Review

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Relation between frailty and adverse outcomes in elderly patients with gastric cancer: a scoping review

Zheng-Ke-Ke Tan, BSc[a], Wen-Zhen Tang, MSc[a], Kui Jia, MSc[b], Dan-Ni Li, BSc[a], Li-Yan Qiu, MSc[a], Xin Chen, BSc[a], Li Yang, BSc[a,*]

Background: Playing an exemplary role, frailty have crucial effect on the preoperative evaluation of elderly patients. Previous studies have shown that frailty is associated with complications and mortality in patients with gastric cancer (GC). However, with the development of the concept of "patient-centered", the range of health-related outcomes is broad. The differences in relation between frailty and various adverse outcomes will be further explored.

Method: The PubMed, Embase, Web of Science, Cochrane Library, China National Knowledge Infrastructure, Wan Fang, and Chinese Biomedical Literature databases were searched for keywords, including frailty (such as frail) and gastric cancer (such as stomach neoplasms or stomach cancer or gastrectomy or gastric surgery). The search period is until August 2023. The included studies were observational or cohort studies with postoperative related adverse outcomes as primary or secondary outcome measures. Valid assessment tools were used. The Quality Assessment Tool for Observational Cohort and Cross-sectional Studies was used to assess methodological quality in the included literature.

Result: Fifteen studies were included, including 4 cross-sectional studies, 8 retrospective cohort studies, and 3 prospective cohort studies. Among them, 6 studies were rated as "Good" and 9 studies were rated as "Fair," indicating that the quality of the literature was high. Then, 10 frailty assessment tools were summarized and classified into two broad categories in accordance with frailty models. Results of the included studies indicated that frailty in elderly patients with GC was associated with postoperative complications, mortality, hospital days, readmissions, quality of life, non-home discharge, and admission to the intensive care unit.

Conclusion: This scoping review concludes that high levels of preoperative frailty increase the risk of adverse outcomes in elderly patients with GC. Frailty will be widely used in the future clinical evaluation of elderly gastric cancer patients, precise risk stratification should be implemented for patients, and frailty management should be implemented well to reduce the occurrence of adverse treatment outcomes.

Keywords: adverse outcomes, elderly, frailty, gastric cancer

Introduction

Gastric cancer (GC) is one of the five most common cancers worldwide. According to GLOBOCAN statistics, the number of new GC cases in the world reached 1.089 million in 2020, and the number of deaths caused by GC accounted for 7.7% of the deaths due to cancer, ranking fourth[1]. The incidence of GC is concentrated in East Asia and Southeast Asia, mostly related to *Helicobacter pylori* infection, which is prone to intestinal and non-cardia type GC[2,3]. As of 2020, 479 000 new cases of GC were reported in China, with 374 000 deaths. Considering the continuous improvement of diagnosis and treatment methods, population-standardized incidence and mortality have exhibited a downward trend in the past two decades[4]. The accumulation of age has an effect on the incidence and mortality of gastric cancer; that is, the number of cases starts to surge at 55 years old, and the peak age is over 75 years old[5,6]. Surgery is the most important treatment of GC by removing the tumour and related tissues with removing the surrounding lymph nodes, but the

HIGHLIGHTS

- Frailty is more common in older patients , recommended to be included in routine preoperative evaluation.
- Existing studies on frailty and various adverse outcomes are fragmented, with different measurement tools and indicators.
- The aim of this review is to determine the extent to which frailty in patients with gastric cancer is associated with adverse outcomes, including postoperative complications, mortality, readmission, prolonged hospital stay, non-home discharge and so on.

Departments of [a]Nursing and [b]Gastrointestinal Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi Zhuang Autonomous Region, People's Republic of China

Z.-K.-K.T. and W.-Z.T. contributed equally.

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**Corresponding author. Address: The First Affiliated Hospital of Guangxi Medical University, Nanning 530000, China. Tel.: +86 151 777 765 39. E-mail: m15177776539@163.com (L. Yang).*

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occurrence of complications hinders postoperative recovery, prolongs hospital stay, forms a vicious circle of poor prognosis, and brings economic and mental burden to the patients and their families[7].

As defined by the European Society for Clinical Nutrition and Metabolism, frailty is a common syndrome in cancer patients that is characterized by weight descent, anorexia inappetence, fatigue, muscle atrophy, and fat loss; tumour patients are divided into three categories: non-debilitating, with muscle atrophy but stable weight, and with weight loss[8]. Frailty is common in elderly cancer patients, and studies have shown that the incidence can reach as high as 64%[9]. In the face of trauma and stress reactions brought about by surgery, the risk of poor prognosis is increased in the frail population, and the mortality rate can reach 10% at 180 days after surgery[10], increasing the direct economic burden[11,12]. The American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society recommended that frailty be included in preoperative assessment to predict the risk of poor prognosis after surgery[13].

Ding *et al.*[14] showed that the prevalence of preoperative frailty in elderly patients with GC is as high as 20.7%, which was positively correlated with postoperative complications, prolonged hospital stay, and other adverse prognoses. However, the relationship between vulnerability and adverse outcomes is inaccurate due to the use of different vulnerability tools and outcome indicators; moreover, research design is mostly single-centre studies, the health outcomes involved were not accurately defined, and thus, systematically summarizing existing studies is necessary[15,16]. Accordingly, the current study evaluated existing insights into the relation between frailty and adverse outcomes in elderly patients with GC in a scoping review to provide guidelines for preoperative comprehensive assessment and the reduction of adverse outcomes in this population.

Methods

We used the Joanna Brigs Institute (JBI) methodology to the conduct of scoping reviews, which based on the framework proposed by Arksey and O'Malley[17]. The evaluation of Scoping reviews follows a systematic approach to map the evidence on the subject and identify key concepts, theories, sources, and knowledge gaps, rather than integrating the evidence and judging quality after rigorous methodological evaluation[18]. The results of the evidence search and selection process were reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews Guidelines (PRISMA) and the protocol for this project is available on Open Science Framework (OSF; https://osf.io/7h3xz/).

Identifying the research question

(1) What tools are available for evaluating preoperative frailty in elderly patients with GC?
(2) What adverse outcomes are associated with frailty in patients with GC? To what extent is it relevant?

Definition and scope

To explore relation between frailty and adverse outcomes in patients with GC scope of the review was defined according to two concept constructs.

Definition of frailty

The current evaluation method was based on two frailty models. The first one, originally a model of frailty phenotype proposed by Fried's team, involved five basic characteristics: weight loss, fatigue, weakness, slow movement, and reduced or lack of physical activity[19]. However, frailty could not be equated with disability, sarcopenia, and comorbidities[20]. The second model, based on a conceptual model of "age-related accumulation of deficits", Rockwood and Mitnitski constructed an assessment of the frailty index, which belief that frailty is a continuous process that accumulates defects with aging and should be fully evaluated from the perspective of the patient as a whole[21].

Definition of adverse outcomes

Synonyms are commonly used in the literature to describe adverse outcomes, including clinical outcomes, adverse prognosis, and health outcomes. At present, adverse outcomes have no clear definition and scope. Outcome indicators are selected in accordance with the personal preferences of researchers. Some studies also regarded postoperative injuries of patients as adverse outcome indicators.

The Global Leadership Initiative on Malnutrition summarized the range of potentially meaningful health outcomes, including 14 indicators across 3 sites in hospitals, nursing homes, and communities. This scoping review included 8 related outcome indicators, as presented in Table 1[22].

Identifying relevant studies

The literature in the PubMed, Embase, Web of Science, Cochrane Library, China National Knowledge Infrastructure , Wan Fang, and Chinese Biomedical Literature databases was searched. The focus was on literature published since the establishment of the database until June 2023. This study used the method of combining subject words and free words, including ("frailty" or "frail") and ("gastric cancer" or "stomach neoplasms" or "stomach cancer" or "gastrectomy" or "gastric surgery"). Other literature was supplemented by searching relevant review citations. The search strategy is presented in Table 2.

Table 1

Potentially meaningful adverse outcomes in our study

Healthcare setting	Health outcome
Hospital	In-hospital mortality
	Major complications
	30-day mortality
	30-day readmission rate
	60-day readmission rate
	Length of hospital stay
Community	Admission rate to hospital
	Quality of life (QoL)

Table 2
Strategy

Database	Search term and strategy	No. matches
PubMed		
#1	Search: (frailty) OR (frail)	
#2	Search: (((gastric cancer) OR (stomach cancer)) OR (gastrectomy)) OR (gastric surgery)	
#3	Search #1 or #2	167
Embase search		
#1	Search 'frailty'/exp OR frailty	
#2	Search frail	
#3	Search #1 OR #2	
#4	Search 'gastric cancer'/exp OR 'gastric cancer' OR (gastric AND ('cancer'/exp OR cancer))	
#5	Search 'stomach cancer'/exp OR 'stomach cancer' OR (('stomach'/exp OR stomach) AND ('cancer'/exp OR cancer))	
#6	Search 'gastrectomy'/exp OR gastrectomy	
#7	Search 'gastric surgery'/exp OR 'gastric surgery' OR (gastric AND ('surgery'/exp OR surgery))	
#8	Search #4 OR #5 OR #6 OR #7	
#9	Search #9 AND ('Article'/it OR 'Article in Press'/it OR 'Letter'/it)	224
Web of science		
#1	Search ALL = ("gastric cancer" OR "stomach cancer" AND "gastrectomy" OR "gastric surgery")	
#2	Search "Frailty" OR "Frail" (Search within all fields of #1)	50
Cochrane library		
#1	Search All Text: (frailty) OR (frail)	
#2	Search All Text: (gastric cancer) OR (stomach cancer) OR (gastrectomy) OR (gastric surgery)	
#3	Search #1 AND #2	28

Study selection

End Note X9 was used to de-duplicate the literature. Two researchers conducted the initial screening of the literature in accordance with the scheduling standard, performed the secondary screening after reading the full text, and included the final literature. Any disagreement between the two researchers could be resolved by a third author.

Selection criteria

(1) The subjects were GC patients underwent surgical treatment.
(2) Study types were cross-sectional, prospective cohort, and retrospective cohort studies.
(3) The concept involved frailty related research and uses reliable assessment tools
(4) The results of studies involved the relationship between frailty and adverse outcomes.

Exclusion criteria

(1) Literature type was review, conference abstract, or individual case.
(2) The full text of the literature could not be obtained.
(3) The language was not Chinese or English.

Charting the data

An Excel chart was created to collect data on the issues studied in this review. The primary features and topic of the scope review related information extracted from each study included the following: first author, year of publication, country, sample, study design, age of study subjects, tumour stage, main treatment, prevalence of frailty, frailty assessment tools, outcome indicator, and major conclusions. Then, the extracted information and data were compared, classified, and summarized in a table.

Collating, summarizing, and reporting results

The included studies were classified into three categories: cross-sectional, prospective, and retrospective studies. The presentation methods of results were divided into two types: descriptive numerical analysis, which was used to summarize the incidence of frailty, statistical tools of frailty, and the incidence of adverse outcomes. A narrative summary is used to summarize the major conclusions drawn from a study around the issues discussed in this review.

Assessment of risk of bias

All included studies assessed the risk of bias by using the Quality Assessment Tool for Observational Cohort and Cross-sectional Studies, which consists of 14 index items[23]. If a standard is met, then it is marked as "Yes." If a standard is not met, then it is marked as "No." If a standard "cannot be determined" (CD) or "not reported" (NR), then it is also deducted. If an entry is not applicable to the study to be evaluated, then it may be marked as "not applicable" (NA) and no points will be deducted. Finally, all the items are counted. If the deducted items are less than or equal to 2 items, then the overall score is "Good." If the deduction is 3–6 items, then the rate as "Fair." If the deduction is greater than 6 items, then the rating is "Poor"[24].

Results

Literature selection and results

A total of 1022 papers were obtained by searching the database, 2 were manually in a snowball process, and 313 duplicate articles were excluded. A total of 672 studies were excluded through the secondary screening of titles and abstracts. After reading the full text, 15 papers were finally included. The literature screening process is illustrated in Figure 1.

Basic features of the included literature

Among the final 15, 4 were cross-sectional studies[14,25–27], 8 were retrospective cohort studies[28–35], and 3 were prospective cohort studies[36–38]. Moreover, 5 studies were from China[14,25,26,35,37], 3 were from Japan[32–34], and 3 were from South Korea[28,30,38], accounting for 73.33% of all the studies in East Asia. Meanwhile, 2 studies were from the United States[29,31], 1 was from Italy[36], and 1 was from Spain[27]. The basic characteristics of the included studies are listed in Table 3.

Risk of bias

The quality of the included literature was above average. Six studies were rated "good" in the methodological quality evaluation, four of which were cross-sectional studies, with the major advantages of consideration of exposure factors, and the relationship between exposure and outcome should not be considered[14,25–27]. In the other two retrospective cohort studies, the major advantages were clear research objectives, researchers

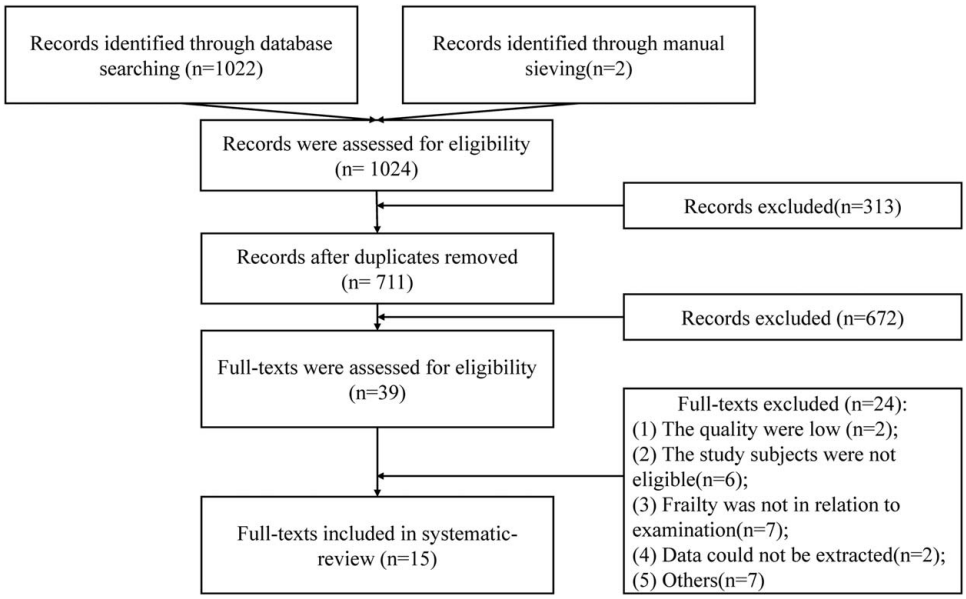

Figure 1. Flow diagram summarizing the article screening process.

considered smoking an exposure factor, and had sufficient time to consider the relationship between exposure and outcome. The limitations were as follows: unclear sample size calculation[31,35].

Nine studies were rated "'fair," with the major limitations being that exposure factors were not reported in the paper, the effect of exposure on outcomes cannot be explored, and sample size evidence was lacking[28–30,32–34,36–38], as presented in Table 4.

Operationalizing and measuring frailty

A variety of frailty assessment tools were used in patients with GC, with eight measures identified in the included studies, namely, the Tilburg Frailty Indicator, frailty phenotype (FP), frailty index (FI), Study of Osteoporotic Fractures Frailty Index (SOF), the High Preoperative Modified Frailty Index (HPMFI), the Groningen Frailty Indicator (GFI), the Clinical Frailty Scale (CFS), the Multidimensional Frailty Score (MFS), and the Modified Frailty Index (mFI), as presented in Table 5.

The nine assessment tools are subjective scales, which are filled by nurses before admission or before operation[14,25–36,38]. HPMFI used three laboratory data associated with frailty, namely, creatinine, haematocrit, and albumin[37]. The number of items ranges from 3 to 40, with FI items being the most numerous[36].

FP, SOF, and HPMFI are prepared on the basis of the Fried phenotype model, but the fading-related items of each tool setting are different[14,26,28,30,37] The remaining seven evaluation tools are based on the cumulative deficit model[25,27,29,31–36,38]. FI and CFS were compiled by Rockwood from the proposed model. Then, GFI and mFI modified and deleted entries on the basis of the above scales.

FP, FI, SOF, and CFS were evaluated in three levels (non-frail, pre-frail, and frail). The remaining assessment tool results were divided into two levels (non-frail and frail) in accordance with the cutoff value.

Identify the relation between frailty and adverse outcomes

A total of 9 adverse outcome indicators were reported in the 15 articles, with 1–4 adverse outcome indicators in a single study. Among them, the incidence of postoperative complications was the most frequent, followed by mortality, including the calculation of overall survival (OS) and tumour-specific survival. In addition, outcome indicators also included readmission rate, length of stay, cure rate, quality of life (QoL), non-home discharge, and admission to ICU. The survival time of patients was obtained by follow-up in four papers, and the relationship between frailty and postoperative survival was analyzed using the Cox model[28,32,33,37], with a follow-up time of 3–5 years. The follow-up time of 3 studies was 1 year[30,35,36,38], that of 1 study was 6 months[29], and those of the 6 other studies were all less than 1 month after surgery[14,25,26,31,34].

Frailty has a relation with postoperative complications

Frailty is closely related to total postoperative complications, and frailty before GC surgery can be used as a predictor. A cross-sectional study showed clearly that the incidence of lung infection was higher in patients with frailty before surgery[26]. A retrospective study suggested that frailty can predict postoperative anastomotic fistula in elder patients with GC[35]. In eight studies, the Clavien–Dindo scale was used to evaluate the severity of surgical complications, and preoperative frailty was mostly positively associated with Grade II complications[25,27,29–33,35–37].

Frailty has a relation with mortality

Among the included literature, eight studies showed that frailty increased the risk of postoperative death. From a time point of view, frailty (pre-frail and frail) is a predictor of short-term survival (within 30 days after surgery)[27,31,36,38] and long-term survival (more than 1 year after surgery)[28,32,33,36–38]. From cause of death, frailty was associated with OS[32,33] and disease-specific survival (DSS)[28,33].

Table 3

Characteristics of the included studies

References	Country	Sample	Design	Age (years)	Tumour stage	Main treatment	Prevalence (%)	Assessment tool	Outcome indicator	The incidence of outcome	Major conclusion
Miao[25]	China	404	Cross-sectional	69 (65–73)	II–IV	Radical gastrectomy	71.6	TFI	Complications, hospital stays, QoL, and disability	Complications 29.1%, prolonged hospital stay 36.5%, low quality of life 26.7% and disability 73.0%	Preoperative multidimensional frailty was the influential factor of total complications, prolonged hospital stay, and low QoL in elderly patients with GC. Multidimensional frailty is a complex interaction among various dimensions that jointly accelerates the development of frailty.
Su[26]	China	217	Cross-sectional	67.33 ± 5.80	I–III	Radical gastrectomy	33.18	FP	Pulmonary infection	Pulmonary infection 66.7%	Frailty is an independent risk factor for postoperative pulmonary infection in elderly patients with GC. Nutritional risk assessment combined with frailty assessment can significantly improve the predictive efficacy of postoperative complications in elderly patients with GC.
Artiles[27]	Spain	256	Cross-sectional	76.1 ± 5.1	—	Major gastrointestinal surgery	38	CFS	Complications and mortality	NR-	Frailty is closely associated with complications and is a good predictor of postoperative complications in elderly patients who undergo major gastrointestinal procedures.
Ding[14]	China	406	Cross-sectional	68.5 (65–73)	I–IV	Gastrectomy	20.7	FP	Complications, hospital stays, and readmission	Complications 24.1%, prolonged hospital stay 24.1% and 90-day hospital readmission 11.1%	Frailty increases the risk of adverse outcomes in elderly GC patients, including total complications, PLOS, and 90-day hospital readmission.
Giannotti[36]	Italy	99	Prospective	80.1 ± 5.88	—	Radical gastrectomy	40.5	FI	Complications and mortality	30-day mortality0.8%, 1-year mortality19%	Functional status, physical performance, and frailty also accurately predicted short-term outcomes. Frailty is not the key predictor of 1-year mortality.
Jeong[28]	South Korea	231	Retrospective	72.04 ± 4.85	I–IV	Gastrectomy	15.2	SOF	Mortality	Mortality 40.8%	Frailty was predictive of GC-specific mortality in the entire cohort.
Lu[37]	China	119	Prospective	82.0 ± 2.4	I–III	Radical laparoscopic gastrectomy	36.13	HPMFI	Complications, overall survival, cancer-specific survival, and Hospital Stays	Complications 55.8%, the 3-year OS rate 37.2%, the 3-year RFS rate 23.3% and Hospital stays (16.5 ± 8.1)	Frailty can significantly affect postoperative complications and the long-term prognosis of elderly patients.
Tegels[29]	USA	180	Retrospective	69.8 (37–88)	0–IV	Gastrectomy	30.24	GFI	Complications, hospital Stays, and mortality	Complications 50%, mortality 23.3%, hospital stays (18.7 ± 12)	Preoperative frailty and nutritional assessment can be used as predictors of postoperative

											mortality and complication in patients with GC.
Vermillion[31]	USA	41455	Retrospective	72.4 ± 7.9	—	Gastrectomy	10.14	mFI-11	Complications and mortality	Major complications 29.1%, 30-day mortality 5.6%	Frailty was strongly associated with increased hospital days, postoperative complications, and 30-day mortality in surgical patients with GC.
Yu[30]	South Korea	223	Retrospective	72.1 ± 4.6	I–IV	Gastrectomy	14.8	SOF	Complications and readmission	Readmission 19.1%	Preoperative frailty in elderly patients with GC increases the risk of complications and mortality. Frailty is a predictor of 1-year readmissions.
Msisawa[32]	Japan	142	Retrospective	—	—	Endoscopic submucosal dissection	28.87	CFS	Complications, cure, and mortality	The perforation rate 2.4% cute 100% and mortality 31.7%	The long-term survival rate of patients with frailty was shorter than that of those without frailty. Death willingness has nothing to do with GC, and most people die from organ failure or other malignant tumours.
Tanaka[33]	Japan	96	Retrospective	82 (80–92)	I–III	Radical laparoscopic gastrectomy	17.71	CFS	Complications, overall survival, Cancer-specific survival, and hospital Stays	Complications 36.2%, the 3-year OS rate 57.3%, the 5-year OS rate 53.7%, the 3-year DSS rate 79.1%	Frailty can have a great effect on the operative morbidity and prognosis of senile patients. The CFS score can be a promising prognostic predictor, particularly for frail patients with advanced GC.
Kim[38]	South Korea	289	Prospective	77.3 (66–94)	I–III	Radical gastrectomy	38.4	MFS	Hospital stays and mortality	Complications 29.7%, hospital stays 0%, 1-year mortality 14.1%	Elderly GC patients undergoing gastrectomy with frailty do not have increased mortality risk. The influence of frailty on postoperative outcomes may vary based on the risk of the surgical procedure.
Osaki[34]	Japan	354	Retrospective	—	T1–T4	Radical gastrectomy	9.8	mFI	Non-home discharge	Non-home discharge 17.1%	Frailty, age, complications, and surgical approach were all predictors of non-home discharge in elderly patients with GC.
Xu[35]	China	1003	Retrospective	—	I–IV	Radical gastrectomy	13.86	mFI	Mortality, complications, and admission to ICU	1-year mortality 18%, anastomotic fistula 7.9% and admission to ICU 31.7%	Frailty can provide prognostic information for 1-year postoperative mortality and admission to ICU.

CFS, Clinical Frailty Scale; DSS, disease-specific survival; FI, frailty index; FP, frailty phenotype; GC, gastric cancer; GFI, Groningen Frailty Indicator; HPMFI, High Preoperative Modified Frailty Index; mFI, Modified frailty index; MFS, Multidimensional Frailty Score; NR, not reported; OS, overall survival; QoL, quality of life; RFS, Recurrence-free survival; SOF, Study of Osteoporotic Fractures Frailty Index; TFI, Tilburg Frailty Indicator.

Table 4

Risk of bias assessment using quality assessment tool for observational cohort and cross-sectional studies (QATOCCS)

Criteria	Miu 2022	Su 2023	Artiles2019	Ding 2023	Giannotti 2019	Jeong 2021	Lu 2018	Tegels 2014	Vermillion 2014	Yu 2017	Msisawa2020	Tanaka2019	Kim 2021	Osaki 2020	Xu 2023
Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the study population clearly specifed and defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all the subjects selected from the same or similar populations.Were inclusion and exclusion criteria for being in the study prespecifed and uniform across participants?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was a sample size justifcation, power description, or variance and effect estimates provided?	Yes	NR	NR	Yes	NR	CD	CD	NR	NR	NR	CD	NR	NR	NR	NR
For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	NA	NA	NA	NA	NR	NR	NR	NR	Yes	NR	Yes	NR	NR	NR	Yes
the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	NA	NA	NA	NA	NR	NR	NR	NR	Yes	NR	CD	NR	NR	NR	Yes
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome?	NA	NA	NA	NA	NR	NR	NR	NR	Yes	NR	No	NR	NR	NR	Yes
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Was the exposure(s) assessed more than once over time?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcome assessors blinded to the exposure status of participants?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NR	Yes	Yes	Yes	CD	Yes	Yes
Was loss to follow-up after baseline 20% or less?	Yes	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	NA	NA	NA	NA	NR	NR	NR	NR	Yes	NR	Yes	NR	NR	NR	Yes
QATOCCS quality rating	Good	Good	Good	Good	Fair	Fair	Fair	Fair	Good	Fair	Fair	Fair	Fair	Fair	Good

CD, cannot determine; NA, not applicable; NR, not reported.

Table 5

Description of frailty measurement tools

frailty measurement tools	Description
Not multidimensional	
FP	The phenotype of frailty as defined included the fulfilment of three out of five criteria: weight loss; exhaustion (fatigue); low physical activity; slowness.
SOF	The frailty as defined included the fulfilment of two out of three criteria: unexplained weight loss; inability to get up from a chair; fatigue.
HPMFI	Preoperative laboratory: indicators albumin, haematocrit and creatinine.
Multidimensional	
FI	Frailty was determined by measuring 70 health deficit indicators (symptoms, signs, functional impairment and laboratory abnormalities), involving self-care ability, psychological, physiological, cognitive and other aspects.
GFI	Frailty was determined by measuring functional loss in 4 areas: physical (activity function, multiple health problems, physical fatigue, vision, and hearing), cognitive (cognitive dysfunction), social (emotional isolation), and psychological (feelings of emotional depression and anxiety), with 15 entries.
Tilburg	Frailty was determined by measuring functional loss in 3 dimensions: Physical (physical health, weight, walking, balance, hearing, vision, grip strength, fatigue), psychological (memory, anxiety, depression, coping ability), social (living alone, social relationships, social support) .
CFS	A 7-point scale that assess physical activity, mobility, physical function and energy status.
MFS	Frailty was determined by measuring functional loss in 9-items: malignant disease, charlson comorbidity index, albumin, ADLs, IADLs, dementia, risk of delirium, mini nutritional assessment, midarm circumference.
mFI	Based on FI, 11 variables were extracted from the National Surgery Quality Improvement Program (NSQIP) database, including functional status, history of diabetes, respiratory problems, congestive heart failure, myocardial infarction, cardiac problems, arterial hypertension, delirium, history related to cognitive impairment or loss, cerebrovascular problems, and history of stroke/decreased peripheral pulses.

ADL, Activities of Daily Living; CFS, Clinical Frailty Scale; FI, frailty index; FP, frailty phenotype; GFI, Groningen Frailty Indicator; HPMFI, High Preoperative Modified Frailty Index; IADL, Instrumental Activities of Daily Living; mFI, Modified frailty index; MFS, Multidimensional Frailty Score; SOF, Study of Osteoporotic Fractures Frailty Index; TFI, Tilburg Frailty Indicator.

Frailty has a relation with hospital stay and readmission

In four of the included studies, compared with non-frail patients, patients with frailty were more likely to have a prolonged hospital stay, which was greater than 75% of the length of hospital stay[14,25,29,38]. However, a prospective study showed no association between preoperative frailty and length of hospital stay[37]. Two studies showed that frailty was positively associated with readmission at 90 days and 1 year due to postoperative complications or the development of stomach cancer[14,30].

Frailty has a relation with QoL, non-home discharge, and admission to ICU

The study of Miu and colleagues described the effect of frailty on QoL, with frailty exerting greater influence on the social and psychological dimensions of patients[25] Osaki *et al*.[34] confirmed that preoperative frailty is a predictor of non-home discharge in elderly patients with GC and transfer to a rehabilitation hospital or a chronic disease hospital. A retrospective study suggested that frailty increases the risk of postoperative ICU admission in patients with GC[35].

Discussion

In this study, the relationship between frailty and postoperative adverse outcomes in elderly patients with GC who were undergoing surgery was reviewed. The following findings were revealed. (1) The assessment tool of frailty was mostly subjective, with a variety of scales and different characteristics, and a large heterogeneity in frailty incidence. (2) Frailty is an effective predictor of postoperative adverse outcomes in a number of elderly patients with GC, but differences in correlation exist with each indicator, and studies on nursing indicators are few.

Study characteristics

Since 2014, studies on the correlation between frailty and adverse outcomes in elderly patients undergoing GC surgery have increased annually. More than 70% of the studies focused on East Asia, including China, South Korea, and Japan, because this region has the highest incidence and mortality of GC in the world[14], the primary cause of which was chronic gastritis caused by *Helicobacter pylori*, followed by smoking. Smoking and drinking are more common in the fattening population[39], and the lack of statistical adjustment for smoking may reduce the internal validity of the study. Vermillion and colleagues introduced smoking into the multifactor analysis, and Xu and colleagues included the influencing factors of smoking and drinking, and reported the relationship between fattening and outcome after adjusting for confounding factors[31,35]. In addition, no other factor data were observed. Among the included studies, four cross-sectional studies were of high quality, and the design did not involve exposure factors, and thus, the relationship between influencing factors and outcomes can only be roughly considered[14,25–27].

Assessment of frailty

In existing studies related to frailty in elderly GC patients, many types of frailty assessment tools are used, and no unified standard is accepted at this moment, making the integration of data for horizontal comparison difficult, which is also the primary reason for the large difference in incidence rates in such studies. As many as nine frailty assessment tools are used in the included literature, mostly using subjective reports from questionnaires, while a few studies used objective values, such as laboratory indicators. The questionnaire is based on two models with different characteristics. The Fried phenotype model only involves the assessment of physiology frail; if one item is met, then the score is 1 point, with fewer items and total score[14,26]. The cumulative flaw model considers that elderly patients should be comprehensively

evaluated, including physical, psychological, and social dimensions. Such tools are characterized by a large number of items and a long evaluation time; the higher the score, the higher the degree of debilitation[27,36]. After rough analysis, we found that the multidimensional tools were excellent predictors in unconventional health outcomes, such as non-home discharge and disability, but lower rates of complications and mortality were shown in the frail population which screened[14,36]. In addition, it showed that mFI screened for a lower frail rate than other tools, which may be related to the fact that it only has 11 entries[34,35].

The questionnaire evaluation method is simple and convenient, with accurate objective indicators, and it can be used for dynamic monitoring during postoperative rehabilitation. However, the biological indicators related to frailty should be studied. Current studies have shown that interleukin 6, tumour necrosis factor alpha (TNF-α), and 75 kDa soluble TNF-α receptor II are strongly correlated with frailty. Chronic inflammation is believed to be the underlying primary mechanism[40,41]. In the future, a combination of subjective and objective evaluation can be used to jointly build a standardized evaluation tool for the preoperative frailty monitoring of elderly GC patients, and a more appropriate frailty assessment tool for elderly Chinese patients can be developed based on the current international frailty assessment methods, combined with cultural background and demographic characteristics.

Relationship between frailty and adverse outcomes

Our scoping review shows that frailty is an essential factor and a good assessment tool for predicting postoperative complications, mortality, readmission rate, hospital days, readmissions, QoL, non-home discharge, and admission to ICU in patients with GC.

Patients with preoperative frailty have a higher risk of mild to severe complications than non-frail patients, but most studies have described only whether complications or severity will occur based on the Clavien–Dindo scale, rather than describing which specific complications were associated[25,36]. Su *et al.*[26] found that frailty is closely related to lung infections. Elderly patients with asthenia have poor lung elasticity and chest wall compliance, prone to ventilator fatigue and respiratory obstruction, and anaesthetic drugs and intraoperative mechanical ventilation will break the respiratory defense function, leading to the occurrence of lung infection[42]. The patient's movement is limited due to postoperative wound pain and catheter indentation, also increasing the risk of lung infection[43]. Meanwhile, another study showed that 28.5% of the patients had systemic complications, including intestinal obstruction, kidney failure, and pneumonia[38]. Xu *et al.*[35] proved that high frailty level would increase the risk of postoperative anastomotic fistula. Patients with weakness may show higher levels of acute reactants and clotting factors, such as CRP, factor VIII, and fibrinogen, after surgery, which correlates with the recovery of postoperative anastomotic fistula or surgical incision[44].

Frailty was negatively associated with postoperative survival in elderly patients with GC. From the perspective of time, it was divided into short-term and long-term survival, and the papers showed that the mortality rate was 0.7–5.6% within 30 days after surgery[31]. The 1-year mortality rate of elderly gastrointestinal surgery patients was 19%, and the studies show that the mortality rate of physiologically frail patients who underwent low-risk surgery before surgery was higher than that of normal patients who underwent high-risk surgery[10,36]. Moreover, frailty, one of the high-risk surgical factor of gastrectomy, would considerably increase the risk of postoperative death, and the mortality rate would be higher with a longer time[10]. From the point of view of cause of death, the influence of frailty on postoperative death is controversial. Msisawa *et al.*[32] suggested that frailty in stage I patients who received endoscopic treatment is primarily associated with non-cancer death, including heart failure, multiple organ failure, or other malignancies. Jeong *et al.*[28] showed that fadility mostly affected the specific survival time of tumours; that is, the death or recurrence of tumours was the key event, and the results showed that the primary cause of death after total gastrectomy in Stages II–IV patients was GC. In summary, this phenomenon may be related to tumour stage and surgical method. Therefore, in future studies, different study groups can be standardized to accurately identify preoperative frailty and achieve precise risk stratification of related complications.

The hospital days of patients with frailty is as high as 70%, and the effects of frailty on physical and psychological dimensions are more significant[25,29,38]. Age and frailty lead to decreased physiological reserve capacity, increased complication rates, or longer postoperative recovery time in the hospital after patients have suffered surgical trauma[14]. Patients with weakened mental endurance and social skills are more likely to achieve a healthy outcome after spending their recovery period in the hospital[45]. At present, Chinese hospitals do not include frailty in routine preoperative assessment. Medical staff should screen for frailty before surgery in a timely manner; develop a pre-rehabilitation plan, including psychological and social frailty care; and implement accurate and targeted vulnerability management.

Patients with additional frailty GC have an increased risk of readmission when compared with normal. Debilitated patients with an advanced tumour stage and age are more likely to be readmitted to the hospital within a year[14,30]. With the popularity of "enhanced recovery after surgery" theory in the world, patients will be discharged from the hospital in a weak and incomplete state, prone to unexpected increases in readmission rates. Current studies have shown that malnutrition and postoperative complications are the major factors that affect readmission rate, and they are significantly associated with frailty[14]. Studies have shown that the three pre-rehabilitation management for frailty, i.e., sports, psychology, and nutrition, can indirectly reduce the readmission rate[46,47]. In addition, Internet services have been widely used in discharge management, which can guide patients through remote network postoperative rehabilitation and timely solve exercise and psychological confusion.

In addition, only one study provided descriptions for each of the other three outcome indicators, presenting limitations. Miu *et al.* showed that frailty is related to low QoL, negative emotions, and social isolation of the elderly after surgery, making them prone to form a vicious circle, and affecting QoL after returning to the family[25]. In addition, the physical dysfunction caused by frailty is also an important factor in the decline of QoL, and physical and mental health can be promoted by appropriately increasing the activity program after surgery[48]. Frailty, complications, and surgery are predictors of non-home discharge, that is the nursing staff transfers patients who do not meet rehabilitation and nutritional standards to an appropriate nursing home, helping patients receive more specialized care during the long recovery period and ensuring the rational allocation of

medical resources in the hospital[34,49]. Xu *et al.*[35] showed that frailty was a more accurate predictor of ICU admission than the prognostic nutrition index, indicating that patients had less physiological reserve capacity and needed more intensive monitoring and instrument support after surgery.

In a meta-analysis conducted in 2023, Liang *et al.*[50] examined the correlation between frailty and poor long-term survival. In a meta-analysis in 2022, Wang *et al.*[51] examined GC patients with frailty may shorten survival after surgery. However, with the development of medical society, health outcomes should not be limited to traditional indicators, such as postoperative complications, survival time, etc. Medical personnel should pay attention to quality of life, self-care ability and negative emotions. It is possible to conduct large sample and multi-centre studies on other outcome measures in the future to apply fateful assessment to the full range of perioperative management to improve patient experience and satisfaction.

Limitations

However, our study has several limitations, as follows. The language of the included studies in this scope review was only in Chinese and English, resulting in an incomplete search. Specific reports of complications were lacking in the included literature; for example, frailty was associated with lung infection in only three of the articles. In addition, the number of high-quality literature is currently limited, and the relationship between exposure factors and outcomes is not described in detail, leading to high-risk bias.

Conclusion

This scoping review summarizes current studies on the relationship between frailty and postoperative adverse outcomes in elderly patients with GC, involving postoperative complications, mortality, length of stay, readmission rates, QoL, non-home discharge, and admission to ICU. The early recognition of the degree of frailty and timely intervention may be reduce the risk of prognosis effectively in elderly patients with GC. It is suggested to develop a unified frailty evaluation standard, add objective biological indicators, and develop dynamic monitoring in the future. With the development of the concept of "patient-centered", health outcomes are not limited to traditional indicators, but pay more attention to the quality of life, psychological and social conditions of patients. Our study has certain potential value, discussing a variety of adverse outcomes together and exploring which one will be more strongly related to frailty next step. With the continuous development of this research field, the implementation of accurate preoperative assessment, risk stratification, and personalized preoperative intervention for different populations is conducive to ensuring postoperative rehabilitation and health outcomes of GC patients.

Ethics approval and consent to participate

Not applicable.

Consent

Informed consent was not required for this review.

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Author contribution

Research design, data analysis and writing were conducted by Z.-K.-K.T. and W.-Z.T. Conceptualization by K.J. Supervision by L.Y., L.-Y.Q., D.-N.L. and X.C. All authors contributed to the critical review of the manuscript before submission.

Conflicts of interest disclosure

None of the authors declare a conflicts of interest.

Research registration unique identifying number (UIN)

UIN was not required for this review.

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