Title
The Derivation and Validation of a Geriatric-Sensitive Perioperative Cardiac Risk Index (GSCRI)

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The Derivation and Validation of a Geriatric-Sensitive Perioperative Cardiac Risk Index (GSCRI)

A thesis submitted in partial satisfaction

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in Clinical Research

by

Rami Alrezk

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ABSTRACT OF THE THESIS

The Derivation and Validation of a Geriatric-Sensitive Perioperative Cardiac Risk Index (GSCRI)

by

Rami Alrezk

Master of Science in Clinical Research

University of California, Los Angeles, 2016

Professor Robert M. Elashoff, Chair

Surgical patients age 65 and over face a high risk of cardiac complications. The Revised Cardiac Risk Index (RCRI) and the Gupta Myocardial Infarction or Cardiac Arrest (MICA) are widely used to predict perioperative cardiac risk but they are not specifically designed to predict that risk in geriatric patients. The objective of this study is to develop and validate a geriatric-sensitive cardiac risk index (GSCRI). Three variables were selected using Lasso regression in the National Surgical Quality Improvement Program (NSQIP) 2013 with the addition of four clinically significant variables. The model was developed using the NSQIP 2013 geriatric cohort (N=485,426) (172,905 age $\geq$ 65) and validated on the NSQIP 2012 geriatric cohort (N=485,426) (210,914 age $\geq$ 65). The Area under the Curve (AUC) for the NSQIP 2012 geriatric cohort for three indices was compared. Gupta MICA had an AUC of 0.70 and the RCRI had an AUC of 0.63. Our GSCRI model showed better performance with an AUC of 0.76

The thesis of Rami Alrezk is approved.

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2016

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Clinical Perspective

There are 40 million people age 65 and over living in the U.S. today (1). Although they account for just 15% of the U.S. population, they receive one-third of all inpatient surgeries (1, 2). By 2030, 72 million Americans will be 65 and over, accounting for 20% of the U.S. population and an increasing number of surgeries(1, 3, 4).

All inpatient surgery carries a risk of cardiac complications for all adult patients, regardless of age (5-7). Cardiac arrest (CA) after non-cardiac surgery is associated with a hospital mortality rate of 65% (8, 9). Myocardial infarction (MI) after non-cardiac surgery is associated with a hospital mortality rate of 15-25% (10-12). Nonfatal MI is associated with increased mortality during the first 6 months after surgery (8, 12). Older adults are more prone to MI and CA during or after surgery (12).

Researchers have developed clinical tools for estimating cardiac risk. The Revised Cardiac Risk Index (RCRI) and Gupta Myocardial Infarction and Cardiac Arrest (MICA) calculator are widely used indices to estimate perioperative risk; however neither tool is specifically designed to assess the risk in geriatric patients. The objective of this study is to develop and validate a geriatric-sensitive cardiac risk index. Geriatric patients have a characteristic, progressive constriction of homeostatic reserves that occurs in every organ system with aging (13). My hypothesis is that a new geriatric-sensitive index, derived specifically from geriatric data, will capture this population's unique response to risk factors. With a growing geriatric population and a projected increase in non-cardiac, usually elective, surgeries (4, 14) and the association with substantial cardiac morbidity and mortality (15, 16), it becomes imperative to have accurate estimations of

the cardiac risk for geriatric patients.

Study Objectives

1. To investigate the performance of the RCRI and Gupta MICA perioperative cardiac risk models in a geriatric population
2. To evaluate the incidence of MICA after non-cardiac non-emergency surgery across the age spectrum
3. To develop a geriatric-sensitive perioperative cardiac risk index (GSCRI) optimized for use with geriatric patients and sensitive to the clinical and physiologic uniqueness of this population (given that prior hypothesis-driven objectives were met)
4. To conduct comparative performance analysis of the GSCRI, RCRI and Gupta MICA models.

I intend to examine the association between the outcome of MICA and age in order to determine if non-linearity exists, as we expect. This would then provide insights about the appropriate statistical derivation methods for yielding the most accurate estimates for the geriatric population. Then we will proceed by accurately deriving these variable estimates for older adults (≥65) to develop a GSCRI. My hypothesis is that what determines the accuracy of the model's performance in predicting the perioperative risk in geriatric patients is not merely the selection of certain relevant variables, but also the accurate weighting of variables by deriving the coefficients for these variables in older adults (≥65).

Methods

Outcome

The end point of interest is intraoperative/postoperative MICA within 30 days of surgery. Cardiac arrest is defined in the National Surgical Quality Improvement Program (NSQIP) as:

> The absence of cardiac rhythm or presence of chaotic cardiac rhythm, intraoperatively or within 30 days following surgery, which results in a cardiac arrest requiring the initiation of CPR, which includes chest compressions. Patients are included who are in a pulseless VT or Vfib in which defibrillation is performed and PEA arrests requiring chest compressions. Patients with automatic implantable cardioverter defibrillator (AICD) that fire but the patient has no loss of consciousness should be excluded. (17)

Myocardial infarction is defined in the NSQIP as:

> An acute myocardial infarction which occurred intraoperatively or within 30 days following surgery as manifested by one of the following: 1-Documentation of ECG changes indicative of acute MI (one or more of the following): (a)- ST elevation > 1 mm in two or more contiguous leads (b)- New left bundle branch (c)- New q-wave in two or more contiguous leads. 2- New elevation in troponin greater than 3 times the upper level of the reference range in the setting of suspected myocardial ischemia. 3- Physician diagnosis of myocardial infarction. (17)

Participants

We utilized the NSQIP cohort, a multicenter database of surgical outcomes collected prospectively by trained professionals in a systematic fashion (17). At each center, a certified Surgical Clinical Reviewer (SCR) collects the data using a variety of methods, including medical chart abstraction. NSQIP developed various mechanisms to ensure data quality, including establishing high inter-rater reliability and auditing of selected participating sites. In addition, SCRs undergo vigorous training and annual certification to ensure they have the knowledge and resources available to collect high quality data (17). NSQIP collected data for over 300 variables, including risk factors and 30-day post-surgery morbidity and mortality outcomes.

In this study, NSQIP years 2012 (N=543,885) and 2013 (N=651,940) were used. Participants who had emergency surgery (2012=54,729; 2013=63,980) or cardiac surgery (2012=3,730; 2013=3,029) were excluded, leaving a sample size of 485,426 (172,905 age ≥ 65) in the 2012 data and 584,931 (210,914 age ≥ 65) in the data from 2013.

The Revised Cardiac Risk Index (RCRI)

The RCRI is a previously published index of post-surgical cardiac risk (5) that uses six risk factors of major cardiac complications. These risk factors are: high risk surgery, history of ischemic heart disease, history of heart failure, history of cerebrovascular disease, diabetes requiring insulin treatment, and serum creatinine > 2.0 mg/dL. The risk factors are binary (present/absent). High-risk surgery is defined as vascular surgery and open intraperitoneal or intrathoracic procedures. Participants with no risk factors were assigned a predicted probability of 0.4%; those with 1 risk factor are assigned 1.0%, 2 risk factors 2.4%, and 3 or more risk factors 5.4% (8) . There were a total of 485,426 (172,905 age ≥ 65) participants in the NSQIP 2012 that were able to have their RCRI score computed.

The Gupta MICA Model

The Gupta MICA is a risk score for perioperative cardiac risk developed in the NSQIP 2007 and validated in the NSQIP 2008 datasets (18). The risk score is comprised of five items: the participant's functional status, American Society of Anesthesiologists (ASA) classification, creatinine levels, age, and type of surgery that will be performed. There were a total of 479,453 (170,737 age ≥ 65) participants in the NSQIP 2012 that had their Gupta MICA score computed.

Analysis

Candidate variables for a GSCRI

Candidate variables for use in the GSCRI were chosen from the NSQIP based on the previous literature and other risk indices currently in use. The variables examined were: sex, high risk surgery, history of congestive heart failure, history of stroke, currently taking insulin, diabetes status, dialysis, being on medication to control hypertension, smoking status, history of chronic obstructive pulmonary disease, ASA classification, functional status, creatinine level, type of surgery to be performed, dyspnea, high blood urea nitrogen levels (BUN), and high risk surgery including vascular surgery, and open intraperitoneal or intrathoracic procedures. Univariate analysis showing the risk factors odds ratio (OR) and confidence interval (CI) are displayed in table 1. For full multivariable model, refer to supplemental table A.

Variable Selection

Risk Factors	Existing Indices		Study Index
	RCRI	Gupta	GSCRI
High-risk surgery	✓		
Type of surgery		✓	✓
Heart failure	✓		✓
Ischemic heart disease	✓		
Cerebrovascular disease	✓		
Stroke history			✓
Diabetes requiring insulin	✓		
Diabetes status			✓
Creatinine level ≥2.0 mg/dL	✓		
Creatinine level ≥1.5 mg/dL		✓	✓
ASA classification		✓	✓
Functional status		✓	✓
Age		✓	

This table summarizes the variables used in each risk model

In order to develop a GSCRI that is more specific to geriatric patients, the aforementioned candidate predictors were used in Least Angle Shrinkage and Selection Operator (LASSO) regression analysis in the NSQIP 2013 data on the geriatric subset (19) implemented in the R package "glmnet". Ten-fold cross validation was used to select the appropriate shrinkage parameter, which was determined to be 0.00001801. Due to the size of the NSQIP dataset and known theoretical underpinnings of the candidate variable list, no variable had coefficients shrunken to zero completely. As a result, in order to develop a parsimonious model, predictors with shrunken coefficients greater than 0.7 were selected for use in the final model in addition to variables with known clinical importance.

Model Building

The variables identified for inclusion from the LASSO model were: history of stroke, ASA classification, and type of surgery. Additional clinically relevant variables such as functional status, creatinine level (>1.5), diabetes status, and a history of CHF were also selected for the final model. These variables, having been selected to be sensitive to geriatric patients, were then used in a logistic regression model in the NSQIP 2013 data to predict myocardial infarction in the geriatric subset. Table 2 shows the final actual GSCRI model.

Model Evaluation

For comparison with the previously published risk scores, the coefficients from the 2013 data were then used to predict the risk of myocardial infarction in the NSQIP 2012 data. There were a total of 485,426 participants in the NSQIP 2012 that were able to have this GSCRI computed. Previous published coefficients of the RCRI and Gupta MICA risk indices were used

to predict the risk of post-surgical myocardial infarction in the NSQIP 2012 data set. The predictive value of the models was used to calculate the area under the receiver operating characteristics curve (AUC of ROC) for the overall sample and within the geriatric (age ≥65) age group and compared between models using the Delong method (20) in the "pROC" package in R version 3.1.0. Plots of observed versus predicted risk (calibration plots) were used to visually assess the fit of these models in the geriatric group.

Analyses were conducted in Stata version 13.1 (College Station, TX) and R version 3.1.0.

Results

Sample Characteristics

In the NSQIP 2012, the majority of the sample was female (58%), middle-aged (age mean=57, sd=16), with few instances of perioperative myocardial infarction (N=2,357, ~.5%). The odds of MI were 4.8 times greater in those 65 or over (~1% *vs* ~0.2%). Figure 1 shows how the risk of MI increases non-linearly with age. Sample characteristics were not substantively different in the NSQIP 2013 data. Clinical characteristics of the derivation and validation cohorts are displayed in supplemental table C.

Development of the GSCRI

The coefficients from the GSCRI in the NSQIP 2013 dataset are displayed in Table 2. All variables were statistically significant predictors of MICA ($p<0.05$).

Comparison of Risk Scores

AUCs for each of the models can be found in Table 3. The GSCRI had a significantly higher AUC than either the RCRI or Gupta MICA in both the geriatric group (AUC=0.76) and overall sample (AUC=0.83). The Gupta MICA also outperformed the RCRI in the geriatric group (0.70 *vs* 0.63) and overall sample (0.72 *vs* 0.68). We additionally found the Gupta MICA model to be poorly calibrated (Figure 2), with an underestimation of risk in the geriatric sample. While both the RCRI and GSCRI also underestimated the risk, the median difference from the observed risk was only -0.28 and -0.04 percentage points different, respectively; whereas the Gupta MICA was off by -0.73% in the geriatric patients.

Discussion

This article demonstrates the concept of developing predictive model in the geriatric population, in contrast to other articles, where the model development is across a wider age spectrum. Currently, geriatric patients have low participation in clinical trials and are often excluded due to age related comorbidities. When included, the data of participants are often pooled together with participants of younger ages who have much lower risk, which possibly leads to inaccurate parameter estimation. Developing predictive models on this pooled data that ignore age categories, can lead to models that are dominated by variables and coefficients not optimized for performance in geriatric patients, and hence provide decreased predictive accuracy and lower sensitivity to certain geriatric characteristics. This holds true especially when

developing predictive models, as even minor inaccuracies in the derivation of the parameter estimates could dramatically affect the discrimination and calibration of a model.

In this study, our hypothesis for the need for specific geriatric analysis and model derivation proved to be valid, and our efforts culminated in producing the Geriatric-Sensitive Perioperative Cardiac Risk Index, GSCRI. Our GSCRI has an AUC of 0.76 and outperformed the RCRI and Gupta MICA models by 13% and 6% in geriatric patients of the validation cohort respectively, with a Δ AUC and P-value of 0.13 (p= <.001), and 0.06 (p= <.001) (see Table 3). Although GSCRI was derived from the geriatric population for the purpose of optimal performance, we wished to test the GSCRI against the RCRI and Gupta MICA in the overall population, as well. We found that the GSCRI has an AUC of 0.83, which outperformed the RCRI and Gupta MICA by 15% and 11% respectively with Δ AUC and P-value of 0.15 (p= <.001) and 0.11 (p= <.001) respectively (Table 3). When testing the Gupta MICA with the published coefficients on geriatric patients, a significant deterioration (~17%) from the previously-published performance in the NSQIP 2007 was noted and a significant underestimation of the risk was also noted, which likely results from assuming a linearity of age and deriving estimates that are not specific for the geriatric population when conducting the analysis for the Gupta MICA calculator.

The final model contains seven variables, and the first three variables (Stroke, ASA Class, Surgical Category) are selected by the robust method of LASSO regression analysis in the NSQIP 2013 data on the geriatric subset. The method selects the most statistically important variables that contribute to the occurrence of the outcome. The other variables (Diabetes, Functional Status, Elevated Creatinine > 1.5 mg/dl, CHF) were added to include clinically significant variables (1)(3). While additional relevant variables could have been added, the increased model complexity would not meaningfully improve the model's predictive ability.

Building a model that was sensitive to geriatric patients, has good performance, and avoids complexity was an ambitious yet feasible task. The multivariable analysis revealed multiple variables that are statistically significant. Creating a parsimonious model was essential to ensure the simplicity and feasibility that physicians working in clinical settings require. When the LASSO method was applied on the geriatric set, it selected three variables, and we wanted to add additional variables that we felt would be clinically essential for accurate estimation of MICA risk in geriatric patients. These are important risk factors that are known to increase the surgical cardiac risk, such as CHF (1), elevated creatinine (1,3), diabetes (1,3) and functional status (3). We chose a creatinine level of 1.5 mg/dl as opposed to 2 mg/dl, because geriatric patients often have decreased GFR with lower serum creatinine levels in comparison with younger patients (4). The performance of the Gradient Boosting Machines model (GBM) achieved a performance of AUC= 0.79, indicating that the most complex model would achieve a performance close to our model (**Δ** AUC=3%); therefore we believe our model was able to achieve good performance without losing interpretability.

These models reflect contemporary risk associated with each surgical category, hence updating these models every few years is imperative to take into account the improved surgical outcomes and decreased complication rates that result from enhanced medical care and improved surgical techniques. This possibly explains why the GSCRI outperformed the other two models in non-geriatric patients, as it has the advantage of being tested on a dataset only one year apart from the derivation dataset, while the Gupta MICA was developed on a 2007 dataset (18). Additionally, the RCRI was not derived to predict the cardiac risk within 30 days of surgery, but is aimed solely at predicting the risk during a hospital stay (5). In the modern world, using equations developed so long ago and on unique populations (i.e. RCRI) is of questionable value,

particularly in an era when curated data sources like the NSQIP and other large data sets are readily available.

With the growth of the geriatric population, and increased awareness of the uniqueness of this growing segment (12, 21), GSCRI represents a step forward for cardiac risk prediction for geriatric patients. Our study demonstrated the necessity of developing risk models optimized for geriatric patients in order to produce accurate predictions. The GSCRI outperforms the Gupta MICA and RCRI in the area under the curve by 7% and 13% respectively.

We believe we might have reached a predictive limit in our ability to predict perioperative risk in geriatrics patients. GBM, an exploratory statistical learning technique was used to examine the maximal predictive ability for the set of predictors available in the NSQIP 2012 dataset. One strength of this technique is the ability to utilize non-linear and high-order interactions that provide the maximal predictive accuracy for the outcome given the dataset; however, it comes at the expense of interpretability. Even with very complex GBM modeling we could not reach a C-statistic that was >0.8 in the geriatric patients as opposed to modeling the risk in younger patients, where we could achieve a C-statistic of 0.88. This result is expected due to the wide variations in the health status of geriatrics patients (). We may need to consider other variables for predicting the risk in geriatrics patients in order to achieve: more accurate predictions. However, we are currently limited by the variables that are available in the NSQIP databases. Therefore, this model is the first of a series of models that will need to be updated constantly by integrating geriatric-relevant data. Hence, our future endeavors will focus on integrating and testing the usability of biologic variables such as inflammatory factors and other significant factors including: nutritional status, functional status, depression, cognition and frailty indices (2, 12, 22-24).

We conducted this study and proceeded with the following steps because we intended to capture the uniqueness of risk factors on the geriatric patients in quantitative fashion We wanted to capture the geriatric uniqueness in quantitative fashion, as an accurate estimation of parameters when developing predictive models, and then translate these into accurate probabilities in mathematical terms. Our study uncovered some inaccuracy in the current perioperative cardiac risk models. Then we applied optimal statistical methods to derive accurate estimates of each risk factor. We then constructed the final model for the GSCRI, which outperformed the most currently used models without risking simplicity.

The findings of the study were driven by our initial hypothesis and, therefore, it is hypothesis-driven study as well as data-driven. We hope our novel index will set a new standard in surgical risk estimation for geriatric patients. To facilitate that purpose, we intend to develop an online calculator to increase the utility of the GSCRI for physicians. Finally, we would like to stress that the GSCRI should be accompanied by clinical evaluation and comprehensive geriatric assessment to add further insights to the actual risk, since no risk model can substitute for the clinical judgment of physicians; it is meant to be a supplemental tool to aid in the process.

Disclosures:

The American College of Surgeons National Surgical Quality Improvement Program and the hospitals participating in the ACS NSQIP are the source of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

Tables and Figures

Figure 1. Association of actual MICA incidence with Age along with the linear and Lowess fit

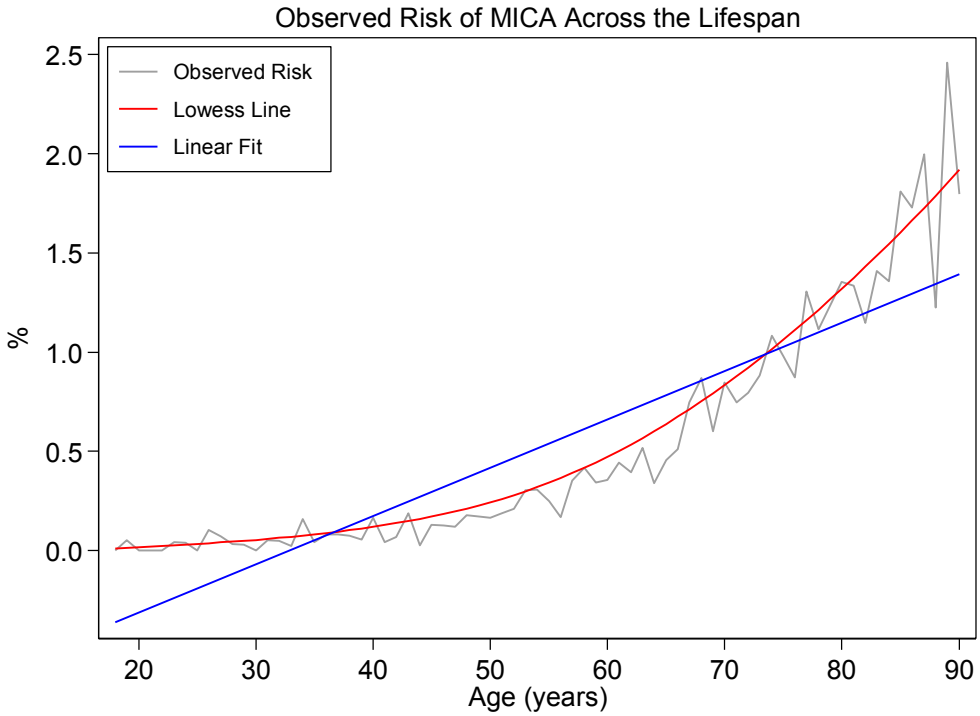
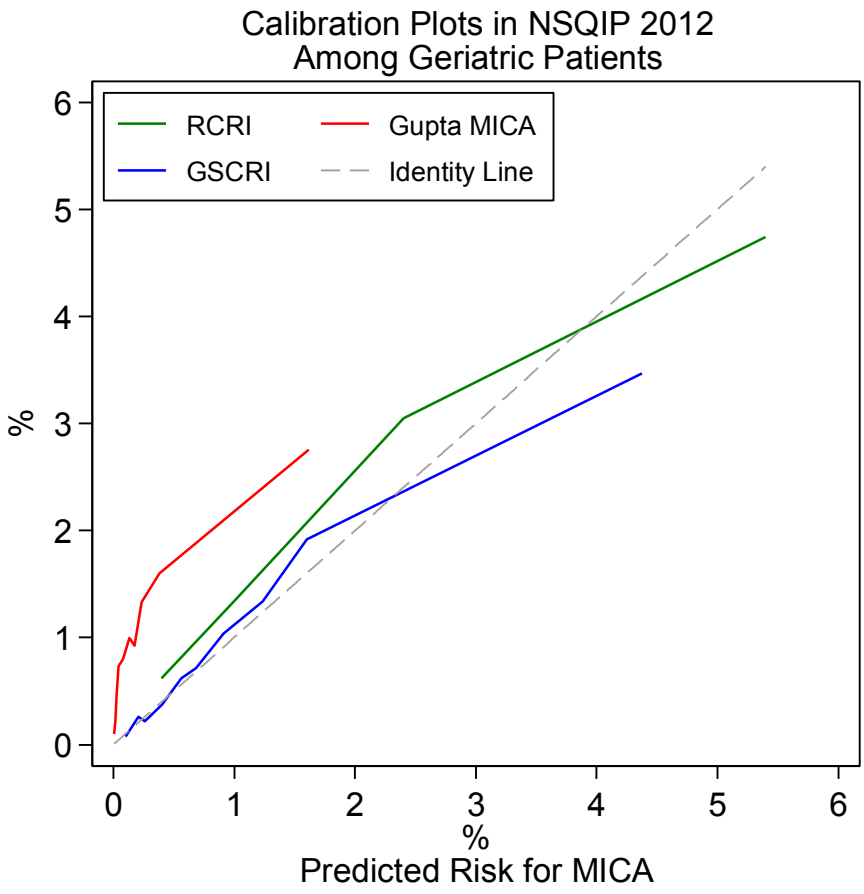


Figure 2. Models Calibration Among Geriatric Patients



Calibration plots comparison of the 3 studied models among geriatric patients. Gupta MICA Model shows under-estimation of the MICA risk in geriatric patients.

Table 1: Odds Ratios for predictors of MICA in Geriatric Patients for Non-Cardiac Surgeries (NSQIP 2012)			
		Age ≥ 65	
Variable	**Group**	**OR (95% CI)**	**P**
Age	*Per 1 Year*	1.05 (1.04, 1.06)	<.001
Sex *Ref=Female*	*Male*	1.55 (1.41, 1.71)	<.001
High Risk Surgery *Ref=No*	*Yes*	1.72 (1.56, 1.90)	<.001
Hx CHF *Ref=No*	*Yes*	5.49 (4.45, 6.78)	<.001
Stroke *Ref=No*	*Yes*	2.91 (2.35, 3.62)	<.001
Taking Insulin *Ref=No*	*Yes*	2.85 (2.52, 3.23)	<.001
Diabetes *Ref=No*	*Yes*	1.98 (1.79, 2.18)	<.001
Dialysis *Ref=No*	*Yes*	5.16 (4.29, 6.21)	<.001
Medications for Hypertension *Ref=No*	*Yes*	2.34 (2.05, 2.66)	<.001
Smoking Status *Ref=Former/Never*	*Current*	1.48 (1.29, 1.69)	<.001
Hx COPD *Ref=No*	*Yes*	2.24 (1.96, 2.55)	<.001
ASA Class *Ref=I*	*II*	4.20 (1.04, 16.93)	0.044
	III	14.93 (3.73, 59.8)	<.001
	IV	48.1 (11.9, 192.8)	<.001
	V	81.13 (14.6, 450)	<.001
Functional Status *Ref=Independent*	*Partially Dependent*	3.02 (2.59, 3.51)	<.001
	Totally Dependent	3.90 (2.88, 5.27)	<.001
Creatinine Category *Ref= < 1.5*	*1.5-2.5*	2.67 (2.33, 3.06)	<.001
	>2.5	4.78 (4.05, 5.64)	<.001
	Missing	0.34 (0.25, 0.45)	<.001
Surgical Category *Ref=Hernia*	*Anorectal*	3.90 (2.41, 6.32)	<.001
	Aortic	7.10 (5.05, 9.97)	<.001
	Bariatric	2.02 (0.96, 4.28)	0.065
	Brain	3.89 (2.26, 6.68)	<.001
	Breast	0.30 (0.15, 0.59)	0.001
	ENT	1.64 (0.74, 3.62)	0.223
	Foregut/hepatopancreatobiliary	4.19 (3.07, 5.74)	<.001
	GBAAS/Intestinal	4.77 (3.52, 6.45)	<.001
	Neck	0.50 (0.23, 1.11)	0.087
	Obstetric/gynecologic	1.13 (0.69, 1.85)	0.630
	Orthopedic	2.99 (2.22, 4.02)	<.001
	Other abdomen	2.94 (1.79, 4.82)	<.001
	Peripheral vascular	4.93 (3.61, 6.73)	<.001
	Skin	3.48 (2.20, 5.51)	<.001
	Spine	2.25 (1.55, 3.27)	<.001
	Thoracic	4.25 (2.85, 6.34)	<.001
	Vein	10.9 (7.96, 14.99)	<.001
	Urology	2.39 (1.71, 3.34)	<.001
Dyspnea *Ref=No*	*Yes*	2.10 (1.86, 2.38)	<.001
BUN *Ref= <30*	*> 30*	2.98 (2.65, 3.35)	<.001
	Missing	0.41 (0.33, 0.50)	<.001
Laparoscopic Surgery *Ref=No*	*Yes*	0.69 (0.56, 0.84)	<.001

Table 2: Coefficients from variables selected by LASSO and Hypothesis in Non-Cardiac Surgery (NSQIP 2013)			
		Non-Cardiac Surgery	
Variable	**Group**	**ln(OR) (95% CI)**	**P**
Stroke *Ref=No*	*Yes*	2.07 (1.80, 2.34)	<.0001
ASA Class *Ref=I*	*II*	0.27 (-0.62, 1.16)	0.5561
	III	1.33 (0.45, 2.21)	0.003
	IV	2.04 (1.16, 2.93)	<.0001
	V	3.63 (2.52, 4.74)	<.0001
Surgical Category *Ref=Hernia*	*Anorectal*	1.02 (0.59, 1.46)	<.0001
	Aortic	1.31 (1.01, 1.62)	<.0001
	Bariatric	0.33 (-0.31, 0.98)	0.3104
	Brain	0.24 (-0.35, 0.83)	0.4256
	Breast	-1.14 (-1.73, -0.54)	0.0002
	ENT	0.32 (-0.41, 1.06)	0.3889
	Foregut/hepatopancreatobiliary	1.04 (0.76, 1.32)	<.0001
	GBAAS/Intestinal	1.14 (0.87, 1.41)	<.0001
	Neck	-0.04 (-0.57, 0.49)	0.8841
	Obstetric/gynecologic	0.12 (-0.32, 0.56)	0.5847
	Orthopedic	0.47 (0.21, 0.74)	0.0005
	Other abdomen	0.18 (-0.29, 0.65)	0.4606
	Peripheral vascular	0.84 (0.56, 1.12)	<.0001
	Skin	0.43 (0.00, 0.86)	0.0497
	Spine	0.42 (0.09, 0.75)	0.0129
	Thoracic	1.07 (0.72, 1.42)	<.0001
	Vein	1.37 (1.08, 1.67)	<.0001
	Urology	0.55 (0.25, 0.85)	0.0003
Functional Status *Ref=Independent*	*Partially Dependent*	0.26 (0.09, 0.43)	0.0027
	Totally Dependent	0.76 (0.47, 1.05)	<.0001
Creatinine Category *Ref= < 1.5*	*> 1.5*	0.61 (0.49, 0.73)	<.0001
	Missing	-0.41 (-0.68, -0.14)	0.0031
Hx CHF *Ref=No*	*Yes*	0.61 (0.40, 0.82)	<.0001
Diabetes *Ref=No*	*Yes*	0.26 (0.16, 0.36)	<.0001
Constant		-6.80 (-7.71, -5.90)	<.0001

Table 3: Differential Performance of Risk Prediction in Geriatric Patients for Non-Cardiac Surgeries (NSQIP 2012)		
	Age ≥ 65 AUC (95% CI)	**Overall** AUC (95% CI)
RCRI	0.63 (0.62, 0.65)	0.68 (0.67, 0.69)
Gupta MICA	0.70 (0.69, 0.71)	0.72 (0.71. 0.73)
GSCRI	0.76 (0.75, 0.77)	0.83 (0.82, 0.83)
	Δ, P-value	**Δ, P-value**
RCRI *vs*. Gupta MICA	0.07, p= <.001	0.04, p= <.001
GSCRI *vs*. RCRI	0.13, p= <.001	0.15, p= <.001
GSCRI *vs*. Gupta MICA	0.06, p= <.001	0.11, p= <.001

Appendix

Supplemental Table A: Multivariable Model with Odds Ratios for predictors of MICA in Age ≥ 65 for Non-Cardiac Surgeries (NSQIP 2012)			
Variable	**Group**	**OR (95% CI)**	**P**
Age	*Per 1 Year*	1.03 (1.03, 1.04)	<.0001
Sex *Ref=Female*	*Male*	1.27 (1.14, 1.41)	<.0001
High Risk Surgery *Ref=No*	*Yes*	1.72 (1.37, 2.16)	<.0001
Hx CHF *Ref=No*	*Yes*	1.65 (1.31, 2.07)	<.0001
Stroke *Ref=No*	*Yes*	2.00 (1.60, 2.51)	<.0001
Taking Insulin *Ref=No*	*Yes*	1.38 (1.17, 1.64)	0.0002
Diabetes *Ref=No*	*Yes*	1.11 (0.97, 1.27)	0.1330
Dialysis *Ref=No*	*Yes*	1.42 (1.04, 1.95)	0.0297
Medications for Hypertension *Ref=No*	*Yes*	1.46 (1.27, 1.68)	<.0001
Smoking Status *Ref=Former/Never*	*Current*	1.25 (1.08, 1.44)	0.0023
Hx COPD *Ref=No*	*Yes*	1.22 (1.06, 1.41)	0.0068
ASA Class *Ref=I*	*II*	2.79 (0.69, 11.27)	0.1498
	III	5.59 (1.39, 22.48)	0.0155
	IV	10.11 (2.50, 40.85)	0.0012
	V	12.32 (2.17, 69.81)	0.0046
Functional Status *Ref=Independent*	*Partially Dependent*	1.39 (1.18, 1.64)	0.0001
	Totally Dependent	1.63 (1.19, 2.24)	0.0023
Creatinine Category *Ref= < 1.5*	*1.5-2.5*	1.36 (1.16, 1.60)	0.0001
	>2.5	1.50 (1.11, 2.04)	0.0081
	Missing	0.77 (0.52, 1.15)	0.2044
Surgical Category *Ref=Hernia*	*Anorectal*	4.28 (2.57, 7.13)	<.0001
	Aortic	3.07 (2.17, 4.34)	<.0001
	Bariatric	2.06 (0.97, 4.42)	0.0616
	Brain	4.55 (2.54, 8.15)	<.0001
	Breast	0.59 (0.29, 1.20)	0.1434
	ENT	2.43 (1.07, 5.53)	0.0339
	Foregut/hepatopancreatobiliary	4.15 (3.02, 5.71)	<.0001
	GBAAS/Intestinal	3.92 (2.88, 5.32)	<.0001
	Neck	0.85 (0.38, 1.93)	0.7024
	Obstetric/gynecologic	2.43 (1.42, 4.16)	0.0012
	Orthopedic	3.73 (2.59, 5.36)	<.0001
	Other abdomen	1.33 (0.79, 2.24)	0.2884
	Peripheral vascular	2.11 (1.54, 2.90)	<.0001
	Skin	2.85 (1.71, 4.74)	0.0001
	Spine	3.11 (2.02, 4.77)	<.0001
	Thoracic	2.40 (1.59, 3.62)	<.0001
	Vein	7.80 (5.31, 11.45)	<.0001
	Urology	2.95 (2.00, 4.35)	<.0001
Dyspnea *Ref=No*	*Yes*	1.24 (1.08, 1.41)	0.0019
BUN *Ref= <30*	*> 30*	1.35 (1.16, 1.57)	0.0001
	Missing	0.84 (0.63, 1.11)	0.2222
Laparoscopic Surgery *Ref=No*	*Yes*	0.93 (0.72, 1.21)	0.5924

Supplemental Table B: Description of Variables from NSQIP 2012				
Variable	**Subgroup**	**Overall**	**MICA=NO**	**MICA=YES**
age	age	(480,553) 57.3 ± 16.2	(478,156) 57.2 ± 16.2	(2,397) 70.6 ± 12.2
asaclas	1:1-No Disturb	(41,655) 8.67%	(41,648) 8.71%	(7) 0.29%
asaclas	2:2-Mild Disturb	(225,203) 46.86%	(224,901) 47.04%	(302) 12.60%
asaclas	3:3-Severe Disturb	(189,671) 39.47%	(188,265) 39.37%	(1,406) 58.66%
asaclas	4:4-Life Threat	(23,896) 4.97%	(23,221) 4.86%	(675) 28.16%
asaclas	5:5-Moribund	(128) 0.03%	(121) 0.03%	(7) 0.29%
fnstatus2	1:Independent	(467,842) 97.35%	(465,731) 97.40%	(2,111) 88.07%
fnstatus2	2:Partially Dependent	(10,630) 2.21%	(10,403) 2.18%	(227) 9.47%
fnstatus2	3:Totally Dependent	(2,081) 0.43%	(2,022) 0.42%	(59) 2.46%
surgcat	0:Hernia	(53,990) 11.23%	(53,903) 11.27%	(87) 3.63%
surgcat	1:Anorectal	(5,743) 1.20%	(5,707) 1.19%	(36) 1.50%
surgcat	2:Aortic	(5,684) 1.18%	(5,573) 1.17%	(111) 4.63%
surgcat	4:Brain	(4,733) 0.98%	(4,708) 0.98%	(25) 1.04%
surgcat	5:Breast	(39,585) 8.24%	(39,571) 8.28%	(14) 0.58%
surgcat	6:Cardiac	(3,691) 0.77%	(3,601) 0.75%	(90) 3.75%
surgcat	7:ENT	(7,553) 1.57%	(7,543) 1.58%	(10) 0.42%
surgcat	8:Foregut/hepatopancreatobiliary	(67,916) 14.13%	(67,623) 14.14%	(293) 12.22%
surgcat	9:GBAAS/Intestinal	(48,907) 10.18%	(48,534) 10.15%	(373) 15.56%
surgcat	10:Neck	(17,416) 3.62%	(17,399) 3.64%	(17) 0.71%
surgcat	11:Obstetric/gynecologic	(36,362) 7.57%	(36,319) 7.60%	(43) 1.79%
surgcat	12:Orthopedic	(84,123) 17.51%	(83,698) 17.50%	(425) 17.73%
surgcat	13:Other abdomen	(7,284) 1.52%	(7,245) 1.52%	(39) 1.63%
surgcat	14:Peripheral vascular	(19,971) 4.16%	(19,731) 4.13%	(240) 10.01%
surgcat	15:Skin	(7,642) 1.59%	(7,594) 1.59%	(48) 2.00%
surgcat	16:Spine	(25,791) 5.37%	(25,703) 5.38%	(88) 3.67%
surgcat	17:Thoracic	(7,117) 1.48%	(7,044) 1.47%	(73) 3.05%
surgcat	18:Vein	(10,407) 2.17%	(10,163) 2.13%	(244) 10.18%
surgcat	19:Urology	(26,638) 5.54%	(26,497) 5.54%	(141) 5.88%
weight	weight	(480,553) 187 ± 52	(478,156) 187 ± 52	(2,397) 179 ± 50
creatcat4	1:Normal	(366,840) 76.34%	(365,080) 76.35%	(1,760) 73.43%
creatcat4	2:Low Abnormal	(15,333) 3.19%	(15,021) 3.14%	(312) 13.02%
creatcat4	3:High Abnormal	(8,480) 1.76%	(8,232) 1.72%	(248) 10.35%
creatcat4	4:Missing	(89,900) 18.71%	(89,823) 18.79%	(77) 3.21%
hibun	0	(350,596) 72.96%	(348,802) 72.95%	(1,794) 74.84%
hibun	1	(19,583) 4.08%	(19,113) 4.00%	(470) 19.61%
hibun	2	(110,374) 22.97%	(110,241) 23.06%	(133) 5.55%
hxchf	1:No	(477,432) 99.35%	(475,175) 99.38%	(2,257) 94.16%
hxchf	2:Yes	(3,121) 0.65%	(2,981) 0.62%	(140) 5.84%
hxcopd	1:No	(459,001) 95.52%	(456,951) 95.57%	(2,050) 85.52%
hxcopd	2:Yes	(21,552) 4.48%	(21,205) 4.43%	(347) 14.48%
dysp	0	(446,237) 92.86%	(444,303) 92.92%	(1,934) 80.68%
dysp	1	(34,316) 7.14%	(33,853) 7.08%	(463) 19.32%
hypermed	1:No	(255,482) 53.16%	(255,017) 53.33%	(465) 19.40%
hypermed	2:Yes	(225,071) 46.84%	(223,139) 46.67%	(1,932) 80.60%
diab	0	(406,737) 84.64%	(405,187) 84.74%	(1,550) 64.66%
diab	1	(73,816) 15.36%	(72,969) 15.26%	(847) 35.34%
dialysis	1:No	(474,318) 98.70%	(472,122) 98.74%	(2,196) 91.61%
dialysis	2:Yes	(6,235) 1.30%	(6,034) 1.26%	(201) 8.39%
stroke	0	(475,866) 99.02%	(473,588) 99.04%	(2,278) 95.04%
stroke	1	(4,687) 0.98%	(4,568) 0.96%	(119) 4.96%
smoke	1:No	(395,003) 82.20%	(393,112) 82.21%	(1,891) 78.89%
smoke	2:Yes	(85,550) 17.80%	(85,044) 17.79%	(506) 21.11%

Supplemental Table C. Clinical Characteristics of the Derivation and Validation NSQIP Cohorts			
Characteristic	**Subgroup**	**Validation Cohort 2012 (n=210,914)**	**Derivation Cohort 2013 (n=172,905)**
Age	*years*	74.1 ± 6.9	74.0 ± 6.9
ASA Class	*1-No Disturb*	1.6%	1.5%
	2-Mild Disturb	34.9%	34.8%
	3-Severe Disturb	55.4%	55.4%
	4-Life Threat	8.1%	8.3%
	5-Moribund	0.0%	0.0%
Functional Status	*Independent*	95.0%	95.4%
	Partially Dependent	4.2%	3.9%
	Totally Dependent	0.8%	0.7%
Creatinine	*Normal*	83.3%	83.5%
	Abnormal	7.9%	7.7%
	Missing	8.8%	8.9%
Surgical Category	*Hernia*	9.4%	9.4%
	Anorectal	1.2%	1.2%
	Aortic	2.7%	2.4%
	Bariatric	0.7%	0.7%
	Brain	0.9%	0.9%
	Breast	6.3%	6.2%
	ENT	0.8%	0.8%
	Foregut/hepatopancreatobiliary	8.4%	8.1%
	GBAAS/Intestinal	10.8%	10.5%
	Neck	2.6%	2.5%
	Obstetric/gynecologic	3.8%	4.0%
	Orthopedic	22.6%	24.0%
	Other abdomen	1.5%	1.4%
	Peripheral vascular	7.7%	7.3%
	Skin	1.6%	1.5%
	Spine	5.2%	5.9%
	Thoracic	2.1%	1.9%
	Vein	3.1%	2.8%
	Urology	8.6%	8.4%
Creatinine	*Normal*	96.3%	96.3%
	Abnormal	3.7%	3.7%
CHF	*No*	98.9%	98.7%
	Yes	1.1%	1.3%
Diabetes	*No*	78.6%	78.4%
	Yes	21.4%	21.6%

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