

Lithiasic acute cholecystitis: application of Tokyo Guidelines in severity grading

Colecistitis aguda litiásica: aplicación de las Guías de Tokio en los criterios de gravedad

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Abstract

Background: Acute calculous cholecystitis (AC) is one of the most frequent surgical emergencies in our field. Laparoscopic cholecystectomy is considered the treatment of choice, although not sufficiently widespread. **Objective:** To analyze the application of the Tokyo Guidelines in the management of AC and to determine the influence of the degree of severity on management and prognosis. **Method:** Prospective, observational study of patients with a primary diagnosis of AC between 2010 and 2015. **Exclusion criteria:** AC recurrence; AC as a secondary diagnosis; acalculous cholecystitis; concurrent biliary pathology. Severity was classified according to Tokyo 2013 Guidelines. **Results:** 998 patients were included: 338 (33.9%) mild AC, 567 (56.8%) moderate AC, and 93 (9.3%) severe AC. A total of 582 (58.3%) patients were operated on. Postoperative complications Dindo-Clavien grade $\geq$ II 12.6%: mild AC 3.6%; moderate AC 12.2%; severe AC 49.0% ($p < 0.001$). Overall mortality 2%: mild AC 0%; moderate AC 0.5%; severe AC 18.0% ($p < 0.001$). **Conclusion:** Urgent laparoscopic cholecystectomy remains the treatment of choice for mild and moderate AC. In patients with severe AC, the risks and benefits of surgery should be assessed, given the high degree of complications and associated mortality.

Keywords: Laparoscopic cholecystectomy. Acute cholecystitis. Cholecystostomy. Tokyo guidelines. Recurrence.

Resumen

Antecedentes: La colecistitis aguda litiásica (CA) es una de las urgencias quirúrgicas más frecuentes en nuestro medio. La colecistectomía laparoscópica se considera el tratamiento de elección, aunque sigue sin ser una realidad su práctica generalizada. **Objetivo:** Analizar la aplicación de las Guías de Tokio en el manejo de la CA y determinar la influencia de la gravedad en el manejo y el pronóstico. **Método:** Estudio prospectivo, observacional, de pacientes con diagnóstico primario de CA entre 2010 y 2015. **Criterios de exclusión:** recidiva de CA, CA como diagnóstico secundario, CA alitiásica u otra patología biliar concomitante. Se ha clasificado la gravedad según las Guías de Tokio de 2013. **Resultados:** Se incluyen 998 CA: 338 (33.9%) leves, 567 (56.8%) moderadas y 93 (9.3%) graves. Se operaron 582 pacientes (58.3%), y posteriormente 15 precisaron rescate. Complicaciones posoperatorias Dindo-Clavien $\geq$ 12,6%: CA leve 3,6%, CA moderada 12,2%, CA grave 49% ($p < 0.001$). Mortalidad global 2%: CA leve 0%, CA moderada 0.5%, CA grave 18% ($p < 0.001$). **Conclusión:** La colecistectomía laparoscópica sigue siendo el tratamiento de elección para la CA leve y

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moderada. En pacientes con CA grave debe valorarse el riesgo-beneficio de la cirugía, dadas las complicaciones y la mortalidad asociadas.

Palabras clave: Colecistectomía laparoscópica. Colecistitis aguda. Colecistostomía. Guías de Tokio. Recidiva.

Introduction

Acute calculous cholecystitis (AC) is one of the main surgical emergencies, especially in the elderly population due to the progressive increase in life expectancy¹. Although its evolution is usually favorable, it can involve complications and has a non-negligible mortality, depending on the characteristics of the disease and the patient².

Although we have not found conclusive meta-analyses³, emergency laparoscopic cholecystectomy (LC) is considered the treatment of choice for AC⁴⁻¹⁰, although patients do not always undergo surgery due to the risks it entails¹¹; patient poor general condition or age have been considered the main risk factors¹²⁻¹⁴, although the advanced age criterion has been varying over time¹⁵⁻¹⁸. The main problem of the referred studies and of the literature in general was the lack of a homogeneous criterion that would allow comparative analyses between the results and different therapeutic options.

The publication in 2007¹⁹ (with updates in 2013²⁰ and 2018²¹) of the Tokyo Guidelines had the purpose to unify diagnostic criteria and classify patients according to defined degrees of severity, and thus facilitate decision-making and subsequent analysis.

The purpose of this study was to analyze our experience in the application of the Tokyo Guidelines to the management of AC, and the influence the degree of severity has on the management and prognosis of patients.

Method

We present an observational clinical study based on prospectively collected data from consecutively-admitted patients with AC in our center from 2010 on, which is when our diagnostic and treatment protocol was modified to be adapted to the Tokyo Guidelines. After these guidelines were updated in 2013, we adapted our protocols again, and the patients included in the database until that moment were revised.

The database includes data from all patients admitted via the emergency department with a diagnosis of a first episode of AC between June 2010 and December 2015. The exclusion criteria were: relapse of a

previous AC episode, AC as secondary diagnosis, acalculous AC or concomitant presence of acute pancreatitis, acute cholangitis or other biliary pathology (benign or neoplastic), except for choledocholithiasis simultaneously diagnosed with AC. The following characteristics were collected for subsequent analysis: age, gender, medical history, history of biliary disorders (acute pancreatitis, acute cholangitis or obstructive jaundice), simultaneous choledocholithiasis and American Society of Anesthesiologists (ASA) classification. We considered patients with ASA III or IV grade as having significant comorbidity. Initial treatment was decided at admission (antibiotic, ultrasound-guided cholecystostomy or cholecystectomy). We defined early cholecystectomy as that performed within the first 48 hours after admission. Treatment duration, readmissions, mortality, and complications (according to Dindo-Clavien scale²²) were recorded. Deferred cholecystectomy is that which was performed after patient discharge, usually from the sixth week onwards. Patient follow-up ended at 30 days of cholecystectomy in those who underwent the procedure (emergency or elective) or until death and at 24 months in the rest.

Diagnosis

Diagnosis was established at the emergency department according to the Tokyo Guidelines²⁰ based on clinical, analytical and radiological criteria (Table 1). Depending on patient status, computed tomography or magnetic resonance imaging was also performed. AC severity was classified as grade I (mild), II (moderate) or III (severe)²⁰ (Table 2).

Management in the emergency department

Treatment was started with fluid therapy, analgesia, omeprazole and antibiotic therapy according to hospital protocol. Subsequently, patients were admitted to the hospitalization area for treatment to be completed. Patients with severe AC were treated on an individual basis, with admission to the intensive care unit when they met the criteria. In selected cases, patients with mild AC were attended to at home by the home hospitalization services²³.

Table 1. Diagnostic criteria for acute cholecystitis according to the Tokyo Guidelines

A. Local signs of inflammation:
– Murphy's sign
– Mass, pain or tenderness at right hypochondrium
B. Systemic signs of inflammation:
– Fever > 37.5 °C
– Elevated C-reactive protein
– Leukocytosis > 10 x 10 ⁹ /L
C. Imaging:
Findings characteristic of acute cholecystitis: edema with > 5-mm wall, distended vesicle, radiological Murphy, perivesicular fluid, cholelithiasis.
Suspected diagnosis: one A criterion + one B criterion
Definite diagnosis: one A criterion + one B + C criterion

Table 2. Criteria for acute cholecystitis severity grading according to the Tokyo Guidelines

– Grade I (mild) AC does not meet criteria for grade II or grade III
– Grade II (moderate) AC is associated with one of the following conditions:
1) Elevated white blood cell count (> 18,000/mm ³)
2) Palpable soft mass on right hypochondrium
3) Symptom duration > 72 hours
4) Marked local inflammation (gangrenous cholecystitis, perivesicular abscess, hepatic abscess, emphysematous cholecystitis, choleperitoneum)
– Grade III (severe) AC is associated with dysfunction of one of the following organs or systems:
1) Cardiovascular: hypotension requiring treatment with dopamine ≥ 5 µg/kg per minute, or any dose of epinephrine
2) Neurological: decreased level of consciousness
3) Respiratory: PaO ₂ /FiO ₂ < 300
4) Renal: oliguria or creatinine > 2.0 mg/dL
5) Hepatic: prothrombin time, INR > 1.5
6) Hematological: platelet count < 100,000/mm ³

AC: acute cholecystitis; FiO₂: fraction of inspired oxygen;
INR: International Normalized Ratio; PaO₂: partial pressure of oxygen.

The antibiotic protocol that was followed, according to the guidelines' recommendations²⁴⁻²⁶, was the following: for mild AC, ceftriaxone + metronidazole; for moderate AC, + ceftriaxone-metronidazole (ertapenem in patients older than 75 years or with risk factors); and for severe AC, piperacillin-tazobactam. In case of allergy, gentamicin + metronidazole was used in mild-moderate AC and tigecycline + amikacin in severe AC. Treatment duration, if cholecystectomy was not performed, was 4-7 days, usually until leukocyte normalization and C-reactive protein decrease to half the initial values; if cholecystectomy was carried out, treatment was discontinued at 24 hours of the

intervention, except in patients with emphysematous AC, vesicular necrosis, perforation or perivesicular abscess, in whom it was also maintained for 4-7 days.

Therapeutic options

Early LC is the treatment of choice in patients with mild-moderate AC; however, for various reasons, such as advanced age, significant comorbidity, anticoagulant therapy, simultaneous choledocholithiasis, surgery refusal or surgeon's decision, antibiotic treatment is carried out with no surgical procedures. In patients with severe AC without significant comorbidity, cholecystectomy is indicated as initial treatment, while in those with significant comorbidity, urgent drainage is indicated by ultrasound-guided cholecystostomy. Patients with severe AC who do not undergo surgery and have a good response to initial medical treatment can complete antibiotic treatment without cholecystostomy being performed. In patients with moderate AC without clinical improvement, cholecystostomy may also be considered. In some selected patients with choledocholithiasis, urgent endoscopic sphincterotomy was carried out for the removal of stones and, subsequently, cholecystectomy.

Surgical treatment

LC is performed with the patient in the French position, access by Hasson umbilical technique and three accessory ports, with a pressure of 12 mmHg being maintained. In case of conversion or laparoscopy contraindication, subcostal laparotomy is performed. Subtotal or partial cholecystectomy has been considered a valid resource in case of difficulty both in laparoscopic surgery and in case of conversion, and it has not been included in the analysis. The placement of drainage is at the surgeon's discretion. Sometimes, the intervention was carried out by senior residents, but always under the supervision of an experienced specialist. Postoperative treatment includes antibiotic according to protocol, analgesia with acetaminophen and metamizole, omeprazole and thromboembolic disease protocol. Oral intake is restarted 6 hours after the procedure with fluids and progressive increase according to tolerance.

Medical treatment

Hospitalized patients who do not undergo invasive procedures receive the same treatment. Oral intake in patients without nausea or vomiting is started when they arrive at the hospitalization area with fluids and

Table 3. Acute cholecystitis results by age groups

Age group (years)	Patients	Significant comorbidity	Grade III (severe)	Cholecystectomy	Dindo-Clavien ≥ II complication	Mortality
10-20	4 (0.4)	0 (0)	0 (0)	2 (50)	0 (0)	0 (0)
20-30	21 (2.1)	2 (9.5)	1 (4.8)	19 (90.5)	4 (19.0)	0 (0)
30-40	52 (5.2)	1 (1.9)	1 (1.9)	45 (86.5)	5 (9.6)	0 (0)
40-50	73 (7.3)	2 (2.7)	0 (0)	57 (78.1)	4 (5.5)	0 (0)
50-60	94 (9.4)	14 (14.9)	7 (7.4)	67 (71.3)	10 (10.6)	1 (1.1)
60-70	155 (15.5)	44 (28.4)	12 (7.7)	108 (69.7)	15 (9.7)	2 (1.3)
70-80	251 (25.1)	107 (42.6)	19 (7.6)	165 (65.7)	32 (12.7)	4 (1.6)
80-90	296 (29.6)	160 (54.0)	47 (15.8)	114 (38.5)	49 (16.5)	11 (3.7)
> 90	52 (5.2)	33 (63.5)	6 (11.5)	5 (9.61)	7 (13.5)	2 (3.8)
Overall	998	363 (36.4)	93 (9.3)	582 (58.3)	126 (12.6)	20 (2.0)

Data expressed as n (%).

is progressively increased according to tolerance. In case of ultrasound-guided cholecystostomy, oral intake is interrupted 6 hours before the test, and restarted after the procedure.

Statistical analysis

Since this was an observational study, no formal sample size estimation was carried out. Quantitative variables were expressed as the mean and standard deviation, and compared with Student's t-test or ANOVA. Quantitative variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test. In the multivariate analysis, variables with $p < 0.2$ or clinically significant were included, and a logistic regression analysis was performed. The level of statistical significance was established at $p < 0.05$. SPSS, version 19.0 (IBM Co, Armonk, NY, USA), was used.

Results

Between June 2010 and December 2015, 998 patients with AC were included, among whom 574 were males (57.5%), mean age was 70.0 ± 16.9 years, and 338 (34%) had mild AC, 567 (57%), moderate AC, and 93 (9%), severe AC.

Table 3 descriptively presents the evolution of results by age divided in decades. Depending on age increase, both the number of patients and the presence of comorbidity, severe AC, complications and

mortality are observed to progressively and almost continuously increase, while, inversely, surgical treatment decreases.

Characteristics of the series

Table 4 shows overall data and data divided according to severity. Although significant differences are observed in practically all parameters, the data suggest that said differences may be influenced by severe AC. Thus, when mild AC and moderate AC are compared, there are no differences in terms of demography, medical history and comorbidity, but they remain for received treatment ($p = 0.000$), antibiotic treatment duration ($p < 0.0001$), mean hospital stay ($p < 0.0001$), complications ($p < 0.0001$), mortality ($p < 0.0001$) and readmissions ($p = 0.044$).

Initial treatment was antibiotic therapy in 404 patients (40.5%), out of whom 15 (3.5%) required surgical rescue: 11 (5%) with moderate AC and 4 (11%) with severe AC; and 8 (2%), rescue with cholecystostomy. Figure 1 analyzes the reasons why surgical treatment not was carried out.

Finally, of the entire series, 582 patients (58%) underwent surgery (Table 5), with differences being observed in all perioperative and postoperative variables according to the grade. There were no differences in the number of biliary fistulas, with a total of 12 (2.0%), among which three were conservatively resolved, four with reoperation and five with Percutaneous Endoscopic Retrograde Cholangiography (PERC).

Table 4. Characteristics of the series, overall and according to acute cholecystitis grade

Characteristics	Overall (n = 998)	Grade I (mild) (n = 338)	Grade II (moderate) (n = 567)	Grade III (severe) (n = 93)	p
Age*	70.0 ± 17	68.7 ± 18	69.9 ± 17	77.5 ± 12	< 0.001
Patients > 80 years	348 (34.9)	106 (31.4)	189 (33.3)	53 (57)	< 0.001
Male gender	574 (57.5)	187 (55.3)	334 (58.9)	53 (57)	0.536
Diabetes	266 (26.7)	86 (25.4)	146 (25.7)	34 (37)	0.721
Anticoagulant therapy	128 (12.8)	39 (11.5)	59 (10.4)	30 (32)	< 0.001
Significant comorbidity	363 (36.4)	105 (31.1)	192 (33.9)	66 (71)	< 0.001
History of biliary disorders	81 (8.1)	25 (7.4)	41 (7.2)	15 (16)	0.012
Cholelithiasis	56 (5.6)	22 (6.5)	26 (4.6)	8 (9)	0.024
Symptoms until admission*	3.3 ± 4	1.5 ± 1	4.1 ± 4	3.8 ± 4	< 0.001
Treatment received					
Antibiotic therapy	381 (38.2)	184 (54.4)	182 (32.1)	15 (16)	< 0.001
Cholecystostomy	35 (3.5)	0 (0)	17 (3.0)	18 (19)	< 0.001
Cholecystectomy	582 (58.3)	154 (45.6)	368 (64.9)	60 (64)	< 0.001
Antibiotic duration*	7.2 ± 4	6.3 ± 3	7.4 ± 4	9.0 ± 5	< 0.001
Hospital stay*	5.7 ± 6	4.2 ± 3	5.5 ± 4	12.5 ± 13	< 0.001
Dindo-Clavien ≥ II complication	126 (12.6)	12 (3.6)	69 (12.2)	45 (49)	< 0.001
Mortality†	20 (2.0)	0 (0)	3 (0.5)	17 (18)	< 0.001
Readmissions‡	29 (2.9)	4 (1.2)	21 (3.7)	4 (5)	0.042
Cholecystitis relapse‡	83 (20.3)	34 (18.5)	43 (21.6)	6 (23)	0.741
Other biliary complication‡	44 (10.8)	20 (10.9)	22 (11.1)	2 (8)	0.832

*Mean±standard deviation in days.

†At 30 days.

‡In non-operated patients.

Except for those indicated with an asterisk, data expressed as n (%).

Risk factors for morbidity and mortality

We have analyzed which factors may have been associated with complications and mortality in patients with AC (Table 6). As independent risk factors for mortality we found severe AC and significant comorbidity. Independent risk factors for Dindo-Clavien ≥ II complications are severe AC and conversion to open surgery.

Severe AC has been a major risk factor in patients both undergoing and not undergoing surgery. Thus, in patients who did not undergo surgery, there was no mortality recorded in mild and moderate AC vs. 7 deaths (21%) in severe AC ($p < 0.0001$); Dindo-Clavien ≥ II complications occurred in 19 (5%) vs. 12 (36%), respectively ($p < 0.0001$). In those patients who underwent surgery, mortality was 3 (0.6%) in mild and moderate AC, and 10 (17%) in severe AC ($p < 0.0001$);

Dindo-Clavien ≥ II complications occurred in 62 (12%) and 33 (56%), respectively ($p < 0.0001$).

Risk factors for severe AC

Given its importance in patient prognosis, we analyzed which factors could have favored severe AC (Table 7). In the multivariate analysis, age older than 80 years (odds ratio [OR] = 1.8; 95% confidence interval [CI]: 1.1-2.8; $p = 0.011$), history of biliary disorders (OR = 2.06; 95% CI: 1.1-3.8; $p = 0.025$) and significant comorbidity (OR = 4.16; 95% CI: 2.5-6.7; $p < 0.0001$) were independent risk factors.

Discussion

AC is one of the most common surgical emergencies in our setting, as demonstrated by the fact of

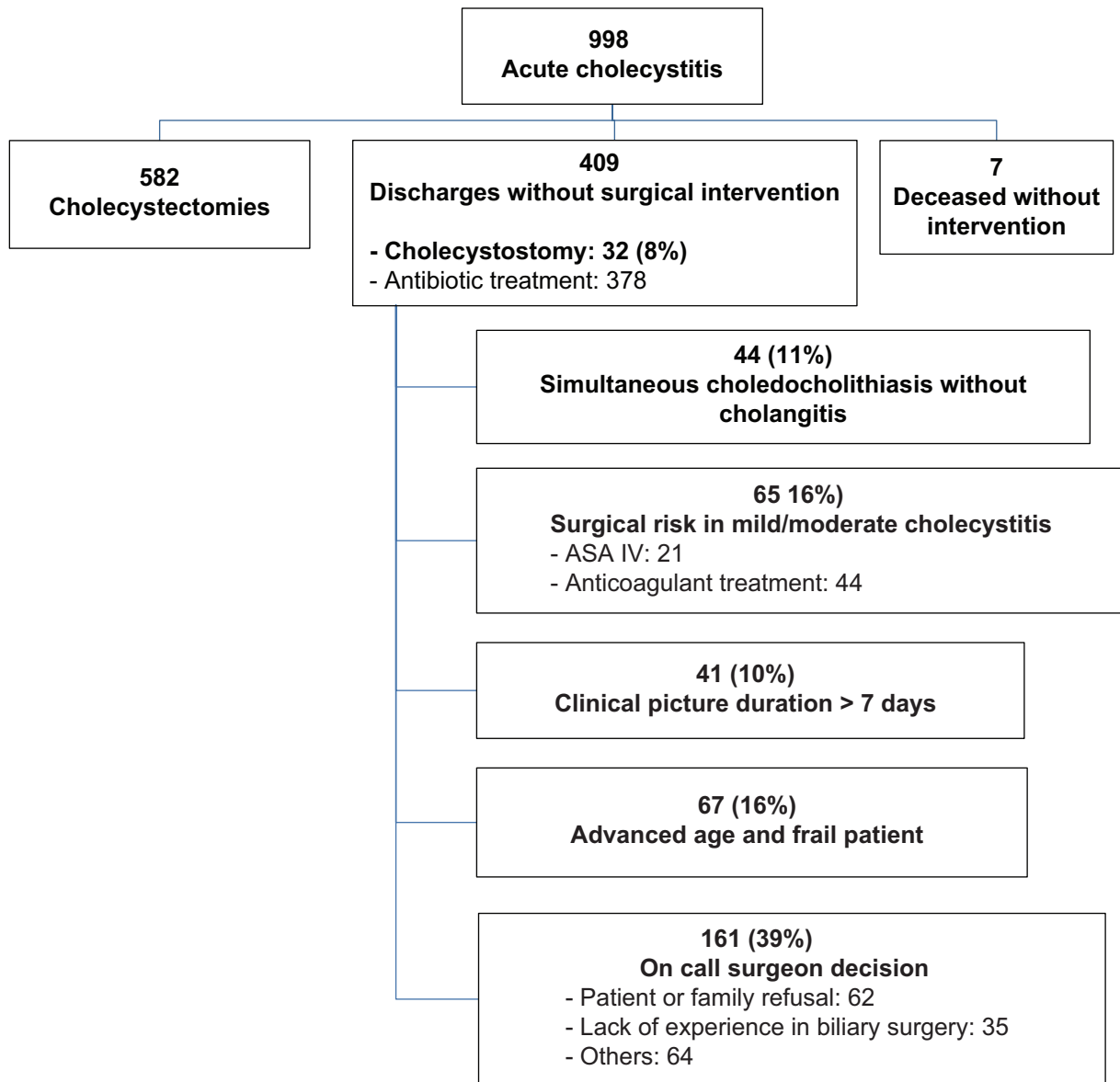


Figure 1. Reasons why surgical treatment was not carried out.

having included almost one thousand cases in less than six years. The increase in its incidence is parallel to the upsurge of life expectancy in our country, the highest in the world²⁷: more than half the cases correspond to patients older than 70 years²⁸. But this is not a mere demographic piece of information, since we have verified that as age advances, comorbidity increases and the number of severe AC cases grows, which translates into an increase in morbidity and mortality.

Advanced age (the designation of which has been shifting from 65 to 80-90 years)^{15-18,28} and associated comorbidity^{18,29,30} have been considered the main risk

factors for complications, with certain analytical, radiological or surgical findings sometimes being considered^{12-14,31}, although without a unanimous definition of severity, which precluded comparing various studies. Other factors analyzed when assessing the risk of cholecystectomy are the number of days of clinical manifestations until surgery, but the lack of measurement homogeneity (some studies take as a starting point clinical manifestations day 0 and others patient admission date) makes comparison and establishment of conclusions difficult^{5,7,9}.

The lack of uniform criteria for AC diagnosis and severity grading prompted the publication in 2007¹⁹

Table 5. Results of patients with acute cholecystitis who underwent surgery

Characteristics	Operated patients (n = 582)	Grade I (mild) (n = 154)	Grade II (moderate) (n = 368)	Grade III (severe) (n = 60)	p
Significant comorbidity	162 (27.8)	29 (18.8)	91 (24.7)	42 (70)	< 0.001
Early cholecystectomy	548 (94.2)	151 (98.1)	344 (93.5)	53 (88)	0.016
Laparoscopic cholecystectomy	545 (93.6)	152 (98.7)	341 (92.7)	52 (87)	0.002
Conversion to open surgery	41 (7.5)	1 (0.7)	31 (9.1)	9 (17)	< 0.001
Findings					
Edematous	197 (34.3)	116 (76.8)	70 (19.2)	11 (18)	< 0.001
Gangrenous	289 (50.3)	31 (20.5)	228 (62.6)	30 (50)	
Perforated/choleperitoneum	89 (15.5)	4 (2.6)	66 (18.2)	19 (32)	
Drain placement	347 (59.7)	51 (33.1)	253 (68.9)	43 (78)	< 0.001
Biliary fistula	12 (2.0)	2 (1.3)	7 (1.9)	3 (5)	0.251
Hospital stay*	5.9 ± 7	3.7 ± 4	5.5 ± 5	13.5 ± 14	< 0.001
Dindo-Clavien ≥ II complication	95 (16.4)	10 (6.5)	52 (14.1)	33 (56)	< 0.001
Mortality†	13 (2.2)	0 (0)	3 (0.8)	10 (17)	< 0.001
Readmissions‡	20 (3.5)	4 (2.6)	12 (3.3)	4 (8)	0.112

*Mean±standard deviation in days.

†At 30 days.

‡Except for those marked with an asterisk, all data expressed as n (%).

(revised in 2013²⁰ and 2018²¹) of the Tokyo Guidelines. These guidelines, beyond being of help for decision-making in routine clinical practice, allow homogeneity of criteria and definitions that will make subsequent comparison of studies and results easier, although initially they would not seem to improve the results of patients with AC³².

Based on these guidelines, we delineated our study: all included patients met the diagnostic criteria and were subsequently classified by severity. The moderate AC group has been the most numerous by including as a criterion the presence of symptoms for more than 72 hours at the beginning of treatment (sometimes, patients with mild symptoms and only slight laboratory anomalies). This may have had an influence on the fact that mild and moderate AC show no differences in terms of demographics, medical history and comorbidity³³, although both are clearly differentiated from severe AC. However, all three groups have clear differences with regard to administered treatment and outcomes.

The Tokyo Guidelines leave certain freedom for treatment selection³⁴, with our first option being surgical treatment, due to the high rate of relapses in non-operated patients (around 20% regardless of AC grade) and poorer evolution of AC relapse with regard

to the first episode^{8,35}. The grade has influenced the results of operated patients: the higher the grade, we have observed more complexity in the surgical procedure, higher need for drains and a higher conversion rate, with longer postoperative stay associated and higher morbidity and mortality, especially in the severe AC group. Nevertheless, bile duct iatrogenic complications have not differed according to the grade, which suggests that morbidity and mortality are determined by AC systemic involvement rather than by technical difficulties of the surgical procedure.

Application of the Tokyo Guidelines to our patients has allowed us to effectively categorize the grade and, according to it, administrate the most appropriate treatment. The results for mild AC have been excellent regardless of the administered treatment. Good results have also been obtained in moderate AC, but these are patients at higher risk and this should be taken into account when treatment is planned. As for severe AC, this is a high-risk group of patients with high morbidity and mortality who will often require intensive care and immediate and individualized treatment, especially in the case of those older than 80 years²⁸.

The multivariate analysis of factors that might have an influence on morbidity and mortality in our patients showed that severe AC and significant comorbidity

Table 6. Risk factors for mortality

	Mortality			Multivariate analysis	
	No (n = 978)	Yes (n = 20)	p	OR (95% CI)	p
Age > 80 years	335 (34.3)	13 (65)	0.004		
Male gender	559 (57.2)	15 (75)	0.1		
Diabetes	256 (26.2)	10 (50)	0.017		
Significant comorbidity	345 (35.3)	18 (90)	0.000	6.4 (1.4-29.3)	0.017
History of biliary disorders	77 (7.9)	4 (20)	0.049		
Grade III (severe)	76 (15.0)	17 (85)	0.000	40.7 (11.3-146.2)	< 0.001
	Dindo-Clavien ≥ II morbidity			Multivariate analysis	
	No (n = 978)	Yes (n = 20)	p	OR (95% CI)	p
Age > 80 years	292 (33.5)	56 (44)	0.016		
Male gender	494 (56.7)	79 (63)	0.2		
Significant comorbidity	293 (33.6)	69 (55)	< 0.001		
History of biliary disorders	66 (7.6)	15 (12)	0.09		
Grade III (severe)	47 (5.4)	45 (36)	< 0.001	7.22 (3.62-14.38)	< 0.001
Cholecystectomy	486 (55.8)	95 (75)	< 0.001		
Open cholecystectomy	26 (5.3)	11 (12)	0.021		
Conversion to open surgery	21 (4.6)	20 (24)	< 0.001	5.68 (2.74-11.77)	< 0.001
Rescue cholecystectomy	9 (2.3)	6 (16)	< 0.001		

CI: confidence interval; OR: odds ratio.
Data expressed as n (%).

Table 7. Risk factors for developing severe acute cholecystitis, multivariate analysis

	Grade III (severe)			Multivariate analysis	
	No (n = 905)	Yes (n = 93)	p	OR (95% CI)	p
Age > 80 years	295 (32.6)	53 (57)	< 0.001	1.80 (1.14-2.85)	0.011
Male gender	521 (57.6)	53 (57)	0.9		
Diabetes	232 (25.6)	34 (37)	0.019		
Significant comorbidity	297 (32.8)	66 (71)	< 0.001	4.16 (2.56-6.77)	< 0.001
History of biliary disorders	66 (7.3)	15 (16)	0.003	2.06 (1.09-3.88)	0.025
Cholelithiasis	48 (5.3)	8 (8)	0.1		

CI: confidence interval; OR: odds ratio.
Data expressed as n (%).

were independent risk factors for mortality, while severe AC and conversion to open surgery were risk factors for morbidity. In view of the poor prognosis of

patients with severe AC, we analyzed which factors can determine its occurrence, and we found significant comorbidity, the presence a history of biliary

disorders and age older than 80 years to be independent factors. Despite the risk significant comorbidity (ASA III-IV) entails in operated patients, our results in mild and moderate AC justify the surgical procedure, given the risk of relapse in case of no intervention; in severe AC, radiological drainage could be more beneficial, unless there is choleperitoneum or if cholecystostomy cannot be performed.

Our experience is consistent with a survey conducted in Spanish surgeons¹: even wanting to operate on all ACs, it is difficult to surpass 60% of operated patients. Patient admission in charge of the hepatobiliary unit and not by on-call surgeon can increase this figure, in addition to patient safety in complex cases. Although we established the seventh day after symptom onset as a theoretical limit for surgery, 94% of surgical procedures were carried out within the first 48 hours, which may have positively influenced our results.

In conclusion, we propose urgent LC at the time of admission as the treatment of choice in mild and moderate AC, regardless of patient age²⁸ (except in cases where there is anesthetic contraindication, other situations such as concomitant choledocholithiasis, or AC of more than 7 days' evolution), based on our good results in operated patients and bearing in mind that AC relapse rate is higher than 20% and has poorer results than the first episode³⁵. Patients with severe AC have high morbidity and mortality and should be treated or, as the case may be, transferred to centers that have appropriate resources and surgeons with experience in biliary surgery.

Conflicts of interest

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Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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