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REVIEW ARTICLE

Frailty and surgical outcomes in gastrointestinal cancer: Integration of geriatric assessment and prehabilitation into surgical practice for vulnerable patients

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Abstract

As life expectancy increases, the older population continues to grow rapidly, resulting in increased requirement for surgery for older patients with gastrointestinal cancer. Older individuals represent a heterogeneous group in terms of physiological reserves, co-morbidity, cognitive impairment, and disability. Owing to the lack of treatment guidelines for vulnerable patients with gastrointestinal cancer, these patients are more likely to be at risk of undertreatment or overtreatment. Hence, the identification of frail patients with gastrointestinal cancer would improve cancer treatment outcomes. Although there is no standardized geriatric assessment tool, a growing body of research has shown associations of frailty with adverse postoperative outcomes and poor prognosis after resection of gastrointestinal tract and hepatobiliary-pancreatic cancers. Emerging evidence suggests that prehabilitation, which includes exercise and nutritional support, can improve preoperative functional capacity, postoperative recovery, and surgical outcomes, particularly in frail patients with gastrointestinal cancer. We reviewed major geriatric assessment tools for identification of frail patients and summarized clinical studies on frailty and surgical outcomes, as well as prehabilitation or rehabilitation in gastrointestinal tract and hepatobiliary-pancreatic cancers. The integration of preoperative geriatric assessment and prehabilitation of frail patients in clinical practice may improve surgical outcomes. In addition, improving preoperative vulnerability and preventing functional decline after surgery is important in providing favorable long-term survival in patients with gastrointestinal cancer. Further clinical trials are needed to examine the effects of minimally invasive surgery, and chemotherapy in frail patients with gastrointestinal cancer.

KEYWORDS
disability, elderly, impairment, oncology, sarcopenia

1 | INTRODUCTION

Gastrointestinal carcinomas are a leading cause of death worldwide.[1] As life expectancy increases, the number of older individuals with gastrointestinal cancer has increased in Japan and worldwide.[2–4] Older individuals are a heterogeneous group, in terms of physiologic reserves, co-morbidity, cognitive impairment, and disability.[5] Because older patients with gastrointestinal cancer are underrepresented in clinical cancer trials, those patients are more likely to be at risk for undertreatment or overtreatment.[6–8]

Frailty is a syndrome characterized by reduced physiological reserve from stressors due to age-related disability.[9,10] Poor treatment tolerance, adverse postoperative outcomes, and poor prognosis have been associated with frail patients with cancer.[4,11,12] Hence, the identification of frail patients with cancer would improve cancer treatment outcomes through patient selection and optimization prior to surgery. Geriatric assessment (GA) is an assessment that includes functional capacity, mobility, cognition, emotional status, nutritional status, comorbidities, polypharmacy, and social support.[13,14] According to this assessment, frailty can be improved by perioperative rehabilitation. Prehabilitation is a preoperative multidisciplinary intervention to prevent or minimize functional decline after surgery and improve postoperative outcomes.[15]

Herein, we reviewed major GA tools to identify frail patients, and summarized clinical studies on frailty and surgical outcomes as well as prehabilitation or rehabilitation in gastrointestinal tract and hepatobiliary-pancreatic (HBP) cancers.

2 | GA TOOLS FOR PATIENTS WITH GASTROINTESTINAL CANCERS

Table 1 shows the diagnostic properties of eight GA tools that have been reported in studies on gastrointestinal tract and HBP cancers. The Geriatric-8 (G8) comprises seven items, as well as an indication of age, as follows: nutritional status, weight loss, body mass index, motor skills, psychological status, number of medications, and self-perception of health.[16,17] Age was considered in three categories (<80, 80-85, and >85 years). Overall, the G8 score ranges from 0 (heavily impaired) to 17 (not at all impaired). The diagnostic accuracy of the G8 has been investigated in three studies.[18–20] The G8 score had moderate-to-high sensitivity (77%-97%), low-to-moderate specificity (44%-64%), and moderately high accuracy for frailty (AUC, 0.71-0.80).

The diagnostic accuracy of the following tools was investigated in the study by Kenig et al[18]: abbreviated Comprehensive Geriatric Assessment (CGA), the Fried Frailty Criteria, the Groningen Frailty Indicator, Balducci Frailty Criteria, and the Clinical Frailty Scale (Table 1). The abbreviated CGA is composed of items from the Geriatric Depression Scale, Mini-Mental State Examination, activities of daily living (ADL), and the independent activities of daily living (IADL).[21] The abbreviated CGA had high sensitivity (84%), specificity (86%), and accuracy for frailty (AUC, 0.85).

The Fried Frailty Criteria defined frailty as a clinical syndrome in which three or more of the following criteria were present: unintentional weight loss, self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.[22] The Fried Frailty Criteria had low sensitivity (52%), high specificity (92%), and moderate accuracy for frailty (AUC, 0.72). The Groningen Frailty Indicator consists of 15 questionnaire screenings for self-reported limitations.[23] The Groningen Frailty Indicator had moderate sensitivity (64%), high specificity (86%), and moderate-to-high accuracy for frailty (AUC, 0.74).

The Balducci Frailty Criteria defined frailty based on fulfilling any of the following criteria from the components of CGA: dependence in one or more ADL, three or more comorbidities, and/or one or more geriatric syndromes.[24] The Balducci Frailty Criteria had high sensitivity (84%), low specificity (50%), and moderate accuracy for frailty (AUC, 0.67). The Clinical Frailty Scale (CFS) is a semiquantitative tool that provides a global score ranging from 1 (very fit) to 9 (terminally ill) to reflect the following domains: disability for basic and instrumental activities of daily living, mobility, activity, energy, and disease-related symptoms.[25] The CFS had low sensitivity (54%), high specificity (100%), and moderate-to-high accuracy for frailty (AUC, 0.77). Usual gait speed had moderate sensitivity (79%), moderate specificity (81%), and moderate-to-high accuracy for frailty (AUC, 0.82) in a study by Pamoukdjian et al.[26]

The Kihon checklist (KCL) can identify individuals at an increased risk of requiring care or support. It consists of 25 questions regarding ADLs, physical strength, nutrition, cognition, and mood.[27] Satake et al[28] found that the KCL had high sensitivity (90%), high specificity (81%), and high accuracy for frailty (AUC, 0.89).

A variety of GA tools have been used due to the lack of an exact definition. According to studies evaluating the diagnostic accuracy of the GA tools, the abbreviated CGA and the KCL may be useful in assessing frailty. However, those studies were mostly retrospective. Hence, geriatric-specific data should be collected routinely in future clinical trials for gastrointestinal cancer to establish a standardized assessment of frailty.

3 | FRAILTY AND OUTCOMES FOLLOWING SURGERY FOR GASTROINTESTINAL TRACT CANCERS

Table 2 shows the association of frailty with outcomes following surgery for gastrointestinal tract cancer. In upper gastrointestinal tract cancers, one study by Tanaka et al[29] examined CFS retrospectively in 96 patients aged over 65 years who underwent laparoscopic gastrectomy for gastric cancer. The authors found that scores of ≥5 on the CFS were associated with worse overall survival (multivariable hazard ratio [HR]: 3.43, 95% confidence interval [CI]: 1.43-8.22, $P = 0.006$) and cancer-specific survival (multivariable HR: 4.00, 95%CI: 1.20-13.3, $P = 0.024$). However, the CFS scores were not significantly associated with the length of postoperative hospital stay or the incidence of overall complications (≥ Clavien-Dindo

TABLE 1 Accuracy of geriatric assessment tools in patients with cancer

Assessment tool	Evaluation items	Author (year)	Sensitivity %	Specificity %	Area under curve
Geriatric-8	(1) age, (2) food intake, (3) weight loss, (4) body mass index, (5) motor skills, (6) psychological status, (7) number of medications, (8) self-perception of health	Kenig et al (2014)	97%	44%	0.71
		Soubeyran et al (2014)	77%	64%	0.80
		Russo et al (2018)	89%	49.5%	0.79
Abbreviated Comprehensive Geriatric Assessment	(items 1-4) geriatric depression scale, (5) bathing, (6) transfer, (7) continence, (8) shopping, (9) preparing own meals, (10) doing housework, (11) doing own laundry, (12) attention and calculation, (13) reading, (14) writing, (15) copying	Kenig et al (2014)	84%	86%	0.85
Fried Frailty Criteria	(1) weight loss, (2) self-reported exhaustion, (3) grip strength, (4) walking speed, (5) physical activity	Kenig et al (2014)	52%	92%	0.72
Groningen Frailty Indicator	(1) shopping, (2) walk outside house, (3) getting (un) dressed, (4) visiting restroom, (5) impaired vision, (6) impaired hearing, (7) weight loss, (8) co-morbidity, (9) cognition, (items 10-14) depression scale, (15) physical fitness	Kenig et al (2014)	64%	86%	0.74
Clinical Frailty Scale	(1) very fit, (2) well, (3) managing well, (4) vulnerable, (5) mildly frail, (6) moderately frail, (7) severely frail	Kenig et al (2014)	54%	100%	0.77
Balducci Frailty Criteria	(1) age, (2) ADL, (3) co-morbidity, (4) geriatric syndromes: delirium, dementia, depression, osteoporosis, incontinence, falls, neglect and abuse, and failure to thrive	Kenig et al (2014)	84%	50%	0.67
Kihon Checklist	Instrumental (3 questions) and social (4 questions) activities of daily living, physical functions (5 questions), nutritional status (2 questions), oral function (3 questions), cognitive function (3 questions), and depressive mood (5 questions)	Satake et al (2016)	90%	81%	0.89
Usual gait speed	<1 m/s	Pamoukdjian et al (2017)	79%	65%	0.82

TABLE 2 Major studies on geriatric assessment and perioperative outcomes in gastrointestinal tract cancers

Author (year)	Study cohort	Geriatric assessment tool/cut-off value (% of frail patients)	Postoperative complications	Postoperative mortality	Length of hospital stay	Patient survival
Gastric cancer						
Tanaka et al (2019)	• Gastric cancer • Age: ≥80 years • n = 96 • Elective resection	• Clinical Frailty Scale • Score ≥5 (n = 17, 18%)	NS	NS	NS	↓ OS: HR 3.4 (95%CI, 1.4-8.2) CSS: HR 4.0 (95%CI, 1.2-13.3)
Colorectal cancer						
Tamura et al (2021)	• Colorectal cancer • Age: ≥65 years • n = 500 • Elective resection	• Kihon Checklist • Score ≥8 (n = 164, 33%)	↑ (CD ≥I, 28% vs 15%, $P = 0.001$)	–	–	–
Bessems et al (2021)	• Colorectal cancer • Age: ≥70 years • n = 149 • Elective resection	• Geriatric-8 and 4-m gait speed test • Score ≤14 and/or 4MGST <1 m/s (n = 53, 36%)	↑ (CD ≥I, 62% vs 28%, $P < 0.001$)	NS	↑ (9 days vs 8 days, $P = 0.009$)	–
Mima et al (2020)	• Colorectal cancer • Age: ≥18 years • n = 729 • Elective resection	• Clinical Frailty Scale • Score ≥4 (n = 253, 35%)	NS	NS	–	↓ OS: HR 2.0 (95%CI, 1.4-3.0) RFS: HR 1.7 (95%CI, 1.3-2.3)
Okabe et al (2019)	• Colorectal cancer • Age: ≥65 years • n = 269 • Elective resection	• Clinical Frailty Scale • Score ≥4 (n = 78, 29%)	↑ (CD III/IV, 23% vs 8%, $P = 0.001$)	NS	↑ (13 days vs 10 days, $P < 0.001$)	–
Fagard et al (2017)	• Colorectal cancer • Age: ≥70 years • n = 190 • Elective resection	• Geriatric-8 • Score ≤14 (n = 115, 61%)	↑ (CD ≥II, 48% vs 31%, $P = 0.020$)	–	–	–
Reisinger et al (2015)	• Colorectal cancer • n = 310 • Elective resection	• Groningen Frailty Indicator • Score ≥5 (n = 41, 25%)	↑ (Sepsis, 15% vs 4.4%, $P = 0.03$)	NS	–	–
Ommundsen et al (2014)	• Colorectal cancer • Age: ≥70 years • n = 178 • Elective resection	• Balducci Frailty Criteria • Frail: n = 76, 43%	–	–	–	↓ OS: HR 3.6 (95%CI, 2.3-5.5)
Tan et al (2012)	• Colorectal cancer • Age: ≥75 years • n = 83 • Elective resection	• Fried Frailty Criteria • Frail: n = 23, 28%	↑ (CD ≥II, 48% vs 18%, $P = 0.006$)	–	–	–
Kristjansson et al (2010)	• Colorectal cancer • Age: ≥70 years • n = 178 • Elective resection	• Abbreviated Comprehensive Geriatric Assessment • Frail: n = 76, 43%	↑ (CD ≥II, 62% vs 33%, $P = 0.002$)	–	–	–

Note: ↑, higher incidence of postoperative complications or mortality, and longer length of hospital stay in frail patients; ↓, shorter overall, cancer-specific, or recurrence-free survival in frail patients; –, not examined.
Abbreviations: CD, Clavien-Dindo grade; CI, confidence interval; CSS, cancer-specific survival; HR, hazard ratio; NS, not significant ($P > 0.05$); OS, overall survival; RFS, recurrence-free survival.

[CD] grade II) (multivariable odds ratio [OR]: 2.72, 95%CI: 0.81-9.20, $P = 0.11$).

An increasing number of studies have investigated the associations of geriatric assessment tools, including the Kihon Checklist, G8, gait speed test, CFS, Balducci Frailty Criteria, Groningen Frailty Indicator, Fried Frailty Criteria, and abbreviated CGA, with postoperative outcomes after resection of colorectal cancer. Tamura and colleagues examined frailty with the use of the Kihon checklist in 500 patients over 65 years who underwent elective colorectal cancer resection.[30] They found that a score of ≥8 on the Kihon checklist was a significant predictor of postoperative overall complications (≥ CD grade I) with an OR of 1.88 (95% CI: 1.66-3.04) in the multivariate analysis.

Two studies examined the associations between CFS score and postoperative outcomes after resection of colorectal cancer. In the study by Okabe, scores of ≥4 on CFS were significantly associated with longer length of postoperative hospital stay (13 days vs 10 days, $P < 0.001$) and higher incidence of severe complications (≥ CD grade III or IV, 23% vs 8%, $P = 0.001$).[31] Mima et al[12] examined the CFS in 729 colorectal cancer patients undergoing curative resection. The authors found that scores of ≥4 on the CFS were independently associated with shorter OS (multivariable HR: 2.04, 95% CI: 1.40-2.99, $P < 0.001$) and recurrence-free survival (multivariable HR: 1.70, 95%CI: 1.25-2.31, $P < 0.001$) in multivariable analyses adjusting for potential confounders, including age and disease stage. However, the CFS scores were not significantly associated with the incidence of severe complications (CD ≥ grade III, $P = 0.67$). In a retrospective study by Fagard and colleagues, a G8 score of ≤14 was associated with a higher incidence of postoperative complications (≥ CD grade II).[32] Bessems et al[33] screened frailty combining G8 and 4-m gait speed test (4MGST) in 149 patients over 70 years who underwent elective colorectal cancer resection. They found that G8 ≤14 and/or 4MGST <1 m/s were associated with a higher incidence of postoperative overall complications (≥ CD grade I, 62% vs 28%, $P < 0.001$) and longer length of hospital stay (9 days vs 8 days, $P = 0.009$).

Ommundsen et al[34] examined the Balducci Frailty Criteria in 178 patients with colorectal cancer over 70 years of age who underwent elective colorectal cancer resection. The authors found that frailty based on the Balducci Frailty Criteria was independently associated with shorter OS (multivariable HR: 3.6, 95% CI: 2.3-5.5) in multivariable analyses adjusting for disease stage. Tan et al[35] examined the ability of the Fried criteria for frailty to predict postoperative complications after resection of colorectal cancer. They found frailty to be an independent predictor of postoperative complications (CD ≥ grade II). The OR of these complications was 4.08 (95% CI: 1.43-11.64). In a retrospective study by Kristjansson et al,[36] frailty based on the abbreviated CGA was an independent predictor of postoperative complications (≥ CD grade II, multivariable OR: 3.13, 95% CI: 1.65-5.92). Reisinger et al[37] examined associations of the Groningen Frailty Indicator, which screened physical, cognitive, social, and emotional status, with postoperative complications after resection of colorectal cancer. The Groningen Frailty Indicator score of ≥5 was associated with a higher incidence of postoperative sepsis (univariable OR: 3.96, 95%CI: 1.14-13.83, $P = 0.03$). The Groningen Frailty Indicator score ≥5 was not significantly associated with the incidence of postoperative mortality ($P = 0.72$) or anastomotic leakage ($P = 0.62$).

4 | FRAILTY AND OUTCOMES FOLLOWING SURGERY FOR HBP CANCERS

Table 3 shows the association between frailty and outcomes following surgery for HBP cancers. Rostoft et al[38] also reviewed the associations between preoperative frailty, geriatric assessment, and surgical outcomes, especially in HBP cancers. Studies from Japan have investigated the associations of geriatric assessment tools, including the Kihon Checklist, G8, and CFS, with postoperative outcomes after resection of hepatocellular carcinoma (HCC). Two studies examined the Kihon Checklist in relation to postoperative outcomes after HCC resection. Tanaka et al[39] screened preoperative frailty using the Kihon Checklist in 217 patients aged ≥65 years who underwent HCC resection. They found that the Kihon Checklist score of ≥8 was associated with a higher incidence of bile leakage (CD ≥ grade III, 11% vs 3.2%, $P = 0.021$), delirium (CD ≥ grade I, 13% vs 1.9%, $P = 0.003$), and 90-day mortality (4.8% vs 0%, $P = 0.024$) in univariable analyses. They also demonstrated that the Kihon Checklist score of ≥8 was an independent predictor of postoperative age-related events, including major respiratory complications, major cardiac events, delirium requiring medication, transfer to rehabilitation facility, and dependency, with an OR of 5.16 (95% CI: 2.30-11.56) in the multivariate analysis.[39] In the study by Ishihara, which included 295 patients with HCC over 65 years of age, the Kihon Checklist score was independently associated with a higher incidence of postoperative delirium (per increase of one point, multivariable OR: 1.14, 95%CI: 1.03-1.26, $P = 0.010$) in the multivariable analyses.[40] They also demonstrated that the optimal cutoff total KCL score for predicting postoperative delirium was 6 points with the use of receiver operating characteristic curves (area under the ROC curves, 0.74).[40] Kaibori et al[41] screened preoperative frailty using the G8 in 71 patients aged >70 years who underwent HCC resection. They found that a G8 score of <14 was independently associated with a higher incidence of postoperative complications (CD ≥ grade II, multivariable OR: 24.36, 95%CI: 1.66-157.08, $P = 0.020$). In another study by Kaibori et al[42] that included 100 patients with HCC over 70 years, patients were screened and reassessed for frailty at 1, 3, and 6 months postoperatively with the use of G8. The authors found that the reduction in the G8 at 6 months was associated with shorter OS (univariable HR: 8.09, 95% CI: 4.03-16.27, $P < 0.001$; multivariable HR: 12.5, 95% CI: 4.54-33.3, $P < 0.001$) and RFS (univariable HR: 5.35, 95%CI: 3.18-9.01, $P < 0.001$; multivariable HR: 6.25, 95%CI: 2.94-12.25, $P < 0.001$) in univariable and multivariable analyses. In one study by Yamada et al[43] that included 92 patients with HCC over 75 years of age, preoperative frailty was screened using the CFS. They found that CFS score ≥4 was independently associated with shorter CSS (multivariable HR: 7.85, 95% CI: 1.57-38.1,

TABLE 3 Major studies on geriatric assessment and perioperative outcomes in hepatobiliary-pancreatic cancers

Author (year)	Study cohort	Geriatric assessment tool/cut-off value (% of frail patients)	Postoperative complications	Postoperative mortality	Length of hospital stay	Patient survival
HCC						
Ishihara et al (2021)	• HCC • Age: ≥65 years • n = 295 • Hepatic resection	• Kihon Checklist • Score ≥6 (n = 127, 43%)	↑ (Postoperative delirium, 15% vs 1.8%, $P<0.001$)	–	–	–
Kaibori et al (2021)	• HCC • Age: ≥70 years • n = 100 • Hepatic resection	• Geriatric-8 • The reduction in G8 score at six months (n = 30, 30%)	NS	–	–	↓ OS: HR 8.1 (95%CI, 4.0-16.3) RFS: HR 5.4 (95%CI, 3.2-9.0)
Yamada et al (2021)	• HCC • Age: ≥75 years • n = 92 • Hepatic resection	• Clinical Frailty Scale • Score ≥4 (n = 21, 23%)	NS	NS	NS	↓ CSS: HR 7.9 (95%CI, 1.6-38.1)
Tanaka et al (2018)	• HCC • Age: ≥65 years • n = 217 • Hepatic resection	• Kihon Checklist • Score ≥8 (n = 63, 29%)	↑ (Bile leakage, 11% vs 3.2%, $P=0.021$; delirium, 13% vs 1.9%, $P=0.003$)	↑ (90-day mortality, 4.8% vs 0%, $P=0.024$)	-	-
Kaibori et al (2016)	• HCC • Age: ≥70 years • n = 71 • Hepatic resection	• Geriatric-8 • Score <14 (n = 39, 55%)	↑ (CD ≥II, 44% vs 3%, $P<0.001$)	NS	↑ (Postoperative hospital stay ≥13 days, 67% vs 38%, $P=0.014$)	-
Pancreatic cancer						
Mima et al (2021)	• Pancreatic cancer • Age: ≥18 years • n = 142 • Elective resection	• Clinical Frailty Scale • Score ≥5 (n = 16, 11%)	NS	NS	–	↓ OS: HR 2.3 (95%CI, 1.1-4.4) CSS: HR 2.5 (95%CI, 1.1-5.3)
Ngo-Huang et al (2019)	• Pancreatic ductal adenocarcinoma • Age: ≥18 years • n = 47 • Elective resection	• Fried Frailty Criteria • Frail: n = 7, 15%	–	–	–	↓ ($P=0.038$)
Mogal et al (2017)	• Pancreatic cancer • n = 9986 • Elective PD	• Modified frailty index • Score/11 ≥ 0.27 (n = 637, 6.4%)	↑ (CD III/IV, 41% vs 29%, $P<0.001$)	↑ (6.3% vs 2.7%, $P<0.001$)	-	-
Augustin et al (2016)	• Pancreatic cancer • Age: ≥18 years • n = 13 020 • Elective PD or DP	• Modified frailty index • Score ≥5 (n = 45, 0.4%)	↑ (CD IV, PD: 37% vs 7.1%, $P<0.001$; DP, 28% vs 3.4%, $P<0.001$)	↑ (PD, 22% vs 1.6%, $P<0.001$; DP, 11% vs 0.6%, $P<0.001$)	↑ (PD, 20 days vs 13 days, $P<0.001$; DP, 17 days vs 8 days, $P<0.001$)	-
Dale et al (2014)	• Pancreatic tumors • Age: ≥18 years • n = 76 • Elective PD	• Fried Frailty Criteria • "Self-reported Exhaustion" (n = 28, 37%)	↑ (CD ≥III, OR, 4.1, $P=0.01$)	–	↑ ($P=0.02$)	-

Note: ↑, higher incidence of postoperative complications or mortality, and longer length of hospital stay in frail patients; ↓, shorter overall, cancer-specific, or recurrence-free survival in frail patients; –, not examined.

Abbreviations: CD, Clavien-Dindo grade; CI, confidence interval; CSS, cancer-specific survival; DP, distal pancreatectomy; HCC, hepatocellular carcinoma; HR, hazard ratio; NS, not significant ($P>0.05$); OS, overall survival; PD, pancreaticoduodenectomy.

P = 0.01) in multivariable analyses. CFS score ≥4 appeared to be associated with a longer length of postoperative hospital stay (20 days vs 15 days, P = 0.08) and a higher incidence of severe complications (≥ CD grade III, 24% vs 8.5%, P = 0.06); however, the differences were not statistically significant.

In pancreatic resection, frailty according to GA tools, including the CFS, Fried Frailty Criteria, and modified frailty index (mFI), has been associated with worse postoperative outcomes. Mima et al[44] examined CFS in 142 patients with pancreatic cancer who underwent curative resection. The authors found that CFS score ≥5 was independently associated with shorter OS (multivariable HR: 2.25, 95% CI: 1.05-4.43, P = 0.038) and CSS (multivariable HR: 2.49, 95%CI: 1.05-5.34, P = 0.039) in multivariable analyses adjusted for age, disease stage, and other potential confounders. However, CFS scores were not significantly associated with the incidence of severe complications (CD ≥ grade III, P = 0.67) or postoperative mortality. The authors also found that CFS score ≥5 was significantly associated with the absence of adjuvant chemotherapy (P < 0.001).

Two studies examined the Fried Frailty Criteria in relation to outcomes after palliative chemotherapy or resection for pancreatic cancer. In a study by Ngo-Huang, frailty based on the Fried Frailty Criteria was associated with shorter OS in patients with pancreatic cancer who underwent palliative chemotherapy or resection for pancreatic cancer in the univariable analysis (univariable HR: 2.50, 95%CI: 1.57-3.98, P < 0.001).[45] However, they did not examine the associations between the Fried Frailty Criteria and adverse events during palliative chemotherapy or postoperative complications. Dale et al[46] screened preoperative frailty using the Fried Frailty Criteria in 76 patients aged >18 years who underwent PD for pancreatic tumors. They found that self-reported exhaustion based on the Fried Frailty Criteria was an independent predictor of severe postoperative complications (CD ≥ grade III, multivariable OR: 4.06, P = 0.01) and longer length of hospital stay (P = 0.02) after adjusting for potential confounders, including age, BMI, comorbidities, and ASA score.

The mFI has been validated in a population of patients with vascular diseases.[47] Augustin et al[48] examined the mFI in relation to postoperative outcomes by utilizing the National Surgical Quality Improvement Program (NSQIP) database that included more than 13 020 patients who underwent pancreaticoduodenectomy (PD) or distal pancreatectomy (DP) for pancreatic cancer. The authors found that scores of ≥5 on the mFI were associated with higher incidence of postoperative complications (CD grade IV, PD: 37% vs 7.1%, P < 0.001; DP: 28% vs 3.4%, P < 0.001) and 30-day mortality (PD: 22.2% vs 1.6%, P < 0.001; DP: 11.1% vs 0.6%, P < 0.001), and longer length of hospital stay (PD: 19.7 days vs 12.5 days, P < 0.001; DP: 17.4 days vs 8.2 days, P < 0.001), compared to mFI of 0. In multivariable analyses adjusting for age, BMI, serum albumin levels, and type of pancreatic resection, scores of ≥5 on the mFI were independently associated with a higher incidence of postoperative complications (CD grade IV, multivariable OR: 6.17, 95%CI: 3.34-11.40, P < 0.001) and 30-day mortality (multivariable OR: 10.9, 95%CI: 4.92-24.01, P < 0.001), compared to an mFI of 0. These findings have been validated in another study by Mogal et al[49] that included 9986 patients with pancreatic cancer who underwent PD in the NSQIP database. Higher scores on the mFI were independently associated with a higher incidence of postoperative complications (CD grade III or IV, multivariable OR: 1.54, 95%CI: 1.29-1.85) and postoperative mortality (multivariable OR: 1.54, 95%CI: 1.05-2.25).

Studies have demonstrated that preoperative frailty is associated with higher incidence of postoperative complications and mortality, and worse prognosis in patients with gastrointestinal tract and HBP cancers. These findings suggest that integration of the GA assessment into clinical practice may improve risk assessment in patients with gastrointestinal cancer, although geriatric-specific data should be collected routinely in future clinical trials to establish a standardized assessment of frailty and treatment strategies for frail patients with gastrointestinal cancer.

5 | EFFECTS OF PRE- OR REHABILITATION ON PERIOPERATIVE OUTCOMES IN PATIENTS UNDERGOING RESECTION OF GASTROINTESTINAL CANCERS

Table 4 shows findings from randomized clinical trials on prehabilitation and rehabilitation in gastrointestinal tract and HBP cancers. Two randomized controlled trials (RCTs) of patients undergoing resection for gastrointestinal cancers, including colorectal cancer, demonstrated that prehabilitation can reduce the incidence of postoperative complications, compared to usual care. In the RCT by Barberan-Garcia and colleagues that included 125 patients over 70 years and/or the American Society of Anesthesiologists (ASA)-physical status (PS) classification score III or IV who underwent major abdominal surgery, including 96 undergoing oncologic surgery, preoperative 60-minute supervised training sessions (1-3 sessions per week; mean duration of 6 weeks) and home-based training enhanced aerobic capacity, and reduced the incidence of postoperative overall complications, compared to usual care (31% vs 62%, P = 0.001).[50] In the RCT by Berkel and colleagues that included 57 patients with colorectal cancer or premalignant lesions over 60 years who had a metabolic equivalent of task score ≤7 on the veteran-specific activity questionnaire, 3 weeks of exercise prehabilitation, consisting of 60 minutes of supervised exercise, improved the incidence of postoperative overall complications (43% vs 72%, P = 0.024), compared to usual care.[51] No differences in length of hospital stay (8.4 days vs 9.1 days, P = 0.14) and hospital readmission rates (14% vs 17%, P > 0.99) were found between the two groups. Two RCTs by Gillis et al and Carli et al evaluated prehabilitation versus postoperative rehabilitation; both interventions included exercise, nutrition, and psychologic interventions in patients who underwent resection for colorectal cancer.[52,53] However, no differences were observed in postoperative overall complication rates, length of hospital stay, and hospital readmission rates between the prehabilitation and rehabilitation groups in the two

TABLE 4 Randomized clinical trials on prehabilitation and rehabilitation in gastrointestinal tract and hepatobiliary-pancreatic cancers

Author (year)	Participants	Intervention	Main findings
Gastrointestinal tract cancers			
Berkel et al (2022)	• Colorectal cancer or premalignant colorectal lesions (n = 57) • Age: ≥60 years • Low preoperative aerobic fitness at the baseline cardiopulmonary exercise test • Prehabilitation (n = 28) vs usual care (n = 29) • Elective colorectal resection	• 60-minute training session supervised by trained physical therapists (3 weeks, 3 sessions per week, 9 sessions in total)	• The overall postoperative complication rate: prehabilitation group (n = 12, 42.9%) vs usual care group (n = 21, 72.4%, *P* = 0.024). • Hospital readmission rate: prehabilitation group (14%) vs usual care group (17%, *P* > 0.99)
Carli et al (2020)	• Colorectal cancer (n = 110) • Fried Frailty Index score ≥2 • Mean age 78 years • Prehabilitation (n = 55) vs rehabilitation (n = 55) • Elective colorectal resection	• Exercise intervention: 60-minute in-hospital supervised training sessions (4 weeks, 1 session per week, 4 sessions in total) and 30-minute home-based training (3 sessions per week) • Nutritional intervention: assessment of nutritional status and protein supplementation • Psychological interventions including counseling regarding smoking and alcohol cessation	• The overall postoperative complication rate: prehabilitation group (n = 25, 45.5%) vs rehabilitation group (n = 25, 45.5%, *P* = 0.90). • Length of hospital stay: prehabilitation group (4 days) vs rehabilitation group (4 days, *P* = 0.80) • Hospital readmission rate: prehabilitation group (3.6%) vs rehabilitation group (9.1%, *P* = 0.18)
Barberan-Garcia et al (2018)	• Gastrointestinal cancer (n = 96) and other diseases (n = 29) • Age >70 years • American Society of Anesthesiologists score III/IV • Prehabilitation (n = 62) vs usual care (n = 63) • Elective major abdominal surgery	• Exercise intervention: 60-minute supervised training sessions (1 to 3 sessions per week; mean duration, 6 weeks) and home-based training	• Overall postoperative complication rate: prehabilitation group (n = 19, 31%) vs usual care group (n = 39, 62%, *P* = 0.001) • Length of stay in the ICU: prehabilitation group (3 days) vs usual care group (12 days, *P* = 0.046)
Gillis et al (2014)	• Colorectal cancer (n = 77) • Mean age 66 years • Prehabilitation (n = 38) vs rehabilitation (n = 39) • Elective colorectal resection	• Exercise intervention: 50-minute home-based, unsupervised training (3 sessions per week; median duration, 24.5 days) • Nutritional intervention: assessment of nutritional status and protein supplementation • Psychological interventions	• The overall postoperative complication rate: prehabilitation group (n = 12, 32%) vs rehabilitation group (n = 17, 44%, *P* = 0.28). • Length of hospital stay: prehabilitation group (4 days) vs rehabilitation group (4 days, *P* = 0.81) • Hospital readmission rate: prehabilitation group (15%) vs rehabilitation group (13%, *P* = 0.78)
HBP cancers			
Nakajima et al (2019)	• HCC, biliary tract cancer, pancreatic cancer, or other HPB malignancies (n = 152) • Median age 69 years • Prehabilitation (n = 76) vs usual care (n = 76) • Highly invasive surgeries (major hepatectomy with at least 3 Couinaud segments, pancreatoduodenectomy, or hepato-pancreatoduodenectomy)	• Exercise intervention: 60-minute home-based training (at least 3 sessions per week) • Nutritional intervention: leucine-rich essential amino acid supplement within 30 minutes after the start and end of exercise therapy	• Severe postoperative complication (CD ≥3) rate: prehabilitation group (n = 32, 42%) vs usual care group (n = 38, 50%, *P* = 0.33) • Postoperative bile leakage: prehabilitation group (n = 8, 11%) vs usual care group (n = 19, 25%, *P* = 0.020) • Length of hospital stay: prehabilitation group (23 days) vs rehabilitation group (30 days, *P* = 0.045)

TABLE 4 (Continued)

Author (year)	Participants	Intervention	Main findings
Ausania et al (2019)	• Pancreatic or peripancreatic malignancies (n = 40) • Median age 66 years • Prehabilitation (n = 18) vs usual care (n = 22) • Pancreatoduodenectomy	• Exercise intervention: 60-minute in-hospital supervised training sessions (5 sessions in total; median duration, 12.6 days) and home-based training • Nutritional intervention: liquid oral nutrition supplements, vitamin supplements, and pancreatic enzyme replacement therapy	• Overall postoperative complication rate: prehabilitation group (n = 6, 33%) vs usual care group (n = 12, 55%, $P = 0.18$) • Postoperative pancreatic fistula: prehabilitation group (n = 2, 11%) vs usual care group (n = 6, 27%, $P = 0.20$) • Delayed gastric emptying: prehabilitation group (n = 1, 5.6%) vs usual care group (n = 9, 41%, $P = 0.01$) • Length of hospital stay: prehabilitation group (11 days) vs usual care group (13 days, $P = 0.45$) • Hospital readmission rate: prehabilitation group (n = 1, 5.6%) vs usual care group (n = 2, 9.6%, $P = 0.67$)
Dunne et al (2016)	• Colorectal liver metastasis (n = 38) • Median age 62 years • Prehabilitation (n = 20) vs usual care (n = 18) • Hepatectomy (n = 29) and laparotomy (n = 5) without hepatectomy because of the identification of unresectable diseases	• Exercise intervention: 30-minute in-hospital supervised cardiopulmonary training sessions (4 weeks, 3 sessions per week, 12 sessions in total)	• Changes in preoperative oxygen uptake at anaerobic threshold (mL/kg/min): prehabilitation group (+1.0) vs usual care group (−0.5, $P = 0.023$) • Changes in QOL by SF-36 scores: prehabilitation group (+12) vs usual care group (+1, $P = 0.028$)
Kaibori et al (2013)	• HCC (n = 51) • Mean age 70 years • Pre- and rehabilitation (n = 25) vs usual care (n = 26) • Elective hepatectomy	• Exercise intervention: 60-minute supervised training (at least 3 sessions per week; 4 weeks prehabilitation and 24 weeks rehabilitation)	• The overall postoperative complication rate: prehabilitation group (n = 2, 8%) vs usual care group (n = 3, 12%, $P = 0.67$). • Length of hospital stay: prehabilitation group (14 days) vs usual care group (18 days, $P = 0.12$)

Abbreviations: CD, Clavien-Dindo grade; HBP, hepatobiliary-pancreatic; HCC, hepatocellular carcinoma; ICU, intensive care unit; QOL, quality of life.

RCTs. There are very few previous prehabilitation studies on upper gastrointestinal tract cancers. In colorectal cancer, prehabilitation for 3-4 weeks prior to surgery can improve functional capacity and survival, and reduce the incidence of overall complication.[51,52,54] Delaying elective colorectal cancer surgery for more than 4 weeks has been associated with increased mortality.[55] These findings suggest that prehabilitation for 3-4 weeks prior to surgery or rehabilitation may improve clinical outcomes in colorectal cancer, although future studies are needed to establish optimal protocols and durations of prehabilitation or rehabilitation.

In HBP cancers, studies have investigated the effects of exercise prehabilitation or multimodal prehabilitation, including exercise and nutrition, on functional capacity, surgical outcomes, and quality of life (QOL) after surgery. Two studies have examined the effects of exercise prehabilitation in patients who underwent hepatectomy. In a prospective study by Kaibori et al[56] that included 51 patients with HCC, 4 weeks of preoperative exercise and 24 weeks of postoperative exercise, in addition to nutrition therapy, improved postoperative oxygen uptake at anaerobic threshold at 6 months (% of baseline, 115% vs 102%, $P = 0.038$), compared to nutrition therapy alone; however, no differences in postoperative overall complication rates and length of hospital stay between the two groups were observed. In the RCT that included 38 patients with colorectal liver metastasis, Dunne et al[57] demonstrated that 4 weeks of exercise prehabilitation, comprising 30 minutes of supervised exercise, improved preoperative oxygen uptake at anaerobic threshold ($P = 0.023$) and preoperative QOL ($P = 0.028$), compared to usual care.

Nakajima et al[58] investigated the effect of exercise and nutritional therapy, consisting of 60 minutes of home-based training (at least three sessions per week) and leucine-rich essential amino acid supplement within 30 minutes after the start and end of exercise therapy, on postoperative outcomes of patients undergoing invasive HBP surgery, including major hepatectomy with at least 3 Couinaud segments, PD, or hepato-pancreatoduodenectomy. The authors found that exercise and nutritional therapy were associated with lower incidence of postoperative bile leakage (11% vs 25%, $P = 0.020$) and shorter length of postoperative hospital stay (23 days vs 30 days, $P = 0.045$), compared to usual care.

In an RCT that included 40 patients with pancreatic or peripancreatic malignancies who underwent PD, Ausania et al[59] demonstrated that 60 minutes of in-hospital supervised exercise and home-based training, and nutritional intervention, consisting of liquid oral nutrition supplements, vitamin supplements, and pancreatic enzyme replacement therapy, reduced the incidence of delayed gastric emptying, compared to usual care (5.6% vs 41%, $P = 0.010$). However, no differences in postoperative overall complication rates (33% vs 55%, $P = 0.18$), postoperative pancreatic fistula (11% vs 27%, $P = 0.20$), and length of hospital stay (11 days vs 13 days, $P = 0.45$) were found between the two groups.

The impact of prehabilitation or rehabilitation in frail patients with HBP cancers remains uncertain. Two studies suggest that prehabilitation for 4 weeks prior to surgery may improve preoperative oxygen uptake at anaerobic threshold and preoperative QOL in patients with HCC or colorectal liver metastasis.[57,60] Prehabilitation for at least 4 weeks prior to surgery might be necessary to improve functional capacity. Neoadjuvant and adjuvant chemotherapy have been shown to improve prognosis in pancreatic cancer. It would be reasonable to assess frailty and perform prehabilitation and rehabilitation during neoadjuvant and adjuvant chemotherapy in frail patients with pancreatic cancer, although future studies are needed.

Three RCTs in hepatocellular carcinoma, colorectal liver metastasis, or pancreatic tumors have evaluated the effects of prehabilitation for older patients without assessing frailty. In those trials, no differences were found between prehabilitation and usual care groups in the incidence of overall complication. In contrast, two RCTs in colorectal cancer have evaluated the effects of prehabilitation especially in high-risk or vulnerable patients, and demonstrated that prehabilitation significantly reduced the incidence of overall postoperative complications, compared to usual care. These findings suggest that prehabilitation may improve preoperative functional capacity and postoperative outcomes, especially in frail patients with gastrointestinal cancer, although future clinical trials are needed to establish optimal protocols and durations of prehabilitation or rehabilitation for frail patients with gastrointestinal cancer.

6 | MINIMALLY INVASIVE SURGERY FOR FRAIL PATIENTS WITH GASTROINTESTINAL CANCERS

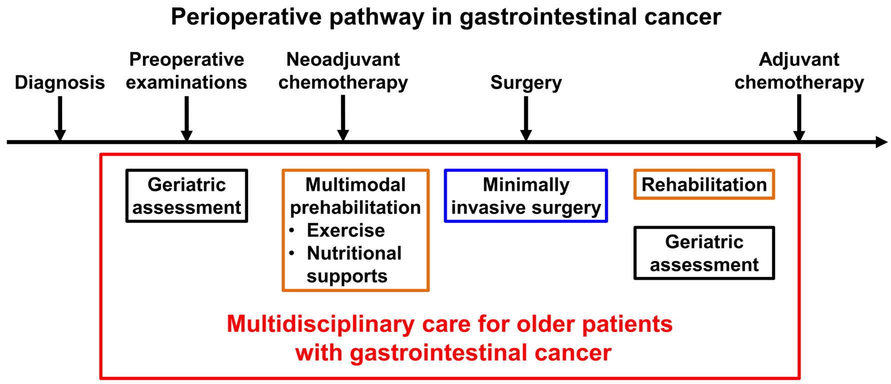
Minimally invasive surgery, including laparoscopic or robotic surgery, has been shown to improve postoperative outcomes, compared to

TABLE 5 Major studies on geriatric assessment and chemotherapy outcomes in patients with gastrointestinal cancers

Author (year)	Study cohort	% of frail patients	Adverse events during chemotherapy	Patient survival according to frailty
Huang et al (2021)	• Esophageal cancer • Age: ≥20 years • n = 87 • Concurrent chemoradiotherapy	n = 41, 47%	↑ (Severe hematological adverse event, 63% vs 20%, $P < 0.001$; emergent room visiting, $P = 0.009$)	↓ OS: HR 2.1 (95%CI, 1.0-4.4)
Jespersen et al (2021)	• Metastatic gastrointestinal cancer (colorectal cancer, esophagus-gastric cancer, biliary and pancreatic cancer, GIST) • Age: ≥70 years • n = 170 • Palliative chemotherapy	n = 49, 29%	↑ [Functional decline, OR: 3.5 (95%CI, 1.0-11.6, $P = 0.04$)]	↓ OS: HR 1.7 (95%CI, 1.2-2.4)
Mima et al (2021)	• High-risk stage II and stage III colorectal cancer • Age: ≥18 years • n = 196 • Adjuvant chemotherapy	n = 36, 18%	↑ (Severe adverse events during oxaliplatin-based chemotherapy, 43% vs 9.4%, $P = 0.036$)	-
Rittberg et al (2021)	• Pancreatic cancer • Age: ≥65 years • n = 87 • Palliative chemotherapy	n = 14, 16%	NS	NS
Ngo-Huang et al (2019)	• Pancreatic ductal adenocarcinoma • Age: ≥18 years • n = 95 • Palliative chemotherapy	n = 29, 31%	NS	↓ ($P = 0.003$)

Note: ↑, higher incidence of adverse events during chemotherapy in frail patients; ↓, shorter overall survival in frail patients; −, not examined.
Abbreviations: CI, confidence interval; HR, hazard ratio; NS, not significant ($P > 0.05$); OS, overall survival.

FIGURE 1 Perioperative pathway in gastrointestinal cancer



open surgery, in terms of less postoperative pain, early postoperative recovery, lower complications, and mortality rates in resections of gastrointestinal tract[61–64] and HBP cancers.[65–68] However, the impact of minimally invasive surgery in frail patients remains uncertain.

In a prospective, observational, multicenter study that included 2968 patients who underwent resection for colorectal cancer by open or laparoscopic approach, Santacruz et al[69] found that laparoscopic surgery was associated with a lower incidence of postoperative overall complications (28% vs 37%, $P < 0.001$) and shorter length of postoperative hospital stay (7 days vs 10 days, $P < 0.001$), compared to open surgery, in high-risk patients with an ASA-PS score of III or IV. Mosquera et al examined associations of surgical approach with postoperative outcomes according to the mFI, utilizing the NSQIP database, which included over 94 811 patients who had undergone resection for colorectal cancer. The authors found that in frail patients with mFI ≥3, the laparoscopic approach was associated with a lower incidence of postoperative complications (35% vs 51%, $P < 0.001$) and 30-day mortality (5.1% vs 11%, $P < 0.001$) compared to open surgery. These findings have been validated in another study by Kothari et al[70] that included 117 064 patients in the NSQIP database. The authors found that in frail patients with mFI ≥4, the laparoscopic approach was associated with a lower incidence of postoperative complications (36% vs 59%, $P < 0.05$) and 30-day mortality (5.4% vs 20.3%, $P < 0.05$), compared to open surgery. Lo et al[71] examined associations of surgical approach with postoperative complications according to the mFI, utilizing the NSQIP database, which included 81 803 patients who had undergone open, laparoscopic, or robotic resection for colorectal cancer. The authors found that in frail patients with an mFI of 3 or 4, the robotic approach was associated with a higher incidence of postoperative major complications, compared to open or laparoscopic surgery (OR: 3.15, 95%CI: 1.34-7.45, $P = 0.009$).

Minimally invasive distal pancreatectomy (MIDP), including laparoscopic or robotic approach, has been shown to improve postoperative outcomes, in terms of less postoperative pain, early postoperative recovery, lower complications, or mortality rates, compared to open distal pancreatectomy (ODP) for treatment of pancreatic body-tail neoplasms.[72,73] Konstantinidis et al[74] examined associations of surgical approach with postoperative outcomes according to the mFI utilizing the NSQIP database, which included 1038 patients who had undergone distal pancreatectomy. The authors found that in frail patients with mFI >0, the laparoscopic or robotic approach was associated with a lower incidence of postoperative CD grade IV complications (2.4% vs 8.3% vs 12%, $P = 0.007$) and mortality (0% vs 2% vs 5.8%, $P = 0.009$), compared to open surgery or converted-to-open surgery.

Studies have demonstrated that laparoscopic surgery is associated with better surgical outcomes in frail patients with colorectal and distal pancreatic cancers, compared to open surgery. These findings suggest that laparoscopic surgery in combination with prehabilitation or rehabilitation may improve clinical outcomes in those patients. Further studies are needed to investigate the safety and effectiveness of minimally invasive surgery, including robotic approach, in high-risk or frail patients with upper gastrointestinal tract and hepatobiliary cancers.

7 | CHEMOTHERAPY IN FRAIL PATIENTS WITH GASTROINTESTINAL CANCER

Table 5 shows the association between frailty and chemotherapy outcomes in patients with gastrointestinal cancer. Huang et al[75] screened pretreatment frailty in 87 patients with esophageal cancer who received neoadjuvant radiotherapy and concurrent chemotherapy with weekly administration of carboplatin and paclitaxel for 5 weeks. They found that pretreatment frailty was associated with a higher incidence of at least one severe hematological adverse event (63.4% vs 19.6%, $P < 0.001$) and poor prognosis (HR: 2.12, 95%CI: 1.01-4.42, $P = 0.046$) during concurrent chemoradiotherapy, when compared to fit patients. In a study by Jespersen[76] that included 170 patients with metastatic gastrointestinal cancers (colorectal cancer, esophagus-gastric cancer, biliary and pancreatic cancer, gastrointestinal stromal tumor) over 70 years of age, pretreatment frailty was associated with a higher incidence of functional decline (OR: 3.5, 95%CI: 1.0-11.6, $P = 0.04$), rapid progressive disease (OR: 3.5, 95%CI: 1.5-8.4, $P = 0.005$), and shorter OS (HR: 1.7, 95%CI: 1.2-2.4, $P = 0.01$) during palliative chemotherapy. Mima et al examined CFS in 196 patients with high-risk stage II or stage III colorectal cancer who underwent curative resection and adjuvant chemotherapy. They found that during oxaliplatin-based adjuvant chemotherapy, frail patients were more likely to experience severe adverse events, compared to non-frail patients (43% vs 9.4%, $P = 0.036$).[77]

Rittberg et al examined the mFI in relation to outcomes of palliative chemotherapy in 87 patients with pancreatic cancer over 65 years of age. The authors found that frailty according to the mFI was not associated with the incidence of adverse events ($P > 0.16$) or OS ($P = 0.60$) during chemotherapy.[78] In a study by Ngo-Huang, frailty based on the Fried Frailty Criteria was associated with shorter OS in patients with pancreatic cancer who underwent palliative chemotherapy ($P = 0.003$), although they did not examine the associations between the Fried Frailty Criteria and adverse events during palliative chemotherapy.[45]

There are few previous studies on geriatric assessment and outcomes of chemotherapy in patients with gastrointestinal cancers. Future clinical trials are needed to establish optimal chemotherapy regimens for frail patients with gastrointestinal cancer.

8 | FUTURE CHALLENGES AND CONCLUSIONS

In this review, we summarized the major GA tools and clinical studies on associations between frailty and perioperative outcomes, and the effects of prehabilitation or rehabilitation on these outcomes in patients with gastrointestinal cancers. A variety of frail measures have been used due to the lack of an exact definition. An increasing number of studies have investigated the association between preoperative frailty and postoperative outcomes after resection of gastrointestinal tract and HBP cancers, especially in older patients. Although these studies were mostly retrospective, and the few prospective studies conducted were small, the results consistently suggest that preoperative frailty is a negative predictor of postoperative outcomes, such as postoperative complications, postoperative mortality, readmission, reoperation, and length of hospital stay.

Evidence on the effects of prehabilitation or rehabilitation on postoperative outcomes in patients with gastrointestinal cancer is still limited. Only two RCTs demonstrated better effects of preoperative exercise on the incidence of postoperative complications, especially in frail patients. Hence, standardized methods must be developed to identify patients who may benefit from prehabilitation and/or rehabilitation. Further clinical trials are required to establish a standardized assessment of frailty in patients with gastrointestinal cancer. In addition, future research should focus on exploring the benefits of combining these GA tools.

Utilizing the NSQIP database, minimally invasive surgery for frail patients with gastrointestinal cancer has been associated with a lower incidence of postoperative complications than open surgery. Neoadjuvant and adjuvant chemotherapy have been shown to improve prognosis in gastrointestinal cancer.[79–83] Mima et al reported that frail patients with colorectal and pancreatic cancers are less likely to receive adjuvant chemotherapy, which leads to poor prognosis.[12,44,77,84] Improvement of perioperative frailty would be key in providing favorable long-term outcomes in patients with gastrointestinal cancers. Further clinical trials are needed to examine the effects of minimally invasive surgery and neoadjuvant and adjuvant chemotherapy in patients with frailty. We proposed an example for the integration of older-patient-specific care into treatment strategies for gastrointestinal cancer, as outlined in Figure 1.

In conclusion, accumulating evidence demonstrates that the integration of preoperative geriatric assessment and prehabilitation for frail patients into clinical practice may improve perioperative and long-term outcomes in patients with gastrointestinal cancer. The increasing numbers of older or frail patients with gastrointestinal cancers require multidisciplinary care; hence, there is an urgent need for future research to establish treatment strategies for these vulnerable patients.

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