

Should We must Push for Primary Surgery Attempt in Case of Acute Cholecystitis? A Retrospective Analysis and a Proposal of an Evidence based Clinical Pathway

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Abstract

The treatment and the correct management of acute calculous cholecystitis (ACC), despite the presence of several studies, meta-analysis and guidelines are still debated and up to 80% of patients with ACC do not receive the definitive surgical treatment during the first hospital admission. A retrospective analysis of patients admitted with non-complicated acute cholecystitis in our hospital has been performed and on the basis of this analysis we proposed evidence based clinical pathway. 502 patients were selected, with a mean age of 62.09 years old, 56% of male sex and a mean Charlson comorbidity index of 2.96.

32.1% of the patients were not operated during all the observed period. Cholecystectomy during the first hospitalization was performed in 44.2% of the cases with a conversion rate of 15.34%, a cumulative hospital stay of 8.08 days and a mean cost of 3904 €. Delayed cholecystectomy after a mean of 119 days was chosen in 23.7% of the patients, 84.80% as elective procedure and 15.2% in urgency. Conversion rate was 13.7%. Cumulative hospital stay was 13.02 days and cumulative costs were 4660 €. Early cholecystectomy resulted better in term of cumulative hospital stay and costs ($p < 0.0001$) without difference in term of conversion rate and complications, according to data in the literature. On the base of these considerations we propose an evidence based clinical pathway for the treatment of ACC.

Keywords: Acute cholecystitis; Timing of laparoscopic cholecystectomy; Clinical pathway

Introduction

Gallstones are a very common cause of admission at the emergency department: in the adult western population about 5-20% has gallstones [1-3] and 20-40% of them have a risk for developing some type of symptom/signs, 1-4% each year [4,5]. Among the severe complications of gallstones the most frequent is the acute cholecystitis (AC). The treatment and the correct management of acute calculous cholecystitis (ACC), despite the presence of several studies, meta-analysis and guidelines are still debated. In the 1800s ACC was treated by performing a cholecistostomy with a permanent biliary fistula; at the end of that century, in 1882, the first open cholecistectomy was performed by Langenbuch and the removal of gallbladder during the initial hospitalization became the gold standard for symptomatic cholelithiasis, also for the high recurrence rate [6]. However Bruggeman in 1927 published an article on *Annals of Surgery* concluded: "I wish to express the hope that someday surgeons will be fairly unanimous in their view on the treatment of acute inflammation of the gall-bladder" [7]. During the prelaparoscopic era several studies demonstrated that the better treatment was early open cholecystectomy within 7 days of the onset of symptoms also in order to reduce rehospitalization for the

high rate of recurrence [8,9]. The change of surgical approach to the gallbladder, with laparoscopy becoming the gold standard technique, maybe played a pivot role in reinforcing the debate about the correct timing for surgical intervention. The technical difficulties in recognition of anatomical structures due to acute inflammation, potential hazard of severe complication as common bile duct lesions and the high conversion rate related brought the surgeon to introduce the delayed laparoscopic cholecystectomy with initial conservative antibiotic treatment until resolution of the acute inflammation followed by elective interval surgery after 8-12 weeks, considering the acute process a relative contraindication to the laparoscopic surgery [10-13]. During these years a lot reports, case series and RCTs were published discussing which is the better timing for laparoscopic cholecystectomy, early or delayed. From the literature data and several meta-analysis [14-17] early laparoscopic cholecystectomy (ELC) and delayed laparoscopic cholecystectomy (DLC) result not different in term of conversion rate to open cholecystectomy or in term of common bile duct injury but with a significative decrease in total hospital stay and a more cost effective approach in ELC group. Despite the presence even of international guidelines for the management of acute cholecystitis [18] up to 80% of patients with acute cholecystitis do not receive the definitive surgical treatment during the first hospital admission [19-23] increasing costs and hospitalization without clinical advantages.

On this setting a retrospective analysis of patients admitted with non-complicated acute cholecystitis in our hospital during the last six years has been performed in order to assess the state of the art in the treatment of ACC in our hospital. On the basis of this analysis we proposed evidence based clinical pathway for our institution with the attempt to improve the outcomes, to simplify the management of acute cholecystitis for all the staff and to ameliorate the use of resources in the management of AC.

Material and Methods

This is a monocentric retrospective analysis of patients admitted to our hospital for ACC from 01/01/2008 to 30/4/2013. Data were collected from the discharge record of our hospital including all patients older than 18 years old, with a non-planned hospital admission: to select only the patients with an ACC we included patients with a code of ACC in the first three field of diagnosis and with an Italian DRG code of biliary tree disease; we excluded patients with a concomitant pancreatitis (ICD9CM code 577.x) or cholangyitis (576.x). Surgical data were extract from the surgical registry; all diagnostic procedures were recorded from the administrative database and results collected from specific registries; time intervals were calculated from the hospital admission. In (Table 1) all the variables analyzed with the respective codes are shown. For each patient Charlson's comorbidity index has been calculated based on the presence of concomitant disease in the index [24]. 30 days, one year mortality and later re-admission for a gallstones related disease (ICD9CM codes 574.x 575.x 576.x 577.x) were collected from the provincial health service database. For those readmissions the same variables were calculated. The total hospital stay was calculated as the sum of each hospital stay length during the period; the cost were calculated for each patients as the sum of payments refunded to the hospital by the regional health care system according to the Diagnostic Related Group (DRG) mechanism.

All the statistical analysis were performed with IBM SPSS 20; means were compared with student's t test, in association with the Pearson's chi square test and the multivariate analysis were performed only with variables that reached significative association. Statistical significance was defined as $p < 0.05$.

	Codes
Acute cholecystitis	574.00 574.01 574.10 574.11 574.30 574.31 574.40 574.41 574.60 574.61 574.70 574.71 574.80 574.81 575.0 575.10 575.12 575.3
RM	88.97
ERCP	51.10 51.11 51.84 51.85 51.86 51.87 51.88
Biliary tree rx	87.5
Abdominal TC	88.01 88.02
Abdominal ultrasound	88.74 88.76
Endoscopic ultrasound	52.13
Surgical intervention	51.2 51.3 51.4 51.5 51.6 51.7 51.81 51.82 51.83 51.91 51.92 51.93 51.94 54.1

Conversion to open Cholecystectomy	V64.41 and operatory room register
Cholecystostomy	51.0
DRG biliary tree disease	193 194 195 196 197 198 207 208 490 493 494 576

Table 1: ICD9CM codes and DRG code used in the selection

Results

with the abovementioned method 502 patients were selected, with a mean age of 62.09 (± 17.90) years old, 56% of male sex and a mean Charlson's comorbidity index of 2.96 (± 1.90). The mean cumulated hospital stay was 11.14 (± 9.23) days with a mean cost of 3544 (± 1969) € for each patient; during the first hospitalization were required second level exams for the study of the common bile duct engagement for 163 (32.5%) patients. Mortality was 0.2% during the hospitalization and one year mortality was 2.8%. Later hospitalization after the first was required for 156 patients (31.1%).

Cholecystectomy during the first hospitalization was performed in 222 patients (44.2%): the mean age was 55.84 (± 16.56), 52.3% were male and the mean Charlson's comorbidity index was 2.21 (± 1.6); The mean interval from admission to intervention was 90 hours (± 117.87); Laparoscopy was attempted in 96.8% of cases while 7(3.2%) were performed with an open approach; 33(15.34%) were converted to open cholecystectomy during the procedure; the mean length of surgery was 84.97 (± 39.69) minutes and the post-operative hospital stay was 4.19 (± 5.26) days; reintervention was required for one patients due to bleeding. The cumulative hospital stay was 8.08 days with a mean cost of 3904 €. Later hospital admissions were required for 4 patients (1.8%) after a mean of 159 days (± 123).

The initial conservative approach with medical therapy and delayed cholecystectomy in a later hospitalization was chosen in 119(23.7%) patients: mean age was 60.83 (± 15.37), 58.8% were male with a mean Charlson's index of 2.72 (± 1.64). Cholecystectomy were performed after a mean of 119 (± 85.26) days, 101 (84.80%) as elective procedure and 18(15.2%) during an urgent hospitalization due to a recurrence, 1.7% were performed with an open approach; conversion rate was 13.7%; the mean length of surgery was 94.85 (± 42.40) minutes, post-operative hospital stay was 4.04 (± 3.44) days. There were no reintervention but was recorded a lesion of the common bile duct during the operation. The cumulative hospital stay was 13.02 (± 8.48) days with a cumulative cost of 4660 (± 1616) €. Later hospital admissions were required for 7 patients (5.8%) after a mean of 366 (± 112) days.

161 (32.1%) patients were not operated during all the observed period but treated only with a medical treatment: mean age was 71.64 (± 17.42), 59.6% were male with a mean Charlson's index of 4.17 (± 1.83). later re-admissions were required for 33 (20.5%) patients after a mean of 200 (± 340) days. All the results are shown in detail in (Table 2 and 3).

Group	Sub groups	N	%	Age	Male sex %	Charlson's Index	Cumulative stays	Cumulative cost	Time intervals	Length of surgery (min)	Conversion %	Laparotomic %			
early surgery		222	44,2	55,84	52,3	2,21	8,08	3904		90,73	84,97	33	15,3	7	3,2
	<72 h	137	61,7	54,21	51,1	2,01	5,05	3539	to surgery (hours)	31,72	85,29	18	13,2	1	0,7
	72 h-7 days	51	23	57,2	45,1	2,37	9,41	3876		110,71	77,33	9	18,8	3	5,9
	>7 days	34	15,3	60,37	67,6	2,74	18,27	5417		298,56	95,14	6	19,4	3	8,8
delayed surgery		119	23,7	60,83	58,8	2,72	13,02	4660	119,5	to readmission (days)	94,85	16	13,7	2	1,7
	election	101	84,8	60,61	59,4	2,7	11,66	4572	128		94,89	10	10,1	2	2
	urgency	18	15,2	62,07	55,6	2,83	20,63	5150	71,15		94,66	6	33	0	0
p				0,007	ns	0,006	<0,0001	<0,0001			0,043	ns	ns		
no surgery		161	32,1	71,64	59,6	4,17	13,97	2223							
tot		502	100	62,09	56,20	2,96	11,14	3544							

Table 2: Patients characteristics

group	Sub groups	Postoperative stays	Investigation for CBD stones	%	In hospital mortality	%	30 days mortality	%	1 year mortality	%	Later admission	%	Time interval (days)
early surgery		4,19	65	29,3	1	0,5	0	0	3	1,4	4	1,8	159,09
	<72 h	3,57	15	10,9	0				0	0	3	2,2	108
	72 h-7 days	4,76	29	56,9	0				1	2	1	2	312
	>7 days	5,82	21	61,8	1	2,9			2	6,1	0	-	-
delayed surgery		4,04	35	29,4	0	0	0	0	0	0	7	5,88	119,5
	election	3,73	29	28,86									366
	urgency	5,74	6	33,3									
p		ns	ns		ns			ns		ns		ns	
no surgery			63	39,1	3	1,9	1	0,6	11	7	33	20,5	200,43
tot			163	32,5	4	0,8	1	0,2	14	2,8	156	31,1	137,64

Table 3: Patients characteristics

Proposed clinical pathway

Starting from the emergency department, where patient is evaluated, the first and most important step is the diagnosis of AC: according to TG13 diagnostic criteria only patients with signs of local inflammation, systemic inflammation and evidence of cholecystitis at US are admitted and involved in this pathway [25]. After an evaluation for the presence of peritonitis, condition that leads the patient to an emergency operation, there is the other critical point: the assessment

of the risk of choledocholithiasis. We decide to adopt the classification proposed by the American Society of Gastrointestinal Endoscopy (ASGE) in its guidelines that describes three class of risk, low, intermediate and high (Table 4) [26].

With a low risk, if the patient is eligible for surgery patient is transferred in general and emergency surgery and cholecystectomy should be performed as soon as possible. If the patient is unfit for surgery should be transferred in emergency medicine or internal

medicine to receive antibiotic therapy and eventual cholecystostomy if the medical treatment is ineffective after 48 hours.

With a high risk for choledocholithiasis patient should undergo directly ERCP in order to remove the stones from the CBD; if ERCP is ineffective is performed a surgical exploration of the CBD.

Patients with intermediate risk for choledocholithiasis are evaluated with colangiogram or Endoscopic US, in base of the availability of the staff, to select patients should receive ERCP. For both group, after diagnostic evaluation patients should be transfer to general and emergency surgery to receive cholecystectomy if fit to surgery or internal medicine/emergency medicine for conservative antibiotic therapy.

The clinical pathway is available in the appendix.

Predictive Factor for choledocholithiasis	
	Evidence of CBD stone at abdominal US
VERY STRONG	Ascending cholangitis
	Total Serum Bilirubin >4 mg/dL
STRONG	Common Bile duct diameter >6mm (with gallbladder in situ) Bilirubin level 1,8-4 mg/dL
MODERATE	Abnormal liver biochemical test other than bilirubin Age older than 55 y Clinical gallstone pancreatitis
Risk class for choledocolithiasis	
HIGH	Presence of any VERY STRONG or Presence of both STRONG predictors
LOW	No predictors present
INTERMEDIATE	All other patients

Table 4: Predictive Factor and Risk Classfor Choledocolithiasis

Discussion

Despite the presence of guidelines and several studies demonstrating the preferable management of ACC, in our hospital only 44% of the patients with ACC underwent cholecystectomy during the first admission period. On the other hand a large number of patients, 119 (23.7%), after the first hospitalization and a conservative medical treatment required a later planned hospital admission in order to perform the surgical intervention in a easier clinical and organizational setting. This presumed advantage however is not supported by our data, according to large case series and metaanalysis [14-17]: this approach to AC results in an augmented cumulated hospitalization during the observed period (13.02 vs 8.08 days, $p < 0.0001$) with a significant increase even for the costs for the regional

health care system (4660 vs 3904 €, $p < 0.0001$) and an augmented cost for the hospital with a mean difference of 2134 € calculated on the basis of the mean cost of daily hospitalization. All this results are according to that reported by Wilson et al. [27]. The advocate more safety of the elective laparoscopic cholecystectomy was not supported by data: the length of surgery resulted increased in delayed group (94.85 vs 84.97 minutes, $p = 0.04$); overall conversion rate to open cholecystectomy did not result different in the two group (13.7% vs 15.3%, $p = ns$): in the subgroup analysis we compared the conversion rate of cholecystectomy during the first hospitalization versus only the elective delayed cholecystectomy and even that difference did not result significative (10.1% vs 15.3%, $p = ns$). In fact in the delayed group for 18 patients (15.3%) we observed an urgent rehospitalisation with cholecystectomy before the planned one, with a mean interval of 71 days, and with a high conversion rate (33%). There were no differences in common bile duct lesions, in-hospital mortality and one year mortality between the two groups.

In the early cholecystectomy group conversions to open cholecystectomy were due to a failed identification of structures in Calot's triangle in 29/33 cases (20 for acute inflammation and 9 to adhesions), Mirizzi's syndrome 1/33, perforation of the gallbladder 1/33 and bleeding 2/33; in the delayed group were due to failed identification of Calot's structures in 15/16 cases (13 for adhesions and 2 for acute inflammation) and for bleeding in one case. Analyzing the reasons of conversion to open cholecystectomy, the only difference is the role of inflammation and adhesions: while in the early group the first reason was the acute inflammation process (60%) in the delayed group the first cause were the adhesion (81%); in fact the medical conservative treatment is effective on the acute inflammation process but cannot restore the normal anatomy having no effect on the formation of adhesions.

The two groups were not homogeneous for age and Charlson's comorbidity, with a major age and a major index in the delayed group: this could be explained as a more prudent approach to older patients with a major comorbidity; however this difference was not significative at multivariate analysis.

Among patients operated in the first admission 137 (61.7%) underwent early cholecystectomy within 72 hours from hospital admission, 23% later than 72 h but within 7 days and 15.3% later than 7 days from admission. We analyzed this subgroup of patients combining with two different cut off: the traditional limit of 72 hours from admission and the limit considered for the early laparoscopic cholecystectomy, 7 days as proposed and discussed in literature [17,28]. Detailed results are shown in table 5: obviously the total hospital stay and the costs were different, due to the different latency from admission and surgery; post-operative stay was increased with a major interval and was significative only with a cut off of 72 hour. We noticed that there are not significative difference in term of conversion rate and length of surgery. These results suggest a not strict limit to perform cholecystectomy during the first hospitalization, as noted by other authors [29-31].

	Tot	Within 72 hours	>72h	<7 days	>7 days
N	222	137	85	188	34
%	44,2	61,7	38,3	84,7	15,3

Age	55,84		54,21	ns	58,47		55,02	ns	60,37
Male sex %	52,3		51,1	ns	54,1		49,5	ns	67,6
Charlson	2,21		2,01	0,026	2,52		2,11	0,041	2,74
cumulative stay	8,08		5,05	<0,0001	12,95		6,23	<0,0001	18,27
Cumulative cost	3904		3539	<0,0001	4493		3631	<0,0001	5417
time to urgery (min)	90,73		31,72	<0,0001	185,85		53,15	<0,0001	298,56
lenght of surgery	84,97		85,29	ns	84,45		83,13	ns	95,14
conversion	33		18	ns	15		27	ns	6
%	15,3		13,2		19,00		14,7		19,4
laparotomic	7		1	0,009	6		4	0,04	3
%	3,2		0,7		7,06		2,13		8,8
degenza post-op	4,19		3,57	0,026	5,19		3,89	ns	5,82
investigations for CBD stones	65		15		50		44,00		21
%	29,3		10,9	<0,0001	58,80		23,40	<0,0001	61,8
in hospital mortality	1		0	ns	1		0	0,018	1
%	0,5				1,18		0,00		2,9
30 days mortality	0		0		0		0		0
%	0						0,00		0
1 year mortality	3		0	0,026	3		1	0,011	2
%	1,4		0		3,53		0,53		6,1
later hospitalization	4		3	ns	1		4	ns	0
%	1,8		2,2		1,18		2,13		0
time interval (days)	159,09		108	ns	312		159,09		-

Table 5: Timing to surgery

The patients not operated during the observed period were considerably older than other and with significant higher Charlson's index: they were not eligible for surgery and in two cases (1.2%) was required cholecystostomy; probably due even to the high comorbidity there were affected by a high rate of gallstones related rehospitalizations (20%). These patients had a 1 year mortality of 7%, but were not associated with later admissions related to gallstones.

Finally the presence of a concomitant lithiasis of the common bile duct is reported in literature ranging from 10% to 25% in gallstones related disease [32-34] and, in a recent prospective study in 8,7% of patients with acute cholecystitis [35]. The suspected choledocholithiasis is one of the major factor implicated in the delaying of surgery, in fact patients require several second level exams to assess the real presence of CBD stones ad endoscopic US, Cholangio MR and ERCP. In our series only 10% of patients operated within 72 hours required second level investigation versus 58% of patients operated after this timing. Among all the patients 163 (32.5%) required a second level investigation for suspected choledocholithiasis: this percentage could express an overestimation of this clinical condition

may be related to the clinical judgment of the single physician and not on the basis of a standardized diagnostic method.

On the base of these considerations we proposed an evidence based clinical pathway for the treatment of ACC. As reported by Sheffield the implementation of a clinical pathway increases the outcome for the patients [36].

The proposed clinical pathway combines different guidelines [18, 26]: is structured as a step by step flow chart to guide physicians and surgeons in the correct way to treat the patients with ACC, surgery is recommended as decisive treatment during the first hospital admission unless contraindication. In the TG13 flowchart for the management of AC [18] patients are stratified on the basis of the severity grading of AC [25] suggesting a conservative approach for patients with moderate AC: as noticed by Campanile et al. [37], the indication of surgery based on this classification is less supported by literature and the application of those guidelines did not showed an improve in the outcome [38]. From this consideration we decided to adopt a surgical approach evaluating the single patient's condition and

the risk related to surgery; among the surgical risk scores there are no scores validated for the acute cholecystitis: P-Poosum is one of the most complete and is yet daily adopted for evaluation of all surgical patients in our institution [39]. For these reasons we chose to adopt it considering a predicted mortality >10% a contraindication to surgery.

All the cholecystectomy should be started in laparoscopy unless contraindications; the optimal timing for surgery is indicated at 72-96 hours, without a strict limit but with the theory of as soon as possible. If the patients is unfit to surgery should receive a conservative medical treatment with antibiotic. For the therapy the 2013 WSES Guidelines for management of intra-abdominal infection were adopted and modified according to the hospital policy and surviving sepsis campaign guidelines [40,41]; the risk of ESBL + infection is calculated with the score proposed by Tumbarello et al. [42]. Details of the antibiotic therapy are shown in (Table 6).

The conservative antibiotic treatment is associated with about 10% of ineffectiveness [9]: after the assessment of failure of medical therapy, generally after 48 hours, as suggested by TG13 [43], for patients unfit to surgery with an high perioperative risk we propose the gallbladder drainage with the percutaneous transhepatic technique (PTGBD) despite in the literature the debate on this clinical approach is still open and there are not strong recommendation based on well-designed studies. For these patients in our institution we plan a later surgical evaluation after 60 days from discharge for possible cholecystectomy in fact as reported in the literature they are afflicted by a recurrence rate up to 50% [44,45].

This study has several limitations: data are extract retrospectively from an administrative discharge record; well defined diagnostic criteria, indication for further CBD test as well indication for early, delayed and no surgery, have not be applied to all patients or at least these information cannot be always retrievable but assumed on the basis of clinical judgment expressed by senior surgeons. With these limitations the coherence of our results can be supported by the fact that they are not different from previous studies. On the other hands our series is large and it is single Institution; moreover it is enforced by data from the provincial health care system database allowing a more detailed analysis of outcome.

ESBL -		ESBL +	
non severe sepsis	severe sepsis	non severe sepsis	severe sepsis
Amoxicillin Clavulanate Ciprofloxacin Metronidazol	+ Piperacillin or Tazobactam + Tigecyclin	Piperacillin Tigecyclin Fluconazol	+ meropenem/ Imipenem/ doripenem ± Vancomicin + Echinocandin
Attribute			No. of points
Recent antibiotic therapy with beta-lactams and/or fluorquinolones ^a			2
Previous ospitalization ^b			3
Transfer from another healthcare facility			3
Charlson comobidity score of >4			2
Recent history of urinary catheterization ^c			2
Age ≥ 70 anni			2

Table 6: Antibiotic Therapy and risk assessment for ESBL

- ^a During the 3 months preceding the index hospitalization
 - ^b During the 12 months preceding the index hospitalization
 - ^c During the 30 days preceding the index admission
- ≥ 3: ESBL carrier possible. Start with tigecycline or carbapenem then shift if not confirmed
- ≥ 8: high probable ESBL. Start with tigecycline or carbapenem. The patient should be isolated.

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References

- Halldestam I, Enell EL, Kullman E, Borch K (2004) Development of symptoms and complications in individuals with asymptomatic gallstones. *Br J Surg* 91: 734-738.
- Stinton LM, Myers RP, Shaffer EA (2010) Epidemiology of gallstones. *Gastroenterol Clin North Am* 39: 157-169.
- Glabek I, Kvaale G, Arnesjö B, Søreide O (1987) Prevalence of gallstones in a Norwegian population. *Scand J Gastroenterol* 22: 1089-1094.
- Friedman GD (1993) Natural history of asymptomatic and symptomatic gallstones. *Am J Surg* 165: 399-404.
- Kimura Y, Takada T, Strasberg SM, Pitt HA, Gouma DJ, et al. (2013) TG13 current terminology, etiology, and epidemiology of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci* 20: 8-23.
- De U (2004) Evolution of cholecystectomy: A tribute to Carl August Langenbuch. *Indian J Surg* 66: 97-100.
- Bruggeman HO (1928) TREATMENT OF ACUTE CHOLECYSTITIS. *Ann Surg* 87: 423-427.
- Järvinen HJ, Hästbacka J (1980) Early cholecystectomy for acute cholecystitis: a prospective randomized study. *Ann Surg* 191: 501-505.
- Papi C, Catarci M, D'Ambrosio L, Gili L, Koch M, et al. (2004) Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. *Am J Gastroenterol* 99: 147-155.
- Kum CK, Goh PM, Isaac JR, Tekant Y, Ngoi SS (1994) Laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg* 81: 1651-1654.
- Kum CK, Eypasch E, Lefering R, Paul A, Neugebauer E, et al. (1996) Laparoscopic cholecystectomy for acute cholecystitis: is it really safe? *World J Surg* 20: 43-48.
- Wilson P, Leese T, Morgan WP, Kelly JF, Brigg JK (1991) Elective laparoscopic cholecystectomy for "all-comers". *Lancet* 338: 795-797.
- Frazer RC, Roberts JW, Symmonds R, Snyder SK, Hendricks J, et al. (1992) What are the contraindications for laparoscopic cholecystectomy? *Am J Surg* 164: 491-494.
- Siddiqui T, MacDonald A, Chong PS, Jenkins JT (2008) Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis of randomized clinical trials. *Am J Surg* 195: 40-47.
- Lau H, Lo CY, Patil NG, Yuen WK (2006) Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis. *Surg Endosc* 20: 82-87.
- Gurusamy K, Samraj K, Gluud C, Wilson E, Davidson BR (2010). Meta-analysis of randomized controlled trials on the safety and effectiveness of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *British Journal of Surgery* 7: 141-150.
- Gurusamy KS, Davidson C, Gluud C, Davidson BR (2013). Early versus delayed laparoscopic cholecystectomy for people with acute cholecystitis. *Cochrane Database Syst Rev*, 6.
- Gurusamy KS, Koti R, Fusai G, Davidson BR (2013) Early versus delayed laparoscopic cholecystectomy for uncomplicated biliary colic. *Cochrane Database Syst Rev* 6: CD007196.

19. Miura F, Takada T, Strasberg SM, Solomkin JS, Pitt HA, et al. (2013) TG13 flowchart for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci* 20: 47-54.
20. Casillas RA, Yegiyants S, Collins JC (2008) Early laparoscopic cholecystectomy is the preferred management of acute cholecystitis. *Arch Surg* 143: 533-537.
21. Riall TS, Zhang D, Townsend CM Jr, Kuo YF, Goodwin JS (2010) Failure to perform cholecystectomy for acute cholecystitis in elderly patients is associated with increased morbidity, mortality, and cost. *J Am Coll Surg* 210: 668-677, 677-9.
22. Senapati PS, Bhattacharya D, Harinath G, Ammori BJ (2003) A survey of the timing and approach to the surgical management of cholelithiasis in patients with acute biliary pancreatitis and acute cholecystitis in the UK. *Ann R Coll Surg Engl* 85: 306-312.
23. Askew J (2005) A survey of the current surgical treatment of gallstones in Queensland. *ANZ J Surg* 75: 1086-1089.
24. Campbell EJ, Montgomery DA, Mackay CJ (2008) A national survey of current surgical treatment of acute gallstone disease. *Surg Laparosc Endosc Percutan Tech* 18: 242-247.
25. Charlson ME, Pompei P, Ales KL, MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 40: 373-383.
26. Yokoe M1, Takada T, Strasberg SM, Solomkin JS, Mayumi T, et al. (2013) TG13 diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci* 20: 35-46.
27. ASGE Standards of Practice Committee, Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, et al. (2010) The role of endoscopy in the evaluation of suspected choledocholithiasis. *Gastrointest Endosc* 71: 1-9.
28. Wilson E, Gurusamy K, Gluud C, Davidson BR (2010) Cost-utility and value-of-information analysis of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg* 97: 210-219.
29. Brooks KR, Scarborough JE, Vaslef SN, Shapiro ML (2013) No need to wait: an analysis of the timing of cholecystectomy during admission for acute cholecystitis using the American College of Surgeons National Surgical Quality Improvement Program database. *J Trauma Acute Care Surg* 74: 167-173.
30. Lee AY, Carter JJ, Hochberg MS, Stone AM, Cohen SL, et al. (2008) The timing of surgery for cholecystitis: a review of 202 consecutive patients at a large municipal hospital. *Am J Surg* 195: 467-470.
31. Degrate L, Ciravegna AL, Luperto M, Guaglio M, Garancini M, et al. (2013) Acute cholecystitis: the golden 72-h period is not a strict limit to perform early cholecystectomy. Results from 316 consecutive patients. *Langenbecks Arch Surg* 398: 1129-1136.
32. Zhu B, Zhang Z, Wang Y, Gong K, Lu Y, et al. (2012) Comparison of laparoscopic cholecystectomy for acute cholecystitis within and beyond 72 h of symptom onset during emergency admissions. *World J Surg* 36: 2654-2658.
33. Peng WK, Sheikh Z, Paterson-Brown S, Nixon SJ (2005) Role of liver function tests in predicting common bile duct stones in acute calculous cholecystitis. *Br J Surg* 92: 1241-1247.
34. Onken JE, Brazer SR, Eisen GM, Williams DM, Bouras EP, et al. (1996) Predicting the presence of choledocholithiasis in patients with symptomatic cholelithiasis. *Am J Gastroenterol* 91: 762-767.
35. Williams EJ, Green J, Beckingham I, Parks R, Martin D, et al. (2008) Guidelines on the management of common bile duct stones (CBDS). *Gut* 57: 1004-1021.
36. Videhult P, Sandblom G, Rudberg C, Rasmussen IC (2011) Are liver function tests, pancreatitis and cholecystitis predictors of common bile duct stones? Results of a prospective, population-based, cohort study of 1171 patients undergoing cholecystectomy. *HPB (Oxford)* 13: 519-527.
37. Sheffield KM, Ramos KE, Djukom CD, Jimenez CJ, Mileski WJ, et al. (2011) Implementation of a critical pathway for complicated gallstone disease: translation of population-based data into clinical practice. *J Am Coll Surg* 212: 835-843.
38. Campanile FC, Catena F, Coccolini F, Lotti M, Piazzalunga D, et al. (2011) The need for new "patient-related" guidelines for the treatment of acute cholecystitis. *World J Emerg Surg* 6: 44.
39. Lee SW, Yang SS, Chang CS, Yeh HJ (2009) Impact of the Tokyo guidelines on the management of patients with acute calculous cholecystitis. *J Gastroenterol Hepatol* 24: 1857-1861.
40. Prytherch DR, Whiteley MS, Higgins B, Weaver PC, Prout WG, et al. (1998) POSSUM and Portsmouth POSSUM for predicting mortality. Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity. *Br J Surg* 85: 1217-1220.
41. Sartelli M, Viale P, Catena F, Ansaloni L, Moore E, et al. (2013) 2013 WSES guidelines for management of intra-abdominal infections. *World J Emerg Surg* 8: 3.
42. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, et al. (2013) Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 39: 165-228.
43. Tumbarello M, Trecarichi EM, Bassetti M, De Rosa FG, Spanu T, et al. (2011) Identifying patients harboring extended-spectrum-beta-lactamase-producing Enterobacteriaceae on hospital admission: derivation and validation of a scoring system. *Antimicrob Agents Chemother* 55: 3485-3490.
44. Tsuyuguchi T, Itoi T, Takada T, Strasberg SM, Pitt HA, et al. (2013) TG13 indications and techniques for gallbladder drainage in acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci* 20: 81-88.
45. de Mestral C, Gomez D, Haas B, Zagorski B, Rotstein OD, et al. (2013) Cholecystostomy: a bridge to hospital discharge but not delayed cholecystectomy. *J Trauma Acute Care Surg* 74: 175-179.