The American Journal of Surgery 218 (2019) 484–489

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Frailty as a prognostic factor for the critically ill older adult trauma patients☆

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ARTICLE INFO

Article history:
Received 21 December 2018
Received in revised form
22 January 2019
Accepted 28 January 2019

Keywords:
Trauma
ICU
In-hospital
Complications
Mortality

ABSTRACT

Background: Frailty is highly prevalent in the elderly and confers high risk for adverse outcomes. We aimed to assess the impact of frailty on critically ill older adult trauma patients.
Methods: We analyzed the ACS-TQIP(2010–2014) including all critically-ill trauma patients ≥65y. The modified frailty index (mFI) was calculated. Following stratified into frail and non-frail, propensity score matching was performed. Our primary outcome measure was in-hospital complications. Secondary outcome measures included mortality and discharge disposition.
Results: We identified 88,629 patients, of which 34,854 patients (frail: 17,427, non-frail: 17,427) were matched. Overall 14% died. Frail patients had higher rates of complications (34% vs. 18%, $p < 0.001$), mortality (18.1% vs. 9.7%, $p < 0.001$), and were more likely to be discharged to rehab/SNF (58.7% vs. 21.2% $p < 0.001$) compared to non-frail patients.
Conclusion: critically-ill frail patients are more likely to have higher morbidity and mortality. Frailty can be used as an objective measure to identify high-risk patients.

Introduction

Over the coming decades, according to the 2015 Census report, the older population of the United States (U.S.) will increase rapidly, and it is estimated that by 2030 one in five Americans will be aged 65 or over.[1] As the population ages, there is a concomitant increase in the utilization of health-care services by geriatric patients. Frailty is a well-established term that denotes a decline in physiological reserves, as well as multi-organ impairments that are independent from the process of aging.[2]

Nonetheless, frailty is more prevalent with increasing age, and it confers a high risk for adverse clinical outcomes, including, but not limited to, falls, mortality, hospitalization, and an adverse discharge disposition to either a skilled nursing facility (SNF) and/or a rehabilitation center.[3,4] Increasingly, frailty is recognized as both a risk factor and a predictor of poor clinical outcomes across various surgical and medical disciplines.[5–8] There are different models to quantify and measure frailty.[9,10] Some rely on the physical phenotype,[11] others on the cumulative deficit model.[12]

Additionally, the increased prevalence of frailty among the geriatric population is expected to lead to a greater utilization of critical-care services.[13] Consequently, the number of frail patients admitted to intensive care units (ICUs) is bound to increase as well. However, some studies have shown that age alone is not predictive of adverse outcomes and prognoses for ICU patients, and that

☆ Poster presentation at the 2018 Annual Scientific Meeting of the American Geriatric Society (AGS), 2nd – 5th May, 2018, Orlando, Florida.

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https://doi.org/10.1016/j.amjsurg.2019.01.035
0002-9610/

severity of the illness, along with comorbidities, primarily determine the overall patient outcomes.[14,15]

At the same time, in contrast to a younger counterpart, a relatively minor injury in a geriatric trauma patient can have devastating consequences, including a greater likelihood of morbidity and mortality. Still, the role of frailty among geriatric trauma patients admitted to the ICU remains unclear and there is a paucity of data describing the association between the two using objective measures of frailty. Therefore, we used the American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP) dataset to assess the impact of an objective measure of frailty on outcomes in critically ill geriatric trauma patients. We hypothesized that frailty among critically ill geriatric trauma patients is associated with higher morbidity and mortality.

Methods

Dataset

We analyzed the aforementioned ACS-TQIP dataset (16), a database that collects data on trauma patients at more than 775 participating trauma centers across the U.S. The program was initiated in 2008. It aims to provide risk-adjusted data for the purposes of reducing variability in adult trauma outcomes and offering best practice recommendations to improve trauma care. TQIP ensures the quality of the data by offering training for data collectors and registrars.[16]

Inclusion criteria & patient stratification

We performed a five-year (2010–2014) analysis and included all geriatric trauma patients (age $\geq$ 65) who were admitted to an ICU for more than 24 h. Patients who died within the first 24 h or spent less than 24 h in the ICU were excluded from the analysis. Then, patients were stratified into two groups, frail and non-frail, using the modified frailty index (mFI) explained below.

Data points

The following data points were collected from the database: demographic characteristics (age, gender, race, and ethnicity); mechanism of injury (blunt vs. penetrating); injury severity parameters [Injury Severity Score (ISS)]; comorbidities [insulin dependent or non-insulin dependent diabetes mellitus, functionally dependent health status, chronic obstructive pulmonary disease (COPD), transient ischemic attack, congestive heart failure, history of myocardial infarction, history of angina, history of peripheral vascular disease, hypertension requiring medication, cerebrovascular accident/residual neurological deficit, and dementia]; complications (respiratory, hematological, cardiovascular, infectious, and renal complications); hospital and ICU length of stay (LOS); ventilator days; discharge disposition; emergency department (ED) physiological parameters [systolic blood pressure (SBP)], heart rate (HR), Glasgow Coma Scale (GCS)), and mortality.

Outcomes

Our primary outcome measure was in-hospital complications, which we analyzed according to five categories: respiratory [acute respiratory distress syndrome (ARDS), pulmonary embolism (PE), and unplanned intubation]; cardiovascular [cardiac arrest and myocardial infarction (MI)]; hematological [deep venous thrombosis (DVT)/thrombophlebitis]; infectious [pneumonia, urinary tract infection (UTI), catheter-related bloodstream infection, deep surgical site infection, organ/space surgical site infection, severe sepsis, and superficial surgical site infection]; and renal [acute kidney injury (AKI)]. Secondary outcome measures included mortality and discharge disposition [skilled nursing facility (SNF) and rehabilitation centers].

Modified frailty index

The mFI was calculated using 11 variables (10 comorbidities and 1 functional status measure) from the Canadian Study of Health and Aging (CSHA): a history of hypertension requiring medication; a history of either peripheral vascular disease or rest pain; a history of a cerebrovascular accident with neurological deficit; a history of myocardial infarction; a history of either prior percutaneous coronary intervention, prior cardiac surgery, or angina; a history of congestive heart failure; a history of either a transient ischemic attack or a cerebrovascular accident; a history of either a chronic obstructive pulmonary disease or pneumonia; a history of diabetes mellitus; a history of impaired sensorium; and, functional status. The 11 variables of the CSHA were matched with 11 variables from the TQIP database, as shown in Table 1. This is a feasible form of measurement because TQIP contains variables found in a patient's history. Additionally, the CSHA-Frailty Index has been described previously, and it is employed as a frailty measuring tool that uses clinically relevant variables in the National Surgical Quality Improvement Program (NSQIP) Dataset.[17] For the frailty calculation, each positive comorbidity is equivalent to one point. The sum of the positive points is then divided by the total number of points available. Thus, the mFI score ranges from 0.0 to 1.0, with 1.0 being the frailest.

Functional health status has been shown to contribute to the ability of statistical models to predict outcomes in older adult patients. In such patients, according to previous literature, a patient's preoperative functional dependency is independently associated with higher rates of complications and mortality.[18,19]

Table 1
Matched modified frailty index variables.

#	TQIP Variable	CSHA Domain
1	Hypertension Requiring Medication	History of Hypertension Requiring Medication
2	History of Peripheral Vascular Disease	History of either Peripheral Vascular Disease or Rest Pain
3	Cerebrovascular Accident/Residual Neurological Deficit	History of Cerebrovascular Accident with Neurological Deficit
4	History of Myocardial Infarction	History Myocardial Infarction
5	History of Angina	History of either Prior Percutaneous Coronary Intervention, Prior Cardiac Surgery, or angina
6	Congestive Heart Failure	History of Congestive Heart Failure
7	Transient Ischemic Attack	History of either Transient Ischemic Attack or Cerebrovascular Accident
8	Chronic Obstructive Pulmonary Disease	History of either Chronic Obstructive Pulmonary Disease or Pneumonia
9	Functionally Dependent Health Status	Functional Status
10	Insulin Dependent/Non-Insulin Dependent Diabetes Mellitus	History of Diabetes Mellitus
11	Altered Level of Consciousness	History of Impaired Sensorium

Statistical analysis

Propensity score matching was performed without replacement to match the two groups (frail vs. non-frail) in a 1:1 ratio. This statistical method, developed by Paul Rosenbaum[20] in 1983, is used in retrospective observational studies, and it serves as an analog to the concept of randomization in clinical trials (pseudo randomization). The following possible confounding variables were included in the propensity model: patient demographics (age, gender, and race), injury parameters (mechanism of injury, ISS), ED physiological vitals (ED HR, ED SBP, GCS), and comorbidities. The predictive capacity of the mFI score was assessed using the area under the Receiver Operator Characteristics (ROC), that is, it was used to confirm the accuracy of the propensity model. The optimum cutoff values for the mFI were determined on the ROC by using the Youden Index.

In our analysis, a p value of $\leq$5% was considered statistically significant. All the statistical analyses were performed using the Statistical Package for Social Services (SPSS, version 24; SPSS, Inc., Armonk, NY).

Results

A total of 88,629 patients were analyzed and matched (frail: 17427, non-frail: 17427). Matched groups were similar in demographics, admission vital signs, injury parameters, and ICU LOS. The mean age was 76.7 ± 7 years (mean ± Standard Deviation), the median GCS was 14 [13–15] (median [Interquartile Range]), and the median ISS was 17 [10–29]. Other results included a mean SBP of 134.8 ± 25.3 mmHg, a mean HR of 93.5 ± 17.8 BPM, and a median ICU LOS of 6 [3–12] days. The most common mode of injury was falls (61%), followed by a motor vehicle accident (31.7%). The most common mechanism of injury was blunt force (92.8%). The data for the matched groups is summarized in Table 2.

Overall, 30.6% of the patients developed complications, while 14% died. Frail patients had higher rates of complications (34.2% vs. 18.1%, p= <0.001), an adverse discharge disposition (SNF/Rehab) (58.7% vs. 21.2%, p= <0.001) [(SNF) (47% vs. 15.6%, p= <0.001), (SNF/Rehab) (11.7% vs. 5.6%, p= <0.001)], and mortality (18.1% vs. 9.7%, p= <0.001) compared to non-frail patients. The primary and secondary outcomes are demonstrated in Table 3.

The most common complications were infectious, followed by respiratory, cardiovascular, hematological, and renal. Among the infectious complications, frail patients were more likely to develop pneumonia (8.4% vs. 4%, p= <0.001), a urinary tract infection (7% vs. 3.2%, p= <0.001), a deep surgical site infection (1.5% vs. 0.6%, p= <0.001), or severe sepsis (2.7% vs. 1.5%, p= <0.001) compared to non-frail patients. However, there was no noticeable difference between the two groups regarding a catheter-related bloodstream infection (p = 0.39), an organ/space infection (p = 0.07), or a superficial surgical site infection (p = 0.39).

When we analyzed the respiratory and cardiovascular complications, frail patients were more likely to develop acute respiratory distress syndrome (8.1% vs. 4%, p= <0.001), a myocardial infarction (7.7% vs. 3%, p= <0.001), or cardiac arrest (3.9% vs. 1.1%, p= <0.001) than non-frail patients. The former group also had higher rates of unplanned intubation (3.4% vs. 2.1%, p= <0.001) than the latter group. Finally, concerning hematological and renal complications, frail patients were more likely to develop DVT/thrombophlebitis (8.1% vs. 3.3%, p= <0.001) and acute kidney injury (5.9% vs. 3%, p= <0.001) compared to non-frail patients.

Even in the frail group, adverse outcomes (including complications, mortality, and an adverse discharge disposition) were linearly increasing with an increasing value of mFI after the cutoff (mFI = 0.27). This relationship is demonstrated in Fig. 1.

On performing ROC curve analysis, an optimal cutoff mFI 0.27 (using Youden Index) was obtained, this cutoff corresponds to a

Table 2
Demographics and injury parameters for the matched data.

Characteristics	Non-Frail (n = 17427)	Frail (n = 17427)	*P-value*
Age, years mean ± SD	76.4 ± 7	76.5 ± 7	0.18
Female, % (n)	43.7% (7615)	44% (7668)	0.31
Whites, % (n)	74.5% (12983)	74.8% (13035)	0.53
BMI, mean ± SD	25.1 ± 9.3	25.3 ± 9.0	0.11
Vital parameters			
GCS, median [IQR]	14 [13–15]	14 [12–15]	0.32
ED SBP, mean ± SD	134.5 ± 25.1	135.2 ± 25.6	0.16
ED HR, mean ± SD	93.2 ± 17.4	93.8 ± 18.2	0.12
Injury Parameters, median [IQR]			
ISS	17 [10–29]	17 [11–29]	0.43
Head AIS	3 [1–2]	3 [1–3]	0.51
Abdominal AIS	2 [1–2]	2 [1–3]	0.65
Thoracic AIS	2 [1–3]	2 [1–2]	0.65
ICU-Course			
ICU LOS, median [IQR]	6 [3–11]	6 [3–12]	0.21
Mechanism of Injury. % (n)			
Blunt	92.4% (16102)	93.2% (16242)	0.24
Penetrating	7.3% (1272)	6.8% (1185)	
Mode of Injury, % (n)			
Falls	60.9% (10613)	61.2% (10665)	0.57
MVC	31.5% (5489)	32.0% (5576)	
Others	7.6% (1324)	6.8% (1185)	

SD: Standard Deviation, BMI: Body Mass Index, GCS: Glasgow Coma Scale, IQR: Interquartile Range, ED: Emergency Department, SBP: Systolic Blood Pressure, HR: Heart Rate, ISS: Injury Severity Score, AIS: Abbreviated Injury Scale, ICU: Intensive Care Unit, LOS: Length of Stay, MVC: Motor Vehicle Crash.

Table 3
Primary and Secondary outcome measures of the study.

Variables	Non-Frail (n = 17427)	Frail (n = 17427)	P-value
Primary			
Complications	18.1%	34.2%	<0.001
Respiratory	5.2%	11.4%	<0.001
ARDS	4.0%	8.1%	<0.001
PE	1.2%	1.1%	0.39
Unplanned Intubation	2.1%	3.4%	<0.001
Cardiovascular	4.2%	10.6%	<0.001
Cardiac Arrest	1.2%	3.9%	<0.001
MI	3%	7.7%	<0.001
Hematological			
DVT/Thrombophlebitis	3.3%	8.1%	<0.001
Infectious	7.3%	16.2%	<0.001
Pneumonia	4.0%	8.5%	<0.001
UTI	3.2%	7%	<0.001
Catheter-related blood stream infection	1.1%	1.0%	0.39
Deep surgical site infection	0.6%	1.5%	<0.001
Organ/space surgical site infection	0.9%	1.1%	0.07
Severe sepsis	1.5%	2.7%	<0.001
Superficial Surgical Site infection	1.1%	1.2%	0.39
Renal			
Acute Kidney Injury	3.0%	5.9%	<0.001
Secondary			
Discharge Disposition			
Home	45.2%	33.1%	<0.001
Skilled Nursing Facility/Rehab	21.2%	58.7%	
Mortality	9.7%	18.1%	<0.001

ARDS: Acute Respiratory Distress Syndrome, PE: Pulmonary Embolism, MI: Myocardial Infarction, DVT: Deep Venous Thrombosis, UTI: Urinary Tract Infection.

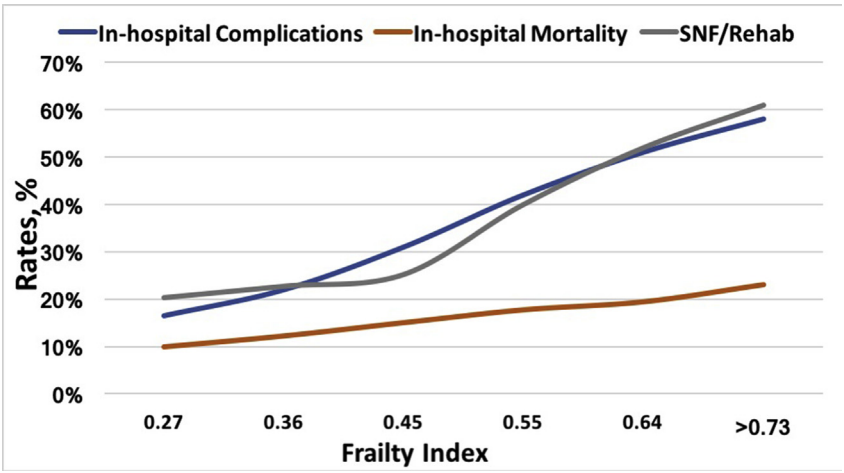

Fig. 1. Rates of in-hospital complications, in-hospital mortality, and SNF/Rehab disposition based on modified frailty index.

sensitivity of 84% and a specificity of 79% for predicting in-hospital complications ($p < 0.001$), a sensitivity of 79% and a specificity of 76% for predicting mortality ($p < 0.001$), and a sensitivity of 81% and a specificity of 78% for predicting discharge disposition ($p < 0.001$).

Discussion

The ongoing growth of the U.S. elderly population is associated with a steady increase in the number geriatric patients admitted to ICUs. Likewise, frailty, described in various fields of medicine, is a reliable tool for predicting adverse outcomes and providing insight into risk stratification. Indeed, the results of our study suggest that frail patients admitted to the ICU are more likely to have higher rates of complications compared to non-frail patients. Furthermore, an adverse discharge disposition and mortality rates were also higher among frail patients. There is growing evidence that frailty may explain the decreased tolerance and increased vulnerability of older adult patients to adverse outcomes in trauma.[21,22] Thus, this study helps to fill gaps in our understanding of how frailty affects outcomes in older adult trauma patients admitted to the ICU. While there is an emerging literature that tackles the impact of frailty on adverse events among older adult trauma patients, there is paucity of data on frailty and ICU outcomes.

While frailty is more common with advancing age, the variety of tools for assessing it has resulted in discrepancies in the literature regarding the reported prevalence of frailty. However, in general, frailty exists in around 11% of patients aged 65 or more and in 43% of patients aged 85 and more.[23,24] From a critical-care point of view, the reported incidence of frailty among geriatric patients admitted to the ICU ranges from 23 to 41%.[25,26] It is crucial to identify frail geriatric patients in the ICU because, for instance, the initiation of aggressive interventions can worsen the decline in their physiological reserve, and it may result in poor outcomes. The immediate identification of such patients in the ICU will also enhance both risk stratification and the prognostic discussion with all family and individuals involved in the care of patients. While no single index can determine the end of life management plan, the modified frailty index can provide some objective data to help guide family discussions as it captures the augmented state of vulnerability frail ICU patients are in and allows us to predict their in-hospital course with a fairly good sensitivity and specificity.

Our study demonstrates increased rates of all postoperative complications among frail patients, with infectious complications being on the first rank, followed by respiratory and cardiovascular complications. Similarly, sepsis, pneumonia, prolonged ventilation, and postoperative renal failure were more common in frail patients undergoing cardiac surgery, as shown by Lee and colleagues.[27] Kolbe et al.[28] and Abt et al.[29] also found that an increasing mFI correlated with a significant increase in Clavien Dindo 4 complications and mortality. Even though they analyzed patients who underwent elective bariatric operations and head/neck cancer operations, they still found that the mFI predicted postoperative outcomes in patients who were less critically ill than those in our cohort were. The Clavien Dindo 4 grade includes postoperative complications that require ICU admission or critical care management.[30] Comparing the mFI with other preoperative risk assessment tools, Shin et al. have shown in their study that the mFI is a strong predictor of Clavien Dindo grade 4 complications with a higher odds ratio than the American Society of Anesthesiologists (ASA) classification, advanced age, and obesity class 3.[31] The complications outcomes in frail patients in this study are consistent with the existing body of literature however when it comes to the rates of unplanned intubation the difference between the two groups though have reached statistical significance but may not necessarily be clinically significant.

Published research findings clearly show that frail patients are less likely to be functionally independent after ICU discharge, and that they will require some sort of home-based or institutional assistance. For instance, one Canadian study[32] involving 421 critically ill patients (admitted to six ICUs) found that frail patients, as measured by the Clinical Frail Scale (10), were less likely to be functionally independent after ICU discharge, and they required home assistance. In our study, we also found that frailty is significantly associated with an adverse discharge disposition. Compared to non-frail patients, frail geriatric trauma patients were more likely to be discharged to an SNF or a rehabilitation center after leaving the ICU. Similarly, in their meta-analysis of the impact of frailty on ICU outcomes, Muscedere et al.[33] found that frail patients were more likely to experience an adverse discharge disposition and less likely to be discharged home.

In our analysis of ICU patients, we found that those who were frail had a higher mortality rate than those who were not. This is in line with a multi-institutional prospective study[26] of geriatric patients aged 65 and older admitted to the ICU, which found that both in-hospital and 6-month mortality was independently associated with frailty (as assessed via the Clinical Frailty Score). These findings are further supported by pooled ICU mortality data that reveals a significant high mortality risk among frail patients, even with

different kinds of frailty scores.[33] Additionally, our analysis showed a linear increment in the rates of adverse outcomes with an increasing mFI, including complications, mortality, and an adverse discharge disposition. As noted above, Abt et al.[29] also found a linear correlation between increasing frailty and mortality using the mFI. Bellamy et al.[19] also described increased rates of systemic complications and LOS with an increasing mFI. In contrast to previously reports, frail and non-frail patients did not have significant differences in their ICU-LOS in our analysis. Even though it cannot be accurately ascertained from a retrospective database, there are multiple reasons to explain this discrepancy one of them is that frail patients had significantly higher rates of mortality and this would have shortened their ICU LOS. Other reasons could be delay in decreasing the acuity of care and the need for vigilant monitoring in non-frail patients.

Given the fact that older adult trauma patients display increased mortality after trauma, goal setting and end-of-life discussion are inevitable responsibilities of the physicians in charge of their care. We believe that the mFI, as a tool to predict outcomes, can be further validated in prospective studies, which will positively influence trauma care, including clinical decision-making and goals of care conversations with patients and their families.

Our study has several limitations. The main one being that the retrospective nature of the study did not allow us to obtain follow-up data for patients admitted to the ICU, i.e., long-term outcomes were not captured. Also, even though we could only evaluate the impact of frailty on outcomes via 11 variables rather than the 70-variable assessment used in the CSHA. In addition, all 11 variables used in the calculation of the modified frailty index were assumed to have an equal contribution to the frailty score even though some variables such as functional dependence, residual neurologic deficit, congestive heart failure may confer more susceptibility and capture better the state of depleted physiological reserves in comparison to others such as hypertension, and history of diabetes. However the reliability and validity of the mFI has been demonstrated extensively with various datasets.[34,35] While the role of frailty among ICU patients has been studied extensively, to the best of our knowledge, this is the first study to analyze its impact on trauma patients admitted to the ICU and to validate the use of the mFI with data from the TQIP database.

Conclusion

Frail patients are more likely to have higher morbidity and mortality on ICU admission. The most common kind of complication among geriatric patients admitted to the ICU is an infectious one, followed by respiratory and cardiovascular complications. Frailty can be used as an objective measure to identify high-risk patients. It improves the accurate prediction of adverse outcomes and leads to better allocation of different health-care resources. Future research demonstrating the validity of the mFI in a prospective setting, as well as interobserver and intraobserver reliability, will be necessary in further defining the exact role of this index in predicting outcomes in actual clinical settings.

Authors contributions

M.H, M.Z, M.F, T.O, V.L, J.N, B.J and N.K study concept and design.

B.J, A.S, M.F, T.O, M.H, J.N, and N.K searched the literature.

B.J, M.Z, M.F, V.L, J.N, M.Z, T.O and N.K acquisition of subjects and/or data.

B.J, A.S, M.F, T.O, M.H, M.Z, and N.K analyzed the data & preparation of manuscript.

All authors participated in data interpretation, manuscript preparation and approval.

Sponsor's role

No identifiable sponsors

Disclosures

There are no identifiable conflicts of interests to report.

The authors have no financial or proprietary interest in the subject matter or materials discussed in the manuscript.

Acknowledgements

None.

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