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Frailty as a Predictor of Outcomes Following Major Lower Extremity Amputation

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Frailty as a Predictor of Outcomes Following Major Lower Extremity Amputation

By

Zachary Fang
B.S., Tufts University, 2011

Advisor: **Theresa Gillespie, PhD**

An abstract of
A thesis submitted to the Faculty of the
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Abstract

Frailty as a Predictor of Outcomes Following Major Lower Extremity Amputation

By: **Zachary Fang**

Objective:
Preoperative clinical frailty is increasingly used as a surrogate for a patient's ability to have a successful operative outcome. While previous reports have analyzed large national databases to correlate frailty with adverse results, there are limited single-center series demonstrating the same. Patients undergoing major lower extremity amputation (LEA) carry a high-risk of perioperative morbidity and mortality, including high 30-day readmission rates. We hypothesized that clinical evidence of preoperative frailty is associated with an increased risk of postoperative readmission.

Methods:
A retrospective review was performed for all patients who underwent above the knee (AKA) or below the knee (BKA) amputation for any indication within a single healthcare system over a five-year period. Data collected included standard demographics, insurance status, follow-up data, and components of the modified frailty index (mFI). Using the mFI, preoperative frailty status was determined for each patient. The primary outcome was 30-day mortality. Secondary outcomes included 30-day readmission and other postoperative complications.

Results:
Among 400 patients who identified, 379 were included in the analysis. The overall readmission and mortality rates as noted in patient charts for this group were 22.7% and 6.1%. Readmission rates increased with increasing mFI score: rates were 5.3%, 15%, 17.5%, 20.3%, 31%, and 35.5% for mFI scores of 0, 1, 2, 3, 4, and ≥5, respectively ($p=0.015$). On multivariate logistic regression comparing mFI score with age, race, operation type, insurance status, and surgical specialty, only mFI score was found to be a significant predictor of readmission (OR 1.417, CI 1.198-1.677, $p<0.0001$).

Conclusions:
Preoperative clinical frailty is associated with an increased 30-day readmission rate in patients undergoing LEA. As the mFI utilizes easily obtained historical information from the medical record, this analysis may be helpful in preoperative decision making for frail patients who are borderline candidates for operative therapy. Furthermore, preoperative frailty status should be considered when proposing standardized benchmarks for readmission.

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INTRODUCTION

Patients who undergo lower extremity amputation (LEA) often have multiple comorbidities and the prognosis is frequently poor, with 30-day and one-year mortality rates of 22% and 44%, respectively (1). The long-term outlook is equally bleak: only 40% of patients who undergo a below the knee amputation (BKA) regain full mobility after two years, and five-year mortality rates are as high as 77% (1, 2). Previous investigations of prognostic factors have been limited to comparisons between surgical subspecialty fields. Frailty assessments have not previously been evaluated as a predictive factor in LEA outcomes (3).

Frailty in medicine is commonly defined as a "biological syndrome that reflects a state of decreased physiological reserve." The exact pathophysiology is currently unknown, but proposed mechanisms include dysregulation of hormones and cytokines in the aging body, accumulation of insults to different organ systems due to disease, and lifelong wear and tear (4). For surgical fields, frailty is rapidly emerging as a potential method of risk-stratifying patients, and research is being performed to validate frailty assessments across a growing variety of subspecialties, operations, and populations (5-8). To date, frailty status has been identified as a predictor of poor outcomes in colorectal, cardiovascular, and gynecological surgical procedures. Outcomes such as mortality, increased 30-day readmission rates, and a variety of other post-operative complications have been consistently correlated with an increase in frailty across different studies (9-18). These findings have led to recognition across a variety of fields that frail patients have worse

outcomes than the non-frail, and that early identification of frailty is an important step in determining treatment, predicting results, and designing effective interventions (4).

One population that has yet to be assessed for the effect of frailty status on outcomes is patients undergoing major lower extremity amputation. Because these patients have such a high burden of comorbidities, a frailty measurement tool could have a significant impact on physicians' ability to effectively risk-stratify and predict outcomes. Subsequent steps could involve intervention-based therapies aimed at changing frailty status or enhanced post-operative surveillance to prevent adverse outcomes.

BACKGROUND

Frailty

Frailty has been discussed as a concept in medicine for more than a quarter of a century (19, 20). Originally described in the elderly population, early studies struggled with multiple definitions of frail as well as different (and often overlapping) methods of assessment (20). Today, frailty is often viewed as a combination of biological syndrome, decline in function, and accumulation of comorbidities (21). The biologic basis of frailty is rooted in the theory that, as we age, our bodies sustain repeated molecular and cellular damage through a combination of genetic and environmental factors (22). While any one insult is not enough to cause an immediate change in outward appearance or function, over time, the accumulation of damage overwhelms our bodies' homeostatic and maintenance systems. It is thought that this leads to changes in organ function and negatively impacts the redundancy found in many organ systems. A reduction in physical activity and decline in nutritional status further contribute to the picture of decreased physiologic reserve (23). At this point, an individual meets the biomedical definition of frailty: "biological syndrome that reflects a state of decreased physiological reserve" (4).

The exact pathophysiology of all preceding steps is currently unknown, but changes in the structure and function of neurons have been associated with many disorders and diseases that are present in the frail patient, such as delirium and neurocognitive decline (24, 25). The endocrine and immune systems have also been implicated, as hormonal and cytokine levels are known to fluctuate with age and cause a muted inflammatory response (26, 27). For example, the older immune system is known to respond abnormally to

stimuli, leading to reductions in the effectiveness of vaccinations in the elderly. Finally, an overall decrease in muscle mass, strength, and power (sarcopenia) is widely regarded as a key component in frailty. Though some degree of sarcopenia is normal in the aging individual, the dysregulation of hormones and cytokines in the frail individual cause a marked increase in weakness and imbalance that contribute to decreased physical activity and the overall picture of frailty (28).

A frail individual may be otherwise "normal" at baseline, but an acute stress event such as a fall or surgery leads to an increase in adverse events, delayed recovery, and often lasting disability. This not only leads to increased hospital costs and lengthier admissions, but the clinical condition of patients who never fully recover can feed back into their underlying frailty, potentially creating a vicious cycle.

There is currently no single standard method of defining or measuring frailty, and more than 20 tools have been developed that are currently in use. This is due in part to the competing models of how frailty is measured: As a growing list of deficits that patients acquire as they age (the cumulative deficit model) or as a amalgam of biological measurements in which different aspects are shared among populations (the phenotype model). It is worth noting that there is significant overlap between the two models and that they seem to be converging as they are refined over time (29).

Perhaps the most comprehensive frailty tool was developed using data from the Canadian Study of Health and Aging (CSHA). First proposed by Rockwood et al., the CSHA frailty

index is considered the prototypical cumulative deficit index; it incorporates more than 70 data points from patient history and physical exams into a measure that accurately assesses the 18- and 70-month risk of death. As a clinical tool, however, a 70-point scale is unwieldy and time-consuming, so other efforts have been made to more quickly and easily assess frailty (30, 31). In contrast to the CSHA index, Fried et al. published a prospective measure of frailty based on five clinically measured characteristics in what proved to be a landmark study describing the phenotypic model of frailty (32). Based on weight loss, exhaustion, low energy, slow gait speed, and weak grip strength, the Fried criteria were found to be strongly correlated with mortality at 3, 5 and 7 years. Though they have been widely adapted into other frailty measures (33), Fried's criteria have been criticized for failing to take into account the neurocognitive aspects that are believed to be important contributors to a patient's overall frailty (34).

Many other tools have been developed to assess frailty specific populations. One widely used instrument is the modified Frailty Index (mFI), an 11-point scale that has been validated to accurately measure frailty and predict outcomes in surgery patients undergoing a variety of procedures (8, 35, 36). Velanovich et al. created the mFI by mapping the 70 points of the CSHA Frailty Index onto the variables collected by the National Surgical Quality Improvement Program (NSQIP) and then validated the resulting 11-point scale in a retrospective population of patients undergoing surgery across 10 different subspecialties. Although they concluded that the relatively simple mFI was easy to use and correctly predicted outcomes, the authors noted that there were several limitations: namely, that researchers were forced to rely on the previous diagnosis

in the medical record and they did not know if the selected variables were the most important in determining frailty status (36). However, because it still consists of far fewer data points than the CSHA Frailty Index but has been proven to accurately predict outcomes, the mFI is an extremely useful tool to assess frailty both prospectively and retrospectively in a thorough yet expedient manner.

Frailty in surgery

For surgical fields, frailty is rapidly emerging as a potential method of risk-stratifying patients, and research is being performed to validate a variety of frailty assessments across a growing selection of subspecialties, operations, and populations (5-7). Mortality, increased surgical complication rates, and increased length of stay are the most common outcomes associated with frailty. In otolaryngologic surgery, Adams et al. found that an increase in the mFI correlated with an increase in mortality (0.2% to 11.9%, $p<0.001$) as well as an increase in overall complications (9.5% to 40.5%, $p<0.001$) (9). Likewise, Hodari et al. found that the mFI could independently predict mortality in esophagectomy patients (OR 31.84, $p=0.015$)(10). Dasgupta et al. used the Edmonton Frail Scale (an assessment tool comprising both cumulative deficits and phenotypic characteristics) to show that lower frailty scores were associated with fewer complications in orthopedic surgery patients (OR 0.27, 95%CI 1.55-16.25)(12, 37). Courtney-Brooks et al. found that 67% of phenotypically frail patients (measured using Fried's criteria) undergoing gynecological oncology procedures experienced post-op complications at 30 days compared with 24% of non-frail ($p=0.04$)(11). In transplant surgery, frailty has been associated with both delayed graft function (38) and early hospital readmission (13).

Similar outcomes have been reported in minimally invasive surgery and colorectal surgery (14-18). These findings support the now widely accepted belief that frail patients have worse outcomes than the non-frail, and that early identification of frailty is an important step in determining treatment and predicting results. They also are representative, however, of the diverse array of tools that have been developed to measure frailty in both clinical and research settings.

Because there is no consensus on how to measure frailty in the surgical patient (39, 40), several subspecialties have tried to develop new frailty indices specific to their needs. At the University of Arizona, researchers modified the CSHA frailty index to a slightly more manageable, but still potentially burdensome, 50-point frailty index and used it to prospectively show that frailty in trauma patients was associated with "unfavorable discharge" (OR 1.3, 95%CI 1.1-1.8) (41) and increased in-hospital complications (OR 2.5, 95%CI 1.5-6.0, $p<0.001$) (42). They then developed a 15-point Trauma-Specific Frailty Index (TSFI) that predicted unfavorable discharge independent of other factors (OR 1.5, 95%CI 1.1-2.5) (43). Unbeknownst to them, however, Farhat et al. had already used the 11-point mFI to show that frailty was associated with increased wound infections and mortality in the elderly trauma population (OR 11.70, $p<0.001$) (44). This vignette highlights some of problems that frailty researchers, and others who develop and apply assessment instruments, face. Each new frailty assessment tool must be validated in a population before it can be used in general practice, but there are often overlapping domains between tools and authors can easily end up repeating the work of others.

Often researchers have attempted to use parts of existing frailty indices to simplify or streamline patient assessments, with varying degrees of success. In coronary artery bypass graft (CABG) and aortic valve replacement (AVR) patients, Afilalo et al. found that slow gait speed (a component of Fried's criteria) was an independent predictor of mortality (OR 3.05, 95%CI 1.23-7.54) (45). In a follow-up study several years later, the same authors found that 35% of frail patients had "poor outcomes" (defined as all-cause mortality or post-op complications) in cardiac surgery compared with 13% of non-frail, as measured by four different frailty scales (46). Using a slightly more expansive measure of frailty that included grip strength, serum albumin, and activities of daily living in addition to gait speed, Green et al. examined patients undergoing transcatheter AVR and found that while frailty was predictive of one-year mortality (HR 3.5, 95%CI 1.4-8.5, p=0.007), it was not an indicator of operative success (47). Ganapathi et al. developed a 6-point frailty index consisting of age, BMI, anemia, history of stroke, hypoalbuminemia, and total psoas volume to show that compared to nonfrail patients, frail patients undergoing surgery of the proximal aorta had increased 30-day mortality (OR 5.0, 95%CI 1.8-14.0, $p<0.01$) and one-year mortality (OR 4.5, 95%CI 2.1-9.6, $p<0.01$)(48).

Amputations

Although frailty research is a current leading research issue in numerous surgical subspecialties, many patient populations have not been included yet in these studies. One group that has yet to be assessed for frailty status versus outcomes is the population of patients undergoing major lower extremity amputation (LEA). The leading cause of amputation in the United States is peripheral artery disease, both in combination with and

without diabetes, the presence of which raises the risk of needing amputation 10-fold (2). Patients who undergo LEA often have multiple comorbidities and the prognosis in most cases is poor, with 30-day and 1-year mortality rates as high as 22% and 44%, respectively(1, 49). The outlook only worsens in the long term: One international medical society, the Trans-Atlantic Inter-Society Consensus (TASC), found that only 40% of patients who undergo a below the knee amputation (BKA) regain full mobility after two years, while 77% are deceased after five years (1, 2).

These numbers have spurred multiple efforts to risk-stratify patients and identify those that may require additional support both inside the hospital and after they are discharged. Belmont et al. surveyed the National Surgical Quality Improvement Program (NSQIP) database and found that renal disease (OR 3.19, 95%CI 2.33-4.38, $p<0.0001$), history of MI or CHF (OR 1.97, 95%CI 1.35-2.88, $p<0.001$), sepsis (OR 1.83, 95%CI 1.34-2.85, $p<0.001$), COPD (OR 1.68, 95%CI 1.13-2.52, $p=0.01$), and increased age (OR 1.03, 95%CI 1.02-1.05, $p<0.0001$) were all predictors of mortality after below the knee amputations (50). Scott et al. performed a similar retrospective analysis of patients undergoing lower extremity amputation in the UK and also found that age >79 (HR 2.78, 95%CI 1.82-4.25, $p<0.001$) and kidney failure (HR 1.57, 95%CI 1.07-2.30, $p=0.02$) were associated with increased mortality(51). Researchers at the University of California, San Diego, developed a 13-point predictive index for 30-day mortality after major lower extremity amputation (52), but for unknown reasons it has not gained wide acceptance, nor has it been incorporated into general practice. It is interesting to note that many of the independent predictors of mortality mentioned above overlap with the components of the

mFI (history of CHF or MI, history of cardiac surgery, COPD, dependent functional status, impaired sensorium).

The eventual cause of death in many LEA patients is usually major cardiovascular adverse events, including stroke and myocardial infarction (1, 2). It remains unclear whether impaired mobility contributes to such poor outcomes, or if it is rather a manifestation of multiple underlying comorbidities. While a significant number of amputations are performed for peripheral vascular disease, some younger patients also undergo LEA for primary orthopedic problems or complications of diabetes (3). Previous investigations have demonstrated a difference in outcomes for patients undergoing LEA by vascular and orthopedic surgeons. Surprisingly, however, frailty assessments have not previously been performed in these two patient groups as a predictive factor in LEA outcomes, nor have there been any studies investigating overlap between the populations.

Significance

Multiple studies have proven the association between frailty and poor surgical outcomes across a variety of procedures. Although a substantial portion of the patient population that undergoes LEA likely meets most frailty criteria, currently no publications provide evidence for a relationship between frailty and outcomes after LEA. In view of the significant 30-day and one-year mortality rates associated with LEA, an assessment of frailty in patients who undergo LEA would be an important step towards the future use of frailty indices to risk-stratify these patients. Ideally, such a tool would be of clinical significance at the time of patient counseling; a frail patient with a predicted poor

outcome may be better served by end-of-life care discussions with subsequent hospice services. Thus, the purpose of this project is to also provide a basis for future studies that prospectively assess frailty in the amputation population as well as the need for extra interventions or precautions in frail patients undergoing LEA in order to improve outcomes.

METHODS

Specific Aims

Aim #1: To conduct a retrospective evaluation of frailty as a prognostic indicator of 30-day mortality and morbidity in all patients undergoing below the knee (BKA) and above the knee (AKA) amputations at two large, academic –associated medical centers.

Aim #2: To provide the basis for a future prospective study that investigates the relationship between frailty and outcomes of lower extremity amputations.

Study Population

All patients who underwent either BKA or AKA procedures at Grady Memorial Hospital (GMH) and Emory University Hospital (EUH) between December 2010 and March 2015 were retrospectively identified. Patients were excluded if they were younger than 18 years. Patient medical records were interrogated to generate a frailty score using the Modified Frailty Index (mFI). Other sociodemographic variables collected included age, race, ethnicity, insurance status, employment status, and gender.

The Modified Frailty Index is a previously validated retrospective tool that was developed using data from the Canadian Study on Health and Aging(36). The 11 historical parameters of the mFI were used to generate a frailty score – each component of the mFI is worth one point; the maximum score (meaning worse frailty) is 11 (Table 1). Briefly, the mFI components are impaired functional status, history of chronic obstructive pulmonary disease (COPD) or current pneumonia, history of congestive heart failure (CHF), history of myocardial infarction (MI), history of cardiac surgery,

percutaneous coronary intervention, or angina within 30 days, hypertension requiring medication, impaired sensorium (e.g. memory loss or dementia), history of transient ischemic attacks, history of stroke or stroke with neurologic deficit, history of peripheral vascular disease, and history of diabetes. Components of the mFI were classified as present if they were documented in the medical record.

Data Sources

Data were collected retrospectively by a single abstractor via medical record review from prospectively maintained data sets at both hospitals. At GMH, patient registries that have been maintained by the Vascular and Orthopedic Surgery Departments were used to identify patients who had amputations performed. At EUH, International Classification of Diseases, Ninth Revision (ICD-9) and Current Procedural Terminology (CPT) codes were used to identify patients from the Clinical Data Warehouse (CDW) maintained by Emory Healthcare. After identification, all pertinent variables were collected by manual chart review. Institutional Research Board (IRB) and Grady Research approvals, along with a HIPAA waiver, were obtained and maintained in active status throughout the conduct of this project. An IRB waiver for consent was also obtained for the duration of this study.

We hypothesized that there is an association between increasing mFI score and higher rates of adverse outcomes. To that end, we calculated *a priori* that we would need to collect data on at least 200 patients (100 frail, 100 non-frail) in order to adequately power this study to detect a 15% difference in 30-day mortality (our primary outcome).

The primary outcome was all-cause mortality within 30 days of a patient's last amputation, or whichever amputation was intended to be their last (as noted in the medical record). Secondary outcomes included unplanned revision, surgical site infection (SSI), stroke, renal failure, prolonged ventilation, sepsis, DVT, MI, 30-day readmission, and 1-year mortality. Outcomes other than 1-year mortality were classified as existing if they occurred within 30 days of amputation. Thirty-day readmission was defined as unplanned readmission to either GMH or EUH within 30 days of discharge after the last amputation. One-year mortality data, when not available in the medical record, was backfilled using each patient's last known contact with the healthcare system. Only complete cases were included for analysis.

Analysis

To account for lower numbers of patients with higher mFI scores, patients with scores >4 were grouped into a "≥5" category in a manner consistent with the literature (6). Modified Frailty Index score was also used to divide subjects into "frail" and "non-frail" categories as previously described, with "non-frail" patients having a score of ≤2 and "frail" subjects having a score of >2 (6, 53).

Baseline demographics were first analyzed by descriptive and bivariate statistics, with each demographic being stratified by mFI score and frail/non-frail categories; this was then repeated for the components of the mFI and each outcome. Univariate analysis was performed to examine differences between subject groups in specific outcomes among mFI scores and frailty status using Chi-square and t-tests.

We also examined the risk of specific outcome variables, e.g. readmission and mortality, and used logistic regression models to identify factors associated with patient

outcomes. The initial logistic model included baseline demographics, mFI score, and the components of the mFI. Stepwise selection was used to identify significant predictors of outcomes at the $\alpha=0.05$ level. A clinically relevant model with mFI score, age and sex was also generated. The components of the mFI were compared to the mFI score to determine which models had better discriminatory ability as measured by the area under the receiver-operator curve (ROC). Modified Frailty Index score was analyzed as both a continuous and a categorical variable to assess the linearity of any significant relationships. Each analysis was performed with mFI as a truncated score (from 0 to ≥ 5) and as a dichotomous variable (frail/non-frail).

Kaplan-Meier survival curves were constructed to examine crude one-year survival differences between individuals with differing mFI scores. Survival curves were generated for both the truncated and the dichotomous mFI scores; Wilcoxon test statistics were generated to detect significant differences between curves at the $\alpha=0.05$ level. A cox proportional hazards model examining factors that influenced one-year mortality was generated using the same variables and technique as the logistic regression models described above.

RESULTS

Of 400 patients who underwent major lower extremity amputation from 2010-2015 (Table 2), 379 were included in the analysis phase; the remainder was excluded due to missing outcomes data. The mean patient age was 59.1 ±15.0 years, with the majority being male (64.0%). Most patients were African-American (69.5%) and either unemployed (35.1%) or retired (35.6%). The mean number of points scored on the mFI was 2.9 ±1.7 (range 0-8). Using a truncated mFI from 0-5 to account for low numbers of high-scoring patients, the most common score was mFI=2 (n=98), followed by mFI≥5 (n=73), mFI=4 (n=70), mFI=3 (n=66), mFI=1 (n=37), and mFI=0 (n=35)(Table 2). Using the dichotomized mFI score, 170 (44.9%) patients scored ≤2 and 209 (55.1%) scored >2 (Table 3). The most common mFI component present was hypertension (78.9%), followed by diabetes mellitus (54.9%) and peripheral vascular disease (54.1%) (Tables 4 and 5). Just over half (52.7%) of all patients underwent below the knee amputation as the definitive treatment for their presenting clinical condition (Table 2). The majority of amputations were performed by vascular surgery services (72.3%), followed by orthopedic surgery (14.2%) and general surgery/trauma (13.5%).

Association Between Modified Frailty Index and 30-day mortality

The 30-day mortality rate was 6.1% overall, 5.3% for patients with mFI ≤2 and 6.7% for patients with mFI >2. Univariate and multivariate analysis did not show an association between mFI and 30-day mortality for either the truncated or dichotomous score. Multivariate logistic regression comparing mFI, sex, age, race, employment status, and insurance status found that only age was a significant predictor of 30-day mortality (OR 1.033 per year, 95%CI 1.003-1.065, p=0.0291).

Association between Modified Frailty Index and additional outcomes

The 30-day readmission rate was 22.7% overall; 14.1% for patients with mFI ≤2 and 29.7% for patients with mFI >2. Univariate analysis revealed that the proportion of patients requiring readmission within 30 days of discharge increased with both the truncated mFI (χ^2=18.1158, p=0.0028) and the dichotomous mFI (p=0.0003) (Tables 6 and 7). On multivariate logistic regression comparing mFI, mFI components, sex, age, race, employment status, and insurance status only mFI (OR 1.49, p<0.0001) and sex (OR 1.81, p=0.0332) were significant predictors of 30-day readmission (Table 8). A multivariate model with mFI as a dichotomous variable (mFI >2 and ≤2) increased the OR estimate for mFI to 2.58 (p=0.0004) (Table 9). When age and sex were forced into the model, the OR estimate for mFI further increased to 2.60 (p<0.0013) (Table 9). A multivariable model containing mFI components but no composite score had a ROC with area of 0.650, while a model including the composite score resulted in a ROC curve with area 0.674.

To determine if the increase in 30-day readmission was non-linear with respect to truncated mFI score, we also performed a multivariate "chunk test" with mFI as a categorical variable, age and sex. A model with indicator variables for each level of frailty was run, with 0 as the reference group. Using this model, the increase in OR was calculated to be 1.65 (95% CI 0.35-7.81) from 0 to 1 point, 2.26 (95% CI 0.58-8.79) from 0 to 2 points, 2.85 (95% CI 0.69-11.83) from 0 to 3 points, 6.08 (95% CI 1.47-25.15) from 0 to 4 points and 7.54 (95% CI 1.85-30.76) from 0 to ≥5 points. The increase in OR supports a linear model for the primary analysis.

There was no association between either truncated or dichotomous mFI and occurrence of unplanned revisions on univariate analysis. Multivariate logistic regression comparing mFI, sex, age, race, employment status, and insurance status found that only age was a significant predictor of unplanned revisions (OR 0.984, 95%CI 0.969-0.999, p=0.0334). Univariate analysis revealed no association between truncated or dichotomous mFI and composite adverse events. On multivariate analysis, however, both truncated mFI score (OR 1.274, 95%CI 1.069-1.517, p=0.0067) and age (OR 0.981, 95%CI 0.963-0.998, p=0.0314) were found to be associated with the composite adverse events outcome. This was not the case with dichotomous mFI (OR 1.623 95%CI 0.978-2.692, p=0.0609).

Survival Analysis

Kaplan-Meier survival curves of major lower extremity patients stratified by mFI score showed decreased one-year survival for patients who scored 3, 4, or ≥5 points compared to 0, 1, or 2 points (Wilcoxon test statistic = 14.2491, p=0.0141) (Figure 1). A simplified Kaplan-Meier curve comparing patients with mFI >2 to those with mFI ≤2 also showed decreased one-year survival for patients with a higher mFI score (Wilcoxon test statistic = 8.3731, p=0.0038) (Figure 2). A multivariable cox proportional hazards model found that the hazard ratio comparing patients with mFI >2 to those with mFI ≤2 was 1.77 (95%CI 0.94-3.35).

Association between expanded mFI variables and outcomes

Multivariable logistic regression comparing the individual variables of the mFI was performed to determine which variables were drivers of significant relationships. History of COPD (OR 6.413 95%CI 2.062-19.940, p=0.0013) congestive heart failure (OR 3.224, 95%CI 1.104-9.421, p=0.0324), and impaired sensorium (OR 8.054, 95%CI 2.308-28.104, p=0.0011) were the only significant predictors at the α=0.05 level (Table 10). For 30-day readmission, impaired functional status (OR 2.486, 95%CI 1.149-5.379, p=0.0208) and congestive heart failure (OR1.901, 95%CI 1.064-3.395, p=0.0299) were both significant predictors at the α=0.05 level (Table 11). The only variable significant at the α=0.05 level for unplanned revisions was history of myocardial infarction (OR 2.100, 95%CI 1.054-4.184, p=0.0349)(Table 12). There were no significant drivers of the adverse events composite outcome (Table 13).

Emory and Grady patients

There was no statistically significant difference in 30-day mortality, 30-day readmission, or adverse events between patients treated at Emory versus those who received care at Grady. Patients at Grady, however, had higher rates of unplanned revisions compared to those at Emory (32.0% vs. 22.6%, p=0.0348). When the cohort was limited to only vascular patients from both institutions, there was no change in which variables were significant for any outcomes. A higher proportion of patients on vascular services had mFI scores >2 (65.7%) compared to orthopedics (29.6%) and trauma (13.5%).

DISCUSSION

This study demonstrates that preoperative frailty as measured by the Modified Frailty Index is significantly associated with 30-day readmission. The lack of a statistically significant relationship between preoperative frailty status and 30-day mortality, the need for further surgical intervention, or overall adverse events could be due to flaws in study design (discussed below). Despite this, these findings add to the growing body of evidence across multiple surgical specialties that the effects of frailty are measurable and/or clinically meaningful in the form of postoperative outcomes.

The association between frailty and 30-day readmission is consistent with previous findings in patients undergoing colorectal or cardiac procedures(16). Not all of our findings, however, are consistent with the literature: multiple studies focused on vascular surgery populations have found significant relationships between frailty and 30-day mortality and composite adverse outcomes (6, 8, 53, 54). The majority of these findings have come from large, national patient registries that include thousands of patients, raising the possibility that our study simply lacks the sample size to detect such a difference and our initial power calculation was inaccurate. It is also possible that the event number is too low to detect a significant difference, especially given that the 30-day mortality rate in our study is significantly lower than the national average. The inclusion of trauma patients, who are on average younger and healthier than the typical vascular patient, could also have affected the observed mortality and frailty rates. In addition to their health status, there is also the possibility that the past medical history of some trauma patients was incomplete due to the emergent nature of their care. Because this study relies on the medical record to measure frailty, some mFI scores could be

incorrect if this information was never properly collected. Finally, information on preoperative sepsis and end-stage renal disease, both medical conditions that are known to affect postoperative outcomes, was not collected.

A possible reason for the lack of detected effect is variability in the definition of adverse events between studies, especially the inclusion of events such as 30-day mortality and the breakdown of outcomes by different classification schemes. For example, several studies used Clavien-Dindo classifications to categorize postoperative complications in addition to specific outcomes (6, 8, 53). We chose not to pursue this classification scheme because this information is not always clearly recorded in the electronic medical record and can be a somewhat subjective measure in that not all studies used the same levels of the Clavien-Dindo classification scheme.

The lack of difference in outcomes (other that unplanned revisions) between Emory and Grady patients is somewhat surprising: the Grady patient population has a higher burden of comorbidities due to increased barriers to healthcare access. If they are less healthy preoperatively than the Emory cohort, they can be expected to have worse outcomes. The Grady cohort, however, is comprised of patients from vascular, orthopedic, and trauma services, whereas the Emory cohort is only comprised of vascular patients. It is likely then that the Emory patients are actually less healthy than the Grady patients who were included in this study, causing the lack of a detected difference. A possible reason for the difference in unplanned revisions is that the trauma patients from Grady were more likely to have infected or “dirty” wounds due to the mechanism of injury. Vascular patients were, on average, more frail (i.e. had higher mFI scores) than their orthopedic or trauma counterparts. It is possible that these are actually 3 different

patient populations, but the extent of the difference is unknown. The fact that the outcomes did not change when the analysis was limited to only vascular patients could be a result of either minimal difference or inadequate numbers of trauma and orthopedic patients to begin with. It is unknown whether there is a difference in overall amputation rates amongst the three groups, though it is likely that vascular and orthopedic rates are similar as many of these patients have the same comorbidities. Because the majority of patients in this study were vascular, our results are most generalizable to vascular patient populations, but we believe that the inclusion of orthopedic and trauma patients enhances the applicability of our findings somewhat.

The retrospective nature of our study places constraints on the definitions of several variables of the mFI, most notably patient independence and recent angina. These factors were taken into account when noted in the medical record, but a prospective study would conceivably have much greater fidelity of patient characteristics. As stated above, the relatively small sample size of patients available may have contributed to lack of significance in several expected relationships. It is also possible that the mFI is a poor scale in a population with a high burden of disease, such as those undergoing major LEA. For instance, the mFI does not account for differing levels of severity within components. A patient with mild memory loss would receive the same score as a severely demented patient for the “impaired cognition” variable. Though these patients clearly have different burdens with respect to their comorbidity, the mFI treats them as equals. This could cause the mFI to have decreased discriminatory power when the majority of a patient’s morbidities are cognitive in nature.

To our knowledge, this is the first study to examine the use of a frailty assessment tool as a predictor of postoperative outcomes in the major lower extremity amputation population. These data are not dependent on a large, national patient data series, which brings both advantages and disadvantages. Although the results presented may not be reflective of national trends, they do provide a window into how the Emory Healthcare and Grady Healthcare systems are performing in terms of outcomes after major lower extremity amputation. For example, the 30-day mortality rate of 6.1% is much lower than the 22% observed by Norgren et al. but this may be closer to the mortality rates at a similarly sized academic institution. One could thus use these numbers to compare Emory to institutions of similar sizes with similar patient populations. Furthermore, the diversity of our patient population (including trauma, vascular, and orthopedic patients) enhances the comparability of our findings to similar groups. Another strength is the complete control over what information was collected and included in our database. Though we relied on the accuracy of the electronic medical record systems at each institution, manual chart abstraction allowed us to scrutinize all of the documentation rather than solely depend on claims data or procedure codes for information.

Readmission within 30 days of discharge in the United States has been estimated to cost somewhere between $12-44 billion dollars per year (55, 56). From a purely financial perspective, the association between frailty and 30-day readmission should thus be given extra weight when confronted with the frail patient who requires an amputation. Though it is widely known that these patients bear some of the heaviest burdens in terms of comorbidities, there is often little special consideration of the needs of new amputees while in the hospital. Easing the transition to home, either with enhanced recovery

programs or some other focused follow-up initiative, should be considered by surgeons before discharging such patients. A 2011 meta-analysis categorized interventions that target readmission into three domains: pre-discharge interventions that prepare patients before they leave the hospital, post-discharge interventions that encourage increased communication and follow-up between patient and provider, and bridging interventions that aim to increase continuity and ease the transition between hospital and community settings (57). Although patient education and pre-discharge planning were the most commonly studied interventions, randomized studies examining the effectiveness of pre-discharge planning have generated mixed results and the differences across studies made it difficult to perform a systematic comparison (57). Several potential interventions, however, may represent the most benefit for major LEA patients. Specifically, a combination of patient discharge instructions and post-discharge telephone call was shown to reduce 30-day readmission by 3-28% in three different studies (58-60).

Multiple future avenues for further research are suggested by this study. If the goal of practitioners is to immediately impact the care of patients undergoing major lower extremity amputation, interventions aimed at reducing 30-day readmission should be implemented for all patients in this population as soon as possible. If, on the other hand, the primary goal is to use frailty to identify and apply interventions only in those most at risk, then several studies should first be performed. As stated earlier, the lack of consensus in the medical community regarding a quick, standard method of assessing frailty is a barrier in both the clinical and research domains. The Modified Frailty Index, though simple and expedient in practice, has not been validated to prospectively assess frailty. The first step would thus be to validate the mFI in a prospective cohort of major

lower extremity amputation patients. Once that is completed (and any necessary modifications are made to the mFI to maximize its discriminatory ability), interventions aimed at reducing 30-day readmission and 30-day mortality could be tested in frail (or high mFI-scoring) patients. Frailty assessment has the potential to serve as a powerful tool in the physician's armamentarium, and the findings of this study will ideally be the first step towards further studies that eventually result in the implementation of an instrument of positive change on patient outcomes.

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Table 1. Components of the Modified Frailty Index

CSHA[a] component	**mFI component**	**Point value**
Problems with dressing Problems with bathing Problems with personal grooming Problems with cooking Problems with going out alone	Impaired functional status – partially or totally dependent	1
Chronic/acute respiratory problems Lung problems	History of COPD[b] or current pneumonia	1
Congestive heart failure	Congestive heart failure present in past 30 days	1
Myocardial infarction	History of myocardial infarction	1
Cardiac problems Cardiac disease	History of cardiac surgery History of percutaneous coronary intervention Angina in past 30 days	1
Hypertension	Hypertension requiring medication	1
Clouding or delirium History relevant to cognitive impairment or loss Family history relevant to cognitive impairment	Impaired sensorium	1
Cerebrovascular problems	History of transient ischemic attack	1
History of stroke	Cerebrovascular accident or stroke with neurologic deficit	1
Decreased peripheral pulses	Peripheral vascular disease or rest pain History of revascularization	1
History of diabetes mellitus	Diabetes mellitus	1
Total	Total	11

[a]: Canadian Study of Health and Aging
[b]: Chronic obstructive pulmonary disease

Table 2: Baseline demographics of patients undergoing major lower extremity amputation from 2010-2015 stratified by Modified Frailty Index (mFI) score (0 to ≥5)

Parameter	Totals (n=379)	mFI=0 (n=35)	mFI=1 (n=37)	mFI=2 (n=98)	mFI=3 (n=66)	mFI=4 (n=70)	mFI≥5 (n=73)
Mean age (std dev)	59 (15)	37 (14)	54 (15)	56 (12)	62 (13)	66 (12)	66 (12)
Male, N (%)	243 (64%)	24 (69%)	30 (81%)	65 (66%)	46 (70%)	39 (56%)	44 (63%)
Race							
Caucasian, N (%)	104 (27%)	16 (46%)	11 (30%)	26 (27%)	16 (24%)	18 (26%)	19 (26%)
African-American, N (%)	265 (70%)	18 (51%)	26 (70%)	70 (71%)	47 (71%)	54 (77%)	57 (78%)
Other, N (%)	10 (3%)	1 (3%)	0 (0%)	2 (2%)	3 (5%)	2 (3%)	2 (3%)
Insurance Status							
Uninsured, N (%)	83 (22%)	14 (40%)	10 (27%)	28 (29%)	11 (17%)	10 (14%)	10 (14%)
Medicaid, N (%)	64 (17%)	5 (14%)	9 (24%)	17 (17%)	13 (20%)	9 (13%)	11 (15%)
Medicare, N (%)	108 (29%)	0 (0%)	5 (14%)	26 (27%)	24 (36%)	30 (43%)	28 (38%)
Private, N (%)	72 (19%)	15 (43%)	11 (30%)	18 (18%)	8 (12%)	14 (20%)	8 (11%)
Medicaid/Medicare, N (%)	52 (14%)	1 (3%)	2 (5%)	9 (9%)	10 (15%)	11 (16%)	21 (29%)
Employment Status							
Employed, N (%)	61 (16%)	16 (46%)	10 (27%)	17 (17%)	7 (11%)	9 (13%)	4 (5%)
Unemployed, N (%)	133 (35%)	12 (34%)	19 (51%)	43 (44%)	21 (32%)	16 (23%)	23 (32%)
Retired, N (%)	135 (36%)	1 (3%)	5 (14%)	27 (28%)	26 (39%)	39 (56%)	42 (58%)
Disabled, N (%)	41 (11%)	2 (6%)	3 (8%)	10 (10%)	9 (14%)	10 (14%)	8 (11%)
Other, N (%)	9 (2%)	4 (11%)	0 (0%)	1 (1%)	3 (5%)	0 (0%)	1 (1%)
Operation							
Above the knee amputation, N (%)	179 (47%)	18 (51%)	19 (51%)	33 (34%)	26 (40%)	42 (60%)	47 (64%)
Below the knee amputation, N (%)	200 (53%)	17 (49%)	18 (49%)	65 (66%)	40 (61%)	32 (46%)	31 (42%)

Table 3: Baseline demographics of patients undergoing major lower extremity amputation from 2010-2015 stratified by Modified Frailty Index (mFI) score ≤2 and >2

Parameter	Totals (n=379)	mFI ≤2 (n=170)	mFI >2 (n=209)
Mean age (std dev)	59 (15)	52 (15)	65 (12)
Male, N (%)	243 (64%)	119 (70%)	124 (59%)
Race			
Caucasian, N (%)	104 (27%)	53 (31%)	51 (24%)
African-American, N (%)	265 (70%)	114 (67%)	151 (72%)
Other, N (%)	10 (3%)	3 (2%)	7 (3%)
Insurance Status			
Uninsured, N (%)	83 (22%)	52 (31%)	31 (15%)
Medicaid, N (%)	64 (17%)	31 (18%)	33 (16%)
Medicare, N (%)	108 (29%)	31 (18%)	77 (37%)
Private, N (%)	72 (19%)	44 (26%)	28 (13%)
Medicaid/Medicare, N (%)	52 (14%)	12 (7%)	40 (19%)
Employment Status			
Employed, N (%)	61 (16%)	43 (25%)	18 (9%)
Unemployed, N (%)	133 (35%)	74 (44%)	59 (28%)
Retired, N (%)	135 (36%)	33 (19%)	102 (49%)
Disabled, N (%)	41 (11%)	15 (9%)	26 (12%)
Other, N (%)	9 (2%)	5 (3%)	4 (2%)
Operation			
Above the knee amputation, N (%)	179 (47%)	70 (41%)	109 (52%)
Below the knee amputation, N (%)	200 (53%)	100 (59%)	100 (48%)

Table 4: Baseline mFI components of patients undergoing major lower extremity amputation from 2010-2015 stratified by mFI score (0 to ≥5)

Parameter	Totals (n=379)	mFI=0 (n=35)	mFI=1 (n=37)	mFI=2 (n=98)	mFI=3 (n=66)	mFI=4 (n=70)	mFI≥5 (n=73)
Impaired functional status, N (%)	57 (15%)	0 (0%)	0 (0%)	6 (6%)	5 (8%)	19 (27%)	32 (44%)
History of chronic obstructive pulmonary disease or current pneumonia, N (%)	28 (7%)	0 (0%)	3 (8%)	2 (2%)	7 (11%)	8 (11%)	11 (15%)
Congestive heart failure, N (%)	81 (21%)	0 (0%)	1 (3%)	3 (3%)	16 (24%)	23 (33%)	40 (55%)
Myocardial infarction, N (%)	49 (13%)	0 (0%)	0 (0%)	2 (2%)	4 (6%)	12 (17%)	33 (45%)
History of percutaneous coronary intervention/cardiac surgery/angina, N (%)	68 (18%)	0 (0%)	1 (3%)	2 (2%)	4 (6%)	25 (36%)	38 (52%)
Hypertension, N (%)	299 (79%)	0 (0%)	18 (49%)	87 (89%)	62 (94%)	67 (96%)	72 (99%)
Impaired sensorium, N (%)	43 (11%)	0 (0%)	0 (0%)	2 (2%)	8 (12%)	15 (21%)	22 (30%)
History of transient ischemic attack, N (%)	10 (3%)	0 (0%)	0 (0%)	1 (1%)	1 (2%)	2 (3%)	7 (10%)
History of cerebrovascular accident, N (%)	60 (16%)	0 (0%)	1 (3%)	1 (1%)	10 (15%)	18 (26%)	34 (47%)
Peripheral vascular disease, N (%)	205 (54%)	0 (0%)	4 (11%)	32 (33%)	39 (59%)	64 (91%)	66 (90%)
Diabetes mellitus, N (%)	208 (55%)	0 (0%)	9 (24%)	58 (59%)	42 (64%)	45 (64%)	61 (84%)

Table 5: Baseline mFI components of patients undergoing major lower extremity amputation from 2010-2015 stratified by mFI score ≤2 and >2

Parameter	Totals (n=379)	mFI ≤2 (n=170)	mFI >2 (n=209)
Impaired functional status, N (%)	57 (15%)	6 (4%)	51 (24%)
History of chronic obstructive pulmonary disease or current pneumonia, N (%)	28 (7%)	5 (3%)	23 (11%)
Congestive heart failure, N (%)	81 (21%)	4 (2%)	77 (37%)
Myocardial infarction, N (%)	49 (13%)	2 (1%)	47 (22%)
History of percutaneous coronary intervention/cardiac surgery/angina, N (%)	68 (18%)	3 (2%)	65 (31%)
Hypertension, N (%)	299 (79%)	106 (62%)	193 (92%)
Impaired sensorium, N (%)	43 (11%)	2 (1%)	41 (20%)
History of transient ischemic attack, N (%)	10 (3%)	1 (1%)	9 (4%)
History of cerebrovascular accident, N (%)	60 (16%)	2 (1%)	58 (28%)
Peripheral vascular disease, N (%)	205 (54%)	37 (22%)	168 (80%)
Diabetes mellitus, N (%)	208 (55%)	67 (39%)	141 (67%)

Table 6. Outcomes after major lower extremity amputation stratified by points scored (0 to ≥5) on Modified Frailty Index (mFI)

Parameter	Totals (n=379)	mFI=0 (n=35)	mFI=1 (n=37)	mFI=2 (n=98)	mFI=3 (n=66)	mFI=4 (n=70)	mFI≥5 (n=73)	P-value
30-day mortality, N (%)	n=23	2 (5.7%)	3 (8.1%)	4 (4.1%)	3 (4.6%)	8 (11.4%)	3 (4.1%)	0.4282
30-day readmission, N (%)	n=86	3 (8.6%)	5 (13.5%)	16 (16.3%)	13 (19.7%)	22 (31.4%)	27 (37.0%)	**0.0013**
Unplanned revisions, N (%)	n=105	10 (28.6%)	13 (35.1%)	24 (24.5)%	13 (19.7%)	23 (32.9%)	22 (30.1%)	0.4414
Adverse Events, N (%)	n=278	23 (65.7%)	28 (75.7%)	68 (69.4%)	44 (66.7%)	56 (80.0%)	59 (80.8%)	0.2126

Adverse events was defined as any postoperative incidence of either 30-day mortality, 30-day readmission, unplanned revisions, SSI, stroke, renal failure, prolonged ventilation, sepsis, DVT, and MI. All adverse events had to occur within 30 days of amputation. P-values correspond to chi-square test for homogeneity or Fisher's exact test where appropriate

Table 7. Outcomes after major lower extremity amputation stratified by points scored on Modified Frailty Index (mFI) score ≤2 and >2

Parameter	Totals (n=379)	mFI ≤2 (n=170)	mFI >2 (n=209)	P-value
30-day mortality, N (%)	n=23	9 (5.3%)	14 (6.7%)	0.5690
30-day readmission, N (%)	n=86	24 (14.1%)	62 (29.7%)	**0.0003**
Unplanned revisions, N (%)	n=105	47 (27.6%)	58 (27.8%)	0.9820
Adverse Events, N (%)	n=278	119 (70.0%)	159 (76.1%)	0.1833

Adverse events was defined as any postoperative incidence of either 30-day mortality, 30-day readmission, unplanned revisions, SSI, stroke, renal failure, prolonged ventilation, sepsis, DVT, and MI. All adverse events had to occur within 30 days of amputation. P-values correspond to chi-square test for homogeneity or Fisher's exact test where appropriate

Table 8. Univariate and adjusted odds ratios for the effect of mFI score (0 to ≥5) on outcomes

Outcome	Univariate OR for mFI (95% Confidence Intervals)	P-value	Adjusted[a] OR for mFI (95% Confidence Intervals)	P-value
30-day mortality	1.033 (0.787-1.358)	0.8136	0.867 (0.630-1.193)	0.3802
30-day readmission	1.447 (1.219-1.717)	**<0.0001**	1.510 (1.245-1.832)	**<0.0001**
Unplanned revisions	1.022 (0.884-1.181)	0.7731	1.156 (0.975-1.371)	0.0960
Adverse events	1.155 (0.997-1.338)	0.0550	1.274 (1.069-1.517)	**0.0068**

[a]: Adjusted for age and sex

Table 9. Univariate and adjusted odds ratios for the effect of mFI score (≤2 vs. >2) on outcomes

Outcome	Univariate OR for mFI (95% Confidence Intervals)	P-value	Adjusted[a] OR for mFI (95% Confidence Intervals)	P-value
30-day mortality	1.284 (0.542-3.044)	0.5699	0.850 (0.333-2.171)	0.7347
30-day readmission	2.583 (1.526-4.372)	**0.0004**	2.604 (1.456-4.657)	**0.0013**
Unplanned revisions	1.005 (0.639-1.580)	0.9820	1.329 (0.798-2.212)	0.2743
Adverse events	1.363 (0.863-2.152)	0.1840	1.623 (0.978-2.692)	0.0609

[a]: Adjusted for age and sex

Table 10. Modified Frailty Index variables as predictors of 30-day mortality

mFI component	OR (95% Confidence Intervals)	P-value
Impaired functional status	0.350 (0.079-1.551)	0.1669
History of COPD or current pneumonia	6.413 (2.062-19.940)	**0.0013**
Congestive heart failure present in past 30 days	3.224 (1.104-9.421)	**0.0324**
History of myocardial infarction	1.391 (0.341-5.676)	0.6459
History of cardiac surgery	0.239 (0.040-1.447)	0.1193
OR percutaneous coronary intervention OR angina in past 30 days		
Hypertension requiring medication	0.507 (0.180-1.427)	0.1984
Impaired sensorium	8.054 (2.308-28.104)	**0.0011**
History of transient ischemic attack	0.001 (0.001-999.99)	0.9855
Cerebrovascular accident OR stroke with neurologic deficit	1.786 (0.512-6.224)	0.3627
Peripheral vascular disease OR rest pain OR history of revascularization	0.531 (0.189-1.492)	0.2297
Diabetes mellitus	0.518 (0.195-1.375)	0.1870

Table 11. Modified Frailty Index variables as predictors of 30-day readmission

mFI component	OR (95% Confidence Intervals)	P-value
Impaired functional status	2.486 (1.149-5.379)	**0.0208**
History of COPD or current pneumonia	1.764 (0.713-4.364)	0.2197
Congestive heart failure present in past 30 days	1.901 (1.064-3.395)	**0.0299**
History of myocardial infarction	1.836 (0.887-3.799)	0.1015
History of cardiac surgery	1.433 (0.732-2.838)	0.3023
OR percutaneous coronary intervention OR angina in past 30 days		
Hypertension requiring medication	1.105 (0.544-2.244)	0.7833
Impaired sensorium	0.791 (0.318-1.968)	0.6147
History of transient ischemic attack	0.240 (0.027-2.096)	0.1969
Cerebrovascular accident OR stroke with neurologic deficit	0.686 (0.332-1.416)	0.3077
Peripheral vascular disease OR rest pain OR history of revascularization	1.643 (0.903-2.989)	0.1037
Diabetes mellitus	1.277 (0.753-2.166)	0.3649

Table 12. Modified Frailty Index variables as predictors of unplanned revisions

mFI component	OR (95% Confidence Intervals)	P-value
Impaired functional status	0.511 (0.217-1.205)	0.1249
History of COPD or current pneumonia	1.149 (0.485-2.722)	0.7517
Congestive heart failure present in past 30 days	0.831 (0.459-1.506)	0.5424
History of myocardial infarction	2.100 (1.054-4.184)	**0.0349**
History of cardiac surgery	1.395 (0.728-2.675)	0.3160
OR percutaneous coronary intervention OR angina in past 30 days		
Hypertension requiring medication	0.878 (0.483-1.595)	0.6694
Impaired sensorium	0.920 (0.381-2.219)	0.8528
History of transient ischemic attack	1.962 (0.518-7.436)	0.3215
Cerebrovascular accident OR stroke with neurologic deficit	0.691 (0.339-1.406)	0.3076
Peripheral vascular disease OR rest pain OR history of revascularization	1.057 (0.619-1.805)	0.8395
Diabetes mellitus	1.101 (0.677-1.791)	0.6977

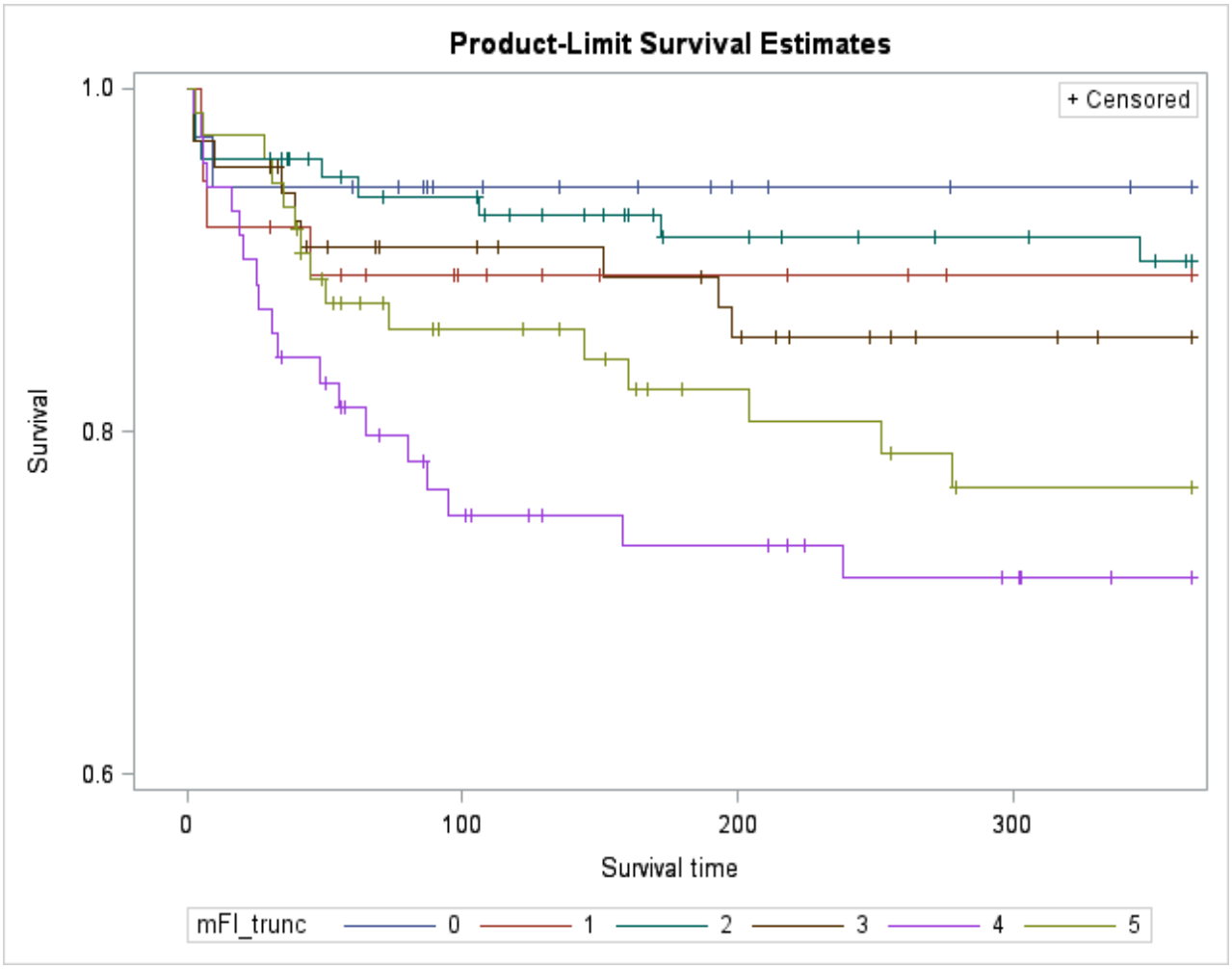
Table 13. Modified Frailty Index variables as predictors of adverse events

mFI component	OR (95% Confidence Intervals)	P-value
Impaired functional status	0.719 (0.345-1.500)	0.3796
History of COPD or current pneumonia	1.473 (0.523-4.153)	0.4635
Congestive heart failure present in past 30 days	1.605 (0.822-3.135)	0.1661
History of myocardial infarction	4.734 (1.381-16.229)	**0.0134**
History of cardiac surgery	1.884 (0.807-4.401)	0.1433
OR percutaneous coronary intervention OR angina in past 30 days		
Hypertension requiring medication	0.589 (0.309-1.126)	0.1093
Impaired sensorium	0.940 (0.408-2.165)	0.8850
History of transient ischemic attack	0.460 (0.117-1.802)	0.2647
Cerebrovascular accident OR stroke with neurologic deficit	0.895 (0.451-1.776)	0.7512
Peripheral vascular disease OR rest pain OR history of revascularization	1.346 (0.793-2.283)	0.2712
Diabetes mellitus	1.124 (0.684-1.846)	0.6453

Table 14. Outcomes at Emory vs. Grady

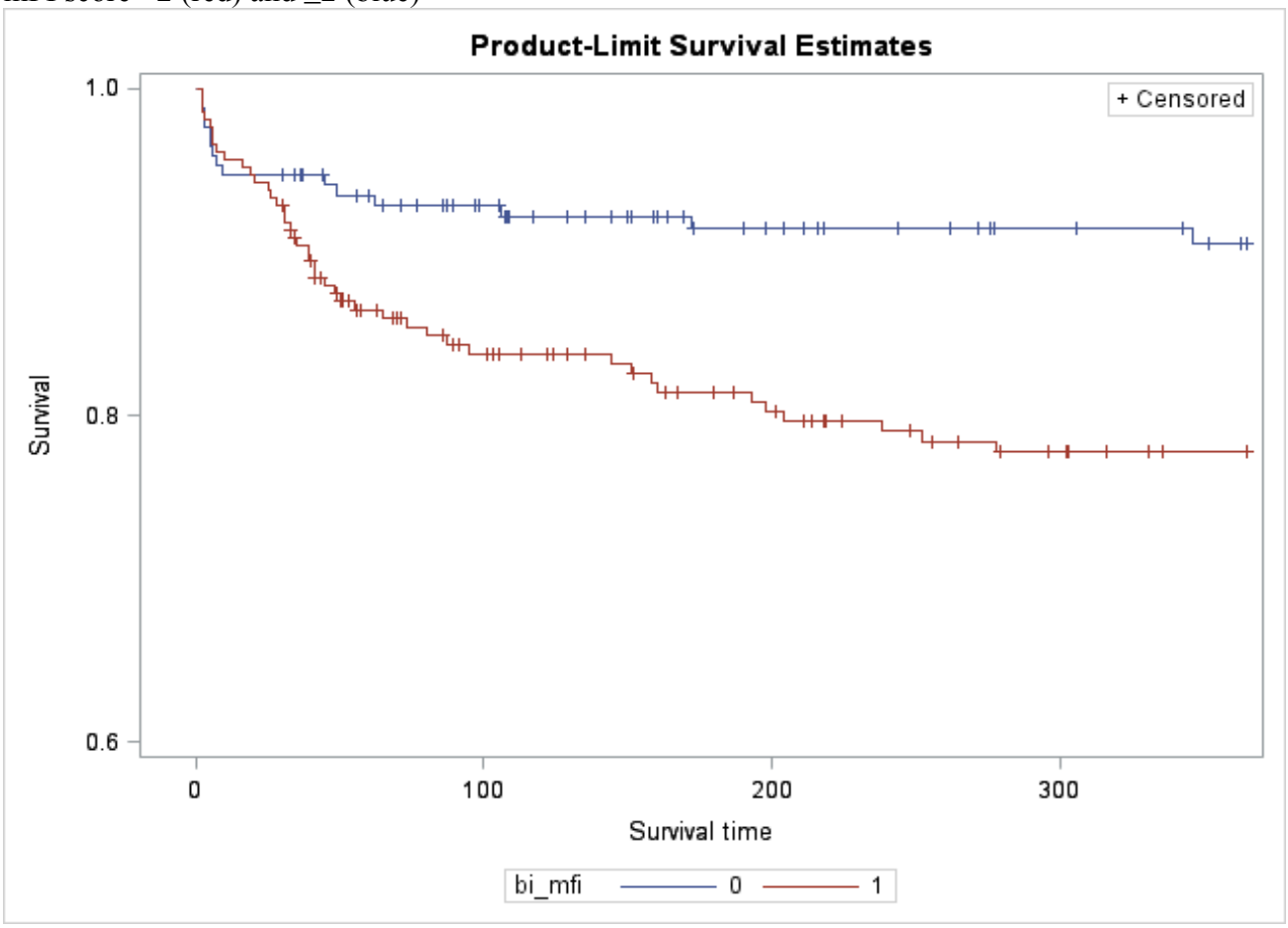
Outcome	Emory (Total = 182)	Grady (Total = 197)	P-value
30-day mortality, N (%)	12 (6.6%)	11 (5.6%)	0.8843
30-day readmission, N (%)	42 (23.0%)	44 (23.9%)	0.8464
Unplanned revisions, N (%)	41 (22.6%)	63 (32.0%)	**0.0348**
Adverse events, N (%)	127 (70.0%)	150 (76.1%)	0.3521

Figure 1: Survival analysis of major lower extremity amputation patients stratified by mFI score



Survival time is measured in days. Wilcoxon test statistic=14.2491, p=0.0141

Figure 2: Survival analysis of major lower extremity amputation patients stratified by mFI score >2 (red) and ≤2 (blue)



Survival time is measured in days. Wilcoxon test statistic=8.3731, p=0.0038