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## **Self-Reported Function More Informative than Frailty Phenotype in Predicting an Adverse Postoperative Course in Older Adults**

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## **Abstract**

**Background—**Current preoperative assessment tools such as the American College of Surgeons Surgical Risk Calculator (ACS Calculator) are suboptimal for evaluating older adults.

**Objective—**To evaluate and compare the performance of the ACS Calculator for predicting risk of serious postoperative complications, with the addition of self-reported physical function versus a frailty score.

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Author Contributions:

Design, manuscript writing/review: AK, TM, MW, CM, AS, ER, DM, NS, YZ, SK, SH, SC DKW, HS, AJ, RF, RAS, JG Analysis, manuscript review: YZ, SC, HJC

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**Design—**Prospective cohort.

**Setting—**Two tertiary care academic medical centers in Massachusetts.

**Participants—**403 patients age 65+ with serious complication risk of 5%

**Measurements—**(1) Self-reported physical function with Late Life Function and Disability Instrument (LLFDI FUNCTION); (2) Frailty Phenotype (FP) with score ranging from 0 to 5 based on presence of slow gait speed, weak handgrip, exhaustion, weight loss, or low activity.

**Main Outcome—**Increase in c-statistic and net reclassification improvement (NRI) for LLFDI-FUNCTION vs. FP in addition to the ACS Calculator for predicting an adverse postoperative course (either serious complication, discharge to nursing home, readmission, or death within 30 days of surgery)

**Results—**Over 30 days, 26% of patients developed an adverse postoperative course. The increase in c-statistic for the ACS Calculator (baseline value 0.645) was slightly higher with LLFDI-FUNCTION vs. FP (0.076 vs. 0.058) with bootstrapped difference in c-statistic of 0.005 (95% CI 0.002–0.007). NRI was also better with LLFDI-FUNCTION.

**Conclusion—**LLFDI-FUNCTION provided slightly better prediction of postoperative complications than the FP. Further studies are needed to confirm these findings and validate the use of the LLFDI-FUNCTION with the ACS Calculator for preoperative assessments of older adults.

### **Keywords**

perioperative medicine; surgical outcomes; self-reported function; frailty

## **INTRODUCTION**

Current preoperative assessment tools focus on predicting discrete medical conditions, not on complications that are viewed more globally (such as discharge to nursing home, readmission, or death).<sup>1–3</sup> More recently, the American College of Surgeons published a universal risk calculator (ACS Surgical Risk Calculator hereafter referred to as the ACS Calculator) that predicts outcomes more broadly. $4$  Although it comprises multiple comorbidities to predict various outcomes, it has limited assessment of physical status.

Frailty has shown the most promise in identifying older adults at high risk of postoperative complications and nursing home discharge.<sup>5–7</sup> Collecting frailty information with the wellestablished Fried Frailty Criteria, however, is not feasible in many places where preoperative evaluation occurs. The Fried Frailty Criteria, which we refer to as Frailty Phenotype (FP), includes measurements of exhaustion, handgrip strength, gait speed, physical activity, and weight loss. Taking these measurements requires significant time (typically 15–20 minutes), training, space (4–5 meters of unimpeded space for gait speed testing), and equipment (dynamometer for handgrip strength). With a more efficient way to measure physical status related to an older adult's risk for adverse surgical outcomes, the practice of preoperative medicine would improve.

Self-reported functional status may be more feasible for identifying high-risk older adults. Function refers to a person's ability to perform specific activities that require gross or fine motor actions.<sup>8</sup> Unlike FP, measuring function through self-report does not require new equipment or training. We previously demonstrated that a self-report instrument could predict adverse postoperative outcomes in older male veterans undergoing total hip and knee replacement.<sup>9</sup> But, there has been little published directly comparing self-reported function versus FP. Therefore, we conducted a prospective cohort study to evaluate the ability of selfreported function versus FP to predict an adverse postoperative course incremental to the ACS Calculator in older adults at elevated risk of postoperative complications.

## **METHODS**

#### **Population and Setting**

We recruited patients age 65 and older on the day of preoperative consultation at the presurgical clinics of academic medical centers. We included older adults undergoing any surgery with risk for a serious complication of 5% or greater as defined by the ACS Calculator. We excluded patients with a positive MiniCog Test (failed five minute recall of three items or combination of partial recall with failed clock drawing)<sup>10</sup> because the selfreport instrument we were evaluating has not been validated for use in patients with cognitive impairment or through proxy. The institutional review boards of the University of Massachusetts Medical School and Boston University Medical Center approved this study.

#### **Outcomes**

We measured the incidence of an adverse postoperative course as the occurrence of one or more of the following outcomes – serious complication, discharge to nursing home, readmission, and death within 30 days of surgery using the definitions published in the ACS National Surgical Quality Improvement Program Operations Manual (ACS Manual).<sup>11</sup> Serious complications included acute myocardial infarction, cardiac arrest, pulmonary embolism or deep venous thrombosis (so long as the treating team initiated treatment), pneumonia, respiratory failure (unplanned intubation), serious infection (sepsis, organ space infection, or deep space infection), renal failure, unplanned return to the operating room, or urinary tract infection. We scored discharge to nursing home as positive for any discharge to a location other than home or group home. Finally, we scored readmissions as positive when they were unplanned and related to the index surgery.

#### **Independent Variables**

We measured self-reported function with the function component of the computer adaptive testing (CAT) version of the Late Life Function and Disability Instrument (LLFDI-FUNCTION) which takes approximately 3 minutes to administer.<sup>12</sup> Members of our team (CM, AJ) developed both the fixed form and CAT versions, the latter using item response theory. Item response theory permits measurement of function from any subset of questions among the 141 items in the question bank. The scores from the LLFDI are transformed to Tscores with a mean of 50 and standard deviation of 10, with higher scores indicating higher function.

In terms of FP, we measured gait speed as usual walking speed over 4m following the protocol of Women's Health and Aging Study.<sup>13</sup> For the remaining four criteria – weight loss, exhaustion, low energy expenditure, and weakness – we prospectively collected information from patients following Cardiovascular Health Study validated definitions.<sup>14</sup> We defined patients as frail if they had at least three frailty criteria, which is consistent with the definition of frailty in the Cardiovascular Health Study<sup>14</sup>

#### **ACS Calculator Variables**

We collected data on 22 variables for each patient following the ACS Manual in order to calculate risk of serious complication using the ACS Calculator. The ACS Calculator does not directly predict our composite outcome, an adverse postoperative course, which also includes nursing home discharge, readmission, and death. However, the same variables are used to compute each of the outcomes. We therefore believe the ACS risk of serious complication (which we will refer to as ACS Risk throughout) would be a suitable proxy for estimating risk of an adverse postoperative course. We used ACS Risk as computed by the online calculator rather than deriving our own model because we felt this would be more representative of how clinicians could currently use the calculator with LLFDI-FUNCTION (i.e. a two-step process of recording LLFDI-FUNCTION and then separately calculating the risk of serious complication with the ACS Calculator). The exact formula for how variables are combined in the ACS Calculator is proprietary.

#### **Analysis**

We calculated frequencies of demographic variables for patients we enrolled and those we could not. (Supplementary Table S1) For those who enrolled, we further calculated the frequencies of the 22 variables used to calculate ACS Risk.

Below we describe the various steps we took in order to compare the performance of LLFDI-FUNCTION versus FP in estimating the risk of an adverse postoperative course in addition to the risk calculated from the ACS Calculator. These steps include examining the threshold values to understand the best categories to model LLFDI-FUNCTION and FP for the Cox proportional hazards model. We then discuss the construction of the Cox models. Finally, we discuss how to evaluate the performance of our models using the c-statistic and net reclassification improvement (NRI).

**Examining for threshold values of ACS Risk, LLFDI-FUNCTION, and FP—**We examined the shape of the association of ACS Risk, LLFDI-FUNCTION and FP with an adverse postoperative course using small increments – viz., ACS Risk of 2%, LLFDI-FUNCTION score of 5, and 1 frailty criterion respectively.

**Cox proportional hazards models—**We constructed multiple Cox proportional hazards models in order to measure the association between our independent variables and time to an adverse postoperative course. We defined the time to an adverse postoperative course as the time to first of any of the four qualifying events. We censored patients not having an adverse postoperative course at 30 days or less in the case of patients who did not return to our

hospital. In cases of same-day surgery and absence of subsequent follow-up, we assumed follow-up of 0.5 days. (Table 3)

**Evaluating Predictive of Performance of Our Models—**We first computed the cstatistic which gives the probability that a randomly selected patient who experienced an adverse postoperative course had a higher predicted probability of an adverse postoperative course based on our Cox models than a patient who did not have an adverse postoperative course. Then we calculated the NRI, which is the improvement in model fit expressed by the proportion of true events for which the model-predicted probability of the event having occurred is increased by the introduction of the new predictor variable (i.e. Model 4 vs. Model 1 and then separately Model 5 vs. Model 1 as listed in Table 3), plus the proportion of non-events for which the corresponding probability is decreased. To compute the c-statistic, we relied on an algorithm published in the literature.<sup>15</sup> To determine model calibration which is the agreement between observed outcomes and predictions, we computed the Hosmer-Lemeshow goodness of fit statistic using an algorithm developed for survival analysis.<sup>16</sup>

**Bootstrapping to determine if the c-statistic and NRI for Model 4 are significantly different than those for Model 5—**In order to determine if there was a difference in model performance, we simulated 1000 samples with replacement from our analysis population ( $n = 403$ ) consistent with other bootstrap examples in the literature.<sup>17</sup> We then used our Cox model to calculate predicted probabilities of an adverse postoperative course and corresponding c-statistic and NRI values for each model and the difference between them for each of the 1000 simulations. Finally, we computed the mean of the differences in c-statistic and NRI for the 1000 simulations with associated 95% confidence intervals.

## **RESULTS**

We included 403 patients in our analysis which were relatively evenly split between our two sites. Most of the patients were among the younger older adult population with 64% between the ages 65 to 75. Sixty-nine percent of the patients were white, 23% were black, and 7% other. Patients who declined to participate were of similar age, race, and gender as those who enrolled. (Supplementary Table S1)

Our study sample reported relatively high function with mean LLFDI-FUNCTION score of  $56.2 \pm 9.7$  which is above the normalized mean of 50 for community dwelling older adults. Few patients had more than three frailty criteria. We therefore analyzed these patients with those having three criteria which is consistent with the definition of frailty described in the Cardiovascular Health Study.<sup>14</sup> (table 1)

#### **Outcomes**

We observed that within 30 days of surgery, 10% of patients had a serious complication, 7% went to a nursing home after index hospitalization for surgery, 9% were readmitted to the hospital, and two patients died. The rate of an adverse postoperative course was 26%. Through examination of the change in this rate over small increments of LLFDI-

FUNCTION, we identified three categories of function (LLFDI-FUNCTION <50, 50–60, >60) with distinct risk – 47.4%, 23.7%, and 14.7% respectively. Similarly we found having more frailty criteria also predicted a higher incidence of each of our outcomes, albeit to a lesser degree than for LLFDI-FUNCTION. (Table 2)

#### **Predictive Performance of LLFDI-FUNCTION and FP**

Both LLFDI-FUNCTION and FP significantly improved the performance of the ACS Calculator. Specifically, the c-statistic increased by 0.051 (95%CI 0.049–0.053) for Model 4 compared with Model 1 and by 0.046 (95%CI 0.045–0.048) for Model 5 compared with Model 1. (Table 3) The NRI for Model 4 Risk was 0.52 compared with 0.40 for Model 5. The 0.52 NRI value for Model 4 comprises a NRI for patients with an adverse postoperative course of −0.03 and a NRI of 0.55 for patients without an adverse course. This suggests that the model with LLFDI-FUNCTION does not improve the classification of risk for those who had an adverse postoperative course (it actually inappropriately decreased the predicted probability 3% of the time more often than it appropriately increased the predicted probability). By contrast, in those who did not develop an adverse postoperative course, it appropriately decreased the predicted probability 55% more of time more than it inappropriately increased the predicted probability. (Supplementary Figure S1) Through bootstrapping, we found the difference in c-statistic for Model 4 vs. Model 5 to be 0.005 (95% CI 0.002–0.007) and difference in NRI to also be significant implying a slight performance edge for LLFDI-FUNCTION. The c-statistic for any single frailty criteria was not greater than for FP as a count of the criteria. Adding both LLFDI-FUNCTION and FP to ACS Risk did not improve predictive performance compared with Model 2. We found that each of the three models were adequately calibrated.

## **Additive Effects of LLFDI-FUNCTION and separately FP to ACS Risk across ACS Risk strata**

**LLFDI-FUNCTION—**In each of the three ACS Risk strata, stratifying further by LLFDI-FUNCTION substantially changed the risk of an adverse postoperative course. For example, for a patient with ACS Risk of 0.06–0.12 (i.e. 6–12% risk for serious complication), the risk of an adverse postoperative course without further risk stratification was 26.4%. Upon further examination within categories of LLFDI-FUNCTION, the risk estimate dropped to 9.6% for those with LLFDI-FUNCTION >60. The risk was 43.8% for those with LLFDI-FUNCTION <50. The other categories of ACS Risk also benefited from further risk stratification with LLFDI-FUNCTION although to a lesser degree.

**FP—**Similar to LLFDI-FUNCTION, the risk of an adverse postoperative course changed substantially within each ACS Risk category, albeit to a lesser extent than LLFDI-FUNCTION. (Supplementary Table S2)

### **DISCUSSION**

We found that self-reported function was more informative than FP in risk stratification of older adults for an adverse postoperative course. Self-reported function also improved risk stratification across the spectrum of ACS Risk.

There are a few other examples directly comparing self-reported physical status instruments like LLFDI-FUNCTION with frailty for the purpose of surgical risk stratification. Kim et al. found that a video animated tool, the Mobility Assessment Tool (MAT-sf), did not significantly improve the ability to predict ACS defined serious complication beyond a base model of age, sex, body mass index, pain score, the Revised Cardiac Risk index, American Society of Anesthesiology (ASA) score, and surgical risk.18 The study population of 197 patients with only 15% event rate limited their analysis. In addition, their base model included multiple other variables and prediction tools that have not been assembled in a common calculator like the ACS Calculator. Our sample was larger, but we also did not have the power to show a difference in serious complications. Nevertheless, the composite outcome we studied was a reasonable postoperative target comprised of individual outcomes which patients and clinicians deem valuable.

Makary et al.<sup>7</sup> found that FP predicted serious complications, length of stay and nursing home discharge in older adult surgical patients. Moreover, they were able to show increases in c-statistic for predicting serious complications and nursing home discharge for FP on top of the ASA score. Their results are not directly comparable with ours given we combined adverse outcomes. Our study distinguishes itself by comparing a three-minute self-report instrument against the longer FP inventory. Because of the convenience of the ACS Calculator, which has already been validated across hundreds of thousands of patients, we feel that the value of adding geriatric assessments must be considered incremental to what the ACS Calculator already offers. The ACS Calculator is an online tool that reports risk of both discrete and global outcomes of surgery using a single set of input condition already available in most medical records at the time of clinician deliberation. Indicating the presence of a certain condition that confers added risk is expedited by the use of drop down menus.

Robinson et al<sup>6,19</sup> and Dasgupta et al.<sup>5</sup> found that an alternative definition of frailty which evaluates an accumulation of deficits<sup>20</sup> was informative for predicting complications and discharge to nursing home. We did not evaluate this definition of frailty in our study given that many of the variables in that model were not available to us. Providers working in systems where this information is already available may find the accumulation of deficits approach more convenient to use. We are unaware of a performance comparison between that approach and self-reported function. Both the Robinson and Dasgupta groups conducted timed up and go tests which require training, marked space and added time above typical preoperative consultation.

Our results have significant implications. For one, self-reported function can improve the ACS Calculator when evaluating older adults going for intermediate to high risk surgery, albeit the improvement in prediction of an adverse postoperative outcome was modest. The ACS model performed relatively poorly in our sample compared to the developers' published performance<sup>4</sup>. This may reflect the greater challenge in predicting an adverse postoperative course in older adults and re-doubles the need for the addition of function and/or other geriatric assessments to risk stratification tools developed in general adult populations.

A second implication comes from our finding that LLFDI-FUNCTION performed slightly better than FP. We surmise that self-reported functional status can capture a wider range of vulnerability than FP. There are only five items included in FP; if we did not capture a patient's vulnerability to surgery by one of these items, we may not have accurately characterized this patient's risk. Moreover, only 18% of our patients had three or more frailty criteria in our population. FP may perform better in settings where the prevalence of frailty is higher but the training, space and time required to collect that information still dims enthusiasm for that approach.

Finally, although interventions to mitigate surgical risk are not well tested, being able to assess accurately the risk of an older adult undergoing surgery is still valuable. Self-reported function can assuage the anxieties of older adults with good function who would otherwise appear to be at elevated risk based on ACS calculator. For those found to be at elevated risk based on the ACS Calculator and self-reported function, providers may decide to refine treatment goals and plan of care.

Our study has several limitations. We did not have sufficient sample size to verify an association between LLFDI-FUNCTION and serious complications (or individual complications within this bundle). Patients may value knowing more globally their risk for an adverse postoperative course. Nevertheless, it would be helpful to know if self-reported function could forecast the risk of discrete complications, particularly if a provider may decide to use a more aggressive prophylaxis regimen in the face of elevated risk.

We are also limited in that we chose to measure an adverse postoperative outcome rather than the Clavien-Dindo which is commonly used in the surgical literature. We focused on the utility of self-reported function and FP incremental to the ACS Calculator, the latter of which is already set up to predict components of our composite outcome – viz., serious complications, nursing home discharge, readmission, and death.

We also did not compare our instrument with other self-report instruments. Indeed researchers may want to improve upon our findings by developing instruments more specifically focused on those aspects of function that are most closely tied to predicting an adverse postoperative course. Another limitation is that our results may also not generalize to patients with cognitive impairment given we excluded patients with positive MiniCog results.

Finally, prior to wider use of the model we derived in this study (namely ACS Risk divided into three categories enhanced with LLFDI-FUNCTION in three categories), prospective studies are necessary to validate our findings.

In summary, self-reported function using LLFDI-FUNCTION improves the ability of the ACS Calculator to identify which older adults are at elevated risk for an adverse postoperative course and is more feasible to administer in typical clinical settings compared with FP. Although adoption of LLFDI-FUNCTION into routine care requires validation in other surgical patient populations, our findings hold great promise for improving the way that clinicians currently perform preoperative evaluation.

## **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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## **Table 1**

## Descriptive Statistics of Older Adult Surgical Population



**Abbreviations:** ACS Risk = American College of Surgeons Universal Risk calculator based risk of serious complications, LLFDI-FUNCTION = function part of the computer adaptive testing version of the Late Life Function and Disability Instrument, MAC = monitored anesthesia care

\* Frequency out of 403 unless otherwise specified

† T-score, mean 50, SD10; higher scores indicate higher function

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Abbreviations: LLFD1-FUNCTION = function part of the computer adaptive testing version of the Late Life Function and Disability Instrument **Abbreviations**: LLFDI-FUNCTION = function part of the computer adaptive testing version of the Late Life Function and Disability Instrument

 $\underset{\text{Any}}{\ast}$  1 of the 4 outcomes in the columns to the left. Any 1 of the 4 outcomes in the columns to the left.

\*\*\*\*<br>Based on the five criteria described by Fried et al. (aka Fried Frailty Criteria) – exhaustion/depression, low activity level/energy expenditure, weight loss weak grip strength, slow gait speed Based on the five criteria described by Fried et al. (aka Fried Frailty Criteria) – exhaustion/depression, low activity level/energy expenditure, weight loss weak grip strength, slow gait speed



Comparison of Performance and Calibration Statistics for ACS Risk of Serious Complications, LLFDI FUNCTION, Frailty Phenotype and Combinations Comparison of Performance and Calibration Statistics for ACS Risk of Serious Complications, LLFDI FUNCTION, Frailty Phenotype and Combinations (n=403)



Abbreviations: ACS =American College of Surgeons Universal Risk Calculator, n/a = not applicable, H-L =Hosmer-Lemeshow, NRI=Net Reclassification Index, ref = reference, LLFDI FUNCTION = **Abbreviations**: ACS =American College of Surgeons Universal Risk Calculator, n/a = not applicable, H-L =Hosmer-Lemeshow, NRI=Net Reclassification Index, ref = reference, LLFDI FUNCTION = Late Life Function part (which is the Activity Limitation scale) of the computer adaptive testing version of the Late Life Function and Disability Instrument Late Life Function part (which is the Activity Limitation scale) of the computer adaptive testing version of the Late Life Function and Disability Instrument

Based on the ACS Calculator (https://riskcalculator.facs.org/RiskCalculator/) which contains 22 demographic and co-morbid condition variables. Based on the ACS Calculator (<https://riskcalculator.facs.org/RiskCalculator/>) which contains 22 demographic and co-morbid condition variables.

 $^{\ast}$  Based on the five criteria described by Fried et al. (aka Fried Frailty Criteria) Based on the five criteria described by Fried et al. (aka Fried Frailty Criteria)

\*\* Calculated from Bootstrapping 1000 samples with replacement from our population with 403 patients. Calculated from Bootstrapping 1000 samples with replacement from our population with 403 patients.

\*\*\*<br> $H-L > 0.05-0.10$  indicates good calibration. H-L > 0.05–0.10 indicates good calibration.