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,
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/m²; (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/m² 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.

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
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 \( \leq 30 \) g/L (OR 2.051, 95% CI 1.032–4.078, \( P = 0.040 \)), obstructive sleep apnea (OR 2.776, 95% CI 1.379–5.86, \( P = 0.004 \)), 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 \( \geq 0.27 \), malnutrition, hemoglobin < 90 g/L, and albumin \( \leq 30 \) 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).
| Demographic data                  | All patients (n = 923) | Without postoperative complications (n = 666) | With postoperative complications (n = 257) | P value |
|----------------------------------|------------------------|----------------------------------------------|------------------------------------------|---------|
| 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                  |                        |                                              |                                          |         |
| < 18.5 kg/m²                     | 58 (6.3%)              | 33 (5.0%)                                    | 25 (9.7%)                                | 0.049   |
| 18.5–23.9 kg/m²                  | 467 (50.6%)            | 347 (52.1%)                                 | 120 (46.7%)                              |         |
| 24–27.9 kg/m²                    | 315 (34.1%)            | 227 (34.1%)                                 | 88 (34.2%)                               |         |
| ≥ 28 kg/m²                       | 83 (9.0%)              | 59 (8.9%)                                    | 24 (9.3%)                                |         |
| General status                   |                        |                                              |                                          | <0.001  |
| ASA class                         |                        |                                              |                                          |         |
| 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<sup>a</sup>         | 212 (23.0%)            | 128 (19.2%)                                 | 84 (32.7%)                               | <0.001  |
| Comorbidities and history<sup>b</sup> |            |                                              |                                          |         |
| Asthma                           | 19 (2.1%)              | 13 (2.0%)                                    | 6 (2.3%)                                 | 0.714   |
| Obstructive sleep apnea<sup>c</sup> | 42 (4.6%)              | 19 (2.9%)                                    | 23 (8.9%)                                | <0.001  |
| Severe arrhythmia<sup>d</sup>    | 77 (8.3%)              | 48 (7.2%)                                    | 29 (11.3%)                               | 0.045   |
| Other cardiac diseases<sup>e</sup> | 24 (2.6%)              | 15 (2.3%)                                    | 9 (3.5%)                                 | 0.285   |
| Mental disorders<sup>f</sup>     | 21 (2.3%)              | 14 (2.1%)                                    | 7 (2.7%)                                 | 0.570   |
| Major neurodegenerative diseases<sup>g</sup> | 16 (1.7%)              | 7 (1.1%)                                     | 9 (3.5%)                                 | 0.023   |
| Visual/hearing impairment<sup>h</sup> | 31 (3.4%)              | 18 (2.7%)                                    | 13 (5.1%)                                | 0.075   |
| Chronic renal insufficiency<sup>i</sup> | 31 (3.4%)              | 17 (2.6%)                                    | 14 (5.4%)                                | 0.029   |
| Chronic hepatic dysfunction<sup>j</sup> | 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<sup>k</sup> | 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<sup>l</sup> | 134 (14.5%)            | 93 (14.0%)                                   | 41 (16.0%)                               | 0.442   |
| Current alcoholism/quit ≤4 weeks<sup>l</sup> | 42 (4.6%)              | 28 (4.2%)                                    | 14 (5.4%)                                | 0.417   |
| Laboratory tests                 |                        |                                              |                                          | <0.001  |
| Hemoglobin < 90 g/L              | 82 (8.9%)              | 41 (6.2%)                                    | 41 (16.0%)                               |         |
Table 1 (continued)

|                              | All patients | Without postoperative complications | With postoperative complications | P value |
|------------------------------|--------------|-------------------------------------|----------------------------------|---------|
|                              | (n = 923)    | (n = 666)                           | (n = 257)                        |         |
| Albumin ≤ 30 g/L             |              |                                     |                                  |         |
| Na⁺ < 135.0 mmol/L           | 44 (4.8%)    | 20 (3.0%)                           | 24 (9.3%)                        | < 0.001 |
| Ca++ < 2.1 mmol/L            | 116 (12.6%)  | 81 (12.2%)                          | 35 (13.6%)                       | 0.550   |
| K⁺ < 3.5 or > 5.5 mmol/L     | 32 (3.5%)    | 21 (3.2%)                           | 11 (4.3%)                        | 0.402   |
| Composite risk index (n)     |              |                                     |                                  | < 0.001 |
| 0                            | 502 (54.4%)  | 413 (62.0%)                         | 89 (34.6%)                       |         |
| 1                            | 306 (33.2%)  | 196 (29.4%)                         | 110 (42.8%)                      |         |
| ≥ 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 (n)

| 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

| General                       | 448 (48.5%)   | 321 (48.2%)                         | 127 (49.4%)                      | 0.346   |
| 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

| < 5 years                     | 259 (28.0%)   | 194 (29.1%)                         | 65 (25.3%)                       | 0.490   |
| 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 (n) |              |                                     |                                  |         |
| 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 |
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).

### 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 | 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

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### 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] vs. 24.0 h [18.0–56.5] 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).
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 (\( \geq 0.27 \)), malnutrition, moderate to severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin \( \leq 30 \) 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,
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 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                        |                      |                         |                        |                        |
| Modified frailty index           |                      |                         |                        |                        |
| 0.00                             | Reference            | Reference               | 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                       |                      |                         |                        |                        |
| 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 univariable 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/m²; (2) unintentional weight loss of greater than 10% within the last 3–6 months; (3) a body mass index of less than 20 kg/m² 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 m² 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 9,986 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 or 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 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) | 0.006                   | –                      | –       |
| 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: χ² = 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 multiform 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 m² 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
Table 4: Postoperative outcomes according to modified frailty index and composite risk index

| Outcome                          | Modified frailty index | Composite risk index | P value |
|----------------------------------|------------------------|----------------------|---------|
|                                  | < 0.27 (n = 698)       | ≥0.27 (n = 225)      |         |
| Postoperative complications a    | 161 (23.1%)            | 96 (42.7%)           | < 0.001 |
| Clavien-Dindo classification c   |                        |                      |         |
| Grade III or higher complications| 57 (8.2%)              | 40 (17.8%)           | < 0.001 |
| Grade IV or higher complications | 36 (5.2%)              | 28 (12.4%)           | < 0.001 |
| Grade V complications            | 4 (0.6%)               | 3 (1.3%)             | 0.483   |
| ICU admission                    | 129 (18.5%)            | 107 (47.6%)          | < 0.001 |
| LOS in ICU, hour d               | 21.0 (17.0, 39.0)      | 28.0 (19.0, 71.0)    | 0.018   |
| Unplanned reintubation           | 6 (0.9%)               | 6 (2.7%)             | 0.081   |
| Unplanned reoperation            | 21 (3.0%)              | 7 (3.1%)             | 0.938   |
| Hospital LOS, day                | 16.0 (13.0, 20.0)      | 19.0 (15.0, 26.0)    | < 0.001 |
| Hospital LOS after surgery, day  | 9.0 (8.0, 12.0)        | 10.0 (8.0, 13.0)     | 0.002   |
| Adverse discharge destination e  | 8 (1.1%)               | 7 (3.1%)             | 0.085   |

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

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 ≥ 0.27), malnutrition, moderate to severe anemia (hemoglobin < 90 g/L), and severe hypoalbuminemia (albumin ≤ 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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