duct stones were significantly independent predictive factors for conversion.

The importance of asymptomatic gallstones and whether they represent an indication for surgery needs to be clarified. According to Murshid [17], the distance to facility (in patients living in the suburbs), long waiting lists in small centers, and even the unavailability of an experienced surgeon may represent an indication to perform the laparoscopic cholecystectomy in absence of symptoms. Murshid’s review finds that young patients with hemolytic anemia of different origins should be operated on due to the progressive increase in diameter of stones [17]. Finally, porcelain gallbladder is a condition in which prophylactic cholecystectomy is indicated in order to prevent gallbladder cancer [17]. Other indications for surgery in patients with asymptomatic gallstones are still the subject of debate. For instance, Tritapepe et al. [18] reported a 3.2-fold higher risk of developing complications in patients...
over 60 years compared to younger patients. While in these patients cholecystectomy should be considered mandatory in the presence of symptoms, the role of prophylactic cholecystectomy to avoid complications (worsened by the advanced age) has yet to be determined.

Furthermore, as diabetes has proven to increase surgical complications [19], some authors [20] have analyzed the effectiveness of prophylactic cholecystectomy in diabetics undergoing operations for other reasons, discovering that they do not benefit from this approach on condition that they were previously asymptomatic. In general, in patients with gallstones detected incidentally during other operations such as for colonic cancer, the prophylactic cholecystectomy has been proven to be affected by an intra- and postoperative risk that is greater than the risk of future morbidity caused by gallstones itself [21].

Another concern regards the risk of gallbladder cancer. Although it is possible to suppose that chronic phlogosis due to the gallstones’ presence may represent the environment in which the gallbladder cancer arises, a study published in 1998 [22] clearly demonstrated that the chronic phlogosis in the mucosa of patients with gallstones show no significant difference compared to that of normal subjects. These findings suggest that chronic inflammatory changes can occur in the gallbladder mucosa prior to the appearance of macroscopic stones [22], and that it cannot be considered the only cause of gallbladder cancer. Moreover, although there is no agreement in the literature on the exact rate of gallbladder cancer in patients with gallstones, the reported risk of cancer in patients with asymptomatic gallstones is lower than 0.01% [23], less than the mortality associated with cholecystectomy itself. However, some regions, such as China, Korea, Japan, India, Central and South America, and Eastern Europe show a high incidence of gallbladder cancer in association with gallstones [24]; therefore, the exact role of genetic and environmental factors in determining this disease needs still to be assessed.
Whether prophylactic cholecystectomy can play a role in these patients is still the subject of debate.

With regard to risk of cancer, another undervalued condition is gallbladder adenomyomatosis [25], because carcinoma has been reported especially in patients with contemporary occurrence of this condition, gallbladder adenomas and gallstones. Degenerative risk suggests that surgery should be mandatory when there is a concomitant presence of these three factors.

Regardless of these specific or rare conditions, we can conclude that there is general agreement that patients with asymptomatic gallstones do not require operation.

To the best of our knowledge, this is the first work which retrospectively analyzes all patients who underwent a laparoscopic cholecystectomy in order to find the percentage of patients submitted to this procedure with no indication or doubtful indications. It is remarkable that 78 patients (that is 9.38% of the cohort) were admitted and subsequently operated on only due to presence of gallstones diagnosed incidentally at FAST, without history associated symptoms. By collecting data from the diagnoses at discharge, the proportion of patients operated on with no indication resulted in an even greater percentage (176 patients who represent 21.18% of the cohort). Almost 98% of this group of patients with indefinite symptoms presented vague symptoms again after the cholecystectomy, demonstrating that the symptoms that led to cholecystectomy were not related to the presence of the gallbladder stone and determining the need of further exams to identify their source.

Speculating about the possible reasons for these data, it is important to note that gallstones are frequently considered the cause of a multitude of abdominal symptoms and, after detection, the patient is usually operated on without further investigations that, conversely, are performed only when symptoms relapse after surgery. Second, it is possible that the increased patient demand due to benefits of laparoscopy and fear of stones complications plays a
determining role. Finally, the need for practice by inexperienced surgeons should be considered.

Given the large diffusion of laparoscopy even for the most challenging operations [26, 27], the improvement in technological devices, and the introduction of less invasive approaches such as natural orifice translumenal endoscopic surgery (NOTES) or single-incision laparoscopic surgery (SILS) [28, 29], not to mention robotic surgery [25], it is speculated that laparoscopic cholecystectomy will be performed even more frequently with some unexpected consequences. For example, it has been proven that the risk of major bile duct injuries is still greater with laparoscopy rather than with the open approach [9, 31]. It is possible to suppose that an irresponsible increase in useless laparoscopic procedures could also result in an increase in bile duct injuries. Moreover, the increased demand for often unnecessary procedures could result in an increased consumption of health care resources. Finally, one question should be addressed: given the importance of surgical skills set in such a different laparoscopic procedure, how critical is the surgeon’s training in determining an increase in useless cholecystectomies? Could the constant introduction of different devices and approaches be responsible for an increase in operations performed on “easy” patients who would not otherwise need surgery?
CONCLUSION

In conclusion, laparoscopic cholecystectomy is indisputably the gold standard in gallstones treatment, although open cholecystectomy still plays a role in complicated cases. Conversion should never be considered a breakdown, but rather a careful choice to safeguard the patient’s life and safety, that should always take priority over cosmesis. The increase in doubtful indications is recognized, and it can be considered a consequence of the new technologies introduced. If not prevented, this trend could continue indefinitely.
REFERENCES


FIGURE LEGEND

**Figure 1.** The operative trend during the nine-year period of study, with regard to the approaches performed. The study started when the laparoscopic cholecystectomy had already become the standard of care at our Department, replacing the open approach in most uncomplicated patients. A residual of the previous trend is evident at the beginning of the 1999, when the percentage of open cholecystectomy was higher.

Legend: VLS: laparoscopic cholecistectomies; OPEN: open cholecystectomies; CONV: conversions.

**Figure 2.** Criteria of inclusion and indications to surgery with related diagnosis at discharge
Competing interests

All the authors declare that they have no competing interests.
Authors' contributions

1) contributions to conception and design: I. Di Carlo, A. Toro
2) acquisition of data, E. Pulvirenti, M, Mannino
3) analysis and interpretation of data: A. Toro, E. Pulvirenti
4) have been involved in drafting the manuscript: A. Toro, E. Pulvirenti
5) revising it critically for important intellectual content: I. Di Carlo, M. Gagner
6) have given final approval of the version to be published: I Di Carlo
CRITERIA OF INCLUSION AND INDICATIONS TO SURGERY

987 CHOLECYSTECTOMIES

831 Laparoscopic Cholecystectomies

105 Primary Open (excluded)

607 (73.05%) Cholelithiasis

84 (10.11%) Acute Cholecystitis

51 (6.14%) Jaundice (Choledocholithiasis)

36 (4.33%) Chronic Cholecystitis

29 (3.49%) Acute Pancreatitis

8 (0.96%) Gallbladder Cancer (diagnosed postoperatively)

6 (0.72%) Gallbladder Adenoma

6 (0.72%) Cholangitis

3 (0.36%) Biliodigestive fistulas

1 (0.12%) Acalculous Cholecystitis

314 (37.79%) Previous episodes of pain

45 (5.42%) Increase of bilirubin

33 (3.97%) Increase of WBC count with pain (no fever, no jaundice)

13 (1.56%) Previous episodes of jaundice

26 (3.13%) Increase of WBC and bilirubin

176 (21.18%) NO INDICATION

51 Converted to Laparotomy (excluded)
Additional files provided with this submission:

Additional file 1: Table 1.doc, 32K
http://www.biomedcentral.com/imedia/3153396168076051/supp1.doc
Additional file 2: Table 2.doc, 32K
http://www.biomedcentral.com/imedia/1510730775807605/supp2.doc
Additional file 3: Table 3.doc, 29K
http://www.biomedcentral.com/imedia/1470230362807605/supp3.doc