Evaluation of a Novel Preoperative Biomarker-Based Score to Assess Morbidity and Mortality Following Hip Fracture

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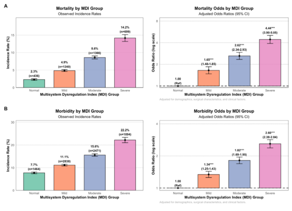
INTRODUCTION:
Hip fractures are strongly associated with poor sequelae and mortality, even following surgical repair. Given high risks for complications and death, preoperative risk stratification is essential to improving outcomes for patients with hip fractures. Previous methods have included frailty indices such as the modified 5-item frailty index (MFI-5) or Risk Analysis Index (RAI), but these may lack relevant physiological information or be cumbersome to calculate. Other frailty measures such as psoas diameter require advanced imaging and may be challenging to capture for many patients. However, recent computational advances have enabled improved analysis of common laboratory biomarkers that may provide an alternative method for assessing preoperative risk in patients with hip fractures. We aimed to evaluate the novel Multisystem Dysregulation Index (MDI), which relies on preoperative laboratory values, in predicting postoperative morbidity and mortality in patients with hip fractures.
METHODS:
Patients treated surgically for hip fractures between 2016 and 2022 within the National Surgical Quality Improvement Program (NSQIP) database were identified using ICD-10-CM and CPT codes. MDI is a novel composite metric quantifying physiological deviation from healthy homeostasis using Mahalanobis distance, a statistical measure that captures multivariate correlation within complex data sets. This was calculated from six routine biomarkers (BUN, albumin, AST, alkaline phosphatase, WBC, sodium) identified as most significant during analysis of the 10 biomarkers available in NSQIP via ablation analysis, and compared to a healthy National Health and Nutrition Survey reference population. MDI scores were categorized into four risk strata (normal/mild/moderate/severe) using chi-square distribution critical values (α=5e-2, 5e-4, 5e-8). Mixed-effects logistic regression models adjusting for demographics and clinical factors evaluated associations with 30-day mortality and morbidity (as defined by Clavien-Dindo Grade 3+ surgical complications). The discriminative performance of MDI was assessed using Odds Ratios (OR), Area Under Curve (AUC), and modified Net Reclassification Index (mNRI), as well as compared to other possible predictors using feature importance analysis with the XGBoost feature selection algorithm.
RESULTS: Of the 65,607 patients managed surgically for hip fractures, 7,931(12.08%) experienced morbidity and 3,780 (5.8%) mortality. Among these patients, increasing MDI was associated with significantly higher morbidity and mortality. Notably, 18714 (28.5%) patients were categorized as severe, and these patients demonstrated dramatically higher risks of morbidity (OR: 2.42; 95% CI: 2.20 to 2.66; *P* = <0.001) and mortality (OR: 3.61; 95% CI: 3.07 to 4.27; *P* = <0.001). When discriminative performance was compared to other medical comorbidities, MDI outperformed the baseline comorbidities model in AUC analysis for both morbidity (Baseline 0.611 [95% CI: 0.604–0.617], MDI 0.640 [95% CI: 0.634–0.647]) and mortality (Baseline 0.739 [95% CI: 0.731–0.747], MDI 0.766 [95% CI: 0.759–0.774]). Results were similarly superior when mNRI was employed (morbidity: 0.2481; 95% CI: 0.2267–0.2718; mortality: 0.3692; 95% CI: 0.3372–0.4000). Feature analysis also identified MDI as the most significant indicator of morbidity and mortality when compared to other predictors such as ASA, age, or BMI.
DISCUSSION AND CONCLUSION:
Of the 65,293 patients managed surgically for hip fractures, 7,867 (12.0%) experienced morbidity and 3,741 (5.7%) mortality. Among these patients, increasing MDI was associated with significantly higher morbidity and mortality. Notably, 4,937 (7.6%) patients were categorized as severe, and these patients demonstrated dramatically higher risks of morbidity (OR: 2.60; 95% CI: 2.38 to 2.84; *P* = <0.001) and mortality (OR: 4.44; 95% CI: 3.90 to 5.05; *P* = <0.001). When discriminative performance was compared to other medical comorbidities, MDI outperformed the baseline comorbidities model in AUC analysis for both morbidity (Baseline 0.610 [95% CI: 0.603-0.617], MDI 0.637 [95% CI: 0.631-0.643]) and mortality (Baseline 0.739 [95% CI: 0.731-0.746], MDI 0.765 [95% CI: 0.757-0.772]). Results were similarly superior when mNRI was employed (morbidity: 0.2353 [95% CI: 0.2117 - 0.2601]; mortality: 0.3564 [95% CI: 0.3262 to 0.3887]. Feature analysis also identified MDI as the most significant indicator of morbidity and mortality when compared to other predictors such as ASA, age, or BMI.



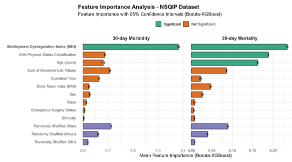


Table 1. Morbidity and Mortality by MDI Stratification

Characteristic	N (%) (Overall N = 65,293)
Demographics	
Age, years, mean (SD)	78.75 (10.80)
Female sex	43,647 (66.8)
Race	
White	57,311 (87.8)
Asian	1,560 (2.4)
Black	3,102 (4.8)
Other	748 (1.1)
Unknown	2,572 (3.9)
Hispanic ethnicity	4,250 (6.5)
Clinical Characteristics	
Body Mass Index (BMI), kg/m ²	
Underweight (<18.5)	5,678 (8.7)
Normal weight (18.5-24.9)	30,690 (47.0)
Overweight (25.0-29.9)	18,573 (28.4)
Class I Obesity (30.0-34.9)	7,165 (11.0)
Class II Obesity (35.0-39.9)	2,118 (3.2)
Class III+ Obesity (≥40.0)	1,069 (1.6)
ASA Physical Status Classification	
Class 1	331 (0.5)
Class 2	10,230 (15.7)
Class 3	42,679 (65.4)
Class 4	11,985 (18.4)
Class 5	68 (0.1)
Procedural Factors	
Year of operation	
2016	8,237 (12.6)
2017	8,848 (13.6)
2018	9,033 (13.8)
2019	10,207 (15.6)
2020	10,006 (15.3)
2021	9,558 (14.6)
2022	9,404 (14.4)
Emergent case	12,356 (18.9)
Outpatient procedure	510 (0.8)

Table 1. Morbidity and Mortality by MDI Stratification Cont.

Frailty and Health Status Measures	
Risk Analysis Index (RAI), mean (SD)	28.86 (6.49)
RAI Category	
Non-frail	913 (1.4)
Pre-frail	16,732 (25.6)
Frail	38,300 (58.7)
Severely Frail	9,348 (14.3)
5-item Modified Frailty Index (mFI-5) Score	
1	15,868 (24.3)
2	34,379 (52.7)
3	12,607 (19.3)
4	2,232 (3.4)
5	207 (0.3)
MDI Score, mean (SD)	1.54 (0.36)
MDI Group	
Normal	18,992 (29.1)
Mild	25,497 (39.1)
Moderate	15,867 (24.3)
Severe	4,937 (7.6)
Outcomes	
Postoperative morbidity	7,867 (12.0)
Mortality	3,741 (5.7)