

Risk factors for acute cholecystitis and for intraoperative complications



Ann. Ital. Chir., 2017 88, 4: 318-325
pii: S0003469X17027294

Octavian Andercou*, Gabriel Olteanu*, Florin Mihaileanu*, Bogdan Stancu*, Marian Dorin**

*Second Surgery Department, University of Medicine and Pharmacy Iuliu Hatieganu ClujNapoca, Romania

**Second Surgery Department, University of Medicine And Pharmacy Targu Mures, Romania

Risk factors for acute cholecystitis and for intraoperative complications

BACKGROUND: Acute cholecystitis is still frequent in emergency surgical departments. As surgical technique, nowadays laparoscopy is widely used and with low complications and with low postoperative morbidity.

MATERIAL AND METHODS: We perform an analytical study about the safety of laparoscopic surgery in patients with acute cholecystitis in a single Surgical Department with an experience of over 20 years in laparoscopic surgery. We included 193 patient admitted in our department during 2014 and 2015.

RESULTS: Of the 193 patients, 43% were diagnosed with acute lithiasic cholecystitis (ALC) whereas 56% had chronic lithiasic cholecystitis (CLC). We assessed the comorbidities of the patient via Pearson's Chi-Square test and we found out that there is a significant relationship between acute cholecystitis and high blood tension, obesity and diabetes. Surgical techniques performed were in 95% of cases laparoscopic cholecystectomy and only in 5% we performed open surgery.

DISCUSSIONS: Experienced surgeons have a lower conversion rate as compared to less experienced surgeons. For this reason, postoperative assessment criteria have been proposed, with a view to identify the risk of conversion

CONCLUSION: In our study laparoscopic surgery for acute cholecystitis is a safe procedure with low intraoperative complication rate and with a reduced hospital stay.

KEY WORDS: Acute cholecystitis, Intraoperative adhesion, Intraoperative bleeding, Laparoscopic cholecystectomy

Introduction

Acute lithiasic cholecystitis is a pathology that is frequently encountered in surgery centres and has an important social and economic impact^{1,2}. The standard treatment for this pathology is surgery. The optimal moment for the surgical intervention is still controversial. Early surgical intervention is supported by the fact that mortality and morbidity are hereby reduced and, on the other

hand, it also has an economic importance through the shortening of the hospitalization period^{3,4}. Since the introduction of the laparoscopic techniques, early surgical intervention has been associated with an increased risk of intraoperative complications and a high conversion rate^{5,6}. For this reason, there are certain studies which recommend the timing of the surgical solution^{7,8} and resorting to a conservative initial treatment. However, in the case of late surgical interventions, there is a risk for certain complications to occur, especially at the level of the main biliary ducts. Since the improvement of the laparoscopic technique, studies have shown that this is a safe technique for resolving acute lithiasic cholecystitis⁹⁻¹⁴. Not only laparoscopic instruments have been improved but also original techniques, derived from the standard one, and which opens the gate to the future (SILS and robotic surgery)^{15,16}. Although laparoscopy is a low-risk technique, the indication to open surgery

Pervenuto in Redazione Maggio 2017. Accettato per la pubblicazione Giugno 2017

Correspondence to: Octavian Andercou, University of Medicine and Pharmacy, Second Surgical Clinic, Clinicilor Street 4-6, 400006, Cluj Napoca Romania (e-mail: andercou@yahoo.com)

in the treatment of acute cholecystitis is still there¹⁷. It is estimated that approximately 48% of acute cholecystitis cases are still resolved via the open technique, although there isn't sufficient data to emphasize its advantages over the laparoscopic technique¹⁷. Earlier studies, from 2001 and 2013 have shown that after laparoscopic cholecystectomy there is a reduced neuroendocrine stress and a better immune postoperative response¹⁸. This response reduces the risk for postoperative complications such as infections, and leading to a faster recovery.

In order to establish optimal treatment procedures for acute cholecystitis, a guide has been developed which establishes the most appropriate moment for surgery and the recommended type of surgical intervention^(20,21). Another controversy is about the conversion rate, which ranges between 5% and 40%²². Of the factors that may lead to conversion from laparoscopic to open surgery, the following need to be mentioned: the difficulty to recognise the anatomical relationships among the different elements due to the presence of fibrotic alterations, the presence of haemorrhage, or the existence of certain severe local²³.

The aim of the present study was to assess the ratio between acute and chronic cholecystitis cases, both lithiasic and alithiasic, to assess the association among different associated diseases and the presence of acute cholecystitis, to assess the optimal operative moment, and to assess the conversion rate according to certain complications that occurred intraoperatively. The study has been conducted in a university surgical centre with over 20 years of experience in laparoscopic surgery. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required. This article does not contain any studies with animals performed by any of the authors.

Material and Method

The institutional review board at our institution approved the protocol for this retrospective study; informed consent was obtained from each patient enrolled in the study.

We have conducted a retrospective clinical analytical study on a number of 193 patients hospitalized and operated upon at the University Department of Surgery in Cluj-Napoca, Romania, during the period 2014-2015, and diagnosed with acute or chronic lithiasic and alithiasic cholecystitis, in whose case laparoscopic cholecystectomy (LAPCHOL) was performed or attempted.

The characteristics monitored within the group of patients were: demographic data, length of hospitalization, associated pathologies, the surgical procedure per-

formed, the conversion rate and reasons, intraoperative and early postoperative complications, as well as the immediate postoperative evolution.

The data obtained was centralized in tables and statistically processed. The information was entered into a data base via Microsoft Excel 2010. For its statistical processing, the Data Analysis program was used.

The statistical analysis part was conducted via the Microsoft Excel 2010 Data Analysis program and SPSS (version 13.0, SPSS Inc., Chicago, IL, USA). Tables and diagrams were used for the graphic representation of the data obtained.

Results

The present study deals with a number of 193 patients diagnosed with cholecystitis. Of these, 83 were diagnosed with acute lithiasic cholecystitis (ALC) (43% of the total number of patients), while 3 patients were diagnosed with acute alithiasic cholecystitis (AAC). The remaining 56% had chronic lithiasic cholecystitis (CLC) and chronic alithiasic cholecystitis (CAC). Diagnosis was established on clinical signs and symptoms and on ultrasound examination for each patient.

The association between the patients' gender and the type of cholecystitis showed that the frequency ratio for cholecystitis cases was 4.07:1 in favour of women. As far as acute cholecystitis is concerned, we identified a number of 69 cases in females, amounting to 83.13% of the total cases of acute cholecystitis.

Via Pearson's Chi-Square test, the hypothesis is accepted according to which there is a statistical connection between the variables cholecystitis type and patients' gender, $p=0.029$ and thus statistically significant.

The distribution of the type of cholecystitis relative to the patients' age showed the highest incidence of cholecystitis cases in the 60-70 age group. In the selected group of patients, there was 1 case under 20 years of age and 14 cases in their twenties and thirties. At the opposite end of the scale, we observe 6 patients aged over 80.

THE ASSESSMENT OF THE ASSOCIATIONS BETWEEN THE PATHOLOGIES ASSOCIATED WITH THE CHOLECYSTITIS TYPE

As far as the associated pathologies are concerned, it was observed that blood arterial hypertension (BP) was encountered in 43.01% of the cholecystitis cases, it being the most frequently encountered of the associated pathologies. Hypertension is important also in terms of the anaesthetic risk and the possibility for certain intraoperative and postoperative complications to occur (Table I).

Following the Chi-Square test, we found a statistical correlation, between arterial hypertension and cholecystitis, $p=0.049$, and thus statistically significant (Table II).

TABLE I - The association of arterial hypertension with cholecystitis type.

			Cholecystitis type				Total
			AAC	ALC	CAC	CLC	
BP	Yes	No. of subjects	2	44	1	36	83
		% of total no.	1.04	22.80	0.52	18.65	43.01
	No	No. of subjects	1	39	4	66	110
		% of total no.	0.52	20.21	2.07	34.20	56.99
Total	No. of subjects		3	83	5	102	193
	% of total no.		1.55	43.01	2.59	52.85	100

TABLE II - The association between obesity and cholecystitis type.

			Cholecystitis type				Total
			AAC	ALC	CAC	CLC	
Obesity	Yes	No. of subjects	1	48	2	19	70
		% of total no.	0.52	24.91	1.04	9.84	36.27
	No	No. of subjects	2	35	3	83	123
		% of total no.	1.04	18.1	1.55	43.01	63.73
Total	No. of subjects		3	83	5	102	193
	% of total no.		1.55	43.01	2.59	52.85	100

TABLE III - The association between the type of cholecystitis and diabetes mellitus.

			Cholecystitis type				Total
			AAC	ALC	CAC	CLC	
DM	Yes	No. of subjects	0	15	0	5	20
		% of total no.	00	7.81	0	2.59	10.40
	No	No. of subjects	3	66	5	97	173
		% of total no.	1.55	35.20	2.59	50.3	89.60
Total	No. of subjects		3	83	5	102	193
	% of total no.		1.55	43.01	2.59	52.85	100

TABLE IV - The distribution of the type of surgical intervention by cholecystitis type.

			Cholecystitis type				Total
			AAC	ALC	CAC	CLC	
Type of Intervention	RLC	No. of subjects	3	76	5	100	185
		% of total no.	1.55	39.38	2.59	51.81	95.86
	CS	No. of subjects	0	4	0	1	5
		% of total no.	0	2.07	0	0.52	2.59
	CONV	No. of subjects	0	2	0	1	3
		% of total no.	0	1.04	0	0.52	1.55
	Total	No. of subjects	3	83	5	102	193
		% of total no.	1.55	43.01	2.59	52.85	100

Obesity was quantified using the body mass index; it is another disease associated with cholecystitis, with a global incidence of 36.27% within the group of patients, 24.91% of whom were diagnosed with acute cholecystitis (Table III).

Following the Chi-Square test, it was demonstrated that there is a statistical connection within the group of patients, between obesity and cholecystitis type, $p=0.001$ and thus statistically significant.

Diabetes mellitus, both the non-insulin dependent and insulin-dependent variety, was studied within the group of patients. DM was present in 10.04% of the patients with cholecystitis and in 7.8% of the patients with acute cholecystitis (Table IV).

Following the Chi-Square test, a statistical connection was identified between diabetes mellitus and cholecystitis type, $p=0.023$ and thus statistically significant.

THE ASSOCIATION BETWEEN THE TYPE OF SURGICAL INTERVENTION AND THE TYPE OF CHOLECYSTITIS

Following the analysis of the distribution of the type of procedure, it was observed that a number of 184 cases underwent retrograde laparoscopic cholecystectomy (RLC) out of the total 193 cases studied, retrograde

TABLE V - Intraoperative adhesions associated with cholecystitis type.

			Adhesions		Total
			Yes	No	
Type of Cholecystitis	AAC	No. of subjects	1	2	3
		% of total no.	0.52	1.04	1.56
	ALC	No. of subjects	23	60	83
		% of total no.	11.92	31.09	43.01
	CAC	No. of subjects	0	5	5
		% of total no.	0	2.59	2.59
	CLC	No. of subjects	32	70	102
		% of total no.	16.58	36.27	52.85
Total	No. of subjects		56	137	193
	% of total no.		29.02	70.98	100

TABLE VI - The association of the type of intervention with the presence of intraoperative adhesions.

			Adhesions		Total
			Yes	No	
Type of Intervention	CS	No. of subjects	3	2	5
		% of total no.	1.55	1.04	2.59
	RLC	No. of subjects	50	135	185
		% of total no.	25.91	69.95	95.85
	CONV	No. of subjects	2	1	3
		% of total no.	1.04	0.52	1.55
	Total	No. of subjects	55	138	193
		% of total no.	28.50	71.50	100

TABLE VII - The association of intraoperative haemorrhage with the type of cholecystitis.

			Intraoperative haemorrhage		Total
			Yes	No	
Type of cholecystitis	AAC	No. of subjects	1	2	3
		% of total no.	0.52	1.04	1.56
	ALC	No. of subjects	6	77	83
		% of total no.	3.56	39.45	43.01
	CAC	No. of subjects	0	5	5
		% of total no.	0	2.59	2.59
	CLC	No. of subjects	4	98	102
		% of total no.	2.08	50.74	52.85
Total		No. of subjects	11	182	193
		% of total no.	6.05	93.95	100

TABLE VIII - The association of intraoperative haemorrhage with the type of intervention.

			Intraoperative haemorrhage		Total
			Yes	No	
Type of Intervention	CS	No. of subjects	0	5	5
		% of total no.	0.0	2.59	2.59
	RLC	No. of subjects	10	175	185
		% of total no.	5.52	90.33	95.85
	CONV	No. of subjects	1	2	3
		% of total no.	0.52	1.04	1.55
Total		No. of subjects	11	182	193
		% of total no.	6.05	93.95	100

laparoscopic cholecystectomy being therefore by far the most widely used technique, amounting to a total of 95.34% of the total cholecystectomy cases. Three cases of conversion to classical surgery (CS) also stand out, 2 of which are in connection with the acute cholecystitis cases

The intraoperative adhesions may be the cause for conversion from retrograde laparoscopic cholecystectomy to classical surgery. We noted the presence of adhesions in 29.02% of the total interventions performed, 11.92% being encountered in the case of acute cholecystitis (Table V).

The intraoperative adhesions are also present in the case of open surgery interventions, even in a higher percentage as compared to laparoscopic surgery (Table VI).

Another factor that may contribute to conversion is the occurrence of diffuse and uncontrollable haemorrhages. This is due to the presence of adhesions and of the inflammatory syndrome, which makes it difficult to recognise the anatomical elements or the normal relationships

TABLE IX - The association of intraoperative bile leakage with the type of cholecystitis.

			Intraoperative bile leakage		Total
			Yes	No	
Type of Cholecystitis	AAC	No. of subjects	0	3	3
		% of total no.	0.0	1.56	1.56
	ALC	No. of subjects	3	80	83
		% of total no.	1.56	41.45	43.01
	CAC	No. of subjects	0	5	5
		% of total no.	0	2.59	2.59
	CLC	No. of subjects	2	100	102
		% of total no.	1.04	51.81	52.85
Total		No. of subjects	5	187	193
		% of total no.	2.59	97.31	100

TABLE X - The association of intraoperative bile leakage with the type of intervention.

			Intraoperative bile leakage		Total
			Yes	No	
Type of Intervention	CS	No. of subjects	0	5	5
		% of total no.	0.0	2.59	2.59
	LRC	No. of subjects	4	181	185
		% of total no.	2.08	93.77	95.85
	CONV	No. of subjects	1	2	3
		% of total no.	0.52	1.04	1.55
Total		No. of subjects	5	188	193
		% of total no.	2.59	97.40	100

among these. Globally, a percentage of 6.05% was observed for intraoperative haemorrhages, their highest frequency being encountered in the case of acute cholecystitis, amounting to 3.56% of the total (Table VII).

Fortunately, we only had one case of intraoperative haemorrhage that required conversion, which amounts to 0.52% of the total number of interventions. It was possible to resolve intraoperatively the other haemorrhage cases, which amount to 5.52% of the total number of procedures, and they did not require either conversion or reintervention (Table VIII).

Another intraoperative incident in the case of retrograde laparoscopic cholecystectomy for acute cholecystitis is the injury to certain (usually anomalous) biliary ducts. Of the 5 intraoperative bile leakage cases, 3 were recorded in the case of acute cholecystitis, which represents 1.56% of the cases (Table IX).

Of the intraoperative bile leakage cases, 1 required CONVERSION, which represents 0.52% of the total number of cases (Table X).

TABLE XI - The association of the length of the hospitalization period with the type of surgical intervention.

Type of intervention	No.	Hospitalization period (days)				Minimum	Maximum	95% confidence interval for the mean	
		Average	Median	Standard deviation				Lower limit	Upper limit
CONV	3	22.6	22.0	12.01		11	35	7.1	52.5
RLC	185	7.5	7.0	4.34		2	38	6.9	8.1
CS	5	9.2	10	3.96		3	13	4.2	14.1

TABLE XII - The association of the length of hospitalization with the type of cholecystitis.

Type of intervention	No.	Hospitalization period (days)				Minimum	Maximum	95% confidence interval for the mean	
		Average	Median	Standard deviation				Lower limit	Upper limit
ALC	83	7.7	7	4.35		2	24	6.77	8.66
CLC	102	7.9	7	5.39		3	38	6.86	8.98

The assessment of the length of the hospitalization period relative to the type of surgical intervention and the type of cholecystitis revealed a shorter hospitalization period in the case of retrograde laparoscopic cholecystectomy, with an average of 7.5 days, as compared to classic cholecystitis (9.2 days). On the other hand, the patients who required conversion to open surgery required additional care, reason for which their average hospitalization period was 22 days (Table XI).

One may observe that there is no statistical difference between the length of the hospitalization period according to the type of cholecystitis (acute lithiasic cholecystitis and chronic lithiasic cholecystitis were taken into consideration), the average number of hospitalization days being 7.7 in the case of acute lithiasic cholecystitis and 7.9 for chronic lithiasic cholecystitis, with a confidence interval of 95% for the mean (Table XII).

The early postoperative complications occurred in 4.68% of the cases, all following retrograde laparoscopic cholecystectomy; thus, 1 case of postoperative haemorrhage, 2 cases of subhepatic abscess, and 2 cases of localized peritonitis were recorded. As for the postoperative complications that occurred following open cholecystectomy, they could not be assessed correctly, due to the low number of patients (only 5) treated via this technique.

Discussions

In the first few years following the introduction of laparoscopic surgery, acute cholecystitis represented a contraindication for resorting to this type of surgery^{24,25}.

The standard treatment consisted in a conservative antibiotic treatment, possibly associated with percutaneous biliary drainage, followed by early open cholecystectomy²⁵. As surgeons gained more experience in laparoscopic techniques, these proved their advantages: low postoperative pain, short hospitalization period, faster social and professional integration, and, last but not least, a much better cosmetic appearance as compared to open surgery²⁷. Although the surgical technique is well standardized, so far it has not been possible to establish the optimal moment for the performance of the surgical intervention. Meta-analyses from 2006 and 2008^{3,9} showed that early laparoscopy reduces the hospitalization period, without influencing the patients' postoperative evolution, however. One of the limitations of our study is the fact that the time from the moment the patient was admitted to hospital to the moment surgery was performed was not specified accurately and in all cases. We performed the early interventions between 24-48 hours, on average, from admittance to hospital. Of course, in situations where certain adhesions associated with inflammatory phenomena were present, the conversion rate was 1.5% (N = 3 cases). In situations where certain intraoperative complications were present, the conversion needs to be regarded as a correct decision on the part of an experienced surgeon, rather than a failure of the operative technique. The causes for conversion are represented in the first place by intraoperative haemorrhage. In our study, only one case of haemorrhage that required conversion was recorded. The conversion rate has several variables. Experienced surgeons have a lower conversion rate as compared to less expe-

rienced surgeons. For this reason, postoperative assessment criteria have been proposed, with a view to appreciating the risk of conversion^{28,29}. According to these scores, cholecystectomy is appreciated as being difficult when the surgical operation requires over 70 minutes³⁰. In our study we did not take into consideration the length of the surgical intervention. We appreciated that, although sometimes the length of the surgical intervention was greater, this was not a reason for conversion.

Besides haemorrhage, another cause for conversion is the injury of the biliary channels. It was present in 2.5% (N = 5) of the cases but only in a single case was conversion necessary. It is an acknowledged fact that in the case of acute cholecystitis, the risk of injury to the biliary channels is higher. This is due to the presence of adhesions and fibrosis phenomena which occur in the confluence area of the cystic duct and the main biliary duct^{31,32}. Not only injuries of the main biliary duct are possible but also injuries of some anatomic variations of biliary channels, such as the duct of Luschka. The injuries of the biliary ducts are an important cause of morbidity and affect the rest of the patient's entire life³³. Only since surgeons have gained more experience in laparoscopic surgery has this complication become ever more rare³⁴, fact also proven in our study. In fact, our surgical centre has a rich experience in laparoscopic surgery, since it has been active in this field for over 20 years.

Among the conversion causes one may also take into account the patient's associated diseases, with reference especially to overweight patients. In the case of these patients, due to their rich fatty tissue in the cystic area, there is a high risk of injury to the biliary channels. In order to avoid this, an attentive dissection and accurate highlighting of the biliary channels are required. Taking into account the risk of bile duct injuries, especially in elderly patients, laparoscopic cholecystectomy is a safe procedure in this particular cases³⁵.

The avoidance of any intraoperative complications is important in the first place for the patient's postoperative evolution, but economic costs are not to be overlooked, either. A patient in whose case they resort to conversion requires a longer special care period, which requires a larger number of hospitalization days. In our study, the maximum hospitalization period was 22 days in the case of such a patient, longer, in a statistically significant way, as compared to patients without conversion. In selected patients, young and with low ASA score, an option for lowering costs in public health system is the so called day surgery with a large applicability in the USA³⁶.

Further studies are concentrating about improvement of the actual technique. Nowadays highly experienced surgeons are performing mini-laparoscopic cholecystectomy. This shows to be more difficult but it is a safe method and guarantees the same clinical results as the standard laparoscopic cholecystectomy³⁷.

Conclusions

Although acute cholecystitis represents an important health issue on a global scale, not enough studies leading to the development of any treatment guides have been conducted yet. Surgical treatment is fundamental and the laparoscopic technique is the primary recommendation. The laparoscopic approach, however, depends on the surgeon's personal experience. Early surgical intervention in the first 48-72 hours greatly reduces the risk of intraoperative complications, which has a positive influence on the patient's postoperative evolution. The patient has a fast postoperative recovery and can be reintegrated faster socially and professionally. So, in our study we have demonstrated that laparoscopic approach to acute cholecystitis is safe, with minimum aggression to the patient and with minimum intraoperative complication and low postoperative morbidity. But it needs a well-trained surgeon to perform safely this technique.

Riassunto

La calcolosi della colecisti rappresenta una patologia chirurgica importante nei servizi chirurgici di urgenza. Il suo trattamento è esclusivamente chirurgico e talvolta difficile. Attualmente la tecnica chirurgica più utilizzata è quella laparoscopica, tecnica con minori complicazioni intraoperatorie e morbidità post-operatoria ridotta.

In questo studio ci siamo proposti di analizzare la sicurezza dell'utilizzo della tecnica laparoscopica nel trattamento di pazienti sofferenti di colecistite acuta. Lo studio è stato effettuato al Reparto di Chirurgia presso il Centro Universitario, con un'esperienza di oltre 20 anni nella chirurgia laparoscopica, e comprende l'arco di due anni, il 2014 e il 2015, prendendo in esame 193 pazienti. Sono stati considerati i dati demografici dei pazienti, le malattie associate che presentavano un fattore di rischio per la colecisti acuta, le complicazioni intraoperatorie e abbiamo valutato il tasso di conversione dalla tecnica laparoscopica alla chirurgia aperta.

RISULTATI: dei 193 pazienti ricoverati, il 43% è stato diagnosticato con colecistite acuta litiasica, e il 56% con colecistite cronica. Utilizzando il test di Pearsons Chi-Square, abbiamo rilevato una correlazione statistica notevole tra la presenza della colecisti acuta e l'ipertensione arteriosa, il diabete mellito e l'obesità. Come metodo di trattamento, nel 95% dei casi è stata utilizzata la tecnica laparoscopica, e solo nel 5% dei casi colecistectomia classica laparotomica. Il tasso di conversione della tecnica laparoscopica è stato di solo 1,5% in relazione ad aderenze intra-addominali presenti. La mortalità è stata zero.

CONCLUSIONE: Secondo i risultati ottenuti, consideriamo che la colecistectomia laparoscopia nella colecisti acuta sia una tecnica chirurgica sicura, con minori complicazioni intraoperatorie, ma richiede un gruppo operatorio

sperimentato. La morbilità post-operatoria è bassa, il che riduce il numero dei giorni di ricovero in comparazione con la tecnica chirurgica laparotomica.

References

1. Strasberg SM: *Clinical practice. Acute calculous cholecystitis*. N Engl J Med, 2008; 358:2804-811.
2. Gutt CN, Encke J, Koninger J, Harnoss JC, Weigand K, Kipfmüller K, et al: *Acute cholecystitis: early versus delayed cholecystectomy, a multicenter randomized trial (ACDC study, NCT00447304)*. Ann Surg, 2013; 258:385-93.
3. Siddiqui T, Macdonald A, Chong Ps, Jenkins Jt: *Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis of randomized clinical trials*. The American Journal of Surgery, 2008. 195:40-47.
4. Van Der Linden W, Edlund G: *Early versus delayed cholecystectomy: The effect of a change in management*. Br J Surg, 1981;68: 753-57.
5. Cuschieri A, Dubois F, Mouiel J, et al: *The European experience with laparoscopic cholecystectomy*. Am J Surg, 1991; 161:385-87.
6. Kum CK, Goh PM, Isaac JR: *Laparoscopic cholecystectomy for acute cholecystitis*. Br J Surg, 1994; 81:1651-654.
7. Koo KP, Thirlby RC: *Laparoscopic cholecystectomy in acute cholecystitis: What is the optimal timing for operation?* Arch Surg, 1996; 131:540-45.
8. Cuschieri A: *Approach to the treatment of acute cholecystitis: Open surgical, laparoscopic or endoscopic?* Endoscopy, 1993; 25:397-98.
9. Gurusamy KS, Samraj K: *Early versus delayed laparoscopic cholecystectomy for acute cholecystitis*. Cochrane Database Syst, Rev. 4; 2006, CD005440.
10. Mestral C, Rotstein Od, Laupacis A, Hoch Js, Zagorski B, Nathens Ab: *A population-based analysis of the clinical course of 10,304 patients with acute cholecystitis, discharged without cholecystectomy*. J Trauma Acute Care Surg, 2013; 74: 26-31.
11. Papi C, Catarci M, D'ambrosio L, et al: *Timing of cholecystectomy for acute calculous cholecystitis: A meta-analysis*. Am J Gastroenterol, 2004; 35:147-55.
12. Chandler CF, Lane JS, Ferguson P, Thompson JE, Ashley S: *Prospective evaluation of early versus delayed laparoscopic cholecystectomy for treatment of acute cholecystitis*. Am Surg, 2000; 66:896-900
13. Lai Pb, Kwong Kh, Leung Kl, et al: *Randomized trial of early versus delayed laparoscopic cholecystectomy for acute cholecystitis*. Br J Surg, 1998; 85:764-67.
14. Lo CM, Liu CL, Fan ST, Lai EC, Wong J: *Prospective randomized study of early versus delayed laparoscopic cholecystectomy for acute cholecystitis*. Ann Surg, 1998; 227:461-67.
15. Carlomagno N, Santangelo M, Romagnuolo G, Antropoli C, La Tessa C, Renda A: *Laparoscopic cholecystectomy: technical compromise between French and American approach*. Ann Ital Chir, 2014; 85:93-100.
16. Caiazzo P, Del Vecchio G, Albano M, Loffredo M, Calbi F, Comentale A, Di Lascio P, Pastore M, Tramutoli PR: *Colecistectomia laparoscopica con singola incisione (S.I.L.S.)*. Esperienza preliminare. Ann Ital Chir, 2010; 81:13-16.
17. Coccolini F, Catena F, Pisano M, Gheza F, Fagioli S, Di Saverio S, Leandro G, Montori G, Ceresoli M, Corbella D, Sartelli M, Sugrue M, Ansaloni L: *Open versus laparoscopic cholecystectomy in acute cholecystitis. Systematic review and meta-analysis*. International Journal of Surgery, 2015; 18:196-204.
18. Di Vita G, Sciumè C, Milano S, Patti R., Lauria GL, Di Bella G, Caruso R, Leo P, Cillari E: *Inflammatory response in open and laparoscopic cholecystectomy*. Ann Ital Chir, 2001; 72:669-74.
20. Yamashita Y, Takada T, Strasberg SM, et al: *TG13 surgical management of acute cholecystitis*. J Hepatobiliary Pancreat Sci, 2013; 20:89-96.
21. Yokoe M, Takada T, Strasberg SM, et al: *TG13 diagnostic criteria and severity grading of acute cholecystitis*. J Hepatobiliary Pancreat Sci, 2013; 20:35-46.
22. Domínguez LC, Rivera A, Bermúdez C, Herrera W: *Analysis of factors for conversion of laparoscopic to open cholecystectomy: A prospective study of 703 patients with acute cholecystitis*. CIR ESP, 2011; 89: 300-06.
23. Costantini R, Caldaralo F, Palmieri C, Napolitano L, Aceto L, Cellini C, Innocenti P: *Risk factors for conversion of laparoscopic cholecystectomy*. Ann Ital Chir, 2012; 83:245-52.
24. 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; 164:491-95.
25. Schirmer BD, Edge SB, Dix, Hyser MJ, Hanks JB, Jones RS: *Laparoscopic cholecystectomy: Treatment of choice for symptomatic cholelithiasis*. Ann Surg, 1991; 213:665-76.
26. Chikamori F, Kuniyoshi N, Shibuya S, Takase Y: *Early scheduled laparoscopic cholecystectomy following percutaneous transhepatic gallbladder drainage for patients with acute cholecystitis*. Surg Endosc, 2002; 16:1704-07.
27. Eldar S, Sabo E, Nash E, Abrahamson J, Matter I: *Laparoscopic cholecystectomy versus open cholecystectomy in acute cholecystitis*. Surg Laparosc Endosc, 1997; 7: 407-14.
28. Takegami K, Kawaguchi Y, Nakayama H, et al: *Preoperative grading system for predicting operative conditions in laparoscopic cholecystectomy*. Surg Today, 2004; 34: 331-36.
29. Kama NA, Kologlu M, Doganay M, et al: *A risk score for conversion from laparoscopic to open cholecystectomy*. Am J Surg, 2001. 181:520-25.
30. Bourgouin S, Mancini J, Monchal T, Calvary R, Bordes J, Balandraud P: *How to predict difficult laparoscopic cholecystectomy? Proposal for a simple preoperative scoring system*. The American Journal of Surgery, 2016. <http://dx.doi.org/10.1016/j.amjsurg.2016.04.003>
31. Nuzzo G, Giulante F, Giovannini I, Ardito F, D'acapito F, Vellone M, et al: *Bile duct injury during laparoscopic cholecystectomy: results of an Italian national survey on 56592 cholecystectomies*. Arch Surg, 2005; 140:986-92.
32. Soderlund C, Frozanpor F, Linde R S: *Bile duct injuries at laparoscopic cholecystectomy: a single-institution prospective study. Acute cholecystitis indicates an increased risk*. World J Surg, 2005; 29:987-93.
33. Lo Nigro C, Geraci G, Sciuto A, Li Voli F, Sciumè C, Modica

- G: *Bile leaks after videolaparoscopic cholecystectomy: duct of Luschka*. Ann Ital Chir, 2012; 83: 303-12.
34. Johansson M, Thune A, Blomqvist A, Nelvin L, Lundell L: *Management of acute cholecystitis in the laparoscopic era: results of a prospective, randomized clinical trial*. J Gastrointest Surg, 2003. 7: 642-45.
35. Caglià P, Costa S, Tracia A, Veroux M, Luca S, Zappulla E, Russo V, Lucifora B, Borzì L, Patanè G, Trovato S, Amodeo C: *Can laparoscopic cholecystectomy be safely performed in the elderly?* Ann Ital Chir, 2012; 83:21-24.
36. Gelmini R, Franzoni C, Saviano M: *Day surgery laparoscopic cholecystectomy: Initial experience in 43 consecutive patients*. Ann Ital Chir, 2013; 84:631-36.
37. Di Bartolomeo N, Mascioli F, Ciampaglia F: *Minilaparoscopic cholecystectomy a one year report*. Ann Ital Chir, 2015; 86:528-31.

READ-ONLY COPY
PRINTING PROHIBITED