Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.320
2022; 25(4): 611-621

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Received : Sep 06, 2022
Accepted : Nov 04, 2022

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RESEARCH

COMPARISON OF THE MODIFIED 5-ITEM FRAILTY INDEX WITH THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS CLASSIFICATION AND CHARLSON AGE COMORBIDITY INDEX FOR PREDICTING POSTOPERATIVE OUTCOMES IN GERIATRIC PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

Abstract

Introduction: Frailty scores estimate postoperative outcomes in elderly patients. This study sought to compare the performance of the modified 5-item frailty index (mFI-5) with the other indexes as postoperative outcome predictors, especially for 1-year mortality in geriatric patients.

Materials and Method: Patients aged ≥ 65 years who underwent elective surgery were enrolled. Along with comparisons in scoring systems, demographics, anesthesia method, operation duration, presence of preoperative transfusion, complications, length of hospitalization, intensive care admission, hospital mortality rate, and 1-year mortality were recorded. Pearson's chi-square test, receiver operating characteristic curve analysis, and binary logistic regression analysis were performed.

Results: Overall, 33% of patients experienced complications and 12% were admitted to intensive care units. The hospital mortality rate was 3.3% (n=10), and the 1-year mortality rate was 27.4% (n=82). The Charlson aged comorbidity index was associated with the overall complications (Area Under Curve (AUC): 0.819, $p<0.001$) very well, and patients with a score over 5 have a 16.075 ($p<0.001$) times higher risk of hospital mortality. The American Society of Anesthesiologists (ASA) classification was associated satisfactorily with overall complications, intensive care admission, hospital mortality, and 1-year mortality (Respectively, AUC: 0.698, 0.662, 0.653, 0.629; $p<0.05$ in all). The mFI-5 score was associated well with intensive care admission (AUC: 0.702, $p<0.001$), and patients with a score over 2 have a 2.741 ($p<0.02$) times higher risk of 1-year mortality.

Conclusions: The mFI-5 was associated with intensive unit admission and 1-year mortality and, was not superior to the ASA classification and the Charlson age comorbidity index classification in predicting the overall postoperative outcomes.

Keywords: Intensive Care Units; Hospital Mortality; Aged; Frail Elderly; Risk Factors.

INTRODUCTION

In the second half of the 20th century, improvements in survival after 65 years of age have led to an increase in life expectancy and a decline in mortality rates at an advanced age (1). The global population of the elderly is projected to double between 2019 and 2050, with all regions expected to experience an increase in their elderly population (2). The increasing proportion of older adults in the general population has resulted in an increase in the number of geriatric patients undergoing surgery.

Elderly patients present additional challenges for perioperative management as a result of the increase in comorbidities and a decrease in physiologic reserve; they also require appropriate, effective, and specialized postoperative care and treatment. Therefore, preoperative recommendations and guidelines for elderly patients can provide a useful starting point for evaluating and optimizing preoperative assessment (3). Traditional methods of operative risk assessment include the ASA physical status classification and the Charlson comorbidity index (CCI) (4, 5). The Charlson comorbidity index (CCI) was developed and validated as a measure of 1-year mortality risk and morbidity (6). In one study, the Charlson age comorbidity index (CACI) was considered a more appropriate prognostic indicator for clinical practice (7).

Frailty scores have been used to predict postoperative complications and outcomes in elderly patients undergoing surgery (8). The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) uses 11 variables listed to predict frailty in preoperative settings. However, the effectiveness of the 11-item modified frailty index (mFI-11) has been questioned since 2012 due to the irregular registration of the 11 original variables. In response, researchers developed the modified frailty index-5 (mFI-5), which includes consistently recorded and validated variables in the NSQIP dataset. In a few studies, the mFI-5 was shown to be as good as the mFI-11 for predicting 30-day mortality (9,10).

Our objective was to compare mFI-5, ASA classification, and CACI as independent predictors of postoperative outcomes in geriatric patients. We were interested in the ability of these measures to predict complications, intensive care unit (ICU) admission, hospital mortality, and specifically 1-year mortality as these outcomes have the potential to significantly impact the quality of life of geriatric patients. We hypothesized that mFI is better than ASA classification and CACI in predicting postoperative outcomes in geriatric patients.

MATERIALS AND METHOD

This prospective observational study included patients aged 65 years and older who underwent elective surgical operations in neurosurgery, urology, orthopedics, or general surgery clinics from the Health Sciences University Hamidiye International Faculty of Medicine Kartal Dr. Lutfi Kirdar City Hospital from July 2019 to May 2021. Patient information and consent were obtained from the preoperative services. Patients who were under the age of 65 years, underwent emergency surgery, and had a psychiatric, genetic, or coagulation disorder, were excluded from the study.

Study Design

Detailed baseline clinical and pathological characteristics were extracted for each patient and included sex, age, educational status, medical history, oncological disease, operation type (Table 1), anesthesia method, and duration of the operation. The European Society of Cardiology and European Society of Anesthesiology on Non-Cardiac Surgery (ESC/ESA-NCS) guidelines were used as references for the classification of surgical interventions (11).

Postoperative complications were graded according to the Clavien–Dindo system (12) which classifies complications into five grades: grade

1 (Any deviation from the normal postoperative course without the need for pharmacological treatment or any interventions except wound infections opening at the bedside. Allowed therapeutic regimens are drugs such as antiemetics, antipyretics, analgesics, diuretics and electrolytes, and physiotherapy), grade 2 (Requiring pharmacological treatment with drugs other than such allowed for grade I complications including blood transfusions and total parenteral nutrition), grade 3 (Requiring surgical, endoscopic or radiological intervention which is classified into two subsections: not under general anesthesia (3a) and under general anesthesia (3b)), grade 4 (Life-threatening complication, including CNS complications and requiring IC/ICU-management, is classified into two subsections: single organ dysfunction including dialysis (4a) and multiorgan dysfunction (4b)), and grade 5 (death of a patient).

ASA classification (4) was extracted directly from the NSQIP. One patient was classified as ASA 1 (indicative of a normal healthy patient) and was enrolled with patients classified as ASA 2 (indicative of mild systemic disease) for a combined analysis. The CACI (7) was calculated based on the following ACS-NSQIP variables and the mFI-5 score (9) was created using previously established methods. Assessment and explanations of risk scores with reference sources mentioned before are depicted in Table 2.

After routine discharge, the length of hospital stay, ICU admission, length of ICU stay, and hospital mortality rate were recorded. The length of hospital stay was compared with Turkey's average duration of 4.1 days, and this statistical measurement was used to calculate prolonged LOS. As none of the patients who were admitted to ICUs stayed longer than 14 days, prolonged ICU stay was not recorded in this study. After one year, the patients or their relatives were contacted via telephone, and the status of the patients was determined.

The primary outcomes of our analyses were the finding of the three risk scores' success that may predict overall complications, ICU admission, prolonged LOS, hospital mortality, and 1- year mortality. Secondary outcomes were the finding of all factors that may affect the postoperative outcomes.

This study was approved by the Health Sciences University Hamidiye International Faculty of Medicine Kartal Dr. Lutfi Kirdar City Hospital Ethics Committee (Protocol No:2019/514/158/4-Date:24.07.2019). All authors have acknowledged that there were no conflicts of interest related to this work to declare. This study was conducted in accordance with the ethical principles of the Helsinki Declaration-2013 and followed good clinical practice guidelines.

Statistical Analysis

The conformity of the variables to the normal distribution was examined using visual (histogram and Q-Q plot) and analytical methods (Kolmogorov-Smirnov test). Median and minimum, maximum or percentages, and frequencies were reported for non-normal distributed continuous or categorical variables, respectively. The Mann-Whitney U test was used for ordinal variables, and Pearson's chi-square test and Fisher's exact tests were used for categorical variables.

In this study, mFI-5, CACI, and ASA classes were determined as three different groups, and the effect size was taken to be the same as the medium (medium=0.25), with a confidence interval (CI) level of 80% and an alpha of 5% in power analysis. Each group consisted of 75 patients, and the total number of patients was 225. (G Power 3.1.9.2. Windows 10). All the scoring systems were assessed as ordinal variables. Data were analyzed using the SPSS version 26 (IBM, Chicago, IL, USA). Receiver operator curve (ROC) analysis was used to evaluate the performance of risk scores as continuous variables for predicting complications, ICU admission, hospital mortality, and 1-year mortality prediction. The cutoff values in the study were calculated according to Youden's index; mFI-5 (group1 = mFI-5 < 2, group2= mFI-5 ≥ 2), CACI (group1= CACI < 5, group2= CACI

Table 1. Operation types.

General Surgery	Orthopedics	Neurosurgery	Urology
- Thyroidectomy (Partial / Total) - Parathyroidectomy - Mastectomy (BCT/Radical) - Esophagectomy - Gastrectomy (Partial/Total) - Colectomy (Hemicolectomy/ Total) - Low Anterior Resection - Hepatectomy - Whipple Procedure - Hernia Surgery (Incisional/ Inguinal/ Umbilical) - Cholecystectomy	- Lower/Upper Limb Tumor Excision - Below/Above Knee Amputation - Knee Replacement Surgery - Total Hip Replacement - Lower/Upper Extremity Fracture Fixation	- Tumor Excision (Frontal/Occipital/Posterior Fossa /Temporoparietal/ Extradural) - Thoracal/Lumbal/Lumbosacral Stabilization - Spinal Instrumentation Removal - Spondylolisthesis Surgery - VP Shunt Surgery - Chronic Subdural/Epidural Hematoma Evacuation Surgery	- Nephrectomy (Partial/ Radical) - Cystectomy - Transurethral Resection - Intervention with ureteroscopy - Retrograde Intrarenal Intervention

Table 2. Risk Stratification Methods

ASA classification (4)	**Class**	**CACI*** (7)	**Score**	**mFI-5**** (9)	**Score**
-A normal healthy patient	ASA 1	-Age (for each decade ≥ 50 years)	1	-Impaired functional status prior to surgery (partial or total dependence)	1
-A patient with mild systemic disease	ASA 2	-MI within 6 months prior to surgery	1	-CHF within 30 days before surgery	1
-A patient with severe systemic disease	ASA 3	-CHF	1	-Hypertension requiring medication	1
-A patient with severe systemic disease that is a constant threat to life	ASA 4	-PVD	1	-Severe COPD or current pneumonia	1
-A moribund patient who is not expected to survive without the operation	ASA 5	-Ulcer disease	1	-Diabetes mellitus	1
-A declared brain-dead patient whose organs are being removed for donor purposes	ASA 6	-Dementia	1		
		-Mild liver disease	1		
		-Diabetes mellitus	1		
		-History of TIA or CVA	1		
		-COPD	1		
		-DM with end-organ damage	2		
		-Hemiplegia	2		
		-ESRD	2		
		-Any tumor	2		
		-Leukemia	2		
		-lymphoma	2		
		-Disseminated cancer	6		
		-AIDS	6		

ASA: The American Society of Anesthesiologists Physical Status Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index, MI: Myocardial infarction, CHF: Congestive heart failure, PVD: Peripheral vascular disease, TIA: Transient ischemic attack, CVA: Cerebrovascular accident, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, ESRD: End-stage renal disease.

* Higher CACI results are associated with higher mortality and morbidity risk.

**Higher score of mFI-5 is associated with higher frailty risk.

≥ 5), and ASA class (group1= ASA class < 3, group2= ASA class ≥ 3) were divided into two groups. Covariates were analyzed using the backward stepwise binary logistic regression method to determine associations with postsurgical outcomes, considering factors such as age, sex, presence of oncological disease, surgical-grade classification, anesthesia method, perioperative transfusion, ICU admission, LOS, and mFI-5, CACI, or ASA class categorization. Statistical significance was set at $p < 0.05$.

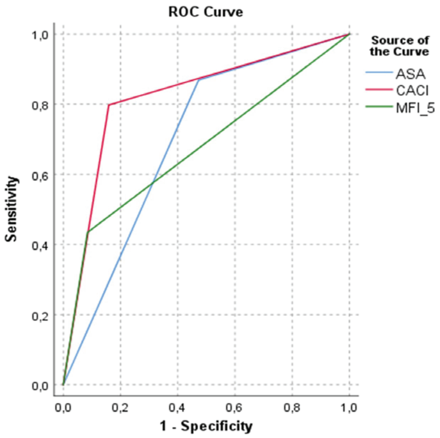
RESULTS

During the study period, 300 patients underwent different types of surgeries at four clinics (neurosurgery, urology, orthopedics, or general surgery). Patient demographics, preoperative characteristics, operative characteristics, and postoperative outcomes are shown in Table 3. The median age was 71 (65-95). Female patients accounted for 47% (n=141) of the study group; one-third of the patients had oncological diseases preoperatively (n=100, 33.3%) and 43% (n=129) of the patients had intermediate surgical risk according to ESC/ESA-NCS guidelines. The median of ASA class values was 3(2- 4), the median of CACI values was 5(2- 13), and the median of mFI-5 scores was 2(0- 5). A total of 175 patients received general anesthesia. Thirty-eight patients (12.7%) required blood product transfusion. Total 33% of the patients (n = 99) experienced a complication; the most common complication grades are grade 1 (n=43, 14.3%) and grade 4 (n=36, 12%) according to Clavien Dindo classification. Only 12% (n= 36) of the patients were admitted to the ICU. The median LOS was 2 days (1–51) and prolonged LOS was observed in 82(27.3%) patients. The overall hospital mortality rate was 3.3% (n=10) and the 1-year mortality rate was 27.4% (n=82).

ROC analysis (Figure1) demonstrated a very good association of CACI (area under the curve [AUC], 0.819; 95% CI, 0.765-0.874), and satisfactory association of mFI-5 (AUC, 0.675; 95% CI, 0.606-0.744) and ASA class (AUC, 0.698; 95% CI, 0.638-0.758) with overall complications. The AUC for mFI-5 and ICU admission were 0.702 (95%CI, 0.601-0.804), 0.669 (95%CI, 0.574-0.763) for CACI, and 0.662 (95%CI, 0.580-0.745) for ASA. As per the AUCs, mFI-5 is a better risk stratification index for ICU admission compared to CACI and ASA classes. The AUC for CACI and hospital mortality was 0.774 (95%CI, 0.653-0.895), for mFI-5 was 0.759 (95%CI, 0.591-0.926), and for ASA class was 0.653 (95%CI, 0.509-0.797). The mFI-5 was not superior to the CACI and ASA classes. All three indices were satisfactory for predicting 1-year mortality.

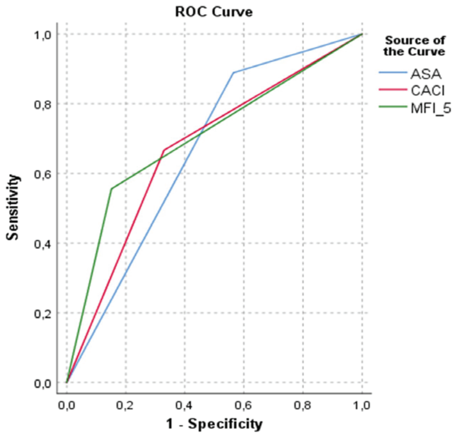
According to the results of binominal logistic regression analysis (Table 4), the risk of complications was 0.215 (95%CI 0.087-0.529, p=0.001) times higher in patients with an mFI-5 score greater than '2', 0.366 (95%CI 0.063-0.300, p=0.025) times higher in patients with an ASA class greater than '3', 0.138 (95%CI 0.152-0.881, p<0.001) times greater in patients with a CACI score greater than '5' and 0.218 (95%CI 0.096-0.492, p<0.001) times greater in patients with oncological diseases. Importantly, patients with an mFI-5 score greater than '2' had 0.165 odds ratio (95%CI 0.061-0.444, p<0.001), male patients had 0.346 odds ratio (95%CI 0.136-0.880, p=0,026), and patients who received transfusion had 0.056 odds ratio (95%CI 0.021-0.152, p<0.001) of ICU admission. Furthermore, patients with a CACI score greater than '5' had a 16.075 odds ratio (95%CI 1.557 -166.006, p=0,020), and patients with oncological diseases had a 0.146 odds ratio (95%CI 0.023-0.935, p=0.042), and patients admitted to ICU had 8.555 odds ratio (95%CI 1.655-44.228, p=0.010) of hospital mortality. Finally, older age had 0.383 odds ratio (95%CI 0.233-0.631, p<0.001), and patients with an mFI-5 score greater than '2' had 2.741 odds ratio (95%CI 1.094-6.869, p= 0.032), prolonged LOS had 9.476 odds ratio 95%CI 4.370-20.549, p<0.001), patients admitted to the ICU had

Figure 1. Receiver operating curve (ROC) analysis is illustrated by comparing risk scores with postoperative complications, ICU admission, hospital mortality, and 12 months mortality. AUC: Area under curve, ASA: The American Society of Anesthesiologists Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index, ICU: Intensive care unit, *: p<0.05, **:p<0.001.



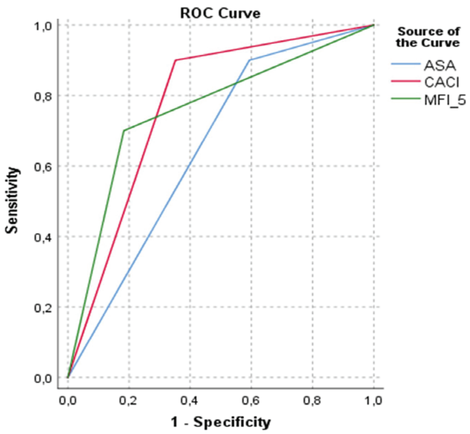
Index	AUC(%95 CI)
CACI	**0.819(0.765-0.874)****
mFI-5	0.675(0.606-0.744)**
ASA class	0.698(0.638-0.758)**

(A)



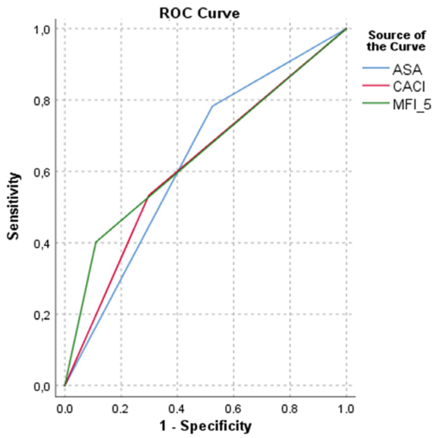
Index	AUC(%95 CI)
CACI	0.669(0.574-0.763)**
mFI-5	**0.702(0.601-0.804)****
ASA class	0.662(0.580-0.745)**

(B)



Index	AUC(%95 CI)
CACI	**0.774(0.653-0.895)****
mFI-5	**0.759(0.591-0.926)***
ASA class	0.653(0.509-0.797)*

(C)



Index	AUC(%95 CI)
CACI	0.617(0.547-0.687)*
mFI-5	0.646(0.574-0.718)**
ASA class	0.629(0.563-0.696)**

(D)

Table 3. Patient demographics, preoperative, operative characteristics, and postoperative outcomes.

Parameter	Frequency (Percentage)	Median (Min-Max)
Age (year)		71(65-95)
Gender (Female/ **Male**)	141(47%)/ **159(53%)**	
Oncologic Disease	100(33, 3%)	
Surgery Classification -Low Risk **-İntermediate Risk** -High Risk	 46(15, 3%) **129(43%)** 125(41, 7%)	
ASA Classification -ASA Class ≥ 3 - ASA Class < 3	 181(60,3%) 119(39,7%)	3(2-4)
Charlson Age Comorbidity Index - CACI ≥ 5 - CACI <5	 182(60,6%) 133((39,4%)	5(2-13)
Modified Frailty Index-5 - mFI-5 ≥ 2 - mFI-5 < 2	 183(61%) 117(39%)	2(0-5)
Anesthesia Method (**General**/ Spinal & Epidural)	175(58, 3%)/ 125(41, 7%)	
Transfusion	38(12, 7%)	
Overall Complications	99(33%)	
Clavien Dindo Classification **-Grade 1** -Grade 2 -Grade 3 Grade 3a/ Grade 3b **-Grade 4** Grade 4a/ Grade 4b	 **43(14,3%)** 17(5,6%) 3(1%) 1(0,3%)/ 2(0,6%) **36(12%)** 32(10,6%)/ 4(1,3%)	
ICU Admission	36(12%)	
LOS -Prolonged LOS	 82(27, 3%)	2(1-51)
Hospital Mortality	10(3, 3%)	
1-Year Mortality	82(27, 4%)	

Values are presented as the number of patients, frequency (percentage), or median(minimum-maximum). ASA: The American Society of Anesthesiologists Physical Status Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index, ICU: Intensive Care Unit, LOS: Length of Hospital Stay

Table 4. Binomial logistic regression analysis for postoperative outcomes.

	p	OR(Odds Ratio)	%95 CI(Confidence Interval)
Complications			
ASA class ≥ 3	**0,025**	0,366	0,063-0,300
mFI-5 ≥ 2	**0,001**	0,215	0,087-0,529
CACI≥ 5	**<0,001**	0,138	0,152-0,881
Oncological Disease	**<0,001**	0,218	0,096-0,492
ICU Admission			
mFI-5≥ 2	**<0,001**	0,165	0,061-0,444
Sex(Male)	**0,026**	0,346	0,136-0,880
Transfusion	**<0,001**	0,056	0,021-0,152
Hospital Mortality			
CACI≥ 5	**0,020**	16,075	1,557-166,006
Oncological Disease	**0,042**	0,146	0,023-0,935
ICU Admission	**0,010**	8,555	1,655-44,228
1-Year Mortality			
Age	**<0,001**	0,383	0,233-0,631
mFI-5≥ 2	**0,032**	2,741	1,094-6,869
LOS	**<0,001**	9,476	4,370-20,549
ICU Admission	**0,012**	17,719	1,862-168,651
Transfusion	**0,005**	5,152	1,632-16,264
Complications	**0,013**	3,625	1,310-10,033

Binomial logistic regression analysis was used for the evaluation of variables affecting complications.

$p < 0.05$ was used to indicate statistical significance. ASA: The American Society of Anesthesiologists Physical Status Classification, mFI-5: Modified 5-item frailty index, CACI: The Charlson age comorbidity index

17.719 odds ratio (95%CI 1.862-168.651, p=0.012), patients who received transfusion had 5,152 odds ratio (95%CI 1.632-16.264, p=0.005), and complications had 3.625 odds ratio (95%CI 1.310-10.033, p=0.013) of 1-year mortality.

DISCUSSION

In our study, 33% of patients experienced complications, the hospital mortality rate was 3.3%, and the 1-year mortality rate was 27.4%. ROC analysis demonstrated a very good association of CACI with overall complications and a good association of mFI-5 with ICU admission and hospital mortality. All three indices were satisfactory predictors of prolonged LOS and 1-year mortality. The patients with higher mFI-5 scores had a greater risk of ICU admission, and 1-year mortality; in addition, patients with higher CACI scores had a greater risk of hospital mortality.

The functional status and preferences of geriatric patients should guide the surgical decisions as most elderly patients value the quality of life rather than the length of life for the remaining time they are alive (13). In this study, 27.4% of patients who underwent surgery died within a year. Therefore, the importance of examining 1-year mortality in our study was once again reinforced. Complications affect the functional results of surgery. Good evaluation of the patient's physiological state in the preoperative period, knowledge, and early recognition of possible complications reduce the risk of disability and/or death reduce significantly (14). In our study, grade 4 (life-threatening) complications were seen in 12% of the patients, and overall complications which include all grades were also found to be associated with increased 1-year mortality.

It is yet to be determined whether ASA class is an independent predictor of medical complications in a wide variety of surgical patients from different institutions. There is also a need to justify the use of ASA as a consistently reliable predictor of outcomes (15). Hackett et al. (16) reported that the ASA classification of physical conditions had strong, independent associations with postoperative medical complications and mortality. In addition, another survey (17) showed that ASA was superior to CCI and CACI in predicting mortality. In contrast, "Rosa et al." (18) reported that in gastric cancer patients, ASA evaluation alone is insufficient to predict postoperative complications and long-term mortality. In our study, the ASA classification was a satisfactory predictor of ICU admission, overall complications, hospital mortality, and 1-year mortality. Although the risk of developing complications was higher in patients with ASA ≥ 3, in the same patient group, no significant relationship was found between ICU admission and hospital mortality.

In recent years, surveys by different surgical clinics (19, 20) have shown that CCI is a good predictor of postoperative mortality and complications. However, as CCI is insufficient in geriatric patients, CCI with age added (CACI) is considered a more appropriate prognostic indicator for clinical use and practice (7). In another study (21), patients with CCI scores greater than 5 had a higher risk of mortality than those in the other group (OR: 4.6[2,4-9.0]). It was observed that patients with systemic complications had a higher mean CCI (p=0.001) compared to the other group. In our study, CACI demonstrated a very good association with the overall complications and was equal to the mFI-5 in predicting hospital mortality. Furthermore, it was determined that the hospital mortality rate increased approximately 16 times in patients with CACI≥ 5.

Compared to an adult, a fragile elderly person is at a higher risk for conditions such as disability, morbidity, and death. Frailty scores have been used to estimate postoperative complications and outcomes in elderly patients undergoing surgery (8). Weaver et al. (22) reported that increased mFI-5 scores were significant in predicting 30-day mortality and morbidity. Another study (23) reported that mFI-5 was as successful as CACI and mFI-11 in predicting postoperative 90-day mortality. In our study, mFI-5 demonstrated a good association between ICU admission and hospital mortality. Higher mFI-5 levels increased the risk of complications, ICU admission, and 1-year mortality.

Ondeck et al. (24) evaluated the predictive power of mFI, mCCI, and ASA for complications, serious complications, mild complications, infectious complications, prolonged hospitalization, and intensive care admission. ASA combined with age was found to be the most useful index for predicting comorbidities. The combination of a demographic parameter and a comorbidity index was found to be the best index for predicting at least five of the six complications.

Different types of surgeries and comorbidities in the same age group provided an advantage in terms of evaluating the indices in different patients simultaneously. This study had some limitations that should be addressed. Adding cardiovascular surgery and thoracic surgery clinics to the study could have made the selected patient group more similar to society. We believe that a study with a larger sample size will better reflect this population. We had to terminate data collection to avoid false results due to the Covid-19 pandemic.

Due to a global increase in the elderly population, the proportion of the geriatric population among those applying to health services is increasing rapidly. According to the results of this study, mFI-5 was associated with ICU admission and 1-year mortality, and CACI was associated with complications and hospital mortality in geriatric patients. Furthermore, mFI-5 was not better than ASA class and CACI in predicting the overall postoperative outcomes. We suggest that the validity and reliability of mFI-5 should be increased by its common usage in multiple centers. Furthermore, creating different evaluation scale combinations with other evaluation indices or parameters is likely to be beneficial.

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