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Pre-surgery age-adjusted Charlson Comorbidity Index is associated with worse outcomes in acute cholecystitis

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ABSTRACT

Background: Beneficial effects of cholecystectomy in acute cholecystitis (AC) might be weakened by complications. The age-adjusted Charlson Comorbidity Index (CCI) assesses disease relevance in the prediction of one-year mortality.
Aims: To evaluate whether age-adjusted CCI predicted complications (including surgical complications, intensive care unit [ICU] admission, and in-hospital death) among patients undergoing cholecystectomy for AC. Associations between age-adjusted CCI and the length of hospital stay have been also evaluated.
Methods: 271 patients were enrolled at Ospedale Policlinico San Martino (Genoa, Italy) between 2005 and 2013. Clinical data and blood samples were collected.
Results: Patients' median age was 67 years. They underwent more frequently video-laparoscopic cholecystectomy with a limited rate of conversion to open cholecystectomy. Surgical complications occurred in 23 patients (8.5%). 6 patients (2.2%) needed ICU admission, while death occurred in 4 patients (1.5%). According to the cut-off point identified by ROC curve, an age-adjusted CCI cut-off value of 5 was found predictive for in-hospital complications also when confounders were considered (OR 1.35, 95% CI 1.02–1.79, $p = 0.035$). No association between adjusted CCI and the length of hospital stay was found.
Conclusions: In patients surgically treated for AC, age-adjusted CCI could represent an additional tool, along with available risk scores, to help surgeons in choosing the best therapeutic option.

1. Introduction

Acute cholecystitis (AC) is one of the most frequent abdominal emergencies representing a major cause of complicated intra-abdominal infection [1]. AC is very frequent among the elderly accounting for up to 50–70% of all cases [2]. Biliary stones are the most common etiology for AC with a prevalence ranging from 10 to 15% [3]. The standard treatment for AC is cholecystectomy, which should be performed as laparoscopic cholecystectomy within 72–96 h from symptom onset according to Tokyo 2013 guidelines (TG13) for surgical management of AC [4,5]. Despite this, the rate of early cholecystectomy is still low, ranging from 15–40% [6,7].

Charlson Comorbidity Index (CCI) is a score defining different clinical conditions and assessing their relevance in the prediction of one-year mortality. A weighted score is assigned to each of 17 comorbidities and, as a consequence, the sum of the index scores represents a marker of disease burden and a strong estimator of mortality [8]. This score has been re-evaluated in order to combine age and comorbidity in a unique score and estimate the relative risk of death [9]. Age-adjusted CCI has been widely evaluated in numerous studies, especially dealing with oncology and surgery [10–12]. On the contrary, in the setting of AC, age-adjusted CCI has been poorly investigated [13].

In light of the progressive aging of the population, an increasing number of patients with multiple comorbidities can need cholecystectomy due to AC. Although guidelines recommend early cholecystectomy for the treatment of AC in order to limit surgical complications and allow a reduced in-hospital length of stay

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Table 1
Baseline characteristics of the overall cohort.

	n = 271
Age at intervention, years	67.0 (53.0–76.0)
Male, n (%)	169 (62.4)
BMI[a], kg/m^2	25.68 (23.78–28.21)
ASA[b] classification	2 (1–2)
I, n (%)	120 (44.3)
II, n (%)	104 (38.4)
III, n (%)	40 (14.8)
IV, n (%)	7.0 (2.6)
V, n (%)	0 (0.0)
VI, n (%)	0 (0.0)
Age-adjusted CCI[c]	4 (2–5)
TGSG[d]	2 (1–2)
I, n (%)	134 (49.4)
II, n (%)	133 (49.1)
III, n (%)	4 (1.5)
Time admission-intervention, days	3.0 (1.0–5.0)
Time intervention-discharge, days	3.0 (2.0–5.0)
Total hospital days, days	7.0 (5.0–12.0)
In-hospital death, n (%)	4 (1.5)
Time and type of surgery	
Delayed, n (%)	31 (11.4)
Early (within 96 h), n (%)	240 (88.6)
OC[e], n (%)	41.0 (15.1)
VLC[f], n (%)	230 (84.9)
Conversion from VLC to OC, n (%)	27 (10.0)
Duration of intervention, min	90.0 (70.0–120.0)
Pathological classification	
Edematous cholecystitis, n (%)	101 (37.7)
Necrotizing cholecystitis, n (%)	107 (39.9)
Suppurative cholecystitis, n (%)	60 (22.4)
Antibiotic therapy	
Ampicillin/sulbactam, n (%)	137 (65.2)
Amoxicillin/clavulanate, n (%)	31 (14.7)
Cefotaxime, n (%)	19 (9.0)
Piperacillin/tazobactam, n (%)	17 (8.1)
Ceftriaxone, n (%)	15 (7.1)
Cephazolin, n (%)	3 (1.1)
Ampicillin, n (%)	1 (0.5)
Meropenem, n (%)	1 (0.4)
Ciprofloxacin, n (%)	16 (7.6)
Levofloxacin, n (%)	1 (0.4)
Metronidazole, n (%)	12 (4.4)
Gentamycin, n (%)	1 (0.4)
Tigecycline, n (%)	2 (0.7)
Surgical complications	
Total, n (%)	29 (10.7)
Minor, n (%)	13 (4.8)
Wound infection, n (%)	13 (4.8)
Major, n (%)	10 (3.7)
Intrahepatic abscess, n (%)	1 (0.4)
Hemorrhage, n (%)	4 (1.5)
Bile leakage, n (%)	2 (0.7)
Biliar tree lesions, n (%)	1 (0.4)
Post-operative pancreatitis, n (%)	2 (0.7)
ICU[g] admission, n (%)	6 (2.2)
Death, n (%)	4 (1.5)
Blood count and biochemistry	
WBC[h], 10^9/L	13.3 (9.80–16.30)
Neutrophils, 10^9/L	9.48 (6.19–12.92)
Lymphocytes, 10^9/L	1.3 (1.0–1.80)
Neutrophil to lymphocyte ratio	7.31 (4.11–11.31)
CRP[i], mg/L	95.0 (18.85–181.50)
Fibrinogen, mg/dL	597.0 (410.0–747.50)
ALP[j], U/L	154.0 (89.5–230.0)
γ-GT[k], U/L	48.0 (24.0–148.75)
Total bilirubin, mg/dL	0.90 (0.59–1.60)
ALT[l],U/L	38.0 (22.0–72.50)
AST[m], U/L	25.0 (17.0–52.50)
Amylase, U/L	26.0 (16.0–61.0)
Lipase, U/L	102.0 (27.0–180.50)

Data are expressed as median (interquartile range [IQR]), number (n), or percentages (%).
[a] BMI: body mass index.
[b] ASA: American Society of Anesthesiologists.
[c] CCI: Charlson Comorbidity Index.
[d] TGSG: Tokyo Guidelines Severity Grading.
[e] OC: open cholecystectomy.
[f] VLC: video-laparoscopic cholecystectomy.
[g] ICU: intensive care unit.
[h] WBC: white blood cell.
[i] CRP: C-reactive protein.
[j] ALP: alkaline phosphatase.
[k] GT: glutamyltransferase.
[l] ALT: alanine transaminase.
[m] AST: aspartate aminotransferase.

[14], only a small percentage of these patients, particularly among the elderly, underwent cholecystectomy within guideline-driven times [15] since comorbidities can hinder the surgical intervention because of a poor prognosis. In this view, the aim of our study is to determine whether there is an association between age-adjusted CCI and complications during the hospital stay in order to help clinicians in choosing the best therapeutic strategy.

2. Materials and methods

2.1. Patients and clinical assessment

A retrospective study was conducted at the Surgery Unit of IRCCS Ospedale Policlinico San Martino (Genoa, Italy) by enrolling 271 patients admitted for AC between August 2005 and November 2013. The study was performed in accordance with the guidelines of the Declaration of Helsinki and approved by the local Ethics Committee. All participants gave their written informed consent before entering the study. Inclusion criteria referred to as TG07 and TG13 diagnostic criteria and severity grading of AC [2,16]. Patients who were younger than 18 on admission were excluded from the study. At the time of admission, patients' characteristics as well as whole blood were collected in order to evaluate circulating inflammatory markers, blood count, and liver enzymes. Age-adjusted CCI contains 17 categories of comorbidities, for each of which is assigned a score of 1–3 or 6 depending on the risk of death associated with this condition in order to predict the 10-year mortality. A free on online calculator is available at: https://www.mdcalc.com/charlson-comorbidity-index-cci. Tokyo Guidelines Severity Grading (TGSG) was defined according to diagnostic criteria and severity assessment of AC of TG07 and TG13 [2,16]. The American Society of Anesthesiologists (ASA) classification is a subjective score about patient's overall health based on five classes (I to V) as summarized by Fitz-Henry [17].

2.2. Study endpoints

The primary endpoint was to determine whether age-adjusted CCI could predict in-hospital complications, including surgical complications, needing of intensive care unit (ICU) admission, and in-hospital death, given that these events can negatively impact on patient's length of hospital stay, especially among the elderly. The secondary end-point was to evaluate the potential association between age-adjusted CCI and the length of hospital stay.

Table 2
Clinical characteristics of four dead patients.

Patient	Sex	Age	TSGS[a]	ASA[b]	Age-adjusted CCI[c]	Cause and time of death
1	Male	85	3	4	7	AC[d] with peritonitis and concurrent liver abscess leading to sepsis. Death occurred in 2011, 4 days after surgery due to MOF[e].
2	Female	85	2	3	6	AC with localized peritonitis in known chronic liver disease. Death occurred in 2013, 21 days after surgery due to hepatic decompensation.
3	Female	69	1	4	8	AC with biliary sepsis and respiratory failure requiring tracheostomy. Death occurred in 2012, 23 days after surgery due MOF.
4	Female	68	2	4	6	AC with peritonitis and biliary sepsis in known liver cirrhosis needing immediate ICU[f] admission. She experienced a progressive worsening of liver function and death occurred in 2012, 5 days after surgery due to liver failure.

[a] TSGS: Tokyo Severity Grading Scale.
[b] ASA: American Society of Anesthesiologists.
[c] CCI: Charlson Comorbidity Index.
[d] AC: acute cholecystitis.
[e] MOF: multiple organ failure.
[f] ICU: intensive care unit.

2.3. Detection of hematological, biochemical, and inflammatory biomarkers

Routine auto-analyzers were used to measure hematological, biochemical, and inflammatory parameters, including white blood cells (WBCs), neutrophils, lymphocytes, glycemia, alkaline phosphatase (ALP), γ-glutamyltransferase (GT), alanine transaminase, aspartate aminotransferase, C-reactive protein (CRP), and fibrinogen.

2.4. Choice of surgical technique

According to TG07 and TG13 guidelines [4,18], the treatment of choice was video-laparoscopic cholecystectomy (VLC) within 72–96 h from admission or symptom onset, except for those cases presenting with high surgical risk or contraindications.

2.5. Definition of minor and major surgical complications

In the present study, minor complications included: wound infection, febricula, and local hematomas. Major complications were defined as intrahepatic abscess, hemorrhage, bile leakage, biliary tree lesions, and post-operative pancreatitis. Moreover, we considered ICU and death as complications following or occurring during the surgical intervention in light of their detrimental impact on patient health and length of hospital stay.

2.6. Statistical analysis

Analyses were carried out using IBM SPSS Statistics for Windows, Version 23.0 (IBM CO., Armonk, NY) and MedCalc 12.5 (MedCalc Software, Ostend, Belgium). Categorical data were presented as relative and absolute frequencies and compared with Pearson $\chi 2$ test, while continuous variables were shown as median and interquartile range (IQR) and their comparison was done using non-parametric Mann–Whitney *U* test. The prognostic ability of age-adjusted CCI was evaluated on the basis of a receiver operator characteristic (ROC) curve. The area under the curve (AUC) was given with 95% confidence interval (CI) and the cut-off point of age-adjusted CCI calculated maximizing the sensitivity in accordance with the Youden's index. The predictive ability of age-adjusted CCI toward in-hospital complications was evaluated by a logistic regression and expressed as odds ratio (OR) and 95% CI. Stepwise backward elimination in the multivariate logistic regression identified only ASA classification and lipase levels (among body mass index, TGSG, CRP, fibrinogen, blood count, amylase, transaminases, ALP, γ-GT, and type of surgical intervention) as risk factors for in-hospital complications. Associations between age-adjusted CCI and the length of hospital stay were calculated by a linear regression. For the multivariate model, we included TGSG, ASA classification, CRP, and type of surgical intervention, which are clinically relevant parameters when considering patients suffering from AC. For all statistical analyses a 2-sided *p*-value <0.05 was considered as statistically significant.

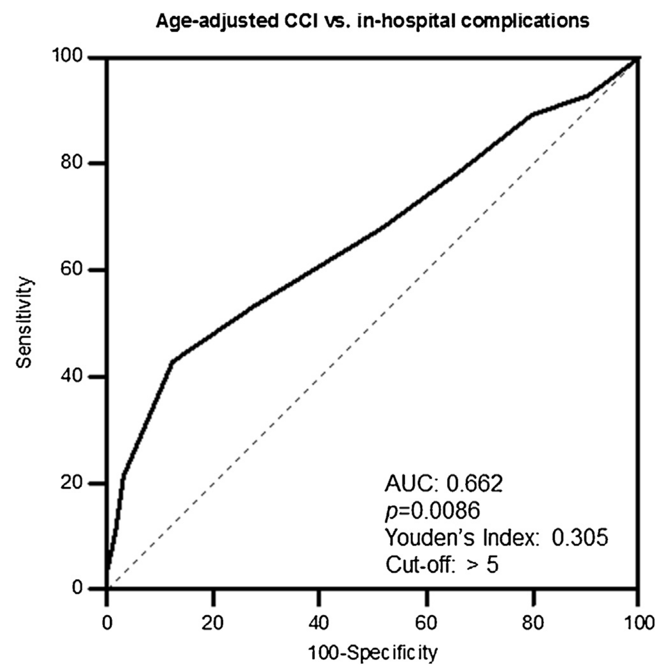

Fig. 1. Receiver operator characteristic curve analysis for age-adjusted Charlson Comorbidity Index (CCI). The prognostic ability of age-adjusted CCI toward the occurrence of in-hospital complications was tested. The cut-off value of 5 was identified.

3. Results

3.1. Patients' characteristics

Baseline clinical characteristics of the overall cohort are listed in Table 1. Patients' median age at the time of surgical intervention was 67 (53.0–76.0), with a slight prevalence of males (62.4%). Median ASA score classification was 2 depicting patients with mild systemic disease. TSGS was 2, with a pronounced, homogeneous concentration of the cohort within the first two grades (49.4% and 49.1% for TGSG I and II, respectively). The median age-adjusted CCI was 4 describing a marked burden of disease and a 53% estimated

Table 3
Baseline characteristics of the overall cohort according to the age-adjusted Charlson Comorbidity Index cutoff >5.

	Age-adjusted Charlson Comorbidity Index		*p*
	≤5 (n = 229)	>5 (n = 42)	
Age at intervention, years	64.0 (51.0–74.0)	76.0 (73.0–81.0)	**<0.001**
Male, n (%)	85 (37.1)	17 (40.5)	0.680
BMI[a], kg/m^2	25.75 (23.97–28.40)	24.81 (22.26–26.88)	0.050
ASA[b] classification	1 (1–2)	2 (2–3)	**<0.001**
I, n (%)	119 (52.0)	1 (2.4)	**<0.001**
II, n (%)	83 (36.2)	21 (50.0)	0.093
III, n (%)	26 (11.4)	14 (33.3)	**<0.001**
IV, n (%)	1 (0.4)	6 (14.3)	**<0.001**
TGSG[c]	1 (1–2)	2 (2–2)	**<0.001**
I, n (%)	126 (55.0)	8 (19.0)	**<0.001**
II, n (%)	103 (45.0)	30 (71.4)	**0.002**
III, n (%)	None	4 (9.5)	**<0.001**
Time admission-intervention, days	2.0 (1.0–4.75)	3.0 (1.75–7.0)	**0.029**
Time intervention-discharge, days	3.0 (2.0–4.0)	5.0 (3.75–9.0)	**<0.001**
Total hospital days, days	7.0 (5.0–10.0)	11.0 (7.50–16.50)	**<0.001**
In-hospital death, n (%)	None	4 (9.5)	**<0.001**
Time and type of surgery			
Delayed, n (%)	25 (10.9)	3 (7.1)	0.461
Early (within 96 h), n (%)	204 (89.1)	39 (92.9)	0.461
OC[d], n (%)	28 (12.2)	13 (31.0)	**0.002**
VLC[e], n (%)	201 (87.8)	29 (69.0)	**0.002**
Conversion from VLC to OC, n (%)	21 (9.2)	6 (14.3)	0.310
Duration of intervention, min	90.0 (70.0–115.0)	97.5 (73.75–131.25)	0.147
Pathological classification			
Edematous cholecystitis, n (%)	86 (37.9)	15 (36.6)	0.875
Necrotizing cholecystitis, n (%)	93 (41.0)	14 (34.1)	0.413
Suppurative cholecystitis, n (%)	48 (21.1)	12 (29.3)	0.252
Surgical complications			
Total, n (%)	16 (7.0)	6 (14.3)	0.063
Minor, n (%)	9 (3.9)	4 (9.5)	0.120
Major, n (%)	7 (3.1)	2 (4.8)	0.571
Intrahepatic abscess, n (%)	1 (0.4)	None	0.668
Hemorrhage, n (%)	2 (0.9)	2 (4.8)	0.055
Bile leakage, n (%)	1 (0.4)	1 (2.4)	0.177
Biliary tree lesions, n (%)	1 (0.4)	None	0.668
Post-operative pancreatitis, n (%)	2 (0.9)	None	0.544
ICU[f] admission, n (%)	2 (0.9)	4 (9.5)	**<0.001**
Blood count and biochemistry			
WBC[f], 109/L (IQR)	12.4 (9.07–15.00)	14.25 (9.62–18.57)	**0.041**
Neutrophils, 10^9/L	9.34 (6.11–12.67)	10.3 (7.64–16.28)	0.094
Lymphocytes, 10^9/L	1.3 (1.0–1.80)	1.3 (0.85–1.58)	0.673
Neutrophil to lymphocyte ratio	6.10 (4.10–10.77)	10.0 (3.88–13.45)	0.160
CRP[g], mg/L (IQR)	70.75 (16.32–165.0)	182.0 (95.5–245.0)	**0.001**
Fibrinogen, mg/dL (IQR)	547.5 (387.5–671.75)	597.0 (455.5–753.0)	0.102
ALP[h], U/L (IQR)	154.0 (86.0–221.0)	164.0 (102.25–334.25)	0.212
γ-GT[i], U/L	43.0 (22.0–129.0)	91.0 (49.0–279.50)	**0.001**
Total bilirubin, mg/dL	0.90 (0.59–1.63)	0.90 (0.70–1.43)	0.735
ALT[j], U/L	37.0 (21.0–73.0)	45.0 (23.0–68.0)	0.564
AST[k], U/L	24.0 (16.0–50.0)	27.0 (21.0–60.0)	0.130
Amylase, U/L	27.0 (18.0–77.50)	18.0 (10.50–49.0)	**0.003**
Lipase, U/L	125.0 (27.0–188.50)	65.0 (19.75–143.75)	0.097

Data are expressed as median (interquartile range [IQR]), number (n), or percentages (%).
p-values were calculated according to Pearson $\chi 2$ test or Mann–Whitney *U* test when appropriate. Statistically significant *p* values are displayed in bold characters.
[a] BMI: body mass index.
[b] ASA: American Society of Anasthesiologists.
[c] TGSG: Tokyo Guidelines Severity Grading.
[d] OC: open cholecystectomy.
[e] VLC: video-laparoscopic cholecystectomy.
[f] WBC: white blood cell.
[g] CRP: C-reactive protein.
[h] ALP: alkaline phosphatase.
[i] GT: glutamyltransferase.
[j] ALT: alanine transaminase.
[k] AST: aspartate aminotransferase.

10-year survival [9]. The most common type of surgical intervention was VLC, which was performed in 94% of patients within 96 h from symptom onset. The rate of conversion from VLC to open cholecystectomy amounted to 10%. Minor and major complications occurred in 13 and 10 patients, respectively, while 6 patients (2.2%) needed ICU admission due to post-operative respiratory failure or development of septic complications. Death occurred in 4 patients (1.5%) and all dead patients experienced septic complications related to their comorbidities (Table 2). The whole cohort displayed a high degree of inflammation at the time of admission,

Table 4
Logistic regression showing the predictive value of age-adjusted CCI toward all in-hospital complications (i.e. surgical complications, intensive care unit admission, and in-hospital death).

	Univariate model			Multivariate model		
	OR[a]	95% CI[b]	*p*-Value	OR	95% CI	*p*-Value
In-hospital complications						
Age-adjusted CCI[c]>5	1.40	1.14–1.72	**0.001**	1.35	1.02–1.79	**0.035**
ASA[d] classification				1.92	1.04–3.54	**0.037**
Lipase				1.00	1.00–1.01	**0.002**

Statistically significant *p* values are displayed in bold characters.
[a] OR: odds ratio.
[b] CI: confidence interval.
[c] CCI: Charlson Comorbidity Index.
[d] ASA: American Society of Anaesthesiologists.

Table 5
Linear regression describing the association between age-adjusted CCI and total hospital stay.

	Univariate model			Multivariate model		
	β	95% CI[a]	*p*-Value	β	95% CI	*p*-Value
Total hospital stay						
Age-adjusted CCI[b]>5	6.019	3.669–8.369	**<0.001**	2.403	−0.750 to 5.555	0.134
TGSG[c]	3.647	1.983–5.311	**<0.001**	0.482	−1.875 to 2.839	0.687
ASA[d] classification	3.717	2.691–4.742	**<0.001**	3.038	1.427–4.648	**<0.001**
CRP[e]	0.074	−0.059 to 0.207	0.275	0.009	−0.112 to 0.130	0.882
Early VLC[f]	−6.718	−8.443 to −4.992	**<0.001**	−5.809	−8.299 to −3.320	**<0.001**

Statistically significant *p* values are displayed in bold characters.
[a] CI: confidence interval.
[b] CCI: Charlson Comorbidity Index.
[c] TSGS: Tokyo Severity Grading Scale.
[d] ASA: American Society of Anaesthesiologists.
[e] CRP: C-reactive protein.
[f] VLC: video-laparoscopic cholecystectomy.

as shown by high WBC and neutrophil counts, CRP, and fibrinogen values, while liver necrosis and cholestasis enzymes were not impaired (Table 1).

3.2. A cut-off value of age-adjusted CCI above 5 predicts in-hospital complications

By a ROC curve analysis, we evaluated whether age-adjusted CCI had significant prognostic accuracy to predict all in-hospital complications, as previously defined (AUC 0.662 [95% CI 0.602–0.718]; $p = 0.0086$, Fig. 1). In accordance with the Youden's index, an age-adjusted CCI value >5 was found as the best cut-off point, having a sensitivity of 42.9% and a specificity of 87.65%. We then compared the whole cohort according to the abovementioned age-adjusted CCI cut-off (Table 3). Patients showing an age-adjusted CCI >5 were older and displayed a higher ASA score, a longer hospital stay, and a higher incidence of in-hospital death as well as of ICU admission (Table 3). Concurrently, deaths were found only in the group with age-adjusted CCI >5. On the contrary, the distribution across TGSG was similar for grade I and II among those with age-adjusted CCI ≤5 (Table 3). With regard to laboratory findings, patients with age-adjusted CCI >5 showed more elevated levels of WBCs and a two-fold increase in CRP and γ-GT values (Table 3). Then, we explored the possibility to use age-adjusted CCI as a tool to evaluate post-surgery in-hospital complications. Indeed, age-adjusted CCI >5 predicted all in-hospital complications (OR 1.40, 95% CI 1.14–1.72, $p = 0.001$) as shown in Table 4. This result was confirmed also in the multivariate model when ASA classification and lipase levels were considered (OR 1.35, 95% CI 1.02–1.79, $p = 0.035$) (Table 4).

3.3. A cut-off value of age-adjusted CCI above 5 is not associated with the length of hospital stay

An age-adjusted CCI >5 was associated with total hospital stay in the univariate model ($\beta = 6.019$, 95% CI 3.669–8.369, $p < 0.001$), but not when TGSG, ASA score classification, CRP, and early VLC were considered ($\beta = 2.403$, 95% CI −0.750 to 5.555, $p = 0.134$) (Table 5).

4. Discussion

The main finding of this study is represented by the predictive role of age-adjusted CCI score toward all in-hospital complications (including surgical complications, needing of ICU admission, and in-hospital death) in patients undergoing cholecystectomy for AC. To date, only one study evaluated the role of CCI in the management of patients with AC [13]. Endo et al. reported that CCI might be a beneficial tool for the early evaluation of patients showing that 30- and 90-day mortality rates were increased for increasing CCI scores. Especially for 30-day mortality, CCI was found as an independent factor in patients with AC of grade I and II according to TGSG [13]. Our results are in touch with those by Endo et al. [13] and Anderson et al. [19] with regard to the median age-adjusted CCI among patients with AC, but differed from those by Boules et al. [20], who found higher levels of age-adjusted CCI among patients undergoing cholecystectomy. Similarly, age-adjusted CCI was found higher in patients with acute, calculous cholecystitis undergoing percutaneous cholecystotomy tube placement [21]. Therefore, age-adjusted CCI might represent a convenient tool to recognize high-risk patients and choose the best treatment for them. For this reason, different studies started to take CCI into consideration when evaluating patients potentially needing surgery for AC. In 2011, Bergman et al. identified age and CCI as factors associated with a decreased probability of surgery within one year in elderly people with symptomatic gallstone disease [22].

In 2013, Anderson et al. investigated complication and mortality rates in patients undergoing cholecystostomy or cholecystectomy by including CCI as a covariate for the logistic regression analysis [19]. Recently, Alvino et al. described lower CCI and ASA scores among patients scheduled for elective cholecystectomy following AC [21]. This year, for the first time, TG18 flowchart for the management of AC included CCI among risk factors for the selection of treatment strategy at each severity grade [14]. We also found that an age-adjusted CCI >5 was associated with an increased in-hospital death. To date, no other study evaluated this aspect to predict the prognosis of patients with AC irrespective of the type of cholecystectomy. Hence, also in light of the recent amendment including CCI within the flowchart for AC [14], we believe that age-adjusted CCI could represent a precious, complementary tool for surgeons and anesthesiologists when cholecystectomy has to be performed in frail patients (i.e. the elderly), among whom comorbidities can strongly impact on the length of hospital stay and the overall survival [15,23]. On this basis, age-adjusted CCI, when performed before surgery, could help, along with other available risk scores, to design a more precise *scenario* of the clinical history of the patient needing cholecystectomy, suggesting the more appropriate therapy (i.e. conservative, surgical or firstly conservative and then surgical).

Finally, we found that an age-adjusted CCI >5 score was not associated with the length of hospital stay when considering also TGSG, ASA score classification, CRP, and early VLC. This means that patients undergoing early VLC might experience a shorter hospital stay irrespective of the pre-surgery clinical situation designed by age-adjusted CCI score, ASA score, and TGSG. This finding is in accordance with a recent meta-analysis showing that among the elderly delayed cholecystectomy is associated to a higher rate of recurrent episodes of AC or pancreatitis [15]. Moreover, our results could be partially in touch with those by Popowicz et al. [24], who found that the hospital stay was significantly longer for patients treated with percutaneous cholecystostomy as compared to those undergoing early cholecystectomy along with a reduced risk for intervention-related complications e irrespective of age, gender, CCI, and TGSG.

Some shortcomings needed to be considered when reading the present paper. Firstly, the limited sample size enrolled at a single center may limit the generalization of our results. Anyway, starting from current results, we are planning to enlarge our cohort and perform additional statistical analyses. Moreover, this study is retrospective and might be prone to selection bias. Finally, we did not have data regarding post-discharge state of health, so we had not been able to evaluate short- and long-term survival after discharge.

5. Conclusions

According to current guidelines, patients suffering from AC should be treated as early as possible from the symptom onset by early VLC irrespective of age-adjusted CCI, which is a useful tool for surgeons to evaluate the prognosis of patients. In light of this, further studies are needed to corroborate our results and to definitively include CCI in the Tokyo Guidelines as an easy-to-measure parameter predicting in-hospital complications and death.

Conflict of interest

None declared.

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