Multidimensional Frailty Score for the Prediction of Postoperative Mortality Risk

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IMPORTANCE The number of geriatric patients who undergo surgery has been increasing, but there are insufficient tools to predict postoperative outcomes in the elderly.

OBJECTIVE To design a predictive model for adverse outcomes in older surgical patients.

DESIGN, SETTING, AND PARTICIPANTS From October 19, 2011, to July 31, 2012, a single tertiary care center enrolled 275 consecutive elderly patients (aged ≥65 years) undergoing intermediate-risk or high-risk elective operations in the Department of Surgery.

MAIN OUTCOMES AND MEASURES The primary outcome was the 1-year all-cause mortality rate. 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 AND RELEVANCE 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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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. 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. 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.

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.

Frail elderly patients who undergo surgery are more likely to encounter postoperative complications (e.g., 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. 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.

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. 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.

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.

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). 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 3 months before surgery. Our CGA set included 6 domains: burden of comorbidity, polypharmacy, physical function, psychological status, nutrition, and risk of postoperative delirium.

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.

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). 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. 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. 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.

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.

Determined through a comprehensive history and medical review, polypharmacy was defined as taking more than 5

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drugs regularly, and inappropriate medication was determined according to the Beers criteria. 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.

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. 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 χ² 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. 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 eTable in the Supplement.

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...
Research  Original Investigation

Table 1. Comparison of Demographic, Laboratory, and Comprehensive Geriatric Assessment Components by All-Cause Mortality Outcome

<table>
<thead>
<tr>
<th>Component</th>
<th>Survival (n = 250)</th>
<th>Death (n = 25)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>75.2 (5.15)</td>
<td>77.6 (7.16)</td>
<td>.10</td>
</tr>
<tr>
<td>Sex, male/female, No.</td>
<td>134/116</td>
<td>17/8</td>
<td>.21</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>59.6 (10.21)</td>
<td>51.9 (8.59)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body mass index&lt;sup&gt;a&lt;/sup&gt;</td>
<td>23.4 (3.24)</td>
<td>20.7 (3.01)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cancer, No. (%)</td>
<td>129 (51.6)</td>
<td>19 (76.0)</td>
<td>.02</td>
</tr>
<tr>
<td>ASA class, 1/2/3/4, No.</td>
<td>29/194/27/0</td>
<td>1/15/8/1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Laboratory values</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC count, ×10&lt;sup&gt;3&lt;/sup&gt;/μL</td>
<td>7.59 (3.05)</td>
<td>8.16 (3.35)</td>
<td>.38</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>12.3 (2.10)</td>
<td>12.0 (2.04)</td>
<td>.39</td>
</tr>
<tr>
<td>Platelet count, ×10&lt;sup&gt;3&lt;/sup&gt;/μL</td>
<td>218.1 (79.05)</td>
<td>218.5 (91.67)</td>
<td>.98</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.89 (0.42)</td>
<td>0.99 (0.49)</td>
<td>.29</td>
</tr>
<tr>
<td>Protein, g/dL</td>
<td>6.5 (0.82)</td>
<td>6.3 (0.93)</td>
<td>.36</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>3.8 (0.58)</td>
<td>3.5 (0.57)</td>
<td>.02</td>
</tr>
<tr>
<td>AST, U/L</td>
<td>51.4 (148.1)</td>
<td>43.3 (46.3)</td>
<td>.79</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>49.3 (143.7)</td>
<td>42.3 (59.3)</td>
<td>.81</td>
</tr>
<tr>
<td><strong>Comprehensive Geriatric Assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>2.2 (1.7)</td>
<td>3.5 (2.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Polypharmacy, No. (%)</td>
<td>122 (48.8)</td>
<td>11 (44.0)</td>
<td>.68</td>
</tr>
<tr>
<td>Inappropriate medication, No. (%)</td>
<td>47 (18.8)</td>
<td>5 (20.0)</td>
<td>.80</td>
</tr>
<tr>
<td>Dependence, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADLs (partial and full)</td>
<td>28 (11.2)</td>
<td>8 (32.0)</td>
<td>.01</td>
</tr>
<tr>
<td>IADLs</td>
<td>21 (8.4)</td>
<td>7 (28.0)</td>
<td>.01</td>
</tr>
<tr>
<td>MMSE-KC score&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23.3 (6.3)</td>
<td>19.1 (8.2)</td>
<td>.003</td>
</tr>
<tr>
<td>SGDS-K score&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.9 (3.9)</td>
<td>4.2 (4.3)</td>
<td>.69</td>
</tr>
<tr>
<td>Risk of delirium, No. (%)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>21 (8.4)</td>
<td>7 (28.0)</td>
<td>.008</td>
</tr>
<tr>
<td>MNA score&lt;sup&gt;e&lt;/sup&gt;</td>
<td>24.1 (4.0)</td>
<td>20.3 (5.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Midarm circumference, cm&lt;sup&gt;a&lt;/sup&gt;</td>
<td>26.0 (2.8)</td>
<td>24.3 (2.0)</td>
<td>.003</td>
</tr>
</tbody>
</table>

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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.

The area under the receiver operating characteristic curve for the models 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 complications 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 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).

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 \(\leq 5\) 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 (\(P < .001\)).

All 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 3).
Frailty Score and Postoperative Mortality Risk

Table 3. Adjusted Odds Ratios for Association Between Multidimensional Frailty Scores and Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Adjusted Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted by Sex and Age</td>
</tr>
<tr>
<td>1-year all-cause mortality</td>
<td>1.67 (1.37-2.03)b</td>
</tr>
<tr>
<td>Discharge to nursing facility</td>
<td>1.37 (1.16-1.61)b</td>
</tr>
<tr>
<td>Postoperative complicationsd</td>
<td>1.44 (1.21-1.70)b</td>
</tr>
</tbody>
</table>

* Odds ratios were determined with logistic regression analysis. Fully adjusted odds ratios were adjusted by age, sex, height, and weight; type of surgery; white blood cell count and hemoglobin, serum urea nitrogen, creatinine, cholesterol, protein, total bilirubin, and aspartate aminotransferase values; and American Society of Anesthesiologists class. Internal validation was done with bootstrapping based on 1000 samples (P = .002).

b P < .001.
c P = .01.
d Postoperative complications included pneumonia, urinary tract infection, delirium, acute pulmonary thromboembolism, and unplanned intensive care unit admission.

Figure 3. Number of Patients and 1-Year All-Cause Mortality Rate by Multidimensional Frailty Score

Bars 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.

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,2 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 Assess-
ment 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.26-30 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%,39 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.

Conclusions

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


SURGICAL CARE OF THE AGING POPULATION

More Powerful Than the American Society of Anesthesiology Score

Michael E. Zenilman, MD

The article by Kim et al1 is important for 2 reasons. First, it is part of a current series that focuses on geriatric indicators for determining the risk of surgery in our elderly patients. Although a wonderful review of best practices for geriatric assessment was published in 2012,2 based on data from the American College of Surgeons National Surgical Quality Improvement Program, Kim et al used their own tool, described in a previous study.3 The earlier study focused on in-hospital mortality; the current one expands the follow-up to 1 year. It is unfortunate that the authors did not measure functional outcome, which in this population is more important than survival, but I am sure they will in the future.

As part of our series on Surgical Care of the Aging Population, JAMA Surgery has also recently published several seminal articles. These articles have shown how a history of falls—a marker of frailty—increases postoperative morbidity and mortality rates,4 how early geriatric consultation and intervention improves functional outcome after trauma,5 and how a “do not resuscitate” order negatively affects survival in patients with bowel obstruction due to cancer.6

The second reason the article by Kim et al is important is that their study is one of few I have seen proving that a well-crafted comprehensive geriatric assessment can be a more powerful predictor of perioperative risk than the time-honored American Society of Anesthesiology score (see Figure 2).1 This is a paradigm shift, and it shows that we are now beginning to understand the true nature of age-related physiological changes in the patients on whom we operate.

ARTICLE INFORMATION

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