Comparing the Performance of Different Instruments for Diagnosing Frailty and Predicting Adverse Outcomes among Elderly Patients with Gastric Cancer

L. Ding^{1,*}, X. Miao^{1,*}, J. Lu², J. Hu¹, X. Xu³, H. Zhu¹, Q. Xu¹, S. Zhu¹

1. School of Nursing, Nanjing Medical University, Nanjing, China; 2. Department of Surgery, the First Affiliated Hospital of Nanjing Medical University, Nanjing, China; 3. Faculty of Health, Queensland University of Technology, Brisbane, Australia; * These authors contributed equally to this work and they are co-first authors: Lingyu Ding and Xueyi Miao

Corresponding Author: Qin Xu, Professor, School of Nursing, Nanjing Medical University, 101Longmian Avenue, Jiangning District, Nanjing, China, Email: qinxu@njmu.edu.cn; Shuqin Zhu, Associate Professor, School of Nursing, Nanjing Medical University, 101Longmian Avenue, Jiangning District, Nanjing, China, Email: zsq@njmu.edu.cn.

Abstract

OBJECTIVES: To examine the diagnostic performance of the Tilburg Frailty Indicator (TFI), 11-factor modified frailty index (mFI-11), and 5-factor modified frailty index (mFI-5) for frailty defined by Frailty Phenotype (FP), as well as to compare the predictive ability of TFI, mFI-11, and mFI-5 for adverse outcomes in hospital among elderly patients undergoing gastric cancer surgery.

DESIGN: A prospective cohort study.

SETTING: Hospitalization setting, Nanjing, China.

PARTICIPANTS: We recruited 259 elderly patients undergoing gastric cancer surgery from a tertiary hospital.

MEASUREMENTS: Frailty was assessed by the FP, TFI, mFI-11, and mFI-5 before surgery, respectively. The receiver operating characteristic (ROC) curves were plotted to compared the diagnostic performance of TFI, mFI-11, and mFI-5 using FP as the reference. ROC curves were used to examine the performance of TFI, mFI-11, and mFI-5 in predicting adverse outcomes. The area under the curve (AUC)>0.70 was regarded as an indicator of good performance.

RESULTS: The prevalence of frailty ranged from 8.5% (mFI-11) to 45.9% (TFI). The AUCs of TFI (AUC: 0.764, p<0.001) was significantly greater than that of mFI-11 (AUC: 0.600, p=0.033) and mFI-5 (AUC: 0.600, p=0.0311) in the detection of frailty defined by FP, with quite different sensitivity and specificity at their original cutoffs. TFI and mFI-11 both had statistically significant but similarly inadequate predictive accuracy for adverse outcomes in hospital, including total complications (AUCs: 0.618; 0.621), PLOS (AUCs: 0.593; 0.639), increased hospital costs (AUCs: 0.594; 0.624), and hypoproteinemia (AUCs: 0.573; 0.600). For the mFI-5, only the predictive ability for hypoproteinemia was statistically significant, with poor accuracy (AUC: 0.592, p<0.0055).

CONCLUSION: The TFI performed slightly better than mFI-11 and mFI-5 in our study. Moreover, future studies are needed to further determine an optimal frailty instrument with great diagnostic and predictive accuracy.

Key words: Elderly, frailty, diagnostic performance, predictive ability, gastric cancer.

Introduction

astric cancer is one of the major global health problems and it is the fourth leading cause of cancer-related death (1). Surgery is still the main therapeutic method (2). Due to the aging population, the number of elderly patients undergoing gastric cancer surgery

is gradually increasing. Their conditions have been seriously influenced by the tumor, aging, and multiple gastrointestinal symptoms, making the phenomenon of frailty prominent and common among them (3). Frailty is defined as a state of decreased physiologic reserves arising from cumulative deficits in multiple homeostatic systems (4). Elderly gastric cancer patients with frailty have a higher risk of adverse postoperative outcomes, such as complications, prolonged length of stay, increased hospital costs, and hypoproteinemia (5-7). Therefore, applying a suitable instrument to identify frailty precisely before surgery and predict adverse outcomes effectively is significant for perioperative management among elderly gastric cancer patients.

There are three widely used conceptual models regarding frailty, including the biological model, deficit accumulation model, and integrative conceptual model. Among them, the biological model is one of the most classical models and reveals the internal physiological process of frailty. Frailty phenotype (FP) is developed based on this model (8). FP is the most commonly used frailty instrument and comprises self-report items as well as objective physical measures (grip strength, walking speed). Although there is still no "gold standard" regarding frailty instruments, FP has been considered as an operational definition of frailty by the American Geriatrics Association and is recognized as one of the optimal risk assessment tools for elderly gastric cancer patients undergoing surgery (9, 10). Another representative instrument of frailty is the frailty index (FI). It is derived from the model of deficit accumulation, which assumes that frailty is a state caused by the accumulation of health deficits in a lifetime (11). However, the original FI is less attractive due to the overload of items (70 items). Thus, 11-factor modified Frailty Index (mFI-11) is developed, which maps the 70 variables from the original FI to 11 preexisting variables from the National Surgical Quality Improvement Program (NSQIP) database (12). Later on, mFI-11 is simplified to a 5-factor modified Frailty Index (mFI-5) (13). Both mFI-11 and mFI-5 can be calculated based on medical records easily. Finally, the most frequently used instrument based on the integrative conceptual model is Tilburg Frailty Indicator (TFI) (14). It expands the dimension of frailty and identifies frailty from three aspects: physical, psychological, and social domains through 15 simple self-report items.

Although FP is considered as an operational definition of frailty, applying FP requires specific equipment and expertise for measuring grip strength and gait speed, which are not always feasible in a busy surgical oncology setting (15). It is necessary to explore whether TFI, mFI-11, and mFI-5, which are concise in items and avoid tedious physical measurement, can be used to replace FP for frailty identification and predicting adverse outcomes in elderly gastric cancer patients undergoing surgery. Some previous studies have compared the performance of these three instruments for diagnosing frailty and predicting adverse outcomes among institutionalized, community-dwelling, inpatient elderly patients (16-18). However, among elderly gastric cancer patients undergoing surgery, the capacity of these instruments for detecting frailty needs further exploration and it remains unclear which frailty instrument has the best predictive accuracy for adverse postoperative outcomes.

Therefore, our study aimed to compare the diagnostic performance of TFI, mFI-11, and mFI-5 for FP-defined frailty, as well as to compare their predictive ability for adverse outcomes among elderly gastric cancer patients undergoing surgery.

Methods

Study design and participants

We conducted a prospective cohort study among elderly patients with gastric cancer at a tertiary hospital in Jiangsu Province, China from March 2021 to July 2021.

The inclusion criteria included patients who: (1) were diagnosed with gastric cancer by endoscopy or pathology; (2) would undergo radical surgery for the first time; (3) aged ≥60 years; (4) signed informed consents and agreed to participate in this study. The exclusion criteria included patients who: (1) had a severe physical disability or cognitive impairment; (2) received preoperative radiotherapy or chemotherapy; (3) combined with other sites of malignant cancers.

The study was approved by the Ethics Committee of Nanjing Medical University, Jiangsu, China (Number: 2020-273). The study was verified by the Chinese Clinical Trial Registry (Number: ChiCTR2100047064).

Measurements

Baseline information

Data were collected on demographic characteristics (age, gender, BMI, marital status, and education), and disease-related information (cancer stage, type of surgery, and nutritional risk screening).

Frailty instruments

The enrolled patients would be measured for frailty within 24 hours after admission using the following four instruments.

The FP includes five components: exhaustion, weight loss,

low physical activity, handgrip strength, and slowness (8). The scores of FP range from 1 to 5. Frailty is defined as a score of 3 to 5. Exhaustion and weight loss were self-report items; low physical activity was assessed using the International Physical Activity Questionnaire-Short Form (IPAQ-SF); handgrip strength was measured on the dominant hand using an electronic hand dynamometer (EH101, Guangdong Province, China); slowness was evaluated using gait speed measurement. More details and measurement criteria are available in "Chinese expert consensus on frailty management" (19). Considering that FP is widely used and recognized, we chose it as the reference standard for the diagnosis of frailty.

The TFI comprises 15 self-report items focusing on physical, psychological, and social domains (14). The 8 items of the physical domain are poor physical health, unexplained weight loss, difficulty in walking, difficulty in maintaining balance, poor hearing, poor vision, lack of strength in hands, and physical tiredness. The 4 items of the psychological domain are problems with memory, feeling down, feeling nervous or anxious, and being unable to cope with problems. The 3 items of the social domain include living alone, lack of social relations loneliness, and lack of social support. The scores of TFI range from 0-15, and a score of 5-15 represents frailty. The TFI has been extensively culturally adapted and validated in China (20).

The mFI-11 consists of the following 11 variables: diabetes; functional status; chronic obstructive pulmonary disease (COPD) or pneumonia; congestive heart failure (CHF); history of myocardial infarction; hypertension requiring medication; peripheral vascular disease or rest pain; impaired sensorium; history of either transient ischemic attack or cerebrovascular accident; history of cerebrovascular accident with neurologic deficit; and prior percutaneous coronary intervention, previous coronary surgery, or history of angina (12). Besides, mFI-5 is simplified from mFI-11 and comprises the following 5 variables: diabetes; functional status; COPD or pneumonia; CHF; hypertension requiring medication (13). The mFI-11 and mFI-5 are calculated by the number of variables present divided by the total variables. An mFI-11 score ≥ 0.27 and an mFI-5 score ≥ 0.4 are defined as frailty, respectively. Both mFI-11 and mFI-5 have been used and validated among elderly surgical patients in China (21, 22).

Outcome measures

The primary outcome was postoperative complications in hospital graded by Clavien-Dindo classification. Total complications were considered as Clavien-Dindo grade ≥ 2 according to previous studies (23).

The secondary outcomes were prolonged length of stay (PLOS), increased hospital costs, and postoperative hypoproteinemia. Based on previous studies, PLOS was defined as a duration (from date of admission to date of discharge) exceeding the 75th percentile in this cohort (24); increased hospital costs were defined as costs greater than the 75th percentile of the entire cohort (24); hypoproteinemia was defined as serum albumin levels<35 g/L at discharge (25).

Variables	n (%)/Mean±SD	Variables	n (%)	
Age (years)	69.1±5.4	FP (0-5)		
BMI (kg/m²)	23.6±2.9	Frail (≥3)	51(19.7)	
Gender		Non-frail (<3)	208(80.3)	
Male	197(76.1)	TFI (0-15)		
Female	62(23.9)	Frail (≥5)	119(45.9)	
Marital status		Non-frail (<5)	140(54.1)	
Married or cohabiting	238(91.9)	mFI-11(0-1)		
Not married or divorced	2(0.8)	Frail (≥0.27)	22(8.5)	
Widowed	19(7.3)	Non-frail (<0.27)	237(91.5)	
Education		mFI-5(0-1)		
Primary or lower	131(50.6)	Frail (≥0.4)	54(20.8)	
Middle or high school	107(41.3)	Non-frail (<0.4)	205(79.2)	
Bachelor degree or higher	21(8.1)	Postoperative complications		
NRS2002		Grade≥2	59(22.8)	
≥3	34(13.1)	Grade<2	200(77.2)	
<3	225(86.9)	Length of stay		
Surgical approach		PLOS	63(24.3)	
Open	62(23.9)	Non-PLOS	196(75.7)	
Laparoscopic	197(76.1)	Hospital costs		
Cancer stage *		Increased hospital costs	65(25.1)	
I	83(32)	Non-Increased hospital costs	194(74.9)	
II	69(26.6)	Albumin(g/L)		
III	101(39)	≥35	155(59.8)	
IV	6(2.3)	<35	104(40.2)	

Note. FP, Frailty Phenotype; TFI, Tilburg Frailty Indicator; mFI-11, 11-factor modified Frailty Index; mFI-5, 5-factor modified Frailty Index; PLOS, Prolonged Length of Stay; BMI, Body Mass Index; NRS2002, Nutritional Risk Screening 2002; * Cancer Stage was graded by Tumor Node Metastasis (TNM).

Statistical analysis

The sample characteristics were described by means (with standard deviations) for continuous variables and frequencies (with percentages) for categorical variables.

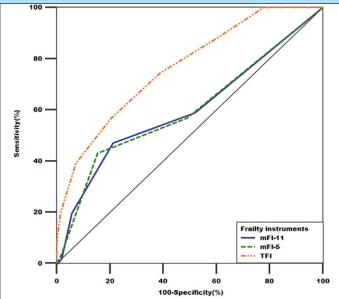
The sample size was estimated based on the PASS version 15.0 (PASS 15 Power Analysis and Sample Size Software, NCSS, LLC). One previous study showed that the prevalence of frailty in preoperative patients with gastric cancer was 17.71% (3). Considering the missing rate of 5%, the minimum sample in our study was 254 patients. The receiver operating characteristic curves (ROCs) were plotted to compared the diagnostic performance of TFI, mFI-11, and mFI-5 for frailty using FP as the reference stand. Meanwhile, ROCs were used to examine the performance of TFI, mFI-11, and mFI-5 for predicting adverse outcomes. The area under the curve (AUC)>0.70 was regarded as an indicator of good performance (26). The nonparametric method described by DeLong et al. was used to performed ROC contrasts between individual frailty instruments and ascertain if there is a statistical difference in AUCs (27). The detailed statistic on sensitivity and specificity were used to compare the clinical validity of each instrument in diagnostic performance and predictive performance, respectively. Statistical analysis was performed using MedCalc for Windows version 19.0 (MedCalc Software, Ostend, Belgium). Statistical significance was defined as a p<0.05.

Results

Participants characteristics

A total of 259 patients were ultimately enrolled in the study. The mean age of study participants was 69.1±5.4 years, with a predominance of male (76.1%). The prevalence of frailty measured by different instruments ranged from 8.5% (mFI-11) to 45.9% (TFI). For the adverse outcomes, the incidence of total complications, PLOS, increased hospital costs, and hypoproteinemia was 22.8%, 24.3%, 25.1%, and 40.2%, respectively. The detailed characteristics of the participants are described in Table 1.

Figure 1. The ROC curves of TFI, mFI-11and mFI-5 against the FP for diagnosis of frailty



Note. ROC contrast: TFI vs mFI-11, P=0.0008; TFI vs mFI-5, P=0.0012; mFI-11 vs mFI-5, P=0.9883. Abbreviations: FP, Frailty Phenotype; TFI, Tilburg Frailty Indicator; mFI-11, 11-factor modified Frailty Index; mFI-5, 5-factor modified Frailty Index; ROC, Receiver Operating Characteristic.

Diagnostic performance for FP-defined frailty

AUCs of TFI, mFI-11 and mFI-5 against the FP for diagnosis of frailty were 0.764 [95%confidence interval (CI): 0.707-0.814; P<0.001], 0.600 (95%CI: 0.538-0.660; P=0.033) and 0.600 (95%CI: 0.538-0.660; P=0.0311), respectively. On ROC contrasts, the AUC of TFI was greater than that of mFI-11 (p=0.0008) and mFI-5 (p=0.0012) in the detection of frailty defined by FP (Figure 1).

At their original cutoffs, the sensitivity of TFI (56.86%) was higher than that of mFI-11 (1.96%) and mFI-5 (3.92%), while the specificity of TFI (79.33%) was lower than that of mFI-11 (98.08%) and mFI-5 (98.08%). At the optimal cutoffs of mFI-11 (0.09) and mFI-5 (0.2), their sensitivity and specificity both tended to be balanced. The optimal cutoff of the TFI was identical to the original cutoff. Table 2 summarizes the diagnostic properties of TFI, mFI-11, and mFI-5 for FP-defined frailty.

Predictive performance for adverse outcomes

TFI and mFI-11 both had statistically significant but inadequate predictive accuracy for adverse outcomes,

including total complications (AUCs: 0.618; 0.621), PLOS (AUCs: 0.593; 0.639), increased hospital costs (AUCs: 0.594; 0.624), and hypoproteinemia (AUCs: 0.573; 0.600). For mFI-5, the predictive ability for hypoproteinemia exclusively was statistically significant, but with poor accuracy (AUC: 0.592).

On ROC contrasts, the predictive accuracy of mFI-11 for total complications and increased hospital costs were better than that of mFI-5. Additionally, there was no statistically significant difference between mFI-11 and TFI in the prediction of four adverse outcomes (Figure 2). The detailed results of predictive performance for adverse outcomes are shown in Table 3.

Discussion

In our study, the prevalence of frailty measured by different instruments ranged from 8.5% to 45.9%. ROC analyses showed that TFI had better diagnostic accuracy in the detection of frailty defined by FP compared with mFI-11 and mFI-5. Besides, TFI and mFI-11 had similarly ability for predicting four adverse outcomes, while the predictive ability of mFI-5 for hypoproteinemia exclusively was statistically significant among elderly patients undergoing gastric cancer surgery.

Our results revealed that the prevalence of frailty varied widely when using different instruments, which is consistent with previous studies among hospitalized and community-dwelling elderly adults (17, 18). Furthermore, we found that the frailty prevalence measured by TFI was higher than the rest of two instruments. The possible reason is that mFI-11 and mFI-5 are purely focus on the physiological level, while TFI also includes psychological and social domains except for physical domains. In the hospital setting, most elderly gastric cancer patients suffer from psychological and social issues, such as anxiety, depression, and low social support, which only can be identified by TFI as part of the determination of frailty (28).

Our findings demonstrated that TFI had significantly better diagnostic performance for frailty defined by FP compared with mFI-11 and mFI-5. This can be explained by the fact that although the TFI and FP are derived from different conceptual models, there is still some overlap in their physical domains (8,14). In contrast, either mFI-11 or mFI-5 mainly focus on the medical history, which is more similar with the concept of comorbidity instead of physical status (12). Some patients with gastric cancer can be judged as frailty through TFI and FP because of poor physical performance mainly caused by the tumor and digestive tract symptoms. While mFI-11 and mFI-5 may neglect the specific poor functional status so that the physical frailty cannot be identified by them completely

Table 2. Diagnostic performance of TFI, mFI-11 and mFI-5 using the FP as reference Standard (N=259)

Table 21 Diagnostic performance of 111, mil 111 and mil 13 asing the 11 as reference standard (17 237)							
	Cut-off	Sensitivity, %	Specificity, %	+LR	-LR	AUC (95% CI)	P value
TFI (0-15) *	≥5	56.86	79.33	2.75	0.54	0.764(0.707-0.814)	< 0.001
mFI-11(0-1)	≥0.27	1.96	98.08	1.02	1.00	0.600(0.538-0.660)	0.033
	≥0.09	47.06	78.85	2.22	0.67		
mFI-5(0-1)	≥0.4	3.92	98.08	2.04	0.98	0.600(0.538-0.660)	0.0311
	≥0.2	43.14	84.62	2.80	0.67		

Note. FP, Frailty Phenotype; TFI, Tilburg Frailty Indicator; mFI-11, 11-factor modified Frailty Index; mFI-5, 5-factor modified Frailty Index; +LR, Positive Likelihood Ratio; -LR, Negative Likelihood Ratio; *The optimal and original cut-points of TFI were identical; The optimal cut-points of mFI-11 and mFI-5 were in bold font; AUC, Area Under the Curve.

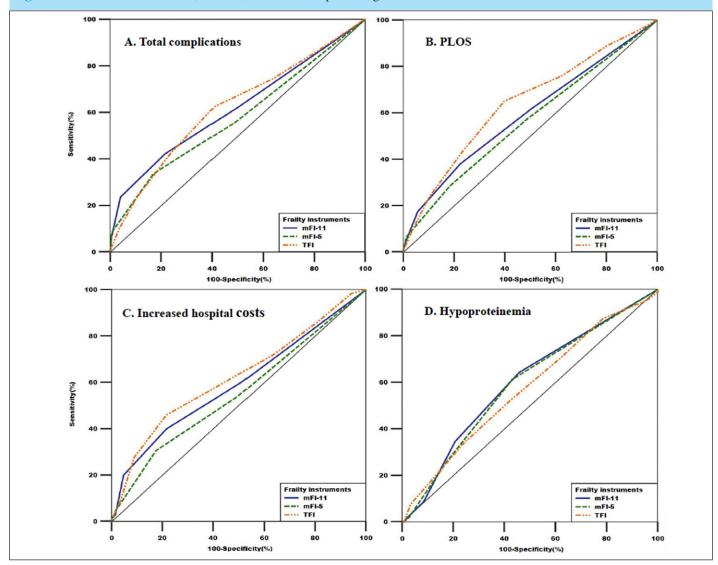


Figure 2. The ROC curves of TFI, mFI-11, and mFI-5 for predicting adverse outcomes

Note. ROC contrasts: Total complication: TFI vs mFI-11, P=0.9553; TFI vs mFI-5, P=0.4102; mFI-11 vs mFI-5, P=0.0221. PLOS: TFI vs mFI-11, P=0.3103; TFI vs mFI-5, P=0.1186; mFI-11 vs mFI-5, P=0.0848. Increased hospital costs: TFI vs mFI-11, P=0.5407; TFI vs mFI-5, P=0.1720; mFI-11 vs mFI-5, P=0.0154. Hypoproteinemia: TFI vs mFI-11, P=0.5563; TFI vs mFI-5, P=0.6777; mFI-11 vs mFI-5, P=0.4869. Abbreviations: TFI, Tilburg Frailty Indicator; mFI-11, 11-factor modified Frailty Index; mFI-5, 5-factor modified Frailty Index; PLOS, Prolonged Length of Stay: ROC. Receiver Operating Characteristic.

(29). Hence, it was unsurprising that mFI-11 and mFI-5 had the poor diagnostic capability for FP-defined frailty among elderly gastric cancer patients.

We found that the sensitivity and specificity of mFI-11, mFI-5, and TFI were quite different at their original cutoffs for discovering frailty. TFI had higher sensitivity compared with mFI-11 and mFI-5, which results in a low false-negative rate, and more elderly gastric cancer patients being frail are identified. This might be crucial as it allows for early warning and intervention as much as possible for elderly gastric cancer patients who are in poor health status (30). Simultaneously, both mFI-11 and mFI-5 had higher specificity than TFI, which contributes to a low false-positive rate and more elderly gastric cancer patients being non-frail can be detected. This can largely avoid adverse psychological impacts on patients and unnecessary medical interventions. In practice, the use of highly sensitive or specific instruments for detecting frailty should depend on the specific context (31). In our study, medical

resources during hospitalization are relatively abundant. To improve the safety and reliability of perioperative management of elderly gastric cancer patients who are originally should be focused on, higher sensitivity may be more important for frailty instruments. Additionally, the optimal cutoff of TFI for diagnosis of frailty was identical with the original cutoff, whereas the optimal cutoffs of mFI-11 (0.27 to 0.09) and mFI-5 (0.4 to 0.2) were both decreased, with more balanced sensitivity and specificity in detection of frailty. It indicates that the cut-off of mFI-11 or mFI-5 can be appropriately adjusted to make it more suitable for elderly gastric cancer patients during hospitalization.

Our findings revealed that mFI-11 had better ability for predicting total complications and increased hospital costs than mFI-5 among elderly gastric cancer patients undergoing surgery. Possibly because mFI-5 lacks some important variables that reflect cardiovascular and cerebrovascular health, such as history of transient ischemic attack, cerebrovascular accident,

Table 3. Predictive performance of TFI, mFI-11 and mFI-5 at original cutoffs for adverse outcomes (N=259)

Table 3. Fredictive performance of 1F1, mF1-11 and mF1-3 at original cutoffs for adverse outcomes (N=239)								
	Cut-off	Sensitivity, %	Specificity, %	+LR	-LR	AUC (95% CI)	P value	
Total complications								
TFI (0-15)	≥5	42.37	76.5	1.8	0.75	0.621(0.559-0.681)	0.0048	
mFI-11(0-1)	≥0.27	6.78	99.5	13.56	0.94	0.618(0.556-0.678)	0.0061	
mFI-5(0-1)	≥0.4	8.47	99.5	16.95	0.92	0.577(0.514-0.637)	0.0730	
PLOS								
TFI (0-15)	≥5	42.86	77.04	1.87	0.74	0.639(0.578-0.698)	0.0007	
mFI-11(0-1)	≥0.27	4.76	98.98	4.67	0.96	0.593(0.531-0.654)	0.023	
mFI-5(0-1)	≥0.4	6.35	98.98	6.22	0.95	0.565(0.502-0.626)	0.1076	
Increased hospital costs								
TFI (0-15)	≥5	46.15	78.35	2.13	0.69	0.624 (0.562-0.683)	0.0035	
mFI-11(0-1)	≥0.27	3.08	98.45	1.99	0.98	0.594 (0.531-0.654)	0.0237	
mFI-5(0-1)	≥0.4	4.62	98.45	2.98	0.97	0.552(0.490-0.614)	0.1942	
Hypoproteinemia								
TFI (0-15)	≥5	33.65	76.13	1.41	0.87	0.573(0.510-0.634)	0.0424	
mFI-11(0-1)	≥0.27	1.92	98.06	0.99	1	0.600(0.538-0.660)	0.003	
mFI-5(0-1)	≥0.4	1.92	97.42	0.75	1.01	0.592(0.530-0.653)	0.0055	

Note. FP, Frailty Phenotype; TFI, Tilburg Frailty Indicator; mFI-11, 11-factor modified Frailty Index; mFI-5, 5-factor modified Frailty Index; PLOS, Prolonged Length of Stay; +LR, Positive Likelihood Ratio; -LR, Negative Likelihood Ratio; AUC, Area Under the Curve.

and prior percutaneous coronary intervention, which are closely related to the adverse outcomes (32,33). Meanwhile, the differences between AUCs of TFI and mFI-11 for predicting adverse outcomes were not statistically significant, and their AUCs were both lower than 0.7, implying that TFI and mFI-11 had comparable ability to predict adverse outcomes, but none of them had an adequate predictive performance. These results are consistent with prior studies. Andreasen et al found that TFI had inadequate accuracy for predicting adverse outcomes in acutely admitted elderly patients (AUC=0.64) (34). Another study concluded that mFI-11 had poor ability to predict major complications among hospitalized elderly patients (AUC=0.645) (35). The inadequate predictive performance of these frailty instruments for adverse clinical outcomes may be explained by the particularity of the participants both in our and previous studies. Among the elderly hospitalized patients, especially the elderly gastric cancer patients undergoing surgery, there are many other problems except for frailty, such as malnutrition and sarcopenia (36, 23). All of these will increase the risk of adverse outcomes. This indicates that using the frailty instrument alone is limited for predicting adverse outcomes in elderly hospitalized patients. A previous study found that adding frailty instruments to current commonly used surgical risk assessment tools, including the American Society of Anesthesiologists (ASA) score and Estimation of Physiologic Ability and Surgical Stress (E-PASS) score can improve the capacity of predicting complications among elderly patients undergoing surgery (37). It implies that we should combine frailty instruments with other effective risk assessment tools in clinical practice to fully improve the quality of in-hospital care for elderly gastric cancer patients undergoing surgery.

At last, although the items of mFI-11 and mFI-5 can be found in electronic health records, which promotes the

feasibility and time-efficiency in practice (38). Given that their inadequate diagnostic performance for frailty and the poor predictive ability of mFI-5 for adverse outcomes, both mFI-11 and mFI-5 do not seem to be suitable frailty instruments for elderly gastric cancer patients undergoing surgery. TFI is simple and convenient to use as a self-reported scale. It can also be assessed by e-mail and telephone, improving the practicability of identifying frailty and predicting adverse outcomes among elderly gastric cancer during hospitalization and post-discharge period (39). Based on its good diagnostic performance for FP-defined frailty and acceptable predictive accuracy for adverse outcomes, TFI appeared to be the most suitable instrument in our study.

Some limitations in our study should be noticed. First, our participants were recruited from a single hospital, which might limit the generalizability of the findings to other hospitals with different medical technology and resources. Additionally, we only involved three instruments in our study. Given that more and more frailty instruments are being developed and applied, the performance of other validated tools needs to be explored among elderly patients with gastric cancer. Moreover, the adverse outcomes in the present study were limited to in-hospital indicators, some important long-term outcomes should be taken into consideration in the future.

Conclusion

In summary, the TFI performed slightly better than mFI-11 and mFI-5 in our study. Moreover, there is still a need to further investigate one optimal instrument which can not only diagnose frailty well but also accurately predict the risk of adverse outcomes among elderly gastric cancer patients. In practice, the detection of frailty should be integrated into routine assessments to improve the quality of perioperative

management among elderly patients with gastric cancer. Finally, except for objective outcomes, further studies should also focus on the predictive ability of diverse frailty instruments for predicting meaningful subjective indicators such as quality of life.

Acknowledgments: We thank the support of the National Natural Science Foundation of China (NSFC) and Jiangsu Higher Education Institutions for this study.

Fundings: Project "The exploration of trajectories and intervention program of frailty for gastric cancer survivors based on the health ecology theory" supported by NSFC (No.82073407); Project "Studies on Construction of Core Competency Model and Development of Assessment Tool for Nurses of Hospice Care" supported by NSFC (No.72004099); Project of "Nursing Science" Funded by the Priority Discipline Development Program of Jiangsu Higher Education Institutions (General Office, the People's Government of Jiangsu Province, 2018, No.87).

Declarations of interest: The authors declare no conflicts of interests

Ethical standards: The study complies with the current laws of the country in which it was performed.

References

- Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-249. doi: 10.3322/caac.21660.
- Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 2017;20:1-19. doi: 10.1007/s10120-016-0622-4.
- Tanaka T, Suda K, Inaba K, et al Impact of Frailty on Postoperative Outcomes for Laparoscopic Gastrectomy in Patients Older than 80 Years. Ann Surg Oncol 2019;26:4016-4026. doi: 10.1245/s10434-019-07640-0.
- Proietti M, Cesari M. Frailty: What Is It? Adv Exp Med Biol. 2020;1216:1-7. doi: 10.1007/978-3-030-33330-0_1.
- Ding L, Lu J, Zhu H, et al. Effects of preoperative frailty on outcomes following surgery among patients with digestive system tumors: A systematic review and metaanalysis. Eur J Surg Oncol 2021; 23:S0748-7983. doi: 10.1016/j.ejso.2021.07.019.
- Richards SJG, Cherry TJ, Frizelle FA, et al. Pre-operative frailty is predictive of adverse post-operative outcomes in colorectal cancer patients. ANZ J Surg 2021;91:379-386. doi: 10.1111/ans.16319.
- Mailliez A, Guilbaud A, Puisieux F, et al. Circulating biomarkers characterizing physical frailty: CRP, hemoglobin, albumin, 25OHD and free testosterone as best biomarkers. Results of a meta-analysis. Exp Gerontol 2020;139:111014. doi: 10.1016/j.exper.2020.111014.
- Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:M146-156. doi: 10.1093/ gerona/56.3.m146.
- Chow WB, Rosenthal RA, Merkow RP, et al. Optimal preoperative assessment
 of the geriatric surgical patient: a best practices guideline from the American
 College of Surgeons National Surgical Quality Improvement Program and the
 American Geriatrics Society. J Am Coll Surg 2012;215:453-66. doi: 10.1016/j.
 jamcollsurg.2012.06.017.
- Lu J, Cao LL, Zheng CH, et al. The Preoperative Frailty Versus Inflammation-Based Prognostic Score: Which is Better as an Objective Predictor for Gastric Cancer Patients 80 Years and Older? Ann Surg Oncol. 2017;24:754-762. doi: 10.1245/s10434-016-5656-7
- Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. Scientific World Journal 2001;1:323-326. doi: 10.1100/tsw.2001.58.
- Velanovich V, Antoine H, Swartz A, et al. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. J Surg Res 2013;183:104-110. doi: 10.1016/j.jss.2013.01.021.
- Subramaniam S, Aalberg JJ, Soriano RP, et al. New 5-Factor Modified Frailty Index Using American College of Surgeons NSQIP Data. J Am Coll Surg. 2018;226:173-181. doi: 10.1016/j.jamcollsurg.2017.11.005.
- Gobbens RJ, van Assen MA, Luijkx KG, et al. The Tilburg Frailty Indicator: psychometric properties. J Am Med Dir Assoc 2010;11:344-355. doi: 10.1016/j. jamda.2009.11.003.
- Kapoor A, Matheos T, Walz M, et al. Self-Reported Function More Informative than Frailty Phenotype in Predicting Adverse Postoperative Course in Older Adults. J Am Geriatr Soc 2017;65:2522-2528. doi: 10.1111/jgs.15108.
- Si H, Jin Y, Qiao X, et al. Comparing Diagnostic Properties of the FRAIL-NH Scale and 4 Frailty Screening Instruments among Chinese Institutionalized Older Adults. J Nutr Health Aging 2020;24:188-193. doi: 10.1007/s12603-019-1301-z.
- Si H, Jin Y, Qiao X, et al. Comparison of 6 frailty screening tools in diagnostic properties among Chinese community-dwelling older people. Geriatr Nurs 2021;42:276-282. doi: 10.1016/j.gerinurse.2020.08.017.

- Chong E, Ho E, Baldevarona-Llego J, et al. Frailty and Risk of Adverse Outcomes in Hospitalized Older Adults: A Comparison of Different Frailty Measures. J Am Med Dir Assoc. 2017;18:638. doi: 10.1016/j.jamda.2017.04.011.
- Geriatric Branch of Chinese Medical Association. Chinese experts' consensus on assessment and intervention for elderly patients with frailty. Chinese Journal of Geriatrics 2017;36:251-256. doi:10.3760/cma.j.issn.0254-9026.2017.03.007.
- Dong L, Liu N, Tian X, et al. Reliability and validity of the Tilburg Frailty Indicator (TFI) among Chinese community-dwelling older people. Arch Gerontol Geriatr 2017;73:21-28. doi: 10.1016/j.archger.2017.07.001.
- Chen Y, Qin J. Modified Frailty Index Independently Predicts Postoperative Delirium and Delayed Neurocognitive Recovery After Elective Total Joint Arthroplasty. J Arthroplasty 2021;36(2):449-453. doi: 10.1016/j.arth.2020.07.074.
- Sun W, Han Q. Relationship between modified frailty index and complications after laparoscopic radical nephrectomy. Clin J Med Office 2021;49(7):815-816,819. doi:10. 16680/j.1671-3826.2021.07.39.
- Hua H, Xu X, Tang Y, et al. Effect of sarcopenia on clinical outcomes following digestive carcinoma surgery: a meta-analysis. Support Care Cancer 2019;27:2385-2394. doi: 10.1007/s00520-019-04767-4.
- Smits FJ, Verweij ME, Daamen LA, et al. Impact of Complications After Pancreatoduodenectomy on Mortality, Organ Failure, Hospital Stay, and Readmission: Analysis of a Nationwide Audit. Ann Surg 2020 Jun 3. doi: 10.1097/ SLA.0000000000003835.
- Hu WH, Eisenstein S, Parry L, et al. Preoperative malnutrition with mild hypoalbuminemia associated with postoperative mortality and morbidity of colorectal cancer: a propensity score matching study. Nutr J 2019;18:33. doi: 10.1186/s12937-019-0458-y.
- Drubbel I, Numans ME, Kranenburg G, et al. Screening for frailty in primary care: a systematic review of the psychometric properties of the frailty index in communitydwelling older people. BMC Geriatr 2014;14:27. doi: 10.1186/1471-2318-14-27.
- DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44(3):837-845.
- Hong JS, Tian J. Prevalence of anxiety and depression and their risk factors in Chinese cancer patients. Support Care Cancer 2014;22:453-459. doi: 10.1007/s00520-013-1997-y.
- Vetrano DL, Palmer K, Marengoni A, et al. Frailty and Multimorbidity: A Systematic Review and Meta-analysis. J Gerontol A Biol Sci Med Sci 2019;74:659-666. doi: 10.1093/gerona/gly110.
- Ambagtsheer RC, Beilby JJ, Visvanathan R, et al. Should we screen for frailty in primary care settings? A fresh perspective on the frailty evidence base: A narrative review. Prev Med 2019;119:63-69. doi: 10.1016/j.ypmed.2018.12.020.
- Dent E, Morley JE, Cruz-Jentoft AJ, et al. Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management. J Nutr Health Aging 2019;23:771-787. doi: 10.1007/s12603-019-1273-z.
- Hacke W, Bassand JP, Virdone S, et al. Prior stroke and transient ischemic attack as risk factors for subsequent stroke in atrial fibrillation patients: A report from the GARFIELD-AF registry. Int J Stroke 2020;15:308-317. doi: 10.1177/1747493019891516.
- Lu DY, Saybolt MD, Kiss DH, et al. One-Year Outcomes of Percutaneous Coronary Intervention in Patients with End-Stage Liver Disease. Clin Med Insights Cardiol 2020;14:1179546820901491. doi: 10.1177/1179546820901491.
- Andreasen J, Aadahl M, Sørensen EE, et al. Associations and predictions of readmission or death in acutely admitted older medical patients using self-reported frailty and functional measures. A Danish cohort study. Arch Gerontol Geriatr 2018;76:65-72. doi: 10.1016/j.archger.2018.01.013.
- Lascano D, Pak JS, Kates M, et al. Validation of a frailty index in patients undergoing curative surgery for urologic malignancy and comparison with other risk stratification tools. Urol Oncol 2015;33:426.e1-12. doi: 10.1016/j.urolone.2015.06.002.
- Guo ZQ, Yu JM, Li W, et al. Survey and analysis of the nutritional status in hospitalized patients with malignant gastric tumors and its influence on the quality of life. Support Care Cancer 2020;28:373-380. doi: 10.1007/s00520-019-04803-3.
- Kapoor A, Matheos T, Walz M, et al. Self-Reported Function More Informative than Frailty Phenotype in Predicting Adverse Postoperative Course in Older Adults. J Am Geriatr Soc 2017;65:2522-2528. doi: 10.1111/jgs.15108.
- Pandit V, Khan M, Martinez C, et al. A modified frailty index predicts adverse outcomes among patients with colon cancer undergoing surgical intervention. Am J Surg 2018;216:1090-1094. doi: 10.1016/j.amjsurg.2018.07.006.
- Gobbens RJ, Uchmanowicz I. Assessing Frailty with the Tilburg Frailty Indicator (TFI): A Review of Reliability and Validity. Clin Interv Aging 2021;16:863-875. doi: 10.2147/CIA.S298191.

How to cite this article: L. Ding, X. Miao, J. Lu, et al. Comparing the Performance of Different Instruments for Diagnosing Frailty and Predicting Adverse Outcomes among Elderly Patients with Gastric Cancer. J Nutr Health Aging. 2021;25(10):1241-1247, http://dx.doi.org/10.1007/s12603-021-1701-8