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수술 후 사망률을 예측하기 위한 다면적 노쇠 평가 도구 개발

Multidimensional Frailty Score for the Prediction of Postoperative Mortality Risk

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김 선 욱

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Multidimensional Frailty Score for the Prediction of Postoperative Mortality Risk

by

Sun-wook Kim

A thesis submitted to the Department of Internal Medicine in partial fulfillment of the requirements for the Degree of Master of Science in Internal Medicine at Seoul National University College of Medicine

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Approved by Thesis Committee:

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ABSTRACT

Background: The number of geriatric patients who undergo surgery has been increasing, and they show an increased mortality rate after surgery compared to younger patients. However there are insufficient tools to predict post-operative outcomes in older surgical patients. We aimed to design a predictive model for adverse outcomes in older surgical patients.

Methods: From October 19, 2011, to July 31, 2012, we enrolled 275 consecutive elderly patients (aged ≥ 65 years) undergoing intermediate-risk or high-risk elective operations in the Department of Surgery of single tertiary hospital. Comprehensive geriatric assessment (CGA) was performed before surgery, and we developed a new scoring model to predict 1-year all-cause mortality using the results of CGA. The secondary outcomes were postoperative complications (eg, pneumonia, urinary tract infection, delirium, acute pulmonary thromboembolism, and unplanned intensive care unit admission), length of hospital stay, and discharge to nursing facility.

Results: Twenty-five patients (9.1%) died during the follow-up period (median [interquartile range], 13.3 [11.5-16.1] months), including 4 in-hospital deaths after surgery. Twenty-nine patients (10.5%) experienced at least 1 complication after surgery and 24 (8.7%) were discharged to nursing facilities. Malignant disease and low serum albumin levels were more common in the patients who died. Among the geriatric assessment domains, Charlson Comorbidity Index, dependence in activities of daily living, dependence in instrumental activities of daily living, dementia, risk of

delirium, short midarm circumference, and malnutrition were associated with increased mortality rates. A multidimensional frailty score model composed of the above items predicted all-cause mortality rates more accurately than the American Society of Anesthesiologists classification (area under the receiver operating characteristic curve, 0.821 vs 0.647; P = .01). The sensitivity and specificity for predicting all-cause mortality rates were 84.0% and 69.2%, respectively, according to the model's cutoff point (>5 vs ≤5). High-risk patients (multidimensional frailty score >5) showed increased postoperative mortality risk (hazard ratio, 9.01; 95% CI, 2.15-37.78; P = .003) and longer hospital stays after surgery (median [interquartile range], 9 [5-15] vs 6 [3-9] days; P < .001).

Conclusions: The multidimensional frailty score based on comprehensive geriatric assessment is more useful than conventional methods for predicting outcomes in geriatric patients undergoing surgery.

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Keywords: Geriatric assessment, frailty, surgery, outcome

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INTRODUCTION

Geriatric patients often have comorbid conditions that may lead to postoperative mortality and morbidity. Moreover, elderly persons have unique physiological changes that impair functional reserve and increase vulnerability for disability.(1) The concept of frailty has been developed to account for this phenomenon and is thought to reflect decreased physiological reserves across multiple organ systems, arising from cumulative comorbid conditions.(2, 3) Surgical disease and surgery itself are substantial stressors that may interrupt physiological homeostasis; therefore, frailty has a clinical significance for older patients who are considering surgery. Moreover, the prevalence of frailty in geriatric surgical patients is much higher than that of a community-dwelling population.(4)

During the past 20 years, the geriatric population has increased dramatically, and the number of elderly patients who undergo surgery has increased even more rapidly. This trend is based on increased life expectancy and improved surgical and anesthetic techniques. Currently, more than half of all operations are performed on elderly patients (aged ≥65 years) in the United States, and this proportion will continue to increase.(5)

Frail elderly patients who undergo surgery are more likely to encounter postoperative complications (eg, pneumonia, delirium, and urinary tract infection), prolonged hospital stays, discharge to nursing homes or long-term care facilities, amplified financial burdens, and higher mortality rates than fit patients.(6) Despite the increase of geriatric surgical patients who are at

perioperative risk, current methods for preoperative risk stratification in the elderly have substantial limitations; most focus on a single organ system or solitary event, or are established from clinical trials that excluded the geriatric population. Thus, these methods cannot measure the older patient's physiological reserves appropriately. Furthermore the elderly population is a heterogeneous group, and chronological age does not always represent biological function, which varies from fit to frail.(7)

In many geriatric fields, the comprehensive geriatric assessment (CGA) is widely used to detect disabilities and evaluate geriatric conditions that can be associated with frailty. The CGA is a systematic multidimensional assessment for the elderly, focusing on somatic, functional, psychological, and social features.(8) It is designed to improve diagnostic accuracy, provide a personalized approach to medical care, and enhance a patient's functional status. Its value has been proven in geriatric medicine in recent years.(9)

Using CGA data, we aimed to develop a scoring model to predict unfavorable outcomes and prolonged hospital stays quantitatively after surgery in elderly patients.

METHODS

Patient Selection

This cohort study was performed at the Seoul National University Bundang Hospital, a 1000-bed teaching hospital. Patients aged 65 years or older who were admitted to the Department of Surgery for elective operations were included in the study. The subjects were consecutively recruited from October 19, 2011, to July 31, 2012. After opting for surgery, they were referred to the geriatric center to undergo CGA. Patients were excluded if they underwent an emergency operation or were at low risk of adverse outcome from surgery according to the American College of Cardiology/American Heart Association 2007 guidelines.(10)

Baseline patient characteristics were collected from electronic medical records and included age, sex, height, weight, type of surgery (laparoscopic or open), type of disease (malignant or benign), and American Society of Anesthesiologists (ASA) classification. The ASA class, which is widely used for surgical patients, indicates an individual's physical health and predicts postoperative morbidity, with scores ranging from 0 (lowest risk) to 5 (highest risk).(11) The study protocol was reviewed and approved by the institutional review board of the Seoul National University Bundang Hospital, which waived the requirement for informed consent.

CGA Protocol

The CGA was performed within a month before surgery, except in 13 patients evaluated 1 to 3months before surgery. Our CGA set included 6 domains: burden of comorbidity, physical function, psychological status, nutrition, polypharmacy, and risk of postoperative delirium.(12)

The burden of comorbidity was quantified using the Charlson Comorbidity Index, which contains 19 categories; each comorbid category has a weighted value based on the 1-year mortality risk.(13)

Physical function was assessed according to activities of daily living (ADLs) and instrumental ADLs (IADLs). The ADLs were measured by using the modified Barthel Index, which consists of 10 items (grooming, bathing, eating, dressing, toilet use, fecal and urinary continence, ability to go up and down stairs, and walking in a hallway).(14) This index ranges from 0 to 100, and 100 means full independence; 75 to 99, partial dependence; and less than 75, full dependence. The IADLs were assessed using the Lawton and Brody Index, which includes 5 items for men (using the telephone, shopping, traveling via car or public transportation, use of medication, and financial management). For women, 3 additional items (the ability to prepare food, laundry, and housekeeping) were also included.(15) Patients with at least 1 IADL dependent were assumed to have IADL dependence.

Psychological status was analyzed using the Korean version of the Mini-Mental State Examination, with scores ranging from 0 to 30. Scores ranging from 17 to 24 indicated mild cognitive impairments and scores less than 17 indicated dementia.(16) Depression was measured using the short form of the Korean Geriatric Depression Scale, with scores ranging from 0 to 15; scores

from 5 to 9 suggest mild depression and scores of 10 or higher, severe depression.(17)

Nutrition was evaluated with the Mini Nutritional Assessment, with scores ranging from 0 to 30; scores of 17 to 23.5 indicated a risk of malnutrition and scores less than 17 indicated malnutrition.(18)

Determined through a comprehensive history and medical review, polypharmacy was defined as taking more than 5 drugs regularly, and inappropriate medication was determined according to the Beers criteria.(19)

The risk of delirium was measured by the Nursing Delirium Screening Scale, with scores ranging from 0 to 5; a score of 2 or higher suggests an increased risk of postoperative delirium.(20)

Study Outcomes

The primary outcome was the 1-year all-cause mortality rate. The secondary outcomes were postoperative complications, length of hospital stay, and discharge to nursing facility. The Ministry of Security and Public Administration provided the dates of all deaths occurring through May 16, 2013. We added the mortality data to our data set using each individual's unique identifier.

Postoperative complications included pneumonia, urinary tract infection, delirium, acute pulmonary thromboembolism, and unplanned intensive care unit admission. Surgical complication was defined according to the American College of Surgeons National Surgical Quality Improvement Program definitions.(21) Unplanned intensive care unit admission was defined as

transferring from the general ward to the intensive care unit at least 72 hours postoperatively for close hemodynamic monitoring, ventilator support, continuous renal replacement therapy, other-site infection, or bleeding. Discharge to a nursing home, transitional care, or any long-term care facility was defined as discharge to nursing facility if the patient had lived at home before being admitted for an elective operation.

Statistical Analysis

Continuous variables were expressed as means (SDs) or as medians (interquartile ranges) if the variables were not normally distributed and were compared by means of unpaired t tests. Discrete variables were expressed as counts and percentages, and χ^2 or Fisher exact tests were used to compare proportions.

The association between the multidimensional frailty score (MFS) and the outcomes was determined by means of a logistic regression model fully adjusted for the relevant prognostic variables. To predict the primary outcome, we took items with statistical significance from each of the univariate analyses for our predictive model. After reviewing previous studies, we used patients' laboratory and demographic data for the model. To assess multicollinearity among explanatory variables used to make a predictive model, we used the variance inflation factor from logistic regression analysis.(22) We validated the predictive model by using bootstrap analysis (n = 1000). We compared our predictive model with the ASA classification,

which is currently used for preoperative risk evaluation, with a pairwise comparison of the receiver operating characteristic curve.

We classified risk according to the proposed model's score and analyzed survival using the Kaplan-Meier survival model. We compared survival rates in 2 groups (high-risk vs low-risk groups) using a log-rank test and time-dependent Cox proportional hazards modeling to control for multiple variables simultaneously. Differences were considered statistically significant at $P < .05$, and all analyses were 2-tailed. We logged and analyzed data using SPSS 18.0 (SPSS Inc) and MedCalc (version 11.0.1.0; MedCalc) software.

RESULTS

Of 358 patients, 52 underwent low-risk surgical procedures, 1 refused CGA, and 30 refused operation. Accordingly, data from 275 patients were used for the analysis (Figure 1). The baseline demographic, laboratory, and surgical characteristics of all participants are listed in the Table 1. The underlying causes for the operations were benign disease (127 patients [46.2%]) and malignant disease (148 patients [53.8%]). In total, 192 patients (69.8%) underwent laparoscopic procedures and 83 (30.2%) underwent open abdominal procedures. The median (interquartile range) length of hospital stay was 10 (7-16) days, and the median length of stay after surgery was 7 (3-11) days.

Through May 16, 2013, a total of 25 patients (9.1%) died (including 4 in-hospital deaths after surgery). The median (interquartile range) follow-up period was 13.3 (11.5-16.1) months. Twenty-four patients (8.7%) were transferred to nursing facilities and 247 patients were discharged home. Twenty-nine patients (10.5%) experienced at least 1 in-hospital complication, including pneumonia (12 patients), urinary tract infection (4 patients), delirium (14 patients), acute pulmonary thromboembolism (2 patients), and unplanned intensive care unit admission (7 patients). Two patients had 3 complications during the postoperative hospital stay and 6 patients had 2.

We evaluated the relationship between the primary outcome and demographics, laboratory results, and CGA components (Table 2).

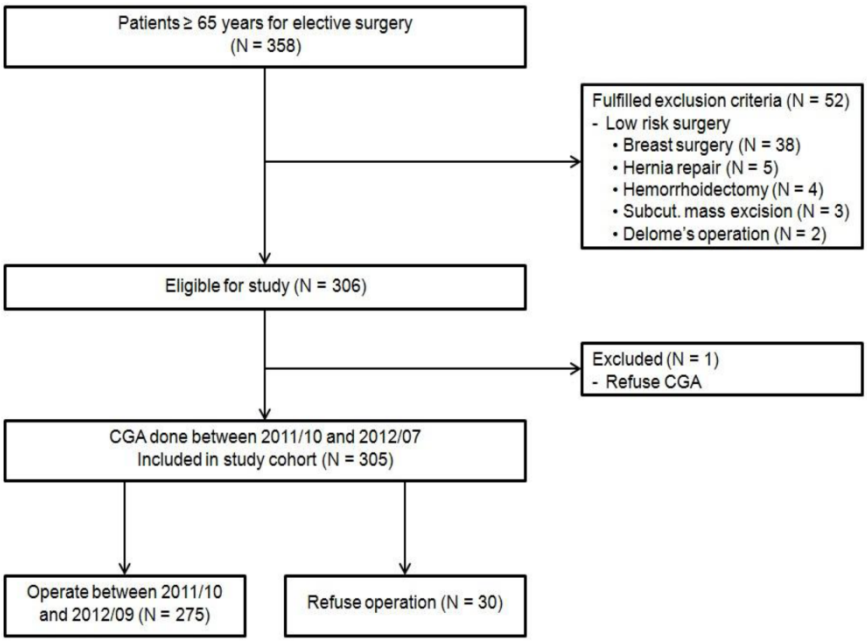


Figure 1. Flow of Patients Through Study

The final study population included 275 elderly patients undergoing intermediate-risk to high-risk operations after comprehensive geriatric assessment (CGA).

Table 1. Demographic, laboratory, surgical characteristics, and CGA components of the whole population

	Operation (n = 275)	Refuse operation (n = 30)
Demographic		
Age, y	75.4 (5.39)	79.0 (7.37)
Sex, male/female, No.	151/124	21/9
Height, cm	159.5 (8.91)	160.1 (7.80)
Weight, kg	58.9 (10.30)	55.4 (9.55)
Body mass index (kg/m^2)	23.1 (3.31)	21.6 (3.43)
Cancer, No. (%)	148 (53.8)	25 (83.3)
Laboratory		
WBC count, x 10^3/μL	7.65 (3.08)	6.98 (3.66)
Hemoglobin, g/dL	12.3 (2.09)	11.9 (2.43)
Platelet count, x 10^3/μL	218.1 (80.1)	206.1 (84.5)
Glucose, mg/dL	127.0 (45.8)	116.6 (35.0)
BUN, mg/dL	14.9 (7.8)	17.1 (6.4)
Creatinine, mg/dL	0.90 (0.42)	0.90 (0.30)
eGFR, mL/min/1.73m^2	83.0 (26.29)	86.6 (41.34)
Cholesterol, mg/dL	156.8 (47.5)	144.4 (37.6)
Protein, g/dL	6.5 (0.83)	6.5 (0.87)
Albumin, g/dL	3.8 (0.58)	3.5 (0.69)
AST, U/L	50.7 (141.9)	34.5 (27.1)
ALT, U/L	48.6 (138.1)	31.1 (29.2)
Surgical		
Laparoscopic/open surgery, No.	192/83	N/A
ASA class, 1/2/3/4, No.	30/209/35/1	1/17/9/3
Comprehensive geriatric assessment		
Charlson Comorbidity Index	2.3 (1.8)	3.4 (2.2)
ADL dependency (partial and full)	36 (13.1%)	10 (33.3%)
IADL dependency	28 (10.2%)	8 (26.7%)
MMSE-KC score	22.9 (6.5)	18.7 (9.8)
SGDS-K score	3.9 (3.9)	4.4 (4.7)

MNA score	23.8 (4.3)	20.4 (6.1)

Data are presented as mean (SD) or number (%).

Abbreviation: WBC; white blood cell, BUN; blood urea nitrogen, eGFR; estimated glomerular filtration rate, AST; aspartate aminotransferase, ALT; alanine aminotransferase, ASA class; The American Society of Anesthesiologist's classification, ADL; activities of daily living, IADL; instrumental activities of daily living, MMSE-KC; Korean version of the mini-mental status examination, SGDS-K; short form of the Korean geriatric depression scale, MNA; mini-nutritional assessment, N/A; not applicable

Table 2. Comparison of demographic, laboratory, and CGA components by all-cause mortality outcome

	Survival group (n = 250)	Mortality group (n = 25)	*P* values
Demographic			
Age (year)	75.2 (5.15)	77.6 (7.16)	0.10
Gender (male/female)	134/116	17/8	0.21
Weight (kg)	59.6 (10.21)	51.9 (8.59)	< 0.001
Body mass index (kg/m^2)	23.4 (3.24)	20.7 (3.01)	< 0.001
Cancer	129 (51.6%)	19 (76.0%)	0.02
ASA class (1/2/3/4)	29/194/27/0	1/15/8/1	< 0.001
Laparoscopic/Open surgery	186/64	6/19	< 0.001
Laboratory			
WBC (x 10^3/μL)	7.59 (3.05)	8.16 (3.35)	0.38
Hemoglobin (g/dL)	12.3 (2.10)	12.0 (2.04)	0.39
Platelet (x 10^3/μL)	218.1 (79.05)	218.5 (91.67)	0.98
Creatinine (mg/dL)	0.89 (0.42)	0.99 (0.49)	0.29
Protein (mg/dL)	6.5 (0.82)	6.3 (0.93)	0.36
Albumin (mg/dL)	3.8 (0.58)	3.5 (0.57)	0.02
AST (IU/L)	51.4 (148.1)	43.3 (46.3)	0.79
ALT (IU/L)	49.3 (143.7)	42.3 (59.3)	0.81
Comprehensive geriatric assessment			
Charlson's comorbidity index	2.2 (1.7)	3.5 (2.3)	< 0.001
Polypharmacy	122 (48.8%)	11 (44.0%)	0.68
Inappropriate medication	47 (18.8%)	5 (20.0%)	0.80
ADL dependency (partial and full)	28 (11.2%)	8 (32.0%)	0.01
IADL dependency	21 (8.4%)	7 (28.0%)	0.01
MMSE-KC*	23.3 (6.3)	19.1 (8.2)	0.003
SGDS-K†	3.9 (3.9)	4.2 (4.3)	0.69

Risk of delirium (≥ 2 Nu-DESC)[‡]	21 (8.4%)	7 (28.0%)	0.008
MNA[‡]	24.1 (4.0)	20.3 (5.0)	< 0.001
Mid-arm circumference (cm)[§]	26.0 (2.8)	24.3 (2.0)	0.003

Data are presented as mean (SD) or number (%).

Abbreviation: ADL; activities of daily living, IADL; instrumental activities of daily living, MMSE-KC; Korean version of the mini-mental status examination, Nu-DESC; the nursing delirium screening scale, MNA; mini-nutritional assessment

[*]; Data were missing for 3 patients, [†]; Data were missing for 2 patients, [‡]; Data were missing for 1 patient, [§]; Data were missing for 6 patients

Patients in the survival group were heavier, predominantly had benign disease, and had higher albumin concentrations. In the CGA, they were likely to have a lower Charlson Comorbidity Index, less ADL and IADL dependence, better cognitive function, lower risk of delirium, better nutritional condition, and longer midarm circumference, but inappropriate medication use and the Korean Geriatric Depression Scale (short-form) scores did not differ significantly between the 2 groups.

We established a new scoring index using the results of CGA, patient characteristics, and laboratory variables (Table 3). Variables that reached a P value of less than .05 and were clinically pertinent were placed in a MFS model. Continuous variables, such as serum albumin level, midarm circumference, and Charlson Comorbidity Index, were divided into tertiles based on the study population. These 3 variables maintained their statistical significance after trichotomization and were entered into the prediction model with each converted score (2, 1, or 0). Three CGA items (ADL dependence, dementia, and malnutrition), which had well-established cutoffs for severity, were scored (2, 1, or 0), and 3 other items (malignant disease, IADL dependence, and risk of delirium) were scored (1 or 0) by their reference values. To exclude multicollinearity among explanatory variables used to make a predictive model, we checked the variance inflation factor from logistic regression analysis. All factors were below 10, so we can exclude the possibility of multicollinearity and put those items into the predictive model. The total score for the MFS model is 15, and higher scores align with a higher postoperative mortality risk.

Table 3. Composition of Multidimensional Frailty Score

Item \ Score	0	1	2
Malignancy	Benign disease	Malignant disease	N/A
Charlson's comorbidity index	0	1 ~ 2	> 2
Albumin (mg/dL)	> 3.9	3.5 ~ 3.9	< 3.5
ADL (Modified Barthel Index)	Independent	Partially dependent	Fully dependent
IADL (Lawton and Brody's index)	Independent	Dependent	N/A
Dementia (MMSE-KC)	Normal	Mild cognitive impairment	Dementia
Risk of delirium (Nu-DESC)	0 ~ 1	≥ 2	N/A
MNA	Normal	Risk of malnutrition	Malnutrition
Mid arm circumference (cm)	> 27.0	24.6 ~ 27.0	< 24.6

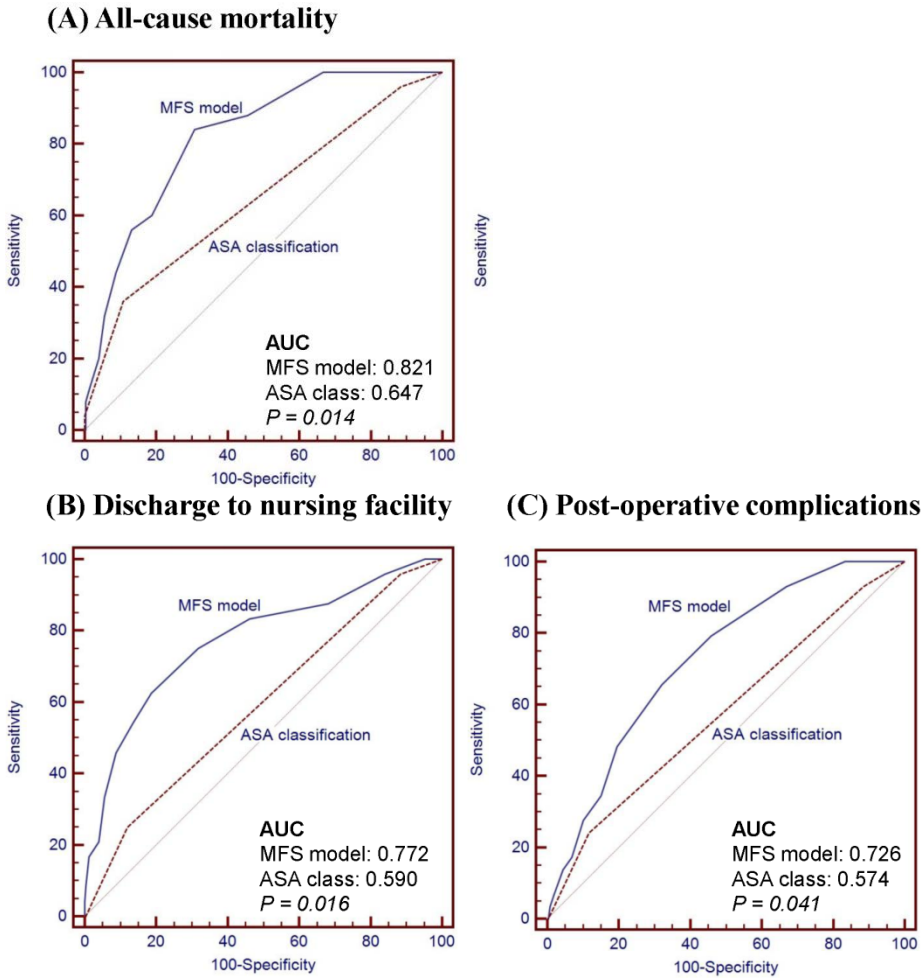
Abbreviation: ADL; activities of daily living, IADL; instrumental activities of daily living, MMSE-KC; Korean version of the mini-mental status examination, Nu-DESC; the nursing delirium screening scale, MNA; mini-nutritional assessment, N/A; not applicable

The area under the receiver operating characteristic curve for the MFS model to predict the all-cause mortality rate was 0.821, and the ASA classification, a conventional preoperative evaluation method, was 0.647. The areas under the receiver operating characteristic curve for the models to predict discharge to nursing facility and postoperative complication were 0.772 and 0.726, respectively; the respective ASA classifications were 0.590 and 0.574. In a pairwise comparison of the receiver operating characteristic curves, the difference between the MFS model and the ASA classification was statistically significant (Figure 2).

The associations between the MFS and outcomes were revealed by multiple logistic regression analysis. The fully adjusted odds ratios per 1 point in the model were 2.05 (95% CI, 1.43-2.94; $P < .001$) for the all-cause mortality rate and 1.42 (1.09-1.86; $P = .01$) for discharge to a nursing facility. However, the MFS model failed to predict postoperative complications (fully adjusted odds ratio, 1.17; 95% CI, 0.92-1.49; $P = .21$) (Table 4).

The Youden Index was used to identify the cutoff point with the highest sensitivity and specificity in classifying the high-risk group.(23) To determine the criteria for the high-risk group using a score above 5, we categorized 98 of 275 participants as the high-risk group, and our model had 84.0% sensitivity and 69.2% specificity to predict the mortality rate. The mortality rate tended to increase with increases in the MFS, representing a trend of dose-response relationships (Figure 3).

Figure 2. Area under receiver operating characteristic curve (AUC) for all-cause mortality rate (A), discharge to nursing facility (B), and postoperative complication (C)



ASA indicates American Society of Anesthesiologists; MFS, multidimensional frailty score.

Table 4. Adjusted odds ratios for association between multidimensional frailty scores and outcomes

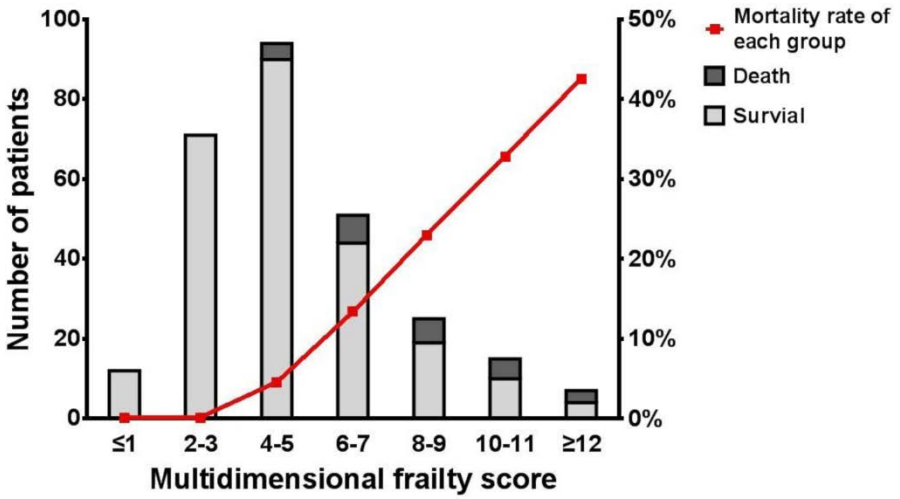
	Age, sex-adjusted OR (95% CI)	Fully-adjusted OR* (95% CI)
1-year all-cause mortality	1.67 (1.37 – 2.03)†	2.05 (1.43 – 2.94)†
Discharge to nursing facility	1.37 (1.16 – 1.61)†	1.42 (1.09 – 1.86)‡
Post-Op complications (pneumonia, UTI, delirium, PTE, un-intentioned ICU admission)	1.44 (1.21 – 1.70)†	1.17 (0.92 – 1.49)§

*; adjusted by age, sex, height, weight, type of surgery, white blood cell count, hemoglobin, BUN, creatinine, cholesterol, protein, total bilirubin, AST, ASA class. Internal validation was done by bootstrap based on 1000 samples ($P = 0.002$)

†; $P < 0.001$, ‡; $P = 0.011$, §; $P = 0.214$

Abbreviation: UTI; urinary tract infection, PTE; pulmonary thromboembolism, ICU; intensive care unit

Figure 3. Number of patients and 1-year all-cause mortality rate by multidimensional frailty score

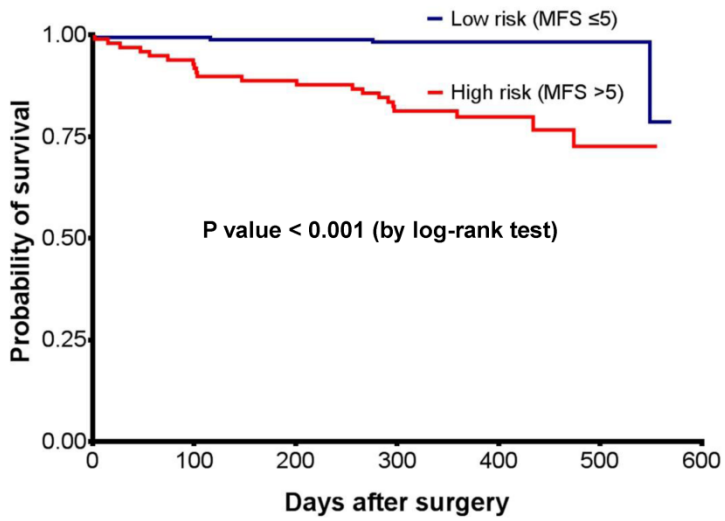


Bar represent numbers of patients (and deaths); black line, mortality rate. As scores increase, the occurrence of the primary outcome (death) increased, and the slope for mortality rates suddenly became steep for patients with scores of 5 or above.

Postoperative survival rates were better in the low-risk group than in the high-risk group (97.7% vs 78.6%; $P < .001$). Mortality estimates based on the Kaplan-Meier curve are shown in Figure 4. Compared with low-risk patients, the adjusted hazard ratio for mortality risk among high-risk patients was 9.01 (95% CI, 2.15-37.78; $P = .003$; adjusted for age, sex, height, weight, type of surgery, white blood cell count, hemoglobin, serum urea nitrogen, creatinine, cholesterol, protein, total bilirubin, aspartate aminotransferase, and ASA class).

With the stated criterion (MFS ≤ 5 vs >5) used to classify risk, the median (interquartile range) numbers of total hospitalization days were 9 (6-12) and 14 (10-23) for the low-risk and high risk groups, respectively ($P < .001$), and the median numbers of postoperative hospitalization days were 6 (3-9) and 9 (5-15), respectively ($P < .001$).

Figure 4. Cumulative all-cause mortality rate according to risk stratification based on multidimensional frailty score



Low risk group	177	176	175	172	99	38
High risk group	98	92	87	80	37	9

Kaplan-Meier plots are shown for all-cause mortality rates in low risk vs high-risk patient groups; results are not adjusted. Numbers at the bottom represent patients who were followed up alive.

DISCUSSION

The main findings of this study were that the postoperative 1-year all-cause mortality rate, length of hospital stay, and likelihood of discharge to nursing facility can be predicted from particular components of the CGA in older surgical patients. The predictive model based on CGA can predict unfavorable outcomes better than the conventional ASA classification. Moreover, a higher score is correlated with a greater mortality risk.

It has been known that some older patients do not have the physiological reserves to endure operations and postoperative burdens,(24) but many physicians measure the patient's reserve subjectively or, even worse, disregard it. This tendency may reflect a lack of insight into geriatric frailty and the absence of appropriate methods for evaluating older surgical patients. In clinical practice, physicians often observe that despite being the same chronological age, some patients can withstand operational stress but others cannot. As a result, some older patients are deprived of the opportunity for surgical treatments solely because of their ages. In contrast, some patients experience postoperative complications and are discharged to long-term care facilities instead of home.

Analyzing findings in 275 patients who underwent CGA before surgery, we observed that the variables associated with frailty had a strong association with postoperative mortality rate and discharge disposition. Because homeostasis in the elderly is narrowly maintained based on cardiovascular, hormonal, and immunologic status, a single stressor could create an imbalance

of general physiology in these patients.(25, 26) Therefore, our findings support the concept of frailty as the capacity to withstand stressors.(27)

We proposed a predictive model, and, using an internal validated scoring system, we identified a group of patients at high risk for postoperative death. We also compared our model with a conventional preoperative screening tool that is suitable and sufficient for younger patients but insufficient to identify the at-risk group among elderly patients.

The elderly population has a high postoperative mortality and morbidity risk; thus, elderly patients would eventually become a socioeconomic burden. Therefore, it will be more important in the future to identify at-risk patients, analyze patients' risk-to-benefit ratio, provide additional information about prognosis, and provide appropriate perioperative medical support based on suitable methods.

Modeling with variables in CGA understandably and inevitably has a certain multicollinearity,(3) but we excluded this possibility by assessing the variance inflation factor. In addition, those variables might have different meanings. For example, serum albumin levels and Mini Nutritional Assessment scores overlapped, both reflecting nutritional status; however, the serum albumin level represents a longer-term nutritional marker than the Mini Nutritional Assessment score, plays a significant role in inflammation and metabolism, and is known as an independent predictor for mortality and morbidity rates in several studies.(28-30) Our MFS model includes both presence or absence of malignant disease and Charlson Comorbidity Index

because presence of malignant disease in the Charlson Comorbidity Index includes cancers initially treated in the last 5 years as well as current diseases.

In the MFS model, we did not apply weighted scores for the variables. However, logistic regression analysis showed no significant difference between our MFS model and a weighted model using β coefficients (data not shown). Thus, we used a nonweighted model for its simplicity.

Our study has several limitations. First, it was performed at a single tertiary care university hospital. Postoperative outcomes are variable and influenced by the skill of surgeons and the quality of the medical team; therefore, this scoring system might not be generalizable to other settings and needs to be validated in a larger population and across multiple institutions. Our model could predict mortality rate and discharge disposition, but it failed to show statistical significance for predicting postoperative complications. The underpowered significance might arise from the few postoperative outcomes in this study population. For example, the incidence of delirium after noncardiac surgery ranges from 5.1% to 52.2%,(31) and it was only 5.1% in our cohort. We considered only diagnosed delirium as a postoperative complication, and the prevalence of cognitive impairment and dementia, the most important risk factors for delirium, was very low in this group. Furthermore, the severity of each complication was not reflected in the outcomes, which can be another explanation for underpowered significance.

Our study also has some strengths. To our knowledge, it is the first large consecutively enrolled study to observe the long-term mortality rate in elderly patients undergoing surgery, and we proposed a model based on CGA. It may

be more useful to stratify preoperative risk using our model than to use ASA classifications in geriatric patients scheduled for surgery. Our findings may provide further insight than current methods into frail older patients, provide more information to patients and families, and assist medical teams in their decision making.

In summary, we found that older surgical patients have surgical risks that can be predicted by careful review of their specific characteristics. If a certain elderly patient was likely to have a longer hospital stay and a greater risk of death or discharge to a nursing facility, physicians may be able to distinguish the high-risk group by using the proposed scoring model based on the MFS. This model may support surgical treatments for fit older patients at low risk of complications, and it may also provide an impetus for better management of geriatric patients with a high risk of adverse outcomes after surgery.

REFERENCES

1. Linda P. Fried LF, Jonathan Darer, Jeff D. Williamson, Gerard Anderson. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care. The journals of gerontology Series A, Biological sciences and medical sciences. 2004;59(3):255-63.

2. Ferrucci L GJ, Studenski S, Fried LP, Cutler GB Jr, Walston JD; Interventions on Frailty Working Group. Designing randomized, controlled trials aimed at preventing or delaying functional decline and disability in frail, older persons-a consensus report. Journal of the American Geriatrics Society. 2004;52(4):625-34.

3. Rockwood K MA. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. 2011;Clin Geriatr Med(17-26).

4. Partridge JSH, D. Dhesi, J. K. Frailty in the older surgical patient: a review. Age and ageing. 2012;41(2):142-7.

5. Etzioni DA LJ, Maggard MA, Ko CY. The aging population and its impact on the surgery workforce. Annals of surgery. 2003;238(2):170-7.

6. Saxton A, Velanovich V. Preoperative frailty and quality of life as predictors of postoperative complications. Annals of surgery. 2011;253(6):1223-9.

7. Lee DH BK, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010;121(8):973-8.

8. Hamaker ME JJ, de Rooij SE, Vos AG, Smorenburg CH, van Munster BC. Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review. The Lancet Oncology. 2012;13(10):e437-e44.

9. Ellis G WM, Robinson D, O'Neill D, Langhorne P. Comprehensive geriatric assessment for older adults admitted to hospital: meta-analysis of randomised controlled trials. BMJ (Clinical research ed). 2011;343(oct27 1):d6553-d.

10. Fleisher LA BJ, Brown KA, Calkins H, Chaikof EL, Fleischmann KE, Freeman WK, Froehlich JB, Kasper EK, Kersten JR, Riegel B, Robb JF, Smith SC Jr,

Jacobs AK, Adams CD, Anderson JL, Antman EM, Buller CE, Creager MA, Ettinger SM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery): developed in collaboration with the American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, and Society for Vascular Surgery. Circulation. 2007;116(17):e418-99.

11. Wolters U WT, Stützer H, Schröder T. ASA classification and perioperative variables as predictors of postoperative outcome. Br J Anaesth. 1996;77(2):217-22.

12. Kim KI PK, Koo KH, Han HS, Kim CH. Comprehensive geriatric assessment can predict postoperative morbidity and mortality in elderly patients undergoing elective surgery. Archives of gerontology and geriatrics. 2013;56(3):507-12.

13. Charlson ME PP, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373-83.

14. Mahoney FI BD. Functional evaluation: the Barthel Index. Md State Med J. 1965;1965(14):61-5.

15. Lawton MP BE. Assessment of older people: self-maintaining and instrumental activities of daily living. The Gerontologist. 1969;9(3):179-86.

16. Lee DY LJ, Ju YS, Lee KU, Kim KW, Jhoo JH, Yoon JC, Ha J, Woo JI. The prevalence of dementia in older people in an urban population of Korea - the Seoul study. Journal of the American Geriatrics Society. 2002;50(7):1233-9.

17. Bae JN CM. Development of the Korean version of the Geriatric Depression Scale and its short form among elderly psychiatric patients. Journal of psychosomatic research. 2004;57(3):297-305.

18. Vellas B GY, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, Albarede JL. The Mini Nutritional Assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition. 1999;1999(15):2.

19. Panel AGSBCUE. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. Journal of the American Geriatrics Society. 2012;60(4):616-31.

20. Gaudreau JD GP, Harel F, Tremblay A, Roy MA. Fast, Systematic, and Continuous Delirium Assessment in Hospitalized Patients: The Nursing Delirium Screening Scale. Journal of Pain and Symptom Management. 2005;29(4):368-75.

21. Khuri SF DJ, Henderson W, Hur K, Demakis J, Aust JB, Chong V, Fabri PJ, Gibbs JO, Grover F, Hammermeister K, Irvin G 3rd, McDonald G, Passaro E Jr, Phillips L, Scamman F, Spencer J, Stremple JF. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. Annals of surgery. 1998;228(4):491-507.

22. O'brien RM. A Caution Regarding Rules of Thumb for Variance Inflation Factors. Quality & Quantity. 2007;41(5):673-90.

23. Fluss R FD, Reiser B. Estimation of the Youden Index and its associated cutoff point. Biom J. 2005;2005(47):4.

24. Revenig LM, Canter DJ, Taylor MD, Tai C, Sweeney JF, Sarmiento JM, et al. Too frail for surgery? Initial results of a large multidisciplinary prospective study examining preoperative variables predictive of poor surgical outcomes. Journal of the American College of Surgeons. 2013;217(4):665-70.e1.

25. Newman AB GJ, Mcburnie MA, Hirsch CH, Kop WJ, Tracy R, Walston JD, Fried LP; Cardiovascular Health Study Research Group. Association of subclinical cardiovascular disease with frailty. The journals of gerontology Series A, Biological sciences and medical sciences. 2001;56(3):158-66.

26. Barzilay JI BC, Moore T, Xue QL, Hirsch CH, Walston JD, Fried LP. Insulin Resistance and Inflammation as Precursors of Frailty. Archives of internal medicine. 2007;2007(167):7.

27. Makary MA, Makary MA SD, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, Takenaga R, Devgan L, Holzmueller CG, Tian J, Fried LP. Frailty as a predictor of surgical outcomes in older patients. Journal of the American College of Surgeons. 2010;210(6):901-8.

28. Corti MC GJ, Salive ME, Sorkin JD. Serum-albumin level and physical-disability as predictors of mortality in older persons. JAMA : the journal of the American Medical Association. 1994;272(13):1036-42.

29. Fried LP KR, Newman AB, Bild DE, Mittelmark MB, Polak JF, Robbins JA, Gardin JM. Risk factors for 5-year mortality in older adults the Cardiovascular Health Study. JAMA : the journal of the American Medical Association. 1998;279(8):585-92.

30. Volpato S LS, Corti MC, Harris TB, Guralnik JM. The value of serum albumin and high-density lipoprotein cholesterol in defining mortality risk in older persons with low serum cholesterol. Journal of the American Geriatrics Society. 2001;49(9):1147-7.

31. Dasgupta M DA. Preoperative risk assessment for delirium after noncardiac surgery: a systematic review. Journal of the American Geriatrics Society. 2006;54(10):1578-89.

국문 초록

서론: 인구의 고령화로 인해 수술을 받는 노인들은 점차 증가하고 있으며, 노인들은 젊은 사람들에 비해 수술 후 사망율이 높다. 그러나 노인 환자의 수술 후 사망율이나 합병증을 예측할 수 있는 도구는 아직 부족하다. 이에 본 연구에서는 노인 수술 환자의 부작용을 예측 할 수 있는 도구를 만들고자 하였다.

방법: 일개 대학 병원의 외과에서 2011 년 10 월부터 2012 년 7 월까지 중등도 위험 및 고 위험 수술을 앞둔 65 세 이상 환자 275 명을 분석 하였다. 수술 전 노인 포괄 평가를 시행 하였으며 이를 바탕으로 1 년 후 사망을 예측 할 수 있는 새로운 점수 모델을 만들었다. 또한 이 도구가 폐렴, 요로 감염, 섬망, 급성 폐 색전증, 계획되지 않은 중환자실 입원 등의 수술 후 합병증과, 재원 기간 및 요양기관으로의 퇴원 등을 예측할 수 있는 지 함께 조사 하였다.

결과: 입원 기간 동안 사망한 4 명을 포함하여 총 25 명(9.1%)이 추적 관찰 기간(중간 값 [사분범위], 13.3 [11.5–16.1] 개월) 동안 사망 하였다. 29 명(10.5%)의 환자가 1 개 이상의 수술 후 부작용을 경험 하였으며, 24 명(8.7%)은 요양 기관으로 퇴원 하였다. 사망한 환자들에게서 악성 종양이 많았고, 혈중 알부민 농도가 낮았다. 노인 포괄 평가 영역에서는 높은 Charlson Comorbidity Index, 일상 생활 의존, 도구적 일상 생활 의존, 치매, 섬망 위험, 짧은 중간

팔 둘레가 높은 사망율과 연관이 있었다. 이를 바탕으로 다면적 노쇠 평가 도구를 만들었으며 이것은 American Society off Anesthesiologists classification 보다 수술 후 사망을 더 잘 예측하였다 (Area under the receiver operating characteristic curve, 0.821 vs 0.647; P = .01). 고 위험군을 5 점 초과로 정의 하였을 때, 사망을 예측 하는데 있어 모델의 민감도와 특이도는 각각 84.0%와 69.2% 였다. 고위험군은 수술 후 사망율이 높았으며 (hazard ratio, 9.01; 95% CI, 2.15–37.78; P = .003), 수술 후 재원 기간이 더 길었다 (중간값 [사분범위], 9 [5–15] vs 6[3–9]).

결론: 노인 포괄 평가를 기반으로 한 다면적 노쇠 평가 도구는 노인 수술 환자에서 수술 후 부작용을 예측하는데 도움이 된다.

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