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The Prediction of Postoperative Delirium Using the Preoperative Assessments of Frailty and Cognitive Impairment in Aged Patients

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Purpose: Frailty and cognitive impairment are closely associated with postoperative delirium. The purpose of this study was to compare the ability of screening tools assessing preoperative frailty and cognitive impairment to predict Postoperative delirium (POD) and the association with prevalence of postoperative complications, Intensive Care Unit (ICU) admission, and the hospital length of stay.

Patients and Methods: Two hundred and ninety-nine patients aged ≥60 years presenting for elective major thoracic or abdominal surgery were divided into preoperative frailty and no frailty groups or cognitive impairment and no cognitive impairment groups. The primary outcome was the incidence of postoperative delirium. The secondary outcomes included postoperative complications, ICU admission, and hospital lengths of stay.

Results: Frailty (25.6% VS 14.6%, P = 0.017) and cognitive impairment (32.7% VS 13.4%, P < 0.001) were associated with POD. However, the area under the receiver operating characteristic curve (AUC-ROC) between frailty (0.657 [95% CI 0.60–0.71]) and cognitive impairment (0.661 [95% CI 0.60–0.71]) for POD was not different (P = 0.9) and both lower than the integrated predictive model of age, body mass index (BMI), American Society of Anesthesiologists (ASA) status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment (0.814 [95% CI 0.77–0.86], P < 0.0001, P < 0.0001). Besides, frailty (15.6% vs 6.3%, P = 0.010) and cognitive impairment (16.3% vs 8.0%, P = 0.029) was associated with the incidence of postoperative complications.

Conclusion: Preoperative frailty and cognitive impairment were associated with POD. However, preoperative frailty or cognitive impairment by themselves were comparably poor predictors of POD. A comprehensive predictive model including age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment was more useful to predict POD.

Keywords: frailty, cognitive impairment, postoperative delirium, surgery, aged, postoperative complication

Introduction

Postoperative delirium (POD) is defined as an acute and fluctuating deficit of attention and cognition after surgery, which manifests with hypoactive, hyperactive, or mixed symptoms.[1] Delirium is a common postoperative complication, especially in elderly surgical patients, and occurs in 10% to 60% of older patients.[2] POD is closely associated with functional decline, longer hospital length of stay, impaired cognition, and death, increasing cost and burden on patients and society.[3,4] In addition, effective treatment of delirium is very difficult, so the prevention of POD is of critical importance, especially in high-risk patients.[5] Identifying predictors of risk preoperatively has the advantage of facilitating prospective decision-making. Advanced age, cognitive or functional impairment, frailty, number of comorbidities, malnutrition, pain, the use of urinary catheters, Intensive Care Unit (ICU) admission, anaemia, and type of surgery have been reported as risk factors for delirium after surgery.[6–8] However, it is challenging to apply all of these risk factors to predictive modelling in clinical practice with a large sample size. A simple predictive assessment to identify high-risk patients would be useful and important.

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Frailty is defined as an excess vulnerability to stressors and is commonly used to reflect decreased reserve across multiple organ systems.[9] Frailty is prevalent among older adults, with a prevalence of 10% in community dwellers and a higher prevalence of 18% to 40% in the hospital population.[9,10] Frail patients had a higher Charlson Comorbidity Index (CCI), and patients with multimorbidity were more likely to screen positive for frailty measures.[11] Frailty has also been shown to be associated with adverse outcomes after surgery.[12,13] Modified frailty index (mFI) is associated with post-operative morbidity and mortality after some general surgery, such as pancreaticoduodenectomy and laparoscopic gastrectomy.[14,15] Some studies suggested that mFI is a superior and independent predictor of adverse outcomes compared to age in neuro-oncological surgeries.[16] Besides, some findings have shown frailty to be associated with higher morbidity, longer hospital length of stay, and a lower probability of discharge to home in spinal surgery[17,18] The mFI was defined by 11 variables within the National Surgical Quality Improvement Program (NSQIP) previously used for the Canadian Study of Health and Aging-Frailty Index and has been proven to adequately reflect frailty and predict mortality and morbidity.[19]

Similarly, preoperative cognitive impairment is common in older surgical patients, and preoperative cognitive screening has been demonstrated to be associated with postoperative cognitive dysfunction.[20] Preoperative screening for frailty and cognitive impairment are both important in identifying patients at high risk for postoperative outcomes. Frailty assessment focuses on the complications of multiple organs, whereas preoperative cognitive assessment focuses only on brain function. There is little consensus about which is more suited for predicting POD and adverse outcomes.

Thus, the primary aim of this study was to explore and compare the ability of cognitive and frailty screening to predict POD. Second, we investigated the relationship between cognition and frailty assessment and the secondary outcome, a composite of postoperative complications, ICU admission, and prolonged hospital length of stay.

Material and Methods

Participants and Recruitment

This study was conducted in compliance with the guidelines stated in the World Medical Association (WMA) Declaration of Helsinki and approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (USTC) and registered with Chinese Clinical Trials.gov (ChiCTR2000039755) and informed consents were obtained. This investigation was to identify the prevalence of preoperative cognitive impairment and frailty and relate these to the incidence of POD, postoperative complications, ICU admission, and hospital lengths of stay following major noncardiac thoracic or abdominal surgery.

Patients scheduled for elective major thoracic or abdominal surgery at the first affiliated hospital of USTC were included in this prospective observational cohort study. Inclusion criteria included: (i) age ≥60 years; (ii) operation time > 60min. Exclusion criteria included: (i) dementia, Mini-Mental Status Examination (MMSE) score < 24 or Clinical Dementia Scale more than 1 before the surgery; (ii) communication difficulties, such as blindness and deafness; (iii) psychiatric illnesses or taking psychotropic drugs; (iv) being unable to complete questionnaires; (v) a history of alcohol or drug abuse.

We studied 299 patients and written informed consent was obtained from all the participants. Patients are assigned to evaluation by trained anesthesiologists 1 day before surgery. Patients, attending anesthesiologist on the operation day and research staff assessing outcomes were blind to the study group assignment. POD was assessed daily for 3 days after surgery.

Anesthesia

Anaesthesia was induced using etomidate, rocuronium and sufentanil for tracheal intubation and maintained by intravenous anaesthesia with propofol, remifentanil and dexmedetomidine and sevoflurane inhalation (depending on the indications). Bispectral index (BIS) monitoring was performed in all patients and was maintained between 40 and 60. Oxycodone was given 30 min before the end of surgery for postoperative pain management as required. In the recovery room, opioid and non-opioid pain medication was administered according to numeric rating scale (NRS). Postoperative pain was most commonly treated with patient-controlled analgesia. Because remifentanil has a rapid offset of action following discontinuation (3–10 minutes) irrespective of the duration of infusion,[21] intraoperative morphine equivalent means sufentanil and oxycodone, according to recommended Oral Morphine Equivalent (OME) conversion factors: morphine (per os) 30mg = sufentanil (iv) 10μg = oxycodone (iv) 10mg.[22,23]

Cognitive and Frailty Measurements

Frailty was defined as satisfying 3 of the following mFI criteria:[24] (1). History of diabetes mellitus; (2). New York Heart Association functional classification 2 or more; (3). History of chronic obstructive pulmonary disease or pneumonia; (4). History of congestive heart failure; (5). History of myocardial infarction; (6). History of percutaneous coronary intervention, prior cardiac surgery, or angina; (7). History of hypertension requiring medication; (8). History of peripheral vascular disease or ischemic rest pain; (9). History of impaired sensorium; (10). History of transient ischemic attack or cerebrovascular accident; (11). History of cerebrovascular accident with neurologic deficit. The functional classification was assessed and documented by the interviewer during the preoperative visit.

The Mini-Mental State Examination (MMSE) is a common measuring tool of a variety of cognitive abilities in clinical trials, comprising 30 questions covering short-term episodic memory, orientation to time and place, attention, visuospatial abilities, and language and motor skills.[25] A score < 27 out of a maximum of 30 was taken to represent impaired cognition.[26]

Outcome Measurements

The primary outcome was the incidence of POD after surgery. Postoperative delirium was measured daily with the Confusion Assessment Method (CAM) for the first 3 days. For intubated patients, POD was measured by CAM-ICU. CAM is the most widely used bedside clinical assessment tool for the identification of delirium, consisting of 4 diagnostic components: acute onset with a fluctuating course, inattention altered level of arousal, and disorganized thinking.[27]

Secondary outcomes included postoperative complications, ICU admission, and hospital lengths of stay. Postoperative complications include cardiovascular, pulmonary, gastrointestinal, renal, infectious, hematologic, neurologic, and wound complications. Postoperative prolonged hospital length of stay means the actual length of stay minus the expected length of stay (the mean length of postoperative hospitalization for all adults in the last year) postoperatively.

Statistical Analysis

Statistical analyses were performed using SPSS 23.0 (IBM SPSS, USA) and MedCalc Statistical Software version 18.6 (MedCalc Software, Belgium). The sample size was based on a preoperative frailty prevalence of approximately 33%, a POD incidence of 48% in the frail patients and 13% in the no frail patients,[28] and a preoperative cognitive impairment prevalence of approximately 38%, a postoperative delirium incidence of 35% in the cognitive impairment patients and 18% in the control group.[29] We would require 290 patients to identify this difference (power of 90%, and $\alpha = 0.05$, two-tailed).

Continuous variables were first assessed for normality using the Kolmogorov–Smirnov test. Group comparisons were made using independent t-tests for normally distributed continuous variables (data reported as mean ± SD), Mann–Whitney *U*-test for nonnormal distributions (data reported as median (25th, 75th percentiles)) and chi-square or Fisher exact test for categorical variables (data reported as count (%)). Besides, we used logistic regression to estimate the odds ratio (OR) values and 95% confidence intervals (CIs) to express the independent predictive risks of the predictors. The area under the receiver operating characteristic (ROC) curve was used to judge the discriminatory ability of the predictors and the ability to predict the occurrence of POD. All testing was two-tailed. The significance threshold was set at $P < 0.05$. Odds ratios and 95% CIs were determined for all tests.

Results

During the study period, we evaluated 653 patients scheduled for elective major thoracic or abdominal surgery. Of these, 338 individuals were ineligible. Of the remaining 315 patients, 13 patients were excluded for operation time < 60 min, and 3 individuals refused the CAM test postoperatively. Data from the remaining 299 patients were analysed in this study (Figure 1).

The overall baseline characteristics (n = 299) are shown in Table 1 and Table 2. Differences were found for age, BMI and ASA between frailty and no frailty group. Age, gender, education and ASA differed between participants with and

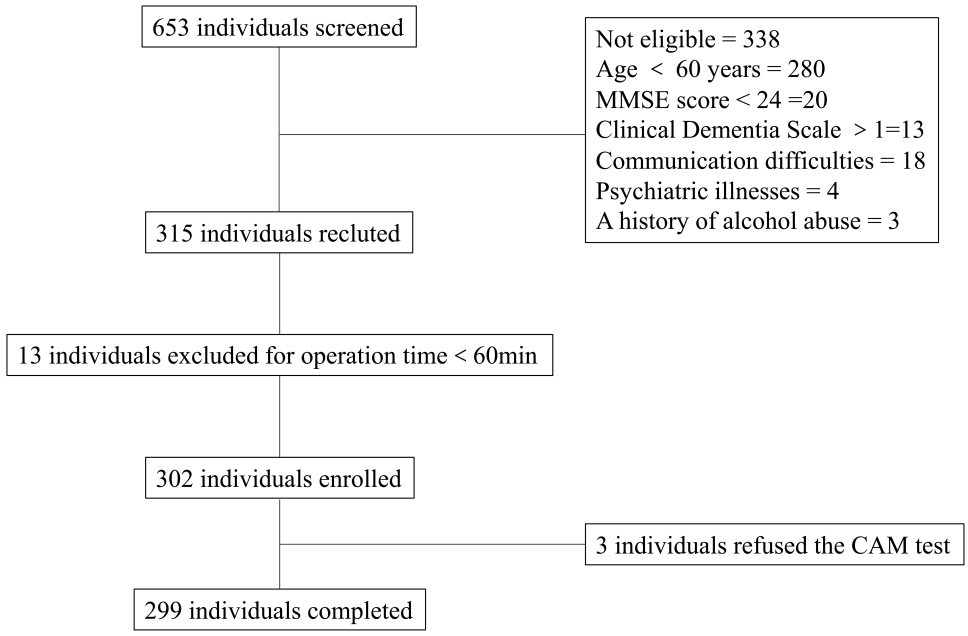

Figure 1 Study Flow. Flow diagram on recruitment and retention.
Abbreviation: MMSE, Mini-Mental State Examination.

without cognitive impairment. In addition, for those assessed preoperatively as frail or cognitively impaired, no significant difference was observed in the pain scores of the two groups in the first 3 days after surgery.

The distribution of the mFI and the MMSE score across the population is shown in Table 1 and Table 2. Based on the mFI, 141 (47.2%) patients were classified as frail. Based on the MMSE, 98 (32.8%) patients in our cohort were classified as having

Table 1 Baseline Characteristics of Frailty and No Frailty Group

	Total	Frailty		P value
	n=299	Frailty n=141	No frailty n=158	
Age	70.30±5.75	72.03±6.05	69.77±5.00	<0.001
Gender (male,%)	212(70.90)	103(73.04)	109(68.99)	0.4
BMI (Kg/m^2)	22.62±3.23	23.34±3.51	21.97±2.82	<0.001
Education (years)	5.00(0.00,8.00)	5.00(0.00,8.00)	5.00(0.00,8.00)	0.3
ASA status				<0.001
II(%)	96(32.11)	1(0.71)	95(60.13)	
III(%)	201(67.22)	138(97.87)	63(39.87)	
IV(%)	2(0.67)	2(1.42)	0(0.00)	
Duration of surgery (min)	201.87±73.25	205.60±78.12	198.54±68.69	0.4
Surgical risk				0.3
Low-risk(%)	0(0.00)	0(0.00)	0(0.00)	
Intermediate-risk(%)	167(55.85)	83(58.9)	84(53.2)	
High-risk(%)	132(44.15)	58(41.1)	74(46.8)	

(*Continued*)

Table 1 (Continued).

	Total n=299	Frailty		P value
		Frailty n=141	No frailty n=158	
NRS (Day1)	2.55±0.63	2.51±0.60	2.58±0.66	0.4
NRS (Day2)	2.01±0.81	2.10±0.81	1.94±0.80	0.1
NRS (Day3)	1.80±0.79	1.81±0.78	1.80±0.80	0.9
Morphine equivalent (mg)	105.00 (90.00,120.00)	102.00(90.00,108.00)	105.00(90.00,120.00)	0.2
Frailty score	2.67±1.17	3.70±0.82	1.74±0.44	<0.001
MMSE score	27.04±1.49	26.84±1.43	27.23±1.53	0.024

Abbreviations: ASA, American Society of Anesthesiologists; MMSE, Mini-mental state examination; BMI, Body mass index.

Table 2 Baseline Characteristics of Cognitive Impairment and No Cognitive Impairment Group

	Total n=299	Cognitive impairment n=98	No cognitive impairment n=201	P value
Age	70.30±5.75	72.78±5.98	69.10±5.24	<0.001
Gender (male,%)	212(70.90)	62(63.39)	150(74.63)	0.042
BMI (Kg/m^2)	22.62±3.23	22.44±3.17	22.71±3.26	0.5
Education (years)	5.00(0.00,8.00)	3.50(0.00,5.00)	5.00(5.00,11.00)	<0.001
ASA status				0.003
II (%)	96(32.11)	20(20.41)	76(37.81)	
III (%)	201(67.22)	78(79.59)	123(61.19)	
IV (%)	2(0.67)	0(0.00)	2(1.00)	
Duration of surgery (min)	201.87±73.25	206.67±74.63	199.53±72.64	0.4
Surgical risk				0.2
Low-risk (%)	0(0.00)	0(0.00)	0(0.00)	
Intermediate-risk (%)	167(55.85)	50(51.02)	117(58.21)	
High-risk (%)	132(44.15)	48(48.98)	84(41.79)	
NRS (Day1)	2.55±0.63	2.51±0.71	2.56±0.60	0.5
NRS (Day2)	2.01±0.81	1.99±0.81	2.02±0.81	0.7
NRS (Day3)	1.80±0.79	1.69±0.74	1.86±0.81	0.1
Morphine equivalent (mg)	105.00 (90.00,120.00)	102.00(90.00,120.00)	105.00(90.00,118.00)	0.8
Frailty score	2.67±1.17	3.01±1.21	2.50±1.12	<0.001
MMSE score	27.04±1.49	25.29±0.75	27.90±0.89	<0.001

Abbreviations: ASA, American Society of Anesthesiologists; MMSE, Mini-mental state examination; BMI, Body mass index.

cognitive impairment. The results of POD testing of patients in the first 3 days after surgery are shown in Table 3 and Table 4. POD developed in 19.7% (N = 59 of 299) patients as detected by the CAM scale, and the median number of days with delirium was 1.00 (1.00, 2.00) days. The incidence of postoperative complications was 10.7% (N = 32 of 299). About 10 (3.3%) patients were admitted to the ICU after surgery. The median prolonged hospital length of stay after surgery was −0.25 (−1.25,1.11) days (Table 3 and Table 4).

Primary Analysis

In the preoperative frailty group, 36 of 141 (25.6%) patients demonstrated POD postoperatively, which was higher than the incidence of POD in the no frailty Group (23 of 158 [14.6%], p = 0.017). In the preoperative cognitive impairment group, 32 of 98 (32.7%) patients demonstrated POD, which was higher than the incidence of POD in the no cognitive impairment Group (27 of 201 [13.4%], P < 0.001). The number of postoperative days with delirium in the preoperative cognitive impairment group was significantly higher than that of the no cognitive impairment group (P = 0.037), but there was no difference in this measure between the frailty and no frailty groups (P = 0.8) (Table 3 and Table 4).

Table 3 Outcomes of Frailty and No Frailty Group

Outcomes	Total	Frailty		P value
		Frailty n=141	No frailty n=158	
POD (1d after surgery,%)	45	30(21.28)	15(9.49)	0.004
POD (2d after surgery,%)	34	19(13.48)	15(9.49)	0.3
POD (3d after surgery,%)	9	6(4.26)	3(1.90)	0.4
POD (the first 3d after surgery,%)	59	36(25.53)	23(14.56)	0.017
Days with delirium	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	1.00 (1.00, 2.00)	0.8
Postoperative complications (%)	32	22(15.60)	10(6.33)	0.010
ICU admission (%)	10	5(3.55)	5(3.16)	0.9
Prolonged hospitalization (days)	−0.25 (−1.25,1.11)	−0.16 (−1.25, 2.30)	−0.36 (−1.25, 0.84)	0.3

Abbreviation: ICU, intensive care unit.

Table 4 Outcomes of Cognitive Impairment and No Cognitive Impairment Group

Outcomes	Total	Cognition		P value
		Cognitive impairment n=98	No cognitive impairment n=201	
POD (1d after surgery,%)	45	23(23.47)	22(10.95)	0.004
POD (2d after surgery,%)	34	22(22.45)	12(5.97)	<0.001
POD (3d after surgery,%)	9	5(5.10)	4(1.99)	0.1
POD (the first 3d after surgery,%)	59	32(32.65)	27(13.43)	<0.001
Days with delirium	1.00 (1.00, 2.00)	1.50 (1.00, 2.00)	1.00 (1.00, 2.00)	0.037
Postoperative complications (%)	32	16(16.33)	16(7.96)	0.029
ICU admission (%)	10	3(3.06)	7(3.48)	0.8
Prolonged hospitalization (days)	−0.25 (−1.25,1.11)	−0.16 (−1.18, 2.89)	−0.36 (−1.25, 0.84)	0.2

Abbreviation: ICU, intensive care unit.

Univariate analysis was conducted and demonstrated that frailty (odds ratio, 1.70; 95% CI (1.33–2.17); P < 0.001) and cognitive impairment (odds ratio, 0.66; 95% CI (0.54–0.81); P < 0.001) were both associated with POD, and the incidence of postoperative delirium increased with the increase of frailty score or the decrease of cognitive score. Besides, age (odds ratio, 1.06; 95% CI, 1.01–1.12; P = 0.013), ASA status (odds ratio, 4.18; 95% CI (1.91–9.13); P < 0.001), duration of surgery (odds ratio, 1.01; 95% CI (1.00–1.01); P = 0.001), Morphine equivalent (odds ratio, 1.02; 95% CI (1.01–1.04); P = 0.003) and Surgical risk (odds ratio, 2.15; 95% CI (1.20–3.84); P = 0.010) were also associated with POD. Multivariate analysis showed that BMI (odds ratio, 0.88; 95% CI 0.79–0.98; P = 0.022), ASA status (odds ratio, 2.92; 95% CI (1.01–8.10); P = 0.040), Morphine equivalent (odds ratio, 1.03; 95% CI (1.01–1.05); P = 0.004) and cognitive impairment (odds ratio, 0.64; 95% CI, (0.48–0.84); P = 0.001) were all associated with POD (Table 5). Thus, the final predictive model contained age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment.

The AUC-ROC was 0.657 (95% CI 0.60–0.71) by frailty and 0.661 (95% CI 0.60–0.71) by cognitive impairment for POD, and there was no difference between the two preoperative assessments (P = 0.9). And the AUC-ROC of the comprehensive predictive model was 0.814 (95% CI 0.77–0.86), with a sensitivity of 79.66%, and the specificity was 79.58%, and the AUC-ROC of this predictive model was significantly higher than when frailty or cognitive impairment was assessed alone (P < 0.0001, P < 0.0001) (Figure 2 and Appendix1).

Secondary Analysis

In the frailty group, the incidence of postoperative complications was 15.6% (22 of 141), 3.5% (5 of 141) of the patients were admitted to the ICU, and the prolonged postoperative hospital length of stay was −0.16[−1.25, 2.30] days. In the no frailty group, the incidence of postoperative complications was lower (6.3% [10 of 158], P = 0.010), but there was no difference in the measures of patients admitted to the ICU (3.2% [5 of 158], P = 0.9) and median prolonged postoperative hospital length of stay (−0.36[−1.25, 084], P = 0.3) after surgery compared with the frailty group (Table 3 and Table 4).

In the cognitive impairment group, the incidence of postoperative complications was 16.3% (16 of 98), 3.1% (3 of 98) of the patients were admitted into the ICU, and the median prolonged postoperative hospital length of stay was −0.16[−1.18, 2.89] days. In the no cognitive impairment group, the incidence of postoperative complications was lower (8.0% [16 of 201], P = 0.029), but there was no difference in the measures of patients admitted to the ICU (3.5% [7 of 201], P = 0.8) after surgery

Table 5 Variables Associated with Postoperative Delirium on Univariate and Multivariate Analysis

	Univariate analysis		Multivariate analysis	
	Odds ratio(95% CI)	**P value**	**Odds ratio(95% CI)**	**P value**
Age	1.06(1.01–1.12)	0.013	1.01(0.95–1.08)	0.7
Gender	1.26(0.66–2.40)	0.5	0.85(0.38–1.88)	0.7
BMI (Kg/m^2)	0.93(0.85–1.03)	0.1	0.88(0.79–0.98)	0.022
Education (years)	1.00(0.94–1.07)	1.0	1.08(0.98–1.19)	0.1
ASA status	4.18(1.91–9.13)	<0.001	2.92(1.05–8.10)	0.040
Duration of surgery (min)	1.01(1.00–1.01)	0.001	1.01(1.00–1.01)	0.1
Morphine equivalent (mg)	1.02(1.01, 1.04)	0.003	1.03(1.01,1.05)	0.004
Surgical risk	2.15(1.20, 3.84)	0.010	1.09(0.48, 2.48)	0.8
Frailty	1.70(1.33–2.17)	<0.001	1.40(1.00–1.96)	0.050
Cognitive impairment	0.66(0.54–0.81)	<0.001	0.64(0.48–0.84)	0.001

Abbreviations: ICU, intensive care unit; BMI, Body mass index; ASA, American Society of Anesthesiologists.

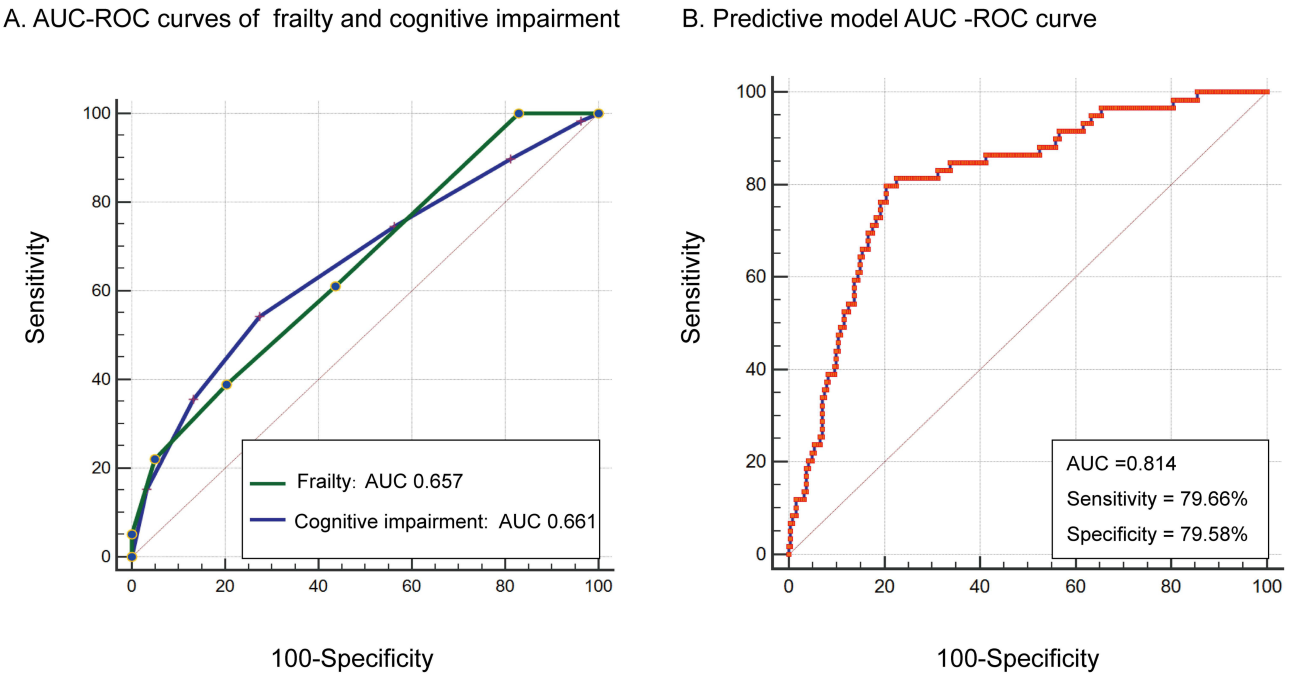

Figure 2 AUC-ROC curves of groups and predictive model. ROC curve of the POD prediction of frailty, cognitive impairment and the model combined with age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment. (**A**) ROC curve analysis for frailty and cognitive impairment. (**B**) ROC curve analysis for the model combined with age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment.
Abbreviations: AUC-ROC, the area under the receiver operating characteristic curve; POD, postoperative delirium.

and median prolonged postoperative hospital length of stay (−0.36[−1.25, 0.84] days, P = 0.2) compared with the cognitive impairment group (Table 3 and Table 4).

Discussion

There is some evidence of the impact of preoperative frailty and cognition on postoperative cognitive change. The incidence of frailty and cognitive impairment was higher in major thoracic and abdominal operations patients and associated with a higher rate of postoperative adverse outcomes.[30–32] However, the relationships between frailty and cognitive impairment and POD in these types of surgeries are not clear. The magnitude of surgical trauma sustained by the elderly patients was also a main contributor to postoperative complications.[33] In this study, we included patients undergoing pulmonary, esophageal and gastrointestinal surgery. Surgical risks are graded according to ESC/ESA guidelines.[34] Hepatobiliary and renal surgery were excluded for the probable affection on the Metabolism of narcotic drugs. We found a high prevalence of preoperative frailty and cognitive impairment in patients undergoing major thoracic or abdominal surgery, and these features were associated with postoperative delirium and complications. However, as it is unclear which of these impairments could better predict POD risk, we compared the findings of two assessment tools in terms of their ability to predict POD. We found that applied singly, preoperative frailty and cognitive impairment screening did not differ statistically in their ability to predict POD, and neither alone was a useful predictor of POD. However, a prediction model combining age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment could help identify patients at high risk of POD.

POD is common in older patients and is associated with worse perioperative outcomes, such as prolonged hospitalization, complications, and high medical expenses.[23] In this study, 19.7% of patients developed POD after major thoracic and abdominal surgery, which was consistent with that in some of the literature.[35] There is currently no convincing evidence of any effective treatment for POD. Considering the high incidence of POD and its close association with postoperative adverse outcomes, older surgical patients were recommended to undergo preoperative screening for geriatric conditions associated with POD.[36]

Our understanding of the association of frailty with poorer outcomes following the acute stress of surgery has significantly expanded in recent years, and incorporating frailty assessment into surgical screenings may be advantageous for predicting functional recovery after surgery.[37] There are several approaches that have been used to characterize frailty. The mFI is based on the proportion of comorbidities present in a patient and perceived as useful and simple for identifying patients at risk for adverse postoperative outcomes.[38] Although the mFI-5 requires fewer than half as many variables as the mFI-11 and is simpler,[39] a more comprehensive understanding of the patient's history of diseases was required before anesthesia, so we chose the mFI-11 in this study. We found that 47.2% patients were considered frail before surgery, which was higher than that in some of the literature about noncardiac surgery,[40] but was similar to that in an article about thoracoabdominal surgery.[41] Furthermore, significant differences in the incidence of POD were observed between the frailty and no frailty groups, but the number of postoperative days with delirium was not different between the two groups.

Cognitive impairment and frailty often coexist in older surgical patients with a higher risk of postoperative adverse outcomes,[42] and preoperative cognitive assessment is also important for prediction of POD. In this study, we chose to use the MMSE to assess preoperative cognition and found that 32.8% patients were cognitively impaired before surgery and that preoperative cognitive impairment was closely associated with POD, which was consistent with the findings in other types of surgical procedures.[43] Besides, cognitive impairment was associated with postoperative days with delirium, which was different from frailty. Postoperative pain was demonstrated to be an independent risk factor for POD.[44] In this study, we adopted patient-controlled analgesia after surgery and found no difference in NRS pain scores between the groups.

Many studies evaluating the association between frailty and cognitive impairment and POD have reported statistically significant odds ratios or differences between participants with and without frailty or with and without cognitive impairment in clinical practice,[42,45] which may not be as rigorous and precise as prospective studies like this one. In this study, the ROC curve was used to judge the discriminatory ability of the frailty and cognitive impairment assessments and to evaluate their ability to predict the occurrence of POD. Our most surprising result was that neither measures of preoperative frailty nor cognitive impairment alone were helpful predictors of POD, which was different from that in some literatures.[46] Although statistically significant, these low values indicate that the predictive ability of these two assessments was too weak to be clinically useful. Because cognitive impairment or frailty alone was not sufficient to predict POD, we used multivariate logistic analysis to identify risk factors for POD. Age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment were selected as independent risk factors into the prediction model and found that this model was effective in predicting POD.

Some investigators have reported a significant association between frailty and postoperative complications,[47] and the results in this study were consistent with these findings. In addition, we also found that preoperative cognitive impairment was closely associated with postoperative complications, which was consistent with the findings in other types of surgical procedures.[47] However, we found no difference in ICU admission and prolonged hospitalization between the frailty and no frailty groups or between the cognitive impairment and no cognitive impairment groups. Presumably, many other factors contribute to ICU admissions, such as type and magnitude of surgical intervention and requests from patients and their families. Since length of stay after different types of surgery may be different, which may affect the outcomes. Unlike most of the previously published literature,[48] in this study, our secondary outcome was postoperative prolonged hospitalization, which defined as the actual length of stay minus the expected length of postoperative stay (the mean length of postoperative hospitalization for all adults undergoing the same surgery in the last year) described by Abraham Sonny et al,[40] rather than total length of hospital stay, and therefore the expected length of stay was procedure specific, which might be the reason for the difference in the results of postoperative prolonged hospitalization in this article compared to other reports.

One of the limitations of our study is that there are several scales for measuring frailty and cognitive impairment, with no gold standard, and we tested only one commonly used measurement for each. It remains possible that other methods may outperform the ones we used. In addition, the mFI includes 11 variables, but the relationship between these 11 indices of frailty and POD was not discussed in this study. Furthermore, because the sample size was relatively small, the inferences should be interpreted with caution. The limited sample size from a single center may place some limitations on generalizability. The literature review table was shown in Appendix 2.

Conclusion

In conclusion, preoperative frailty and cognitive impairment were closely associated with POD in older patients undergoing major thoracic and abdominal operations. However, the use of preoperative frailty or cognitive impairment measures alone was comparably poor predictors of POD. A comprehensive assessment of age, BMI, ASA status, duration of surgery, morphine equivalent, surgical risk, frailty and cognitive impairment together was useful to predict POD. Moreover, frailty and cognitive impairment were associated with an increased number of postoperative complications. Although further studies using different screening tools in a larger cohort are needed, our results will be helpful for perioperative prediction and prevention of POD.

Data Sharing Statement

The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request. Please send your request for original data to the e-mail address of Professor Sheng Wang at iamsheng2020@ustc.edu.cn. No data other than those contained in the manuscript were shared.

Ethics/Copyright Approval Statement

This study was approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (USTC) and registered with Chinese Clinical Trials.gov (ChiCTR2000039755). An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

Patient Consent Statement

The patients volunteered to participate and signed an informed consent form either by themselves or their guardians.

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Disclosure

The authors report no conflicts of interest in this work.

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