Original Research Paper

Volume-8 | Issue-4 | April-2018 | PRINT ISSN No 2249-555X

Surgery

RANDOMIZED SINGLE CENTRE STUDY, SURGICAL TIMING AND CONVERSION FACTORS IN 100 CONSECUTIVE PATIENTS TREATED FOR ACUTE CHOLECYSTITIS.

Buffone A*	Department of "Chirurgia Generale e Specialità Medico Chirurgiche", University of Catania, Endocrinesurgery Unit, "Policlinico-Vittorio Emanuele" Hospital, Via Santa Sofia 78, Catania, Italy. *Corresponding Author
Lo Bianco S	University of Catania, Endocrinesurgery Unit, "Policlinico-Vittorio Emanuele" Hospital, Via Santa Sofia 78, Catania, Italy.
Terranova L	University of Catania, Endocrinesurgery Unit, "Policlinico-Vittorio Emanuele" Hospital, Via Santa Sofia 78, Catania, Italy.
Provenzano D	University of Catania, Endocrinesurgery Unit, "Policlinico-Vittorio Emanuele" Hospital, Via Santa Sofia 78, Catania, Italy.
Basile G	Department of "Chirurgia Generale e Specialità Medico Chirurgiche", University of Catania, Endocrinesurgery Unit, "Policlinico-Vittorio Emanuele" Hospital, Via Santa Sofia 78, Catania, Italy.
Cannizzaro M A	Department of "Scienze Mediche, Chirurgiche e tecnologie Avanzate – G. F. Ingrassia", University of Catania. Endocrinesurgery Unit, "Policlinico-Vittorio Emanuele" Hospital, via Santa Sofia 78, 95123, Catania, Italy.

ABSTRACT

Introduction: The aim of this study is to evaluate which factors might influence the decision and the time of conversion in the laparoscopic treatment of acute cholecystitis.

Materials and methods: A monocentric retrospective study was performed on 100 patients affected by acute cholecystitis. The group A, consisting of 15 males (30%) and 35 females (70%) was treated with early laparoscopic cholecystectomy. The group B, consisting of 16 males (32%) and 34 females (68%), was undergoing delayed laparoscopic cholecystectomy approximately after 40 days.

Results: The differences between group A and group B were the incidence of laparotomic conversion (22% in the group A vs 10% in the group B) and the operating time (110' group A vs 75' group B). Time of hospitalization was shorter in patients undergone to early surgery (5 days) compared to patients undergone to delayed surgery (8,5 days). Postoperative complications rate was of 10% in group A and 6% in group B. Cases of mortality were not reported. Factors that influenced conversion to laparotomic surgery were: belonging to male sex, leukocytosis (>18000 WBC) and PCR (>20 MG/DL). In acute forms edema and tissues friability were common causes that hindered the dissection of the concerning structures. Instead, the new formed adherences observed in patiens undergone to delayed surgery has not been an obstacle to dissection.

Conclusions: Laparoscopic surgery represents gold standard in the acute cholecystitis treatment. In our experience, delayed surgery showed a lower rate of conversion and morbility.

KEYWORDS : Cholecystitis, laparoscopy, laparotomy.

Introduction

Acute cholecystitis is the most frequent complication in patients with cholelithiasis. The 1-2% of patients with asymptomatic gallstones and the 1-3% with mild/moderate symptoms present annually acute episodes (acute cholecystitis, acute cholangitis, severe jaundice, pancreatitis) or complications [1-3]. Laparoscopic cholecystectomy represents the gold standard of treatment even for acute forms in which is reported a higher conversion rate.

In our UOC we evaluate, in acute cholecystitis, how the decision about timing of conversion to laparotomy and predictive factors could influence the choice of surgery.

Materials and methods

We made a study of 100 patients with acute cholecystitis undergone videolaparoscopic cholecystectomy at the U.O.C. Endocrine Surgery of the University Hospital Policlinico-Vittorio Emanuele of Catania, from January 1st 2010 to January 1st 2014. The aim of this study is to verify the precise timing and which factors could influence conversion to open cholecystectomy.

The 100 patients (31 male, 69 female) were divided in two groups A and B of 50 patients each one:

- The Group A was composed of 15 males (30%) and 35 females (70%). The average age was 53 years (range 41-76 year). The patients of this group were subjected to early laparoscopic cholecystectomy among 10 and 72 hours of hospitalization, without onse of symptoms;
- The group B was composed of 16 males (32%) and 34 females (68%). The average age was 58 years (range 45-82 year). In this group were included patients treated with delayed laparoscopic cholecystectomy; these patients were accepted from PS and first treated with conservative medical therapy and, after approximately 40 days, with elective laparoscopic cholecystectomy.

The antibiotic prophylaxis was administrated in all patients with a single dose of third generation cephalosporin. To the first group 1 gram was administrated 30 minutes before surgery and then until 2 days after surgery. To the second group were administrated 2 gram daily (1 gram every 12h) from the first hospitalization until "cooling" of inflammatory process (4-6 days); during the second hospitalization, the same antibiotic dosage was administrated, as in the first group.

The diagnosis of acute cholecystitis was formulated by examining clinical and medical history, abdominal objectivity, laboratory data and ultrasound exam.

The enrolment criterions were:

- Age greater than 18 years
- Signs and symptoms of acute cholecystitis: epi-mesogastric pain, later moved to right upper quadrant, rear irradiation, nausea/vomit, fever, jaundice in approximately 20-30% of cases – almost always not associated with lithiasis of common bile duct – contracture in the right upper quadrant, who presented distended gallbladder, positive Murphy, generally murky peristalsis.
- Leukocytosis (12000 ≤WBC ≥22000 mm^3 neutrophilia (between 80 and 92%); Alkaline phosphatase ≥200 UI/L; GPT (92-212

UI/L); GOT (t79-231UI/L); total bilirubin (1,9-3,4 mg/dL); direct bilirubin (0,60-1,3 mg/dL); PCR ≥11,5 mg/dL;
- Ultrasound showing gallbladder wall thickness greater than 4 mm, gallbladder distension, inflammatory pericholecystic liquid, positive Murphy, presence of stones in the infundibulum.

We have registered age, weigh, sex, tobacco and alcohol usage, preoperative comorbidities (diabetes mellitus, liver disease, COPD, heart disease, cancer), ASA scale, previous abdominal surgery, time between onset of symptoms and surgery (timing), operative time, hospital stay and total hospital stay.

Patients excluded from the study were those with: emphysematosis cholecystitis; Mirizzi Syndrome; ASA IV; septic shock; pregnangcy; severe cardiopathy; patients entered group B after stabilization who presented resumption of symptomatology within the time between discharge and second hospitalization.

Patients affected by cirrhosis (child-Pugh C) and in therapy with oral anticoagulants derived from coumarin assigned to B group. All the remaining patients were randomized using sealed envelopes (flow Diagram). Cholecystectomy was performed by the same operator, with the same technique and working tools. Surgical times followed to perform urgency laparoscopic cholecystectomy were those developed for elective surgery. Only in a presence of a marked distension of the gallbladder was performed a puncture from outside (fig.1).

The data obtained were analysed with "statistica v.10" software.

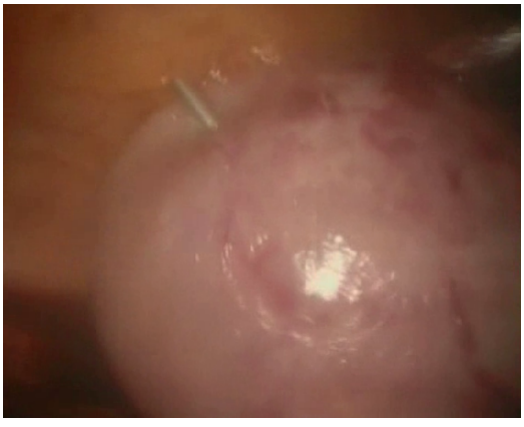

Fig.1 – gallbladder drainage

Results

In group A, 50 patients undergone to early cholecystectomy surgery between the 10° and the 72° hour following the hospitalization; cholangiopancreatography RM was not performed. The mean operating time was 110 minutes (from 70 to 150 minutes). The time limit for conversion in case of intraoperative technical issues were 60-90 minutes. In the 22% of patients (11/50 of which 7 M and 4 F) was necessary to perform conversion to laparotomy; of these conversion, 6 patients had leucocytosis ≥ 18.000 mm^3. In 13 patients (26%) it was performed an intraoperative cholangiography with negative results, for the presence at ultrasound of minutes calculations mixed to biliary sludge. In 36 patients (72%) we had to empty the gallbladder due to the volume and thickening of the walls.

In 11 patients (80% of cases) the conversion was required because of the presence of significant edema that altered inextricably both the cystic duct and the cystic artery made, moreover, making more difficult to obtain surgical grip, the dissection of the elements of the triangle Calot, the correct identification of the adjacent structures. In one case (20%), we proceeded to conversion due to the difficulty and impossibility to locate the source of bleeding for a cystic artery laceration. After numerous attempts to isolate cystic duct and artery, it was decided to convert when reached the 50 minutes, despite the range was 60 to 90 minutes.

The mean hospital stay was 5 days (range 3-9 days). Postoperative complications appeared in 10% of cases (5/50): wound infection (1/50), atrial fibrillation (1/50), incisional hernia on the 10th day (1/50), 2 losses of about 200cc of bile per day resolved with endoscopic sphincterotomy (2/50).

The patients of Group B have been treated by delayed cholecystectomy after 40 days from acute cholecystitis; in all of them a cholangiopancreatography MRI was performed which has excluded the presence of gallstones in the common bile duct. The mean operating time was 75 minutes (range 60-125 minutes).

The conversions were 5 (10%) 2 males and 3 females: 4 cases for surgical issues in the dissection of the Calot triangle (anatomy altered by adhesions and, in only 2 cases, by fibrosclerotic tissue) and one for bleeding cystic artery lesion. The Intraoperative cholangiography was not performed in no one of the patients.

The average stay of the second hospitalization was 3,5 days (range 3-5 days); the total average hospitalization were 8,5 (first hospital stay was 5 days, range 4-8). Postoperative complications appeared in 3 cases: 1 hematoma at the point of insertion of the Hasson trocar, 1 leakage of bile, about 250cc die, resolved with endoscopic sphincterotomy, 1 suppurative infection of the laparotomy wound.

We found difficulties in the adhesion lysis between gallbladder and neighboring organs in 4% of patients in Group B, of which only 30% needed conversion. The time of conversion was similar to first group. We had no operative mortality. The histological diagnosis in all patients was: acute cholecystitis (77 pts), empyema (19pts), acute cholecystitis gangrenous (4 pts).

The average intervention time between group A and group B does not shows significant differences (P> 0.01). In the acute phase, males show an increased conversion rate (9/50); 5 of these have presented a leucocytosis ≥ 18.000 mm3 and PCR ≥ 20mg /dl.

The operating time in patients undergone to conversion was extended to 60-80 minutes. In 8 patients of group A the hospital stay was 2 days longer than in the other 3 who stayed for the same time of those undergone to laparoscopic cholecystectomy; while in group B only 1 hospitalization lasted 2 days longer.

The hospital stay was significantly longer in the second group B (P <0.01) (result from the sum of two admissions).

Discussion

The 2-20% of the world population has gallstones and 15% of these develop acute cholecystitis with a mortality rate of 0-10% [5-8].

The therapeutic approach of acute cholecystitis has been modified in recent times [9].

The concept of "cooling" acute cholecystitis and treating it later, after the complete resolution of the acute event is a source of debates:

1) Every flogistic event that affects the gallbladder causes a fibrotic reaction [10];
2) 26% of patients with acute empyetic or gangrenous cholecystitis does not respond to conservative therapy and require surgical treatment in acute phase [10];

Also, a review of the literature on comparative studies on early or delayed laparoscopic cholecystectomy reveals that:

- there is no statistically significant difference in biliary tract lesions (0.5% in patients undergoing early cholecystectomy vs 1.4% delayed)[11];
- there is no difference in morbidity and mortality between the two groups [11];
- the global and post-operative hospital stays are lower in patients undergoing early cholecystectomy[11-15].
- advanced age does not preclude the indication for laparoscopic cholecystectomy [16].

The Socieété FranCaise de Chirurgie Digestive [17] defines early surgery less than 7 days from hospitalization and delayed after 6-12 week interval. According to other studies, the interval between admission and intervention varies from: 5 Days [18],72 hours [19], 48 hours[20] or 24 hours [21]. In fact in the first 48 hours, the inflammation increases the

parietal edema that facilitates the dissection of the gallbladder from liver bed; after this period, the inflammation induces parietal alterations (necrosis, fibrosis and parietal abscesses) and tenacious adhesions of the bowel to the surrounding structures.

Although initially it was considered a contraindication, today Laparoscopic cholecystectomy is considered the treatment of choice for acute cholecystitis (EAES Consensus Conference 2006) [22-24].

Despite the surgeon's experience, compared to uncomplicated, today the conversion rate in acute cholecystitis is still high (from 10% to 21.7%); the wall edema and inflammatory adhesions make difficult the identification and isolation of the structures, increasing surgical risk (hemorrhage, lesion of the main bile duct) [24].

Many studies have been conducted to identify the risk factors responsible for conversion: belonging to male sex [25-32], age [29-42], obesity [32-47], previous surgeries [48], increased wall thickness of the gallbladder [49], increased CRP levels (CRP ≥ 3 mg/ dL), white blood cells and alkaline phosphatase [50-54], onset ≥ 72 hours sympstoms, acute cholecystitis [59-60], portal hypertension [61], Mirizzi syndrome, cancer of the gallbladder [62], and experience of the surgeon [63-65]. However, the increased CRP ≥ 3 mg/dL, the duration of preoperative symptoms, the male and increased white blood cell count ≥ 180.000 mm^3 seems to be the most important risk factors for the conversion [44]. Rattner indicates a series of laboratory factors (leukocytosis ≥ 14,000 / mm3, increased alkaline phosphatase) predictive of conversion laparotomy [64].

These data were confirmed by Laporte in a review of 246 patients from 4 controlled clinical trials [65-66]; in this study were found a series of laboratory risk factors predictive of conversion laparotomy and divided into preoperative factors (over 65 years of age, leukocytosis ≥ 13.000 / mm^3 and gangrenous cholecystitis) and intraoperative factors (hydrops or empyema of the gallbladder, gangrenous cholecystitis) [24]. All these criteria are variable depending on the experience of several teams; in fact, the value of WBC oscillates between 13.000/mm^3 [24] - 14.000/mm^3 [66] and 17.000/mm^3 [53]-18.000/mm^3 [67] and CRP ≥ 20 mg/dL. These factors does not induces the surgeon to choose laparotomy, but the possibility of conversion is only determined during surgery, considering the value of these risk factors relative than absolute [63-67]. Our approach has changed, giving more value to these predictive factors.

We also considered the conversion an event to decide during the surgery if there are obvious difficulties. In our experience we have found more conversions, in Group A, due to edema, increasing the caliber of the cystic and nearby structures. Conversion to open surgery is not specifically a disadvantage for the patient but rather an act of safety to prevent complications. If the anatomy is unclear, the surgeon should never hesitate to convert [5].The laparoscopic surgery is converted into open surgery if you encounter difficulties in organ dissection. For this reason, we placed a time limit (30-60 min) for conversion, if there is any difficulty in displaying the calot triangle. Instead, we proceed directly to open surgery if the patient hasleukocytosis ≥ 18,000 mm3, PCR> 20 mg/dl and fever.

Currently many surgeons believe that the incidence of laparotomy conversions, in early laparoscopic cholecystectomies, for acute cholecystitis, is greater than those performed after conservative medical treatment. These data are a source of controversy, in fact, other authors have shown a higher conversion rate in delayed surgery [67]. The SociétéFrançaise de Chirurgie Digestive and meta-analysis of Cocrhane found no statistically significant difference in conversions between the two groups of patients. A lower incidence of laparotomy conversions is demonstrated in the early operated patients group (20.3% in patients treated immediately vs 23.6% of patients undergoing deferred treatment). The most frequent causes of laparotomy conversions are inflammation of the Calot triangle in the early surgery and post-inflammatory fibrous adhesions in delayed surgeries. In addition, during the conservative medical therapy, they may also onset of complications such as:

- Non-regression or aggravation of cholecystitis (17.5% -30%); this makes necessary in many cases (50%) an urgent surgery with a higher incidence of laparotomy conversions (45%);
- secondary common bile duct lithiasis (9.3%) [69];
- biliary pancreatitis (4.3%)[70](Tab.1).

Tab. 1 Comparison of early and delayed laparoscopic cholecystectomy

Authors	N. of patients	Percentage of conversion early VLC (gruppo A)	Percentage of conversion delayed VLC (gruppo B)	Mean days of hospitalization early VLC (gruppo A)	Mean days of hospitalization delayed VLC (gruppo B)
Lo et al [5]	86	11%	23%	6	11
Lai et al [6]	91	21%	24%	7,6	11,6
Chandler et al[7]	43	24%	36%	5,5	7,1
Buffone et al 2015	100	22%	4%	5	3,5 (+5 first admission)

Conclusion

Nowadays is still a topic of discussion about acute cholecystitis treatment if to perform laparoscopic or traditional treatments. Although there is an almost univocal consent considering laparoscopic cholecystectomy as treatment of choice for acute cholecystitis, also if not all the gallbladders can be performed with this method both for the patient's general condition and for comorbidities. In these cases it is preferred undoubtedly an open access.

In relation to the results obtained from our study, we believe it is necessary to consider the predictive factors for conversion and do not hesitate to perform a traditional cholecystectomy when these are meaningful; moreover, even today, there is no agreement on early or delayed treatment and time to conversion. So, our idea is to reduce the inflammation and perform surgery after 4-6 weeks. If inflammation does not regress and there areleukocytosis ≥ 18.000 mm3 and CRP≥20mg/dl, open surgery is performed directly.

In our opinion it is necessary to expand the number of cases to study for data collection with national trial to test the complications and therefore patient safety.

The surgeon should never hesitate to convert when the anatomy of Calot triangle and adjacent structures is unclear.

References

1. Kimura Y, Takada T, Kawarada Y, Nimura Y, Hirata K, Sekimoto M, et al (2007) Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis : Tokyo Guidelines. J Hepatobiliary Pancreat Surg. 4(1): 15-26 (clinical practice guidelibes CPGs).
2. Tazuma S. (2006) Gallstone disease: epidemiology, pathogenesis and classification of biliary stones (common bile duct and intrahepatic). Best. Pract. Res. Clin. Gastroenterol. 20: 1075-83.
3. Friedman GD. (1993) Natural history of asymptomatic and symptomatic gallstones. Am J Surg.165:399-404.
4. Tang, Ph. D, Alfred Cuschieri. (2006) Conversion during laparoscopic Cholecystectomy: risk factors and effects on patient outcome. J Gastrointest. Surg 10:1081-1091
5. Portincasa, Moschetta, Palasciano. (2006) Cholesterol Gallstones disease. Lancet. 15(368):230-9.
6. Lee SW, Yang SS, Change CS, Yeh HJ. (2009) Impact of the Tokyo guidelines on the management of patient with acute calculous cholecystitis. J Gastroenterol Hepatol. 24:1857-61.
7. Meyer KA, Capos NJ, Mittelpunkt AI. (1967) Personal experiences with 1261 cases of acute and chronic cholecystitis and cholelithiasis. Surgery. 61:661-8
8. Sekimoto M, Okuma K, Imanada Y, Mayumi T, et al. (2010) The practical guideline for acute cholangitis were published in 2005. In this study we utilized administrative data to examine trends in patients characteristics, process of care, patient outcome, and medical resource utilization for patients with acute cholecystitis. J Abdom Emerg Med. 30: 413-9.
9. Amendolara M, Perri S, Pasquale E, Biasiato R. (2001) Surgical treatment in acute cholecystitis emergencies. Chir Ital 53(3):375-81
10. Strasberg SM 1995), Hertl M, Soper NJ. (1995) An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg 180:101-25.
11. Gurusamy RS, Samraj K. (2006) Early versus delayed laparoscopic cholecystectomy for acute cholecystitis. The Chocrane Library 4:1-51
12. Sauerland S, Agresta F, Bergamaschi R, Borzellino G, Dudzynski A, et al. (2006) Laparoscopy forabdominal emergencies. Surg Endosc 11:14-29
13. Laporte S, Navarro F. (2003) Qual è il momento migliore per operare una colecistite acuta per via laparoscopic. J Chir 140:193-196.
14. Kolla SB, Aggarwal S, Kumar A, Kumar R, Chumber S, et al. (2004) Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective randomized trial. Surg Endosc 18:1323-1327.
15. Lau H, Lo CY, Patil NG, Yuen WK. (2006) Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis. Surgical Endoscopy 20:82-7.
16. Pessaux P, Tuech JJ, Deouet N. (2000) Laparoscopic cholecystectomy in the elderly: a prospective study. Surg Endosc 14:1067-1069
17. Peschaud F, Alves A, Berdah S, Kianmanesh R, Lurent C, et al. (2006) Indicazioni alla laparoscopia in chirurgia generale e digestiva. J Chir 6:65-79
18. Lupascu C. (2005) Care este momentul optimum pentru a opera laparoscopic o colecestita acuta? Journal de Chirurgie 1:21-23.
19. Yuksel O, Salman B, Yilmaz U, Akyurek N, Tatlicioglu E. (2006) Timing of laparoscopic choecystectomy for subacute calculos cholecystitis: early or interval – a prospective study. J Hepatobiliary Pancreat Surg 13:421-426.
20. Uchiyama K, Onishi H, Tani M, Kinoshita H, Ueno M, Yamaue H. (2004) Timing of laparoscopic cholecystectomy for acute cholecystitis with cholecystolithiasis.

Hepatogastroenterology 51:346-348
21. Cuschieri A,Dubois F,Mouiel P, Becker H,Buess G,et al.(1991) The European exeperience with laparoscopic cholecystectomy. Am J Surg 16:385-387.
22. Cuschieri A. (1993) Approach to treatment of acute cholecystitis: open surgical, laparoscopic or endoscopic? Endoscopy 25:397-98.
23. Watteville JC, Testas P. (1994) La coelioscopia nelle urgenze digestive. In: Testas P, Delaitre B (eds). Chirurgia digestiva per via coelioscopica. Edizioni Vigot, Friburgo 199-16.
24. Stevens KA, Chi A, Lucas LC, Porter JM, Williams MD. (2006) Immediate laparoscopic cholecystectomy for acute cholecystitis: no need to wait. Am J Surg 192:756-761
25. Livingston EH, Rege RV. (2004) A nationwide study of conversion from laparoscopic to open cholecystectomy. American Journal of Surgery 188:205-11
26. Alponat A, Kung CK, Koh BC, Rajnakowa A, Goh PM. (1997) Predictive factors for conversion of laparoscopic cholecystectomy. World J Surg 21: 629-633
27. Lein HH, HuangCS. (2002) Male gender : Risk factor for severe symptomatic cholelitiasis . World J Surg 26: 598-601.
28. Zisman A, Gold-Deutch R, Zisman E, et al. (1996) Is male gender a risk factor for conversion to laparoscopic into open cholecystectomy ? Surg Endosc 10 : 892-894
29. Russell JC, Walsh SJ, Reed-Fouquet L, Mattie A, Lynch J. (1998) Symptomatic cholecystectomy for acute cholecystitis : A different disease in men?Connecticut Laparoscopic Cholecystectomy Registry, Ann Surg 227: 195-200
30. Lee HK, Han HS, Min SK, Lee JH. (2005) Sex based analysis of the outcome of laparoscopic cholecystsetcomy for acute cholecystitis . Br J Surg 92: 463-466.
31. Brunt LM, Quasebart MA, Dunnegan DL, Soper NJ. (2011) Outocmes analysis of laparoscopic cholecystectomy in the extremely alderly . Surg Endosc 15: 700-705.
32. Kartal A, Aksoy F,Vatansev C, Sahin M, Ylmaz O, Belviranli M,Karahan O. (2001) Does estrogen cause low conversion rates in laparoscopic cholecystecyomies for acute and chronic cholecystitis in women? JSLS. 5(4):309-12.
33. Wiebke EA, Pruitt AL, Howard TJ, et al. (1996) Conversion of laparoscopic to open cholecystectomy .An analysis of risk factors. Surg Endosc 10: 742-745.
34. Merriam LT, Kanaan SA, Dawes LG, et al. (1999)Gangrenous cholecystitis: analysis of risk factors and experience with laparoscopic cholecystectomy. Surgery 126:680-686
35. Liu CL, Fan ST, Lai EC, Lo CM, Chu Km. (1996) Factors affecting conversion of laparoscopic cholecystectomy to open surgery . Arch Surg 131: 98-101
36. Lo CM, Fan ST, Liu CL, Lai EC, Wong J. (1997) Early decision for conversion of laparoscopic to open cholecystectomy for treatment of acute cholecystitis. Am J Surg 173: 513-517.
37. Tagle FM, Lavergne J, Barkin JS, Unger SW. (1997) Laparoscopic cholecystectomy in the elderly. Surg Endosc 11: 636-638.
38. Fried GM, Barkum JS, Sigman HH, et al, (1994) Factors determining conversion to laparostomy in patients undergoing laparoscopic cholecystectomy . Am J Surg 167: 35-39.
39. Bingener J, Richards ML, Schwesinger WH, Strodel WE, Sirinek KR. (2003) Laparoscopic cholecystectomy for elderly patients. Gold standard for golden years? Arch Surg 138: 531-535.
40. Kama NA, Doganay M, Dolapci M, Reis E, Atli M, Kologlu M. (2001) Risk factors resulting in conversion of laparoscopic cholecystectomy to open surgery. Surg Endosc 15: 965-968-
41. Lo CM, Lai EC, Fan ST, Liu CL, Wong J. (1996) Laparoscopic cholecystectomy for acute cholecystitis in the elderly. World J Surg 20: 983-986.
42. Ammori, Vezakis, Davides, Martin, Larvin, Mc Mahom. (2001) Laparoscopic cholecystectomy in morbidly obese patients. Surg. Endosc 15:1336-1339.
43. Angrisani L, Lorenzo M, De Palma G et al. (1995) Laparoscopic cholecystectomy in obese patients compared with nonobese patients. Surg Laparosc Endosc 5:197-201.
44. Simopoulos, Polycronidis, Botaitis, Perente, Pitiakoudis. (2005) Laparoscopic cholecystectomyin obese patients. Obes Surg 15:243-246.
45. Gatsoulis, Koulas, Kiparos, et al. (1999) Laparoscopic cholecystectomyin obese and nonobese patients. Obes Surg 9:459-461.
46. Hawn MT, Bian J, Leeth, et al. (2005) Impact of obesity on resource utilization for general surgical procedures. Ann Surg 241:821-828.
47. Karayiannakis AJ, Polychronidis A, Perente S, Botaitis S, Simopoulos C. (2004) Laparoscopic cholecystectomy in patients with previous upper or lower abdominal surgery. Surg Endosc 18: 97-101.
48. Hutchinson, Traverse, Lee. Laparoscopic cholecystectomy. (1994) Do preoperative factors predict the need to convert to open? Surg Endosc 8:875-878.
49. Shafer M, Schneiter R, Krahenbuhl L. (2003) Incidence and management of Mirizzi syndrome during laparoscopic cholecystectomy. S urg Endosc 17: 1186-1190-
50. Rattner DW, Ferguson C, Warshaw AL. (1993) Factors associated with successful laparoscopic cholecystectomy for acute cholecystitis. Ann Surg 217:233-236.
51. Eldar S, Sabo E, Nash E, Abrahamson J, Matter I. (1997) Laparoscopic versus open cholecystectomy in acute cholecystitis. Surg Laparosc Endosc 17:407-414.
52. Lai PB, Kwong KH, Leung KL, Kwok SP, Chan AC, Chung SC, et al. (1998) Randomized trial of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br J Surg 85:764-7
53. Brodsky A, Matter I, Sabo E, Cohen A, Abrahamson J, Eldar S. (2000) Laparoscopic cholecystectomy for acute cholecystitis: can the need for the conversion and the probability of complications be predict?A prospective study. Surg End 14: 755-760.
54. Peng WK, Sheikh Z, Nixon SJ, Paterson-Brown S. (2005) Role of laparoscopic cholecystectomy in the early management of acute gallbladder disease. British Journal of Surgery 92:586-91
55. Madan AK, Aliabadi-Wahle S, Tesi D, Flint LM, Steinberg SM. (2002) How early is early laparoscopic treatment of acute cholecystitis? Am J Surg 183:232-236
56. Willsher PC, Sanabria JR, Gallinger S, et al. (1999) Early laparoscopic cholecystectomy for acute cholecystitis : a safe procedure.J Gastrointest Surg 3:50-53.
57. Habib FA, Kolachalam RB, Khilnani R,Preventza O, Mittal VK. (2001) Role of laparoscopic cholecystectomy of gangrenous cholecystitis .Am J Surg 181:71-75.
58. Cox MR, Wilson TG, Luck AJ, Jeans PL, Padbury RTA,Toouli J. (1993) Laparoscopic cholecystectomy for acute inflammation of gallbladder. Ann Surg 218:630-634.
59. Rutledge D, Jones D, Reqe. R (2000) Consequences of delay in surgical treatment of biliary disease. Am J Surg 180:466- 469
60. Morino M, Cavuoti G, Miglietta C, Giraudo G, Simone P. (2000) Laparoscopic cholecystectomy in cirrhosis:controindication or privileged indication?Surg Laparosc Endosc 10:360-363.
61. Lam, Yuen, Wai et al. (2005) Gallbladder cancerr presenting with acute cholecysti: a population-based study. Surg Endosc 19: 697-701.
62. MacFadyen BV Jr, Vecchio R, Ricardo AE, Mathis CR. (1998) Bile duct injury after laparoscopic cholecystectomy; The United States experience.Surg Endosc 12:315-321
63. Capizzi FD, Fogli L, Brulatti M, et al. (1993) Conversion rate in laparoscopic cholecystectomy: Evolution from 1993 and current state . J Laparoendosc Adv Surg Tech 13(2). 89-91.
64. Buffone A, Basile G, Catania, G,Belvedere A, Cirino E. (2005) Acute postoperative acalculous cholecystitis. Chirurgia italiana 57 (6): 743-748.
65. Cagir, Rangraj, Maffuci, Herz.(1994) The learning curve for laparoscopic cholecystectomy. J laparoendosc Surg 4:419-427.
66. Peters , Krailadsiri, Incarbone, et al. (1994) Reason for conversion from laparoscopic to open cholecystectomy in a urban teaching hospital. Am J Surg 168: 555-559.
67. Tambyraja AL, Kumar S, Nixon SJ. (2004) Outcome of laparoscopic cholecystectomy in patients 80 years and older. World J Surg 28: 745-748.
68. Liguori G, Bortul M, Castiglia D. (2003) The treatment of laparoscopic cholecystectomy for acute cholecystitis. Annali Italiani di Chirurgia 74:517-21
69. Papi C, Catarci M, D'Ambrosio L, Gili L, Koch M, Grassi GB, et al.(2004) Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. Am J Gastroenterol 99:147- 55.
70. Lawrentschuk N, Hewitt PM, Pritchard MG. (2003) Elective laparoscopic cholecystectomy: implications of prolonged waiting times for surgery. ANZ Journal of Surgery 73:890-3.