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RESEARCH

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The composite risk index based on frailty predicts postoperative complications in older patients recovering from elective digestive tract surgery: a retrospective cohort study

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Abstract

Background: Limitations exist in available studies investigating effect of preoperative frailty on postoperative outcomes. This study was designed to analyze the association between composite risk index, an accumulation of preoperative frailty deficits, and the risk of postoperative complications in older patients recovering from elective digestive tract surgery.

Methods: This was a retrospective cohort study. Baseline and perioperative data of older patients (age ≥ 65 years) who underwent elective digestive tract surgery from January 1, 2017 to December 31, 2018 were collected. The severity of frailty was assessed with the composite risk index, a composite of frailty deficits including modified frailty index. The primary endpoint was the occurrence of postoperative complications during hospital stay. The association between the composite risk index and the risk of postoperative complications was assessed with a multivariable logistic regression model.

Results: A total of 923 patients were included. Of these, 27.8% (257) developed postoperative complications. Four frailty deficits, i.e., modified frailty index ≥0.27, malnutrition, hemoglobin < 90 g/L, and albumin ≤30 g/L, were combined to generate a composite risk index. Multivariable analysis showed that, when compared with patients with composite risk index of 0, the odds ratios (95% confidence intervals) were 2.408 (1.714–3.383, $P < 0.001$) for those with a composite risk index of 1, 3.235 (1.985–5.272, $P < 0.001$) for those with a composite risk index of 2, and 9.227 (3.568–23.86, $P < 0.001$) for those with composite risk index of 3 or above. The area under receiver-operator characteristic curve to predict postoperative complications was 0.653 (95% confidence interval 0.613–0.694, $P < 0.001$) for composite risk index compared with 0.622 (0.581–0.663, $P < 0.001$) for modified frailty index.

Conclusion: For older patients following elective digestive tract surgery, high preoperative composite risk index, a combination of frailty deficits, was independently associated with an increased risk of postoperative complications.

Keywords: Older patient, Frailty, Malnutrition, Digestive system surgical procedures, Postoperative complications

Background

Frailty is a geriatric syndrome characterized by declined physiologic reserve and impaired capacity to maintain homeostasis [1, 2]. The etiology of frailty is multifactorial but may include the accumulation of degenerative changes and disease-associated deficits across multiple systems,

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involving functional, medical, nutritional, psychosocial, and cognitive domains, all of which increase vulnerability to stress. In particular, the progressive nutritional and medical deteriorations caused by new-onset diseases such as cancer contribute to the development or aggravation of frailty. With the accelerated aging process, the proportion of older people (aged ≥65 years) in the Chinese population is rapidly increasing [3]. It is estimated that more than 50% of older people will receive at least one surgery during their remaining lifespan [4]. However, frailty among older patients not only decreases their resilience to surgical trauma, but also delays their postoperative recovery. This brings a great challenge to the perioperative care providers.

It is recommended that frailty assessment should be routinely performed for older patients before surgery [5, 6]. Numerous instruments, including the modified frailty index (mFI), have been developed to assess frailty [7–15]. Current evidence indicates that the presence of frailty is associated with increased perioperative morbidity and mortality [7, 10, 14, 16–24]. However, limitations exist in the available results. For example, as one of the most frequently used preoperative frailty scales, the mFI does not include recent changes induced by surgical diseases for which surgeries are planning to be performed [7, 16–24]. These changes, such as loss of body weight, low albumin, and anemia, may also aggravate frailty and be associated with worse outcomes [25–28]. Additionally, there are also studies reporting “negative” results [29–31]. Therefore, further studies are required to improve the method for frailty evaluation and to clarify the correlation between preoperative frailty and postoperative outcomes.

We hypothesized that a higher preoperative composite risk index, accumulation of frailty deficits including the mFI, was associated with an increased risk of adverse postoperative outcomes in older patients. The primary purpose of this study was to analyze the relationship between the composite risk index and the occurrence of postoperative complications (POCs) in older patients recovering from elective digestive tract surgery.

Methods

Study design

This retrospective cohort study was performed in Peking University First Hospital, a tertiary general hospital in Beijing, China. The study protocol was approved by the Biomedical Research Ethics Committee of Peking University First Hospital (2019[296], Beijing, China). As the study was purely observational and no patient follow-up was performed, the Ethics Committee agreed to waive the written informed consent from patients. All personal data were kept strictly confidential.

Patient selection

Older patients (age ≥ 65 years) who underwent elective digestive system surgery from January 1, 2017 to December 30, 2018 in Beijing University First Hospital were screened utilizing the medical records system. Patients who met the following criteria were excluded: (1) underwent combined surgery; (2) incomplete or missing perioperative data.

Data collection

All data were extracted from the electronic medical records system of Peking University First Hospital. To eliminate the risk of diagnostic bias, covariates and outcomes were separately collected by different investigators (CZ and FY) who were strictly trained and blinded to the purpose of the study.

Baseline data were collected and included demographic characteristics (age, sex, and body mass index), surgical diagnosis, comorbidity, body weight change in the last 3–6 months, history of smoking and drinking [32], and main laboratory test results. Physical status was classified according to the American Society of Anesthesiologists (ASA) Classification. The 11 components of the mFI were collected according to the National Surgical Quality Improvement Program definitions (Supplementary Table 1); each item was assigned the same weight of 1 point. The mFI score was calculated by summarizing the total points and then dividing them by 11. The resulting index ranges from 0 to 1.0, with a higher score indicating more severe frailty [7]. Nutritional status was assessed according to the National Institute for Health and Clinical Excellence (NICE) guidance for “Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition (2006)”, which defines malnutrition as meeting any of the following: (1) a body mass index of less than 18.5 kg/m^2; (2) unintentional weight loss of greater than 10% within the last 3–6 months; or (3) a body mass index of less than 20 kg/m^2 and unintentional weight loss of greater than 5% within the last 3–6 months [33].

Intraoperative data were also collected and included type and duration of surgery, type of anesthesia, the seniority of anesthesiologists, estimated blood loss, and intraoperative blood transfusion. The type of surgery was stratified into five categories according to the Operative Stress Score, i.e., very low stress, low stress, moderate stress, high stress, and very high stress (Supplementary Table 2) [34]. If more than one surgical procedure (such as unplanned reoperation for bleeding or other complications) was performed during hospitalization, only the first procedure was taken into analysis.

The primary outcome was the development of POCs during hospital stay. POCs were defined as any deviation from a normal postoperative course that was harmful to patients' recovery and required different levels of therapeutic intervention, i.e., graded II or higher according to the Clavien-Dindo classification (Supplementary Table 3) [35]. If multiple complications occurred in a patient, only the most severe one was analyzed. Secondary outcomes included the intensive care unit (ICU) admission after surgery, length of ICU stay, unplanned reintubation/reoperation, total length of hospital stay and length of hospital stay after surgery, and adverse discharge destination.

Statistical analysis

The baseline and perioperative data were compared between patients with POCs and those without. Continuous variables were analyzed with independent samples *t* tests or Mann-Whitney *U* tests. Categorical variables were analyzed using chi-square tests, continuity-corrected chi-square tests, or Fisher's exact tests. Time-to-event variables were analyzed with Kaplan-Meier survival analyses, with the differences between groups tested with Log-Rank tests. Univariable logistic regression analyses were used to screen potential risk factors of POCs. Independent variables with P values <0.20 in univariate analysis and those that were considered clinically important were included in a multivariable logistic regression model to identify independent predictors of POCs with the Wald (backward) method.

According to the results of primary multivariable analysis, we divided the mFI dichotomously and selected other independent predictors of POCs that reflected the frailty features of the study cohort. We combined these parameters to generate a composite risk index. We then performed another multivariable logistic regression analysis to evaluate the effects of the composite risk index in predicting POCs after adjustment for confounding factors.

We also compared postoperative outcomes among patients with different mFI or composite risk index scores. Outcomes of two groups were compared as above. For outcomes of three or more groups, categorical variables were compared with the Chi-squared tests or Fisher's exact tests and post hoc Chi-squared tests or Fisher's exact tests. Time-to-event variables were analyzed with Kaplan-Meier survival analyses and Log-Rank tests. The predictive performances of the mFI and composite risk index in predicting POCs were assessed using the receiver-operating characteristic (ROC) curve analysis. The area under the curve and 95% confidence interval (CI) were provided to describe their discriminative power.

Two-tailed P values of <0.05 were considered statistically significant. Bonferroni correction was performed for multiple comparisons. Statistical analysis was performed with the SPSS version 25.0 (IBM SPSS, Inc., Chicago, IL).

According to the "ten events per variable" rule and the number of independent variables (15 or 12) included in the multivariable logistic regression models, the number of patients with primary outcome (257) was sufficient [36], although estimation of sample size was not performed in advance. Therefore, the sample size of participants (923) included in our study was adequate and could guarantee the stability of the regression estimates.

Results

Patients

From January 1, 2017 to December 31, 2018, a total of 5191 patients underwent digestive tract surgery. Of these, 3378 patients were excluded because they did not meet the inclusion criteria (age < 65 years or emergency surgeries); 890 patients were excluded because they met the criteria of exclusion (ambiguous medical or personal histories, incomplete preoperative laboratory test results, combined surgeries, or missing data of postoperative complications). At last, 923 patients were included in the final analysis (Fig. 1).

The study population had a mean age of 73.5 years; 37.6% (347/923) were female. Of the included patients, 23.8% (220) had a mFI of 0.00, 30.8% (284) a mFI of 0.09, 21.0% (194) a mFI of 0.18, 12.7% (117) a mFI of 0.27, 8.1% (75) a mFI of 0.36, and 3.6% (33) a mFI of 0.45 or above, and 23.0% (212) met the criteria of malnutrition. During surgery, 6.1% (56) underwent low-stress procedures, 28.8% (266) moderate-stress procedures, 57.0% (526) high-stress procedures, and 8.1% (75) very high-stress procedures. After surgery, 27.8% (257) developed complications, 25.6% (236) were admitted to the ICU; the median length of hospital was 16.0 days (Table 1; Supplementary Tables 1, 2, 3 and 4). Baseline and intraoperative data according to modified frailty index and composite risk index are listed in Supplementary Table 5.

Association between mFI and POCs

As the mFI score increased from 0 to 0.45 or above, the incidence of POCs in the six mFI subgroups increased accordingly (Fig. 2A). Univariable analyses identified 17 factors (excluding composite risk index) with $P < 0.20$. Among these, high mFI was associated with an increased risk of POCs (Supplementary Table 6).

Fifteen factors were included in the multivariable logistic model. After correction for confounding factors, high mFI remained to be significantly associated with an increased risk of POCs; when compared with

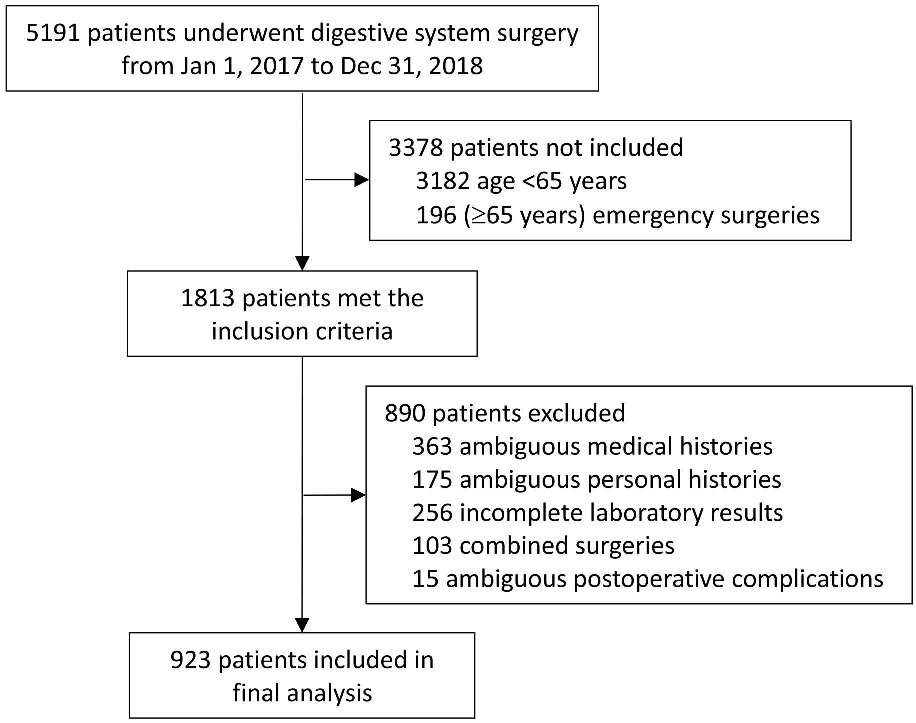

Fig. 1 Flowchart of the study

patients with mFI of 0, the odd ratios (ORs) were 1.113 (95% confidential interval [CI] 0.703–1.764, $P=0.648$) for those with mFI of 0.09, 1.519 (95% CI 0.931–2.476, $P=0.094$) for those with mFI of 0.018, 2.250 (95% CI 1.316–3.848, $P=0.003$) for those with mFI of 0.27, 3.663 (95% CI 1.996–6.721, $P<$ 0.001) for those with mFI of 0.36, and 5.495 (95% CI 2.396–12.60, $P<$ 0.001) for those with mFI of 0.45 or above (Table 2). Among other independent factors, malnutrition (OR 1.522, 95% CI 1.068–2.170, $P=0.020$), hemoglobin <90 g/L (OR 1.794, 95% CI 1.072–3.001, $P=0.026$), albumin ≤30 g/L (OR 2.051, 95% CI 1.032–4.078, $P=0.040$), obstructive sleep apnea (OR 2.776, 95% CI 1.379–5.586, $P=0.004$), surgery with moderate or higher stress (compared with low-stress procedures, moderate-stress procedures: OR 10.34, 95% CI 1.371–78.04, $P=0.023$; high-stress procedures: OR 15.86, 95% CI 2.106–119.4, $P=0.007$; very high-stress procedures: OR 22.40, 95% CI 2.755–182.2, $P=0.004$), and long-duration surgery (per hour: OR 1.127, 95% CI 1.003–1.266, $P=0.045$) were also associated with increased risk of POCs (Table 2).

Association between composite risk index and POCs

According to the above multivariable analysis results, a cutoff point of 0.27 was adopted to dichotomously divide patients according to the mFI. Four independent factors which represent various aspects of frailty, i.e., mFI of ≥0.27, malnutrition, hemoglobin <90 g/L, and albumin ≤30 g/L, were combined to generate a composite risk index, each assigned with 1 point. As the composite risk index increased from 0 to 3 or above, the incidence of POCs in the four subgroups increased accordingly (Fig. 2B). Univariable analysis revealed that high composite risk index was associated with an increased risk of POCs (Supplementary Table 6).

Twelve factors, including the composite risk index, were included in a multivariable regression model. After correction for confounding factors, the composite risk index remained to be significantly associated with an increased risk of POCs; when compared with patients with a composite risk index of 0, the ORs were 2.408 (95% CI 1.714–3.383, $P<$ 0.001) for those with a composite risk index of 1, 3.235 (95% CI 1.985–5.272, $P<$ 0.001) for those with a composite risk index of 2, and 9.227 (95% CI 3.568–23.86, $P<$ 0.001) for those with a composite risk index of 3 or above. Among other independent factors, obstructive sleep apnea (OR 2.817, 95% CI 1.400–5.670, $P=0.004$), surgery with moderate or higher stress (compared with low-stress procedures, moderate-stress procedures: OR 10.23, 95% CI 1.347–77.71, $P=0.025$; high-stress procedures: OR 15.55, 95% CI 2.052–117.9, $P=0.008$; very high-stress procedures: OR 22.82, 95% CI 2.791–186.7, $P=0.004$) were also associated with increased risk of POCs (Table 3).

Table 1 Baseline and perioperative data

	All patients (*n* = 923)	Without postoperative complications (*n* = 666)	With postoperative complications (*n* = 257)	*P* value
Demographic data				
Age, year	73.5 ± 6.2	73.3 ± 6.1	74.1 ± 6.3	0.092
Female gender	347 (37.6%)	243 (36.5%)	104 (40.5%)	0.263
Body mass index				**0.049**
< 18.5 kg/m^2	58 (6.3%)	33 (5.0%)	25 (9.7%)	
18.5–23.9 kg/m^2	467 (50.6%)	347 (52.1%)	120 (46.7%)	
24–27.9 kg/m^2	315 (34.1%)	227 (34.1%)	88 (34.2%)	
≥ 28 kg/m^2	83 (9.0%)	59 (8.9%)	24 (9.3%)	
General status				
ASA class				**< 0.001**
I	7 (0.8%)	5 (0.8%)	2 (0.8%)	
II	537 (58.2%)	430 (64.6%)	107 (41.6%)	
III	361 (39.1%)	225 (33.8%)	136 (52.9%)	
IV	18 (2.0%)	6 (0.9%)	12 (4.7%)	
Modified frailty index				**< 0.001**
0.00	220 (23.8%)	177 (26.6%)	43 (16.7%)	
0.09	284 (30.8%)	221 (33.2%)	63 (24.5%)	
0.18	194 (21.0%)	139 (20.9%)	55 (21.4%)	
0.27	117 (12.7%)	75 (11.3%)	42 (16.3%)	
0.36	75 (8.1%)	41 (6.2%)	34 (13.2%)	
0.45	23 (2.5%)	9 (1.4%)	14 (5.4%)	
0.55	7 (0.8%)	3 (0.5%)	4 (1.6%)	
0.64	3 (0.3%)	1 (0.2%)	2 (0.8%)	
Malnutrition[a]	212 (23.0%)	128 (19.2%)	84 (32.7%)	**< 0.001**
Comorbidities and history [b]				
Asthma	19 (2.1%)	13 (2.0%)	6 (2.3%)	0.714
Obstructive sleep apnea [c]	42 (4.6%)	19 (2.9%)	23 (8.9%)	**< 0.001**
Severe arrhythmia [d]	77 (8.3%)	48 (7.2%)	29 (11.3%)	**0.045**
Other cardiac diseases [e]	24 (2.6%)	15 (2.3%)	9 (3.5%)	0.285
Mental disorders [f]	21 (2.3%)	14 (2.1%)	7 (2.7%)	0.570
Major neurodegenerative diseases [g]	16 (1.7%)	7 (1.1%)	9 (3.5%)	**0.023**
Visual/hearing impairment	31 (3.4%)	18 (2.7%)	13 (5.1%)	0.075
Chronic renal insufficiency [h]	31 (3.4%)	17 (2.6%)	14 (5.4%)	**0.029**
Chronic hepatic dysfunction [i]	49 (5.2%)	27 (4.1%)	22 (8.2%)	**0.006**
Hyper−/hypothyroidism	19 (2.1%)	14 (2.1%)	5 (1.9%)	0.881
Chronic corticosteroid therapy [j]	26 (2.8%)	16 (2.4%)	10 (3.9%)	0.220
Malignant tumor	741 (80.3%)	514 (77.2%)	227 (88.3%)	**< 0.001**
Current smoker/quit ≤4 weeks [k]	134 (14.5%)	93 (14.0%)	41 (16.0%)	0.442
Current alcoholism/quit ≤4 weeks [l]	42 (4.6%)	28 (4.2%)	14 (5.4%)	0.417
Laboratory tests				
Hemoglobin < 90 g/L	82 (8.9%)	41 (6.2%)	41 (16.0%)	**< 0.001**

Table 1 (continued)

	All patients (*n* = 923)	Without postoperative complications (*n* = 666)	With postoperative complications (*n* = 257)	*P* value
Albumin ≤30 g/L	44 (4.8%)	20 (3.0%)	24 (9.3%)	**< 0.001**
Na^{+} < 135.0 mmol/L	116 (12.6%)	81 (12.2%)	35 (13.6%)	0.550
Ca^{++} < 2.1 mmol/L	32 (3.5%)	21 (3.2%)	11 (4.3%)	0.402
K^{+} < 3.5 or > 5.5 mmol/L	99 (10.7%)	70 (10.5%)	29 (11.3%)	0.734
Composite risk index [m]				**< 0.001**
0	502 (54.4%)	413 (62.0%)	89 (34.6%)	
1	306 (33.2%)	196 (29.4%)	110 (42.8%)	
2	92 (10.0%)	50 (7.5%)	42 (16.3%)	
≥ 3	23 (2.5%)	7 (1.1%)	16 (6.2%)	
Intraoperative data				
Type of surgery				**< 0.001**
Simple general surgeries [n]	80 (8.7%)	77 (11.6%)	3 (1.2%)	
Gastric	154 (16.7%)	100 (15.0%)	54 (21.0%)	
Intestinal	556 (60.2%)	414 (62.2%)	142 (55.3%)	
Hepatopancreatobiliary	133 (14.4%)	75 (11.3%)	58 (22.6%)	
Surgery by Operative Stress Score [o]				**< 0.001**
Low stress	56 (6.1%)	55 (8.3%)	1 (0.4%)	
Moderate stress	266 (28.8%)	215 (32.3%)	51 (19.8%)	
High stress	526 (57.0%)	357 (53.6%)	169 (65.8%)	
Very high stress	75 (8.1%)	39 (5.9%)	36 (14.0%)	
Duration of surgery, hour	3.2 (2.4, 4.3)	3.0 (2.3, 4.0)	3.6 (2.6, 5.0)	**< 0.001**
Type of anesthesia				0.346
General	448 (48.5%)	321 (48.2%)	127 (49.4%)	
Combined PNB-general	438 (47.5%)	322 (48.3%)	116 (45.1%)	
Combined epidural-general	32 (3.5%)	19 (2.9%)	13 (5.1%)	
Neuraxial	5 (0.5%)	4 (0.6%)	1 (0.4%)	
Seniority of anesthesiologists				0.490
< 5 years	259 (28.0%)	194 (29.1%)	65 (25.3%)	
5 to 10 years	175 (19.0%)	123 (18.5%)	52 (20.2%)	
> 10 years	489 (53.0%)	349 (52.4%)	140 (54.5%)	
Blood transfusion	64 (6.9%)	33 (5.0%)	31 (12.1%)	**< 0.001**
Estimated blood loss, ml	100 (50, 200)	50 (50, 150)	100 (50, 200)	**< 0.001**
Postoperative data				
Postoperative complications [p]	257 (27.8%)	–	257 (100.0%)	–
Clavien-Dindo classification [q]				–
Grade II	160 (17.3%)	–	160 (62.3%)	
Grade III	33 (3.6%)	–	33 (12.8%)	
Grade IV	57 (6.2%)	–	57 (22.2%)	
Grade V	7 (0.8%)	–	7 (2.7%)	
ICU admission	236 (25.6%)	106 (15.9%)	130 (50.6%)	**< 0.001**
LOS in ICU, hour	24.0 (18.0, 48.0)	20.0 (16.0, 24.0)	41.0 (20.0, 91.0)	**< 0.001**

Table 1 (continued)

	All patients (*n* = 923)	Without postoperative complications (*n* = 666)	With postoperative complications (*n* = 257)	*P* value
Unplanned reintubation	12 (1.3%)	0 (0%)	12 (4.7%)	**< 0.001**
Unplanned reoperation	28 (3.0%)	0 (0%)	28 (10.9%)	**< 0.001**
Hospital LOS, day	16.0 (14.0, 21.0)	15.0 (13.0, 19.0)	21.0 (16.0, 29.0)	**< 0.001**
Hospital LOS after surgery, day	10.0 (8.0, 12.0)	9.0 (7.0, 10.0)	13.0 (11.0, 20.0)	**< 0.001**
Adverse discharge destination [r]	15 (1.6%)	0 (0%)	15 (5.8%)	**< 0.001**

Data are n (%), mean ± SD, or median (interquartile range). *P* values in bold indicate < 0.05

ASA American Society of Anesthesiologists, *PNB* peripheral nerve block, *ICU* intensive care unit, *LOS* length of stay

[a] Defined by any of the following: (1) a body mass index of less than 18.5 kg/m^2; (2) unintentional weight loss of greater than 10% within the last 3–6 months; or (3) a body mass index of less than 20 kg/m^2 and unintentional weight loss of greater than 5% within the last 3–6 months [33]

[b] Data on 11 items of the modified frailty index are presented in Supplementary Table 1

[c] Diagnosed by previous polysomnography, or history inquiry and physical examination, and/or STOP-Bang/Berlin questionnaire

[d] Include atrial fibrillation, frequent (> 6 beats/min) or multifocal ventricular premature beat, paroxysmal supraventricular tachycardia, second/third-degree atrioventricular block, and sick sinus syndrome

[e] Include congenital heart disease, cardiomyopathy, and valvular heart disease

[f] Include diagnosed depression, anxiety, schizophrenia, phobia, and hallucination

[g] Include Alzheimer's disease, Parkinson's disease, and dementia

[h] Refers to estimated glomerular filtration rate < 45 ml/min/1.73 m^2 or on dialysis [37]. The CKD-EPI equation was adopted to calculate the estimated glomerular filtration rate [38]

[i] Defined as Child-Pugh class B and C

[j] With a duration of > 1 month

[k] Smoking refers to daily smoking of cigarettes up to half a pack for at least two years

[l] Alcoholism refers to ethanol consumption ≥40 g/d for men and ≥ 20 g/d for women, lasting for more than 5 years. Ethanol (g) = alcohol consumption (ml) × ethanol content (%) × 0.8 [32]

[m] A composite of four items, i.e., modified frailty index ≥0.27, malnutrition [33], moderate or severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin ≤30 g/L). Each item was assigned the same weight of 1 point

[n] Refers to low-risk and 23-h-stay operations including hernia repair, laparoscopic cholecystectomy, appendectomy, and hepatic cyst fenestration

[o] Stratified into five categories of physiologic stress, i.e., very low stress, low stress, moderate stress, high stress, and very high stress [34]. Also see Supplementary Table 2

[p] Indicate those of Clavien-Dindo grade II or higher. Also see Supplementary Table 4

[q] Clavien-Dindo classification of postoperative complications [35]

[r] Defined as discharge to destinations other than home (e.g., a long- or short-term care facility)

Postoperative outcomes according to mFI and composite risk index

Compared with patients with a mFI of < 0.27, those with a mFI of ≥0.27 had a higher incidence of POCs (23.1% [161/698] vs. 42.7% [96/225], *P* < 0.001) and a higher rate of ICU admission (18.5% [129/698] vs. 47.6% [107/225], *P* < 0.001); they also had longer lengths of ICU stay (median 21.0 h [interquartile range 17.0–39.0] vs. 28.0 h [19.0–71.0], *P* = 0.018), hospital stay (16.0 days [13.0–20.0] vs. 19.0 days [15.0–26.0], *P* < 0.001), and hospital stay after surgery (9.0 days [8.0–12.0] vs. 10.0 days [8.0–13.0], *P* = 0.002; Table 4).

Compared with patients with a composite risk index of 0, those with a composite risk index of 1 and ≥ 2 had higher incidences of POCs (17.7% [89/502] with 0 vs. 35.9% [110/306] with 1 vs. 50.4% [58/115] with ≥2, *P* < 0.001), higher rates of ICU admission (14.7% [74/502] with 0 vs. 33.0% [101/306] with 1 vs. 53.0% [61/115] with ≥2, *P* < 0.001), and higher rate of unplanned reintubation (0.8% [4/502] with 0 vs. 1.0% [3/306] with 1 vs. 4.3% [5/115] with ≥2, *P* = 0.027); they also had longer lengths of ICU stay (median 20.0 h [interquartile range 17.0–32.5] with 0 vs. 24.0 h [18.0–56.5] with 1 vs. 32.0 h [20.5–96.0] with ≥2, *P* < 0.001), hospital stay (16.0 days [12.8–19.0] with 0 vs. 18.0 days [15.0–24.0] with 1 vs. 21.0 days [16.0–27.0] with ≥2, *P* < 0.001), and hospital stay after surgery (9.0 days [7.0–11.0] with 0 vs. 10.0 days [8.0–13.0] with 1 vs. 11.0 days [9.0–14.0] with ≥2, *P* < 0.001; Table 4).

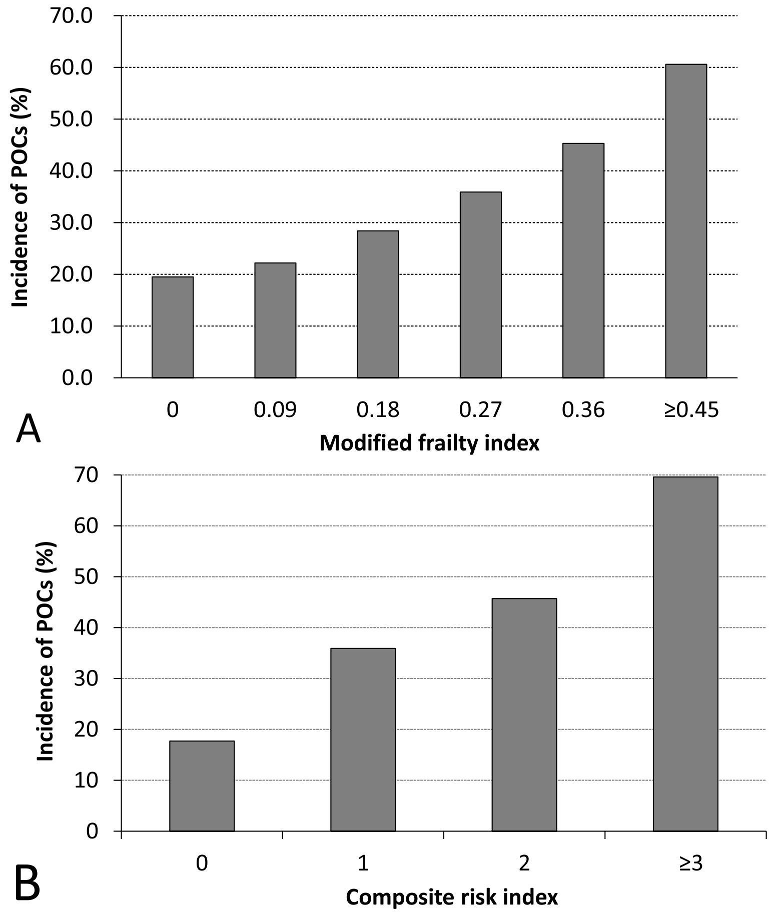

Fig. 2 Incidence of postoperative complications in subgroups according to modified frailty index (**A**) and composite risk index (**B**). When compared with patients with mFI = 0, mFI = 0.09: $P = 0.471$, mFI = 0.18: $P = 0.035$, mFI = 0.27: $P = 0.001$, mFI = 0.36: $P < 0.001$, and mFI ≥ 0.45: $P < 0.001$ (chi-square tests; $P < 0.003$ was considered statistically significant after Bonferroni correction). When compared with patients with composite risk index of 0, composite risk index of 1: $P < 0.001$, composite risk index of 2: $P < 0.001$, composite risk index of 3 or above: $P < 0.001$ (chi-square tests; $P < 0.008$ was considered statistically significant after Bonferroni correction). Abbreviations: *POCs* Postoperative complications

Comparison of mFI and composite risk index for POCs prediction

The area under receiver-operator characteristic curve of mFI in predicting POCs was 0.622 (95% CI 0.581–0.663, $P < 0.001$); that of composite risk index in predicting POCs was 0.653 (95% CI 0.613–0.694, $P < 0.001$). There was no significant difference in the discriminative power between the two instruments (Supplementary Fig. 1).

Discussion

Our results confirmed that high composite risk index, a combination of mFI (≥0.27), malnutrition, moderate to severe anemia (hemoglobin <90 g/L), and severe hypoalbuminemia (albumin ≤30 g/L), was an independent predictor for increased risk of POCs in older patients recovering from elective digestive tract surgery. Furthermore, there was a "dose-effect" relationship, i.e., the higher the composite risk index, the higher the incidence of POCs.

In the present study, POCs occurred in 27.8% of older patients following elective digestive tract surgery. In previous studies of patients undergoing various digestive tract surgeries, the reported incidence of POCs varied from 26.9 to 45.2% [39–42]; the incidence of POCs in our patients was well within this range. Along with the aging population, the number of older patients undergoing surgical procedures has been increasing in recent years. However, despite improvements in perioperative management, the incidence of POCs in older patients remains higher than that in young patients [16, 24]. Therefore, it is extremely necessary to identify the risk factors of POCs in older surgical patients. As one of the age-related factors, frailty is attracting more and more attention.

The frailty index evaluates "accumulated deficits" across multiple domains involving the functional, cognitive,

Table 2 Predictors of postoperative complications

Variables	Univariable analyses		Multivariable analysis [a]	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age, year	1.020 (0.997–1.044)	0.092	–	–
Modified frailty index				
0.00	Reference		Reference	
0.09	1.173 (0.759–1.813)	0.471	1.113 (0.703–1.764)	0.648
0.18	1.629 (1.032–2.571)	0.036	1.519 (0.931–2.476)	0.094
0.27	2.305 (1.393–3.815)	0.001	2.250 (1.316–3.848)	0.003
0.36	3.413 (1.943–5.998)	< 0.001	3.663 (1.996–6.721)	< 0.001
≥ 0.45	6.333 (2.921–13.73)	< 0.001	5.495 (2.396–12.60)	< 0.001
Malnutrition [b]	2.041 (1.476–2.822)	< 0.001	1.522 (1.068–2.170)	0.020
Severe arrhythmia [c]	1.638 (1.008–2.661)	0.046	–	–
Obstructive sleep apnea [d]	3.347 (1.790–6.258)	< 0.001	2.776 (1.379–5.586)	0.004
Major neurodegenerative diseases [e]	3.416 (1.259–9.273)	0.016	–	–
Visual/hearing impairment	1.918 (0.926–3.974)	0.080	–	–
Chronic renal insufficiency [f]	2.199 (1.068–4.530)	0.033	–	–
Chronic hepatic dysfunction [g]	2.216 (1.237–3.967)	0.007	–	–
Malignant tumor	2.238 (1.468–3.411)	< 0.001	–	–
Hemoglobin < 90 g/L	2.894 (1.827–4.582)	< 0.001	1.794 (1.072–3.001)	0.026
Albumin ≤30 g/L	3.327 (1.804–6.136)	< 0.001	2.051 (1.032–4.078)	0.040
Surgery by Operative Stress Score [h]				
Low stress	Reference		Reference	
Moderate stress	13.05 (1.764–96.51)	0.012	10.34 (1.371–78.04)	0.023
High stress	26.04 (3.573–189.7)	0.001	15.86 (2.106–119.4)	0.007
Very high stress	50.77 (6.675–386.1)	< 0.001	22.40 (2.755–182.2)	0.004
Duration of surgery, hour	1.312 (1.200–1.434)	< 0.001	1.127 (1.003–1.266)	0.045
Estimated blood loss, 100 ml	1.094 (1.045–1.146)	< 0.001	-	-

[a] Factors with *P* values < 0.20 in univariate analyses or considered clinically important were included in the model. Body mass index was excluded because it was covered by malnutrition; ASA classification was not included because of correlation with the modified frailty index; type of surgery was not included because of correlation with the surgery by Operative Stress Score; intraoperative blood transfusion was not included due to correlation with preoperative anemia or estimated blood loss. The multivariable logistic regression analysis was performed with the backward stepwise method. Hosmer-Lemeshow test for goodness of fit of the multivariable model: $\chi^2 = 11.657$, $df = 8$, $P = 0.167$

[b] Defined by any of the following: (1) a body mass index of less than 18.5 kg/m^2; (2) unintentional weight loss of greater than 10% within the last 3–6 months; (3) a body mass index of less than 20 kg/m^2 and unintentional weight loss of greater than 5% within the last 3–6 months [33]

[c] Include atrial fibrillation, frequent (> 6 beats/min) or multifocal ventricular premature beat, paroxysmal supraventricular tachycardia, second/third-degree atrioventricular block, and sick sinus syndrome

[d] Diagnosed by previous polysomnography, or history inquiry and physical examination, and/or STOP-Bang/Berlin questionnaire

[e] Include Alzheimer's disease, Parkinson's disease, and dementia

[f] Refers to estimated glomerular filtration rate < 45 ml/min/1.73 m^2 or on dialysis [37]. The CKD-EPI equation was adopted to calculate the estimated glomerular filtration rate [38]

[g] Defined as Child-Pugh class B and C

[h] Stratified into five categories of physiologic stress, i.e., very low stress, low stress, moderate stress, high stress, and very high stress [34]. Also see Supplementary Table 2

emotional, sleep, nutritional, social, and medical history. The score of frailty index is obtained by dividing the sum of deficits present by the total number of deficits measured [9]. The measurement process of the frailty index, however, is time-consuming and necessitates professional skills [6, 43]. As a shortened scale, the mFI consists of 10 items on comorbidities and 1 item on functional status. It can be easily acquired from routine clinical practice, either prospectively or retrospectively [7]. The effect of mFI has been validated in patients scheduled for elective digestive tract surgery. In a retrospective study of 58,448 adult patients undergoing colectomies, Obeid et al. [40] found a significant association between mFI and POCs; the incidence of serious POCs (Clavien-Dindo class IV/V) increased from 3.2 to 56.3% as the mFI score increased from 0 to 0.55. In another retrospective study

Table 3 Effects of preoperative composite risk index in predicting postoperative complications

Variables	Univariable analyses		Multivariable analysis [a]	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Age, year	1.020 (0.997–1.044)	0.092	–	–
Composite risk index [b]				
0	Reference		Reference	
1	2.604 (1.878–3.612)	< 0.001	2.408 (1.714–3.383)	< 0.001
2	3.898 (2.437–6.236)	< 0.001	3.235 (1.985–5.272)	< 0.001
≥ 3	10.61 (4.239–26.54)	< 0.001	9.227 (3.568–23.86)	< 0.001
Severe arrhythmia [c]	1.638 (1.008–2.661)	0.046	–	–
Obstructive sleep apnea [d]	3.347 (1.790–6.258)	< 0.001	2.817 (1.400–5.670)	0.004
Major neurodegenerative diseases [e]	3.416 (1.259–9.273)	0.016	–	–
Visual/hearing impairment	1.918 (0.926–3.974)	0.080	–	–
Chronic renal insufficiency [f]	2.199 (1.068–4.530)	0.033	–	–
Chronic hepatic dysfunction [g]	2.216 (1.237–3.967)	0.007	–	–
Malignant tumor	2.238 (1.468–3.411)	< 0.001	–	–
Surgery by Operative Stress Score [h]				
Low stress	Reference		Reference	
Moderate stress	13.05 (1.764–96.51)	0.012	10.23 (1.347–77.71)	0.025
High stress	26.04 (3.573–189.7)	0.001	15.55 (2.052–117.9)	0.008
Very high stress	50.77 (6.675–386.1)	< 0.001	22.82 (2.791–186.7)	0.004
Duration of surgery, hour	1.312 (1.200–1.434)	< 0.001	–	–
Estimated blood loss, 100 ml	1.094 (1.045–1.146)	< 0.001	–	–

[a] Factors with *P* values < 0.20 in univariate analyses or considered clinically important were included in the model. Body mass index was excluded because it was covered by malnutrition; ASA classification was not included because of correlation with the modified frailty index; type of surgery was not included because of correlation with the surgery by Operative Stress Score; intraoperative blood transfusion was not included due to correlation with preoperative anemia or estimated blood loss. The multivariable logistic regression analysis was performed with the backward stepwise method. Hosmer-Lemeshow test for goodness of fit of the multivariable model: $\chi^2 = 5.634$, $df = 8$, $P = 0.688$

[b] A composite of four items, i.e., modified frailty index ≥0.27, malnutrition [33], moderate or severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin ≤30 g/L). Each item was assigned the same weight of 1 point

[c] Include atrial fibrillation, frequent (> 6 beats/min) or multifocal ventricular premature beat, paroxysmal supraventricular tachycardia, second/third-degree atrioventricular block, and sick sinus syndrome

[d] Diagnosed by previous polysomnography, or history inquiry and physical examination, and/or STOP-Bang/Berlin questionnaire

[e] Include Alzheimer's disease, Parkinson's disease and dementia

[f] Refers to estimated glomerular filtration rate < 45 ml/min/1.73 m^2 or on dialysis [37]. The CKD-EPI equation was adopted to calculate the estimated glomerular filtration rate [38]

[g] Defined as Child-Pugh class B and C

[h] Stratified into five categories of physiologic stress, i.e., very low stress, low stress, moderate stress, high stress, and very high stress [34]. Also see Supplementary Table 2

of 9986 adult patients undergoing pancreaticoduodenectomy, Mogal et al. [41] reported that high mFI (≥0.27) was significantly associated with increased risks of any complications, major complications (Clavien-Dindo class III or higher), and 30-day mortality. Consistent with previous studies [16–24, 40, 41], high mFI score was also independently associated with an increased risk of POCs in our patients. Specifically, we found that those with a mFI of ≥0.27 developed more POCs; they also required more ICU admission, and stayed longer in the ICU and the hospital. We therefore adopted ≥0.27 as the cut-off point of the mFI. Similar cut-off point was also suggested by some others [21, 41].

It should be noted that the mFI does not fully evaluate the entire spectrum of frailty because it consists of only two domains (comorbidities and functional decline). In our results, other frailty-related parameters, including malnutrition, moderate to severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin ≤30 g/L), were also independently associated with increased risk of POCs. As an important dimension of frailty [6], malnutrition is common among older surgical patients and is related to increased perioperative morbidity and other worse outcomes [25, 44, 45]. Considering the data availability in our medical records system, we defined malnutrition using the NICE criteria

Table 4 Postoperative outcomes according to modified frailty index and composite risk index

	Modified frailty index		P value	Composite risk index [a]			P value
	< 0.27 (n = 698)	≥0.27 (n = 225)		0 (n = 502)	1 (n = 306)	≥2 (n = 115)	
Postoperative complications [b]	161 (23.1%)	96 (42.7%)	**< 0.001**	89 (17.7%)	110 (35.9%)*	58 (50.4%)*†	**< 0.001**
Clavien-Dindo classification [c]							
Grade III or higher complications	57 (8.2%)	40 (17.8%)	**< 0.001**	24 (4.8%)	36 (11.8%)*	37 (32.2%)*†	**< 0.001**
Grade IV or higer complications	36 (5.2%)	28 (12.4%)	**< 0.001**	15 (3.0%)	20 (6.5%)*	29 (25.2%)*†	**< 0.001**
Grade V complications	4 (0.6%)	3 (1.3%)	0.483	2 (0.4%)	0 (0.0%)	5 (4.3%)*†	**< 0.001**
ICU admission	129 (18.5%)	107 (47.6%)	**< 0.001**	74 (14.7%)	101 (33.0%)*	61 (53.0%)*†	**< 0.001**
LOS in ICU, hour [d]	21.0 (17.0, 39.0)	28.0 (19.0, 71.0)	**0.018**	20.0 (17.0, 32.5)	24.0 (18.0, 56.5)	32.0 (20.5, 96.0)*†	**< 0.001**
Unplanned reintubation	6 (0.9%)	6 (2.7%)	0.081	4 (0.8%)	3 (1.0%)	5 (4.3%)*	**0.027**
Unplanned reoperation	21 (3.0%)	7 (3.1%)	0.938	14 (2.8%)	13 (4.2%)	1 (0.9%)	0.197
Hospital LOS, day	16.0 (13.0, 20.0)	19.0 (15.0, 26.0)	**< 0.001**	16.0 (12.8, 19.0)	18.0 (15.0, 24.0)*	21.0 (16.0, 27.0)*†	**< 0.001**
Hospital LOS after surgery, day	9.0 (8.0, 12.0)	10.0 (8.0, 13.0)	**0.002**	9.0 (7.0, 11.0)	10.0 (8.0, 13.0)*	11.0 (9.0, 14.0)*	**< 0.001**
Adverse discharge destination [e]	8 (1.1%)	7 (3.1%)	0.085	6 (1.2%)	6 (2.0%)	3 (2.6%)	0.399

Data are n (%) or median (interquartile range). P values in bold indicate < 0.05. *P < 0.05/3 = 0.017 (Bonferroni-corrected post hoc multiple comparisons) when compared with the patients with a composite risk index of 0. †P < 0.017 when compared with the patients with a composite risk index of 1

ICU intensive care unit, *LOS* length of stay

[a] A composite of four items, i.e., modified frailty index ≥0.27, malnutrition [33], moderate or severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin ≤30 g/L). Each item was assigned the same weight of 1 point

[b] Indicate those of Clavien-Dindo grade II or higher. Also see Supplementary Table 4

[c] Clavien-Dindo classification of postoperative complications [35]

[d] Results of patients who were admitted to the ICU

[e] Defined as discharge to destinations other than home (e.g., a long- or short-term care facility)

which focuses on weight loss and body mass index [33]. The rate of malnutrition was 23.0% in our patients, like other studies in a similar patient population [45, 46]. The prevalence of anemia increases with age [47, 48], mainly due to nutrient deficiency, chronic renal disease and/or inflammation, and unexplained reasons [49]. Although controversial, serum albumin is still recommended for preoperative nutritional screening [50]. Hypoalbuminemia is a valid predictor of poor postoperative outcomes [26, 27, 51]. In the present study, we enrolled patients undergoing digestive system surgeries; the majority (80.3%) of them turned out to have digestive tract malignancies. Our patients were at high risk of malnutrition, anemia, and hypoalbuminemia.

Since the above four risk factors are all related to frailty characteristics of the study patients and are easily acquired in routine clinical practice, it is feasible to use the combination of these factors as an evaluation tool of preoperative frailty. We therefore tested the value of a composite risk index, a combination of mFI ≥0.27, malnutrition, moderate to severe anemia, and severe hypoalbuminemia, in predicting the risk of POCs in our patients. Our results showed that patients with a high composite risk index developed more POCs, required more ICU admission and unplanned reintubation, and stayed longer in the ICU and the hospital. Multivariable analysis also confirmed that higher composite risk index was associated with higher risk of POCs. The effect of the composite risk index in predicting POCs is similar, if not superior, to that of the mFI. Our results may help perioperative clinicians to better predict the postoperative outcomes and help patients for decision-making before surgery. Furthermore, since the three parameters added to mFI in the composite risk index are all modifiable, our results indicate potential targets of intervention. Further studies are required to explore whether preoperative individualized intervention can improve outcomes of these high-risk patients.

Our study had several limitations. First, the study was performed retrospectively with data not specifically intended for frailty assessment; data on other frailty domains such as sarcopenia, and psychosocial and cognitive parameters, were unavailable. These might lead to an underestimation of the frailty syndrome. Second, the primary outcome of our study was limited to in-hospital POCs; the occurrence of post-discharge complications was not collected. These may confound the effects of frailty on the outcomes. Finally, as a single institution study, our results may not be extrapolated to patients in other centers. Despite these, our findings have clinical significance for improvement of perioperative care and management and generate hypotheses for further exploration.

Conclusions

Our results showed that high preoperative composite risk index, a combination of frailty (mFI $\geq$0.27), malnutrition, moderate to severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin $\leq$30 g/L), was independently associated with an increased risk of in-hospital POCs in older patients undergoing elective digestive tract surgery. Further studies are required to explore whether individualized preoperative intervention can improve outcomes in high-risk patients.

Abbreviations

MFI: Modified Frailty Index; POCs: Postoperative complications; ASA: American Society of Anesthesiologists; ICU: Intensive care unit; ROC: Receiver-operating characteristic; PNB: Peripheral nerve block; LOS: Length of stay; OR: Odds ratio; CI: Confidential interval.

Supplementary Information

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Additional file 1: Supplementary Table 1 Composition of Modified Frailty Index.

Additional file 2: Supplementary Table 2 Surgical procedures stratified according to Operative Stress Score.

Additional file 3: Supplementary Table 3 Clavien-Dindo classification of postoperative complications.

Additional file 4: Supplementary Table 4 Individual complications of Clavien-Dindo classification grade II or higher.

Additional file 5: Supplementary Table 5 Baseline and intraoperative data according to modified frailty index and composite risk index.

Additional file 6: Supplementary Table 6 Factors in association with postoperative complications (univariate analyses).

Additional file 7: Supplementary Figure 1 The area under receiver-operator characteristic curves of modified frailty index and composite risk index in predicting postoperative complications.

Additional file 8: STROBE Statement—Checklist of items that should be included in reports of cohort studies.

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Standards of reporting

The manuscript adheres to the STROBE guideline.

Authors' contributions

D-XW and C-QL contributed to the conception, study design, and supervision. C-QL recruited patients and performed frailty evaluation. CZ collected other baseline and intraoperative data. FY collected postoperative data. X-YL contributed to statistical analyses. D-XW, C-QL, and X-YL analyzed and interpreted the data. C-QL drafted the manuscript. All authors critically revised the manuscript, agreed to submit it to the current journal, gave final approval of the version to be published, and agreed to take responsibility and be accountable for the contents of the article.

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Availability of data and materials

The datasets that support the findings of the study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The Biomedical Research Ethics Committee of Peking University First Hospital in Beijing, China, reviewed and approved the study protocol (2019[296]), and agreed to waive the informed consent from the included patients considering the purely observational study design and that no patient follow-up was performed. All methods were performed in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

None of the authors have any conflicts of interest to declare.

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