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CT ABBREVIATED ASSESSMENT OF SARCOPENIA FOLLOWING TRAUMA: THE CAAST MEASUREMENT PREDICTS 6-MONTH MORTALITY IN OLDER ADULT TRAUMA PATIENTS

Christine Leeper, MD, Elizabeth Lin, BS, Marcus Hoffman, MD, Anisleidy Fombona, BA, Tianhua Zhou, BA, Matthew Kutcher, MD, Matthew Rosengart, MD, MPH, Gregory Watson, MD, Timothy Billiar, MD, Andrew Peitzman, MD, Brian Zuckerbraun, MD, and Jason Sperry, MD MPH

University of Pittsburgh Medical Center (C.L., M.H., M.K., M.R., G.W., T.B., A.P., B.Z., J.S.), Pittsburgh, Pennsylvania; and the University of Pittsburgh School of Medicine (E.L., A.F., T.Z.), Pittsburgh, Pennsylvania.

Abstract

Background—Older adult trauma patients are at increased risk of poor outcome, both immediately after injury and beyond hospital discharge. Identifying patients early in the hospital stay who are at increased risk of death after discharge can be challenging.

Correspondence to: Jason Sperry.

Christine Leeper, MD, General Surgery Resident, Postdoctoral Research Fellow, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, leepercm@upmc.edu

Elizabeth Lin BS, University of Pittsburgh School of Medicine, M240 Scaife Hall, 3550 Terrace St, Pittsburgh, PA 15261, line@upmc.edu

Marcus Hoffman MD, Trauma & Acute Care Surgery Fellow, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, hoffmanmk@upmc.edu

Anisleidy Fombona BA, University of Pittsburgh School of Medicine, M240 Scaife Hall, 3550 Terrace St, Pittsburgh, PA 15261, Fombona.Anisleidy@medstudent.pitt.edu

Tianhua Zhou BA, University of Pittsburgh School of Medicine, M240 Scaife Hall, 3550 Terrace St, Pittsburgh, PA 15261, Zhou.Tianhua@medstudent.pitt.edu

Matthew Kutcher, MD, Surgical Critical Care Fellow, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, kutcherme@upmc.edu

Matthew Rosengart, MD MPH, Associate Professor, Surgery and Critical Care Medicine, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, rosengartmr@upmc.edu

Gregory Watson, MD, Assistant Professor, Surgery and Critical Care Medicine, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, watsong@upmc.edu

Timothy Billiar, MD, Chair, Department of Surgery, George Vance Foster Endowed Professor, Distinguished Professor of Surgery, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, billiartr@upmc.edu

Andrew Peitzman, MD, Distinguished Professor of Surgery, Mark M. Ravitch Professor and Vice-Chairman, Department of Surgery, UPMC Vice-President for Trauma and Surgical Services, University of Pittsburgh School of Medicine, F-1281, UPMC-Presbyterian, Pittsburgh, Pa 15213, peitzmanab@upmc.edu

Brian Zuckerbraun, MD, Associate Professor, Surgery and Critical Care Medicine, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, zuckerbraunbs@upmc.edu

Jason Sperry, MD MPH, Associate Professor, Surgery and Critical Care Medicine, Associate Director of Acute Care Surgery Fellowship, Suite F1268 PUH, University of Pittsburgh Medical Center, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213, Office: 412-802-8270, Fax: 412-648-6872, sperryjl@upmc.edu

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Authorship Statement

All authors contributed significantly and substantially to this work and are willing to take public responsibility for one or more aspects of the study including design, literature search, data collection and analysis, writing and critical revisions of the manuscript.

Methods—Retrospective analysis was performed using our trauma registry linked with the social security death index from 2010–2014. Age was categorized by 18–64 and ≥ 65 years. We calculated mortality rates by age category then selected elderly patients with mechanism of injury being a fall for further analysis. CT Abbreviated Assessment of Sarcopenia for Trauma (CAAST) was obtained by measuring psoas muscle cross-sectional area adjusted for height and weight. Kaplan-Meier survival analysis was performed and proportional hazards regression modeling was utilized to determine independent risk factors for in-hospital and out-of-hospital mortality.

Results—23,622 patients were analyzed (age 18–64: 16,748 and age ≥ 65: 6,874). In-hospital mortality was 1.96% for age 18–64 and 7.19% for age ≥ 65 ($p<0.001$); post-discharge 6-month mortality was 1.1% for age 18–64 and 12.86% for age ≥ 65 ($p<0.001$). Predictors of in-hospital and post-discharge mortality for age 18–64 and in-hospital mortality for age ≥ 65 group included injury characteristics such as ISS, admission vitals and head injury. Predictors of post-discharge mortality for age ≥ 65 included skilled nursing prior to admission, disposition, and mechanism of injury being a fall. In total, 57.5% ($n=256$) of older patients who sustained a fall met criteria for sarcopenia. Sarcopenia was the strongest predictor of out-of-hospital mortality in this cohort with hazard ratio 4.77 (95% CI 2.71–8.40; $p<0.001$)

Conclusion—Out of hospital does not assure out of danger for the elderly. Sarcopenia is a strong predictor of 6-month post-discharge mortality for older adults. The CAAST measurement is an efficient and inexpensive measure that can allow clinicians to target older trauma patients at risk of poor outcome for early intervention and/or palliative care services.

Keywords

sarcopenia; elderly; post-discharge mortality; frailty; muscle mass

Introduction

Trauma patients who are 65 years of age or older have worse outcomes compared to a younger population after injury (1); however, it is becoming evident that in-hospital death is an incomplete measure of the natural history of injury in the elderly. Several studies have demonstrated that older trauma patients are at an increased risk of death after hospital discharge compared to age and gender matched controls (2–4). It is apparent that survival to hospital discharge does not guarantee a positive long-term outcome.

A variety of factors have been associated with post-discharge death, including discharge disposition, hospital and ICU length of stay, and injury scales such as the Injury Severity Score or Abbreviated Injury Scores for specific body regions (2, 5–8). However, not all of these predictors are readily available to clinicians at the time of admission or early in the hospital stay, and some are not sufficiently specific to allow providers to identify those patients at risk of poor outcome so that they may target interventions to those most appropriate. Further, these factors rely heavily on injury characteristics and do not provide any insight into the patient's premorbid condition or functional status, which are important factors in post-discharge death particularly for older adults (9). Sarcopenia is a reduction in lean body mass associated with the process of aging that results in decreased strength and functional capacity (10). There is a paucity of literature that investigates the implications of

sarcopenia in an older adult trauma population, perhaps due to the complexity of measuring and defining this entity. Measures such as age and body mass index alone are not reliable correlates of muscle mass (11–14). Recent evidence suggests that psoas muscle cross-sectional area is a standard surrogate measure of sarcopenia that can be readily and reliably measured by clinicians using standard image viewing software (15).

We hypothesized that in younger populations, injury characteristics and injury severity would predict both in-hospital and post-discharge mortality. In the older adult group, we expected to see similar characteristics predicting in-hospital mortality. However, for post-discharge mortality, we hypothesized that measures of frailty (discharge disposition, age, and sarcopenia) rather than injury characteristics or severity would be independent predictors of mortality.

Methods

CT Abbreviated Assessment of Sarcopenia following Trauma - The CAAST measurement

Muscle mass was measured by analysis of abdominal CT performed for diagnostic purposes on arrival to the hospital immediately following the injury event. The images were reviewed by trained research assistants using iSite Picture Archiving and Communication System (PACS) image management technology. Research personnel were trained in the technique of psoas measurements by the senior investigator. All measurements were verified by the primary investigator to ensure accuracy and consistency across raters. Psoas major muscle cross-sectional area (mm^2) was recorded for each patient at the level of the third lumbar vertebrae, confirmed using tissue-specific Hounsfield unit ranges. This measured value was then normalized for stature using a calculated value of body surface area (m^2) [Mosteller formula = $(\text{weight}(\text{kg}) \times \text{height}(\text{cm})/3600)^{1/2}$] to generate the CAAST value, an adjusted measure of muscle mass. Patients were considered to be sarcopenic if they fell below the 5th percentile for muscle mass, or two standard deviations below a healthy adult population (male: $<524 \text{ mm}^2/\text{m}^2$ and female $<385 \text{ mm}^2/\text{m}^2$) (18–20). All research procedures and analyses conducted for this study were approved by the local institutional review board.

Study Description

We performed a retrospective review of subjects presenting to our single institution between 2010–2014. Inclusion criteria were age ≥ 18 , level 1 or level 2 trauma alert, and the availability of at least 6 months of follow up data. Data was abstracted from the trauma registry at our quaternary referral, Level 1 trauma center that has more than 5,000 adult trauma admissions a year. Variables of interest included basic demographics, admission vital signs, injuries and injury severity score, procedures, complications and inpatient mortality. We then linked our trauma registry with the social security death index data from the same five year time period allowing the identification of post-discharge mortality. The follow-up period was limited to the first six months after discharge, as out of hospital death during this time was thought to be more likely related to the inciting trauma event as compared to out of hospital deaths years later (8, 16).

Subjects were stratified by age (18–64 years versus 65+ years) with two outcomes of interest: in-hospital and post-discharge death. Kaplan-Meier survival analysis was performed and four unique proportional hazards regression models were generated. A subset of elderly patients with mechanism of injury of fall was then selected for further analysis to identify predictors of mortality in this vulnerable group. In previous research (7, 17), falls were a particularly strong predictor of poor outcome in the elderly. Falls as a mechanism of injury may be an indicator or symptom of frailty; therefore, a measure of sarcopenia was obtained for this smaller cohort which was then included in the proportional hazards regression modeling. Subjects were excluded from this analysis if they did not have an admission CT scan.

Data Analysis

Statistical analyses were performed with Stata 13.0 statistical software (StataCorp, College Station, TX). Data were summarized as mean (SD), median (interquartile range), or percentage. Student's *t* or Mann-Whitney statistical tests were used to compare continuous variables, while χ^2 or Fisher's exact test was used for categorical variables. Univariate analysis was conducted to determine association between selected variables and the outcome of interest, mortality. Cox regression modeling was performed to control for potential confounders in determining the contribution of variables to the temporal development of in-hospital and post-discharge death. Survival time for the in-hospital analysis was set using length of stay (days), defined as the time from admission to discharge from the hospital, and was right-censored at 30 days. Survival time for the post-discharge analysis was set using time from hospital discharge until death as documented in the SSI, and was right-censored at 180 days (6 months). All factors in the univariable analysis with $p \leq 0.2$ and important predictors previously described were included in the proportional hazards regression model. Variables were chosen for the final model using backward stepwise selection. Collinear diagnostics were used to exclude predictors that captured redundant information about the outcome. A test of the proportional hazards was performed for each covariate and globally using a formal significance test based on Schoenfeld residuals. Harrell's *C* concordance statistic was employed to assess the fit of each model. Differences were considered significant for $p < 0.05$.

Results

The study cohort included 23,622 patients (age 18–64: 16,748 and age >65: 6,874) admitted to our Level 1 trauma center between 2010 and 2014 (Table 1). In-hospital mortality was 1.96% for age 18–64 and 7.19% for age >65 ($p < 0.001$); post-discharge 6-month mortality was 1.1% for age 18–64 and 12.86% for age >65 ($p < 0.001$). Other significant differences between younger and older age groups included female sex, race, ISS, and penetrating mechanism. The older group was more likely to be admitted to an ICU and to have a diagnosis of traumatic brain injury. While the median ISS was higher in the older group, the younger group had an increased proportion of individuals with severe injuries indicated by ISS > 25.

Median time to in-hospital death was 1 day [IQR 1–5] for the 18–64 year old group and 3 days [IQR 1–7] for 65+ year old group. Median time to out-of-hospital death was 56 days [IQR 23–122] for the 18–64 year old group, 37 days [IQR 10–92] for the age 65+ mechanism of injury being falls group, and 88 days [IQR 25–130] for the age 65+ other mechanism group (Figure 1).

Predictors of in-hospital mortality for the age 18–64 group (Table 2) included age, male sex, Injury Severity Score >25, admission GCS 8, admission hypotension (SBP <90 mmHg), head AIS 3, and penetrating mechanism. The model for post-discharge mortality in this group was nearly identical with the addition of cervical spine fracture and discharge to a skilled nursing facility as independent predictors, while admission systolic blood pressure did not contribute.

Predictors of in-hospital mortality for the age >65 group (Table 3) included age, Injury Severity Score, admission GCS 8, admission hypotension (SBP <110), cervical spine fracture, and ICU admission. The model for post-discharge mortality in this group relied less upon on injury characteristics, and included age, male sex, residence in a skilled nursing facility or personal care home before the trauma, and discharge to a skilled nursing facility. However, in this older adult cohort, fall as a mechanism of injury remained an independent predictor and, in fact, was one of the strongest contributors to post-discharge death in the model.

Further analysis on this particularly vulnerable cohort was performed using the CAAST measurement described above. Of patients with age >65 with mechanism of injury being a fall, a total of 445 patients with an admission CT, height and weight measures were included in the sarcopenia analysis. This cohort was 57.5% female with 11.0% in-hospital mortality and 19.8% out-of-hospital mortality. The sarcopenia measure, average psoas major muscle area adjusted for body surface area (mm^2/m^2), is normally distributed with a mean of 420.29 (105.36). For every 1 mm^2/m^2 decrease in cross sectional area, patients had a 1% increase in the odds of mortality.

We further categorized patients as sarcopenic versus not sarcopenic using the 5th percentile for muscle mass by gender as a cutoff (male: <524 mm^2/m^2 and female <385 mm^2/m^2). In total, 57.5% (n=256) of patients in this cohort met criteria for sarcopenia; by gender, this included 72.49% of men (n=137) and 46.48% of women (n=119) (p<0.001). Notably, sarcopenia was not associated with age (p=0.377). Of patients who were sarcopenic, 32.59% died within 6 months of the trauma event as compared to 8.72% who were not sarcopenic (p<0.001). Sarcopenia was the strongest predictor of out-of-hospital mortality in this cohort of older adult patients who sustained a fall with a hazard ratio of 4.77 (95% CI 2.71–8.40; p<0.001) (Table 4).

We then performed a dose response analysis by dividing cross sectional area into quartiles; compared to the quartile with the highest cross sectional area (Q4), patients with decreasing CSA had an increased odds of mortality of 1.76 (Q3; p=NS), 3.51 (Q2; p=0.006) and 9.15 (Q1; p<0.001). Median time to outpatient death for patients who were sarcopenic was 38 days (8–74), compared to 75 days (31–114) for patients who were not sarcopenic (p=0.242).

Discussion

Death rates in this trauma cohort compared to the annual death rate for the general population during the same time period (21) demonstrated a significantly higher rate of death for trauma patients across all age decades. Predictors of inpatient mortality in both young and old age groups included age, Injury Severity Score >25, admission GCS 8, and admission hypotension (SBP <90 mmHg). Six-month out-of-hospital mortality was predicted by the above, discharge disposition and cervical spine fracture for the younger group. Injury by fall was the single predictive injury characteristic in the older group; other predictors included age, male sex, residence in a skilled nursing facility or personal care home before the trauma, and discharge to a skilled nursing facility. This older cohort who sustained a fall had a significantly increased risk of 6-month out-of-hospital death as compared to the younger group and older group with any other mechanism. Falling is likely an indicator of frailty, with sarcopenia serving as a surrogate marker of this disease. The incidence of sarcopenia in this cohort was 72.49% for males and 46.48% for females, and was unrelated to patient age. Sarcopenia was the strongest predictor of 6-month post-discharge mortality with a hazard ratio of 4.77.

A variety of factors have been associated with post-discharge death, including discharge status, hospital and ICU length of stay, and injury scoring systems like Injury Severity Score or Abbreviated Injury Scores for various body regions (2, 5–8), as well as other injury characteristics including spinal cord injury, head injury, and mechanism of injury being a fall (7).

Our study indicates that older adult patients at increased risk of mortality in the first six months after a trauma can be identified by a single measurement, cross-sectional area of the psoas major muscle adjusted for body surface area. This quick, inexpensive and readily available measure can be calculated by clinicians in minutes at the time of the patient's admission. The goal of utilizing an admission measure of sarcopenia is to inform clinicians early of a patient's risk of poor outcome and need for intervention. Sarcopenic, frail patients may be admitted to the ICU with a lower threshold, offered physical therapy and nutrition services, counseled appropriately about the risks and benefits of medical/surgical interventions, and offered consultation with a palliative care provider to clarify goals of care and connect patients with needed services.

Since it was first described in 1988 (22), sarcopenia has received increasing recognition for its role in the development of frailty and disability in older adults (23, 24), which is estimated to cost the US health system approximately \$18.4 billion per year (25). Recent work also depicts the detrimental impact of sarcopenia on survival in patients with chronic disease (26, 27) and malignancy (18). Further, sarcopenia has been shown to influence drug pharmacokinetics (28) and can lead to increased drug toxicities (29). Finally, sarcopenic patients have been found to accrue increased costs in the first 6 months after a surgical procedure (30). However, little work has been done to date in clarifying the impact of sarcopenia in an older adult trauma population.

Fairchild *et al.* studied 252 blunt trauma patients over 65 years old and found increased risk for discharge to skilled nursing facility or rehabilitation unit in patients with lower mean muscle cross-sectional area. Injury Severity Score was not associated with dependence at discharge; other predictors included gender, weakness, hospital complications, and cognitive impairment (31). Several studies focus on falls and frailty fractures; falls are common and costly accidents that lead to death and disability for older adults and present a source of significant stress for caregivers (32, 33). Globally, 28–35% of older adults fall each year (34). Sarcopenia and the associated pathology of osteoporosis play an important role for this cohort as these factors are associated with increased risk of hip fracture (35–37).

The etiology of sarcopenia is multifactorial; one prominent contributor is physical inactivity. The mechanism by which this occurs starts with decreased muscle contraction that leads to decreased muscle growth factors (insulin growth factor (IGF-Ea) and mechanogrowth factor(MGF)), ultimately resulting in type 2 muscle fiber atrophy (12, 38, 39). A frequent companion to inactivity in geriatric patients is malnutrition, specifically the lack of adequate protein intake required to sustain muscle mass. Increased inflammatory cytokines, decreased vitamin D levels and other endocrine dysregulation also contribute to the complex etiology behind the development of sarcopenia (12, 13). To date, proper nutrition, aerobic exercise and strength training are the only interventions that have been proven effective in preventing or delaying the onset of frailty in older adults (40).

The CAAST measurement is an efficient and inexpensive measure that serves as a useful adjunct to the clinical history and physical exam regarding a patient's likelihood of frailty and malnutrition. Sarcopenia is an important component of frailty, a complex clinical syndrome defined by elements of physical and cognitive decline that predicts disability and vulnerability in aging adults. Frailty indices have been validated in geriatric trauma patients as a predictor of favorable outcome (41); the 50 item-questionnaire has been modified to a 15 item Trauma-Specific Frailty Index for use in a trauma population in an attempt to decrease the burden of administering this cumbersome measurement (14). However, these indices still may be impractical for routine clinical use in a busy acute care and trauma population. Current measurements of malnutrition such as the Subjective Global Assessment (SGA) rely on historical information about the patients GI symptoms, weight changes and diet as well as subjective visual assessment of muscle, fat and body fluid volume (42). As an ever increasing proportion of our society is obese, these measures may be suboptimal in determining patients who are malnourished and overweight. As in previous studies of critically ill patients (11), sarcopenia was detected in our cohort in patients of all body mass indices, some of whom may have been classified erroneously by traditional measures of nutrition as having normal nutritional status.

Previously, use of muscle cross-sectional area as a sarcopenia measure was limited to the research realm and required the use of costly software programs for use with MRI/CT, bone density scanning, or complex calculations based on multiple muscle groups. More recently, Jones *et al.* have demonstrated the reliable and practical use of the ruler measurement feature offered by most PACS software to calculate psoas muscle cross-sectional area in a clinical setting (15). In contrast to more burdensome measures, this single measure of cross-sectional muscle area from a CT scan may be used to identify patients at risk of frailty as it predicts

important outcomes such as discharge disposition in elderly trauma patients (31) and in our study, predicts 6-month mortality in an older adult trauma population after a fall. Other strengths of this sarcopenia measure include its objectivity; it does not rely on subjective opinion about a patient's habitus or functional status. Furthermore, it makes use of existing available data and does not demand subject participation, which is often not possible in an injured patient.

Notably, in our study the development of sarcopenia was not associated with the chronologic age of the patient. These results are consistent with previous studies that demonstrate no correlation between frailty and age (12–14). The age at which patients develop frailty, disability and cognitive deterioration varies substantially. Sarcopenia is one measure that may help to explain some of the heterogeneity in the aging process. Interestingly, our older trauma cohort had an increased incidence of sarcopenia in men (72.49%, vs 46.48% in women), which corroborates other work done with inpatient and community cohorts (43, 44). Further work is needed to clarify the contribution of gender and the hormonal milieu to the development of sarcopenia.

Limitations of our study include the retrospective nature of data collection as well as the patient cohort being from a single trauma center which may limit generalizability. Other limitations include the fact that this measure captures only muscle mass, and does not take into account other important markers of frailty including functional and nutritional status. Further, our data was limited in that we could not account for the severity of pre-existing medical comorbidities. Finally, our results presume that death within the first six months is due to sequelae of the trauma and not to an unrelated disease process; without cause of death, we can only note the temporal association and not true causation. Further study including prospective analysis will expand upon this research to include patients across a broad spectrum of ages and mechanisms. Sarcopenia was not related to age in our study, and we hypothesize that the CAAST measurement will be a useful and relevant assessment tool for both younger and older adults.

In conclusion, out of hospital does not assure out of danger for the elderly. CT Abbreviated Assessment of Sarcopenia for Trauma (CAAST) is an efficient and inexpensive early measure that can allow clinicians to target older trauma patients at risk of poor outcome for intensive intervention such as admission to a higher level of care, physical therapy, nutrition counseling, and/or palliative care services.

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Figure 1.
Kaplan-Meier 6-month post-discharge survival by age group and mechanism

Figure 2.
Kaplan-Meier 6-month post-discharge survival by sarcopenia criteria

Table 1

Study population characteristics by age group

		Age 18–64 (n=16,748)	Age >65 (n=6,874)	P value
Female sex, n (%)		5,234 (31.25)	3,814 (55.48)	*<0.001
Race, n (%)				
	White	12,234 (82.67)	6,307 (94.74)	*<0.001
	Black	2,607 (16.27)	301 (4.52)	*<0.001
	Other	167 (1.04)	50 (0.75)	NS
Injury Severity Score, median (IQR)		5 (2–10)	9 (4–13)	*<0.001
ISS>25, n (%)		679 (4.40)	235 (3.42)	*<0.001
Length of Stay, days median (IQR)		2 (1–5)	4 (2–7)	*<0.001
Mechanism of Injury, n (%)				
	Blunt	14,318 (84.92)	6,805 (98.98)	*<0.001
	Penetrating	2,430 (15.08)	69 (1.02)	*<0.001
Admission hypotension, n (%)		SBP<90mmHg 398 (2.46)	SBP<110mmHg 157 (2.31)	NS
Admission GCS 8, n(%)		1,094 (6.53)	320 (5.99)	NS
ICU admission, n (%)		2,822 (16.85)	2,233 (32.58)	*<0.001
Traumatic Brain Injury, n (%)		2,363 (14.11)	2,160 (31.42)	*<0.001
Admit from SNF, n (%)		69 (0.41)	551 (8.01)	*<0.001
Discharge to SNF, n (%)		1,355 (8.09)	2,786 (40.52)	*<0.001
Mortality, n (%)				
	In-hospital	328 (1.96)	494 (7.19)	*<0.001
	Post-discharge	179 (1.1)	821 (12.86)	*<0.001

Table 2

Age 18–64, all mechanisms of injury: proportional hazards regression modeling to determine independent risk factors for in-hospital and post-discharge mortality

	In-hospital mortality			Post-discharge mortality		
	Hazard Ratio	95% Confidence Interval	p value	Hazard Ratio	95% Confidence Interval	p value
ISS>25	1.99	1.66–2.40	<0.001	1.54	1.06–2.24	0.024
GCS 8	8.79	7.33–10.54	<0.001	1.50	1.07–2.12	0.020
Head AIS 3	1.85	1.53–2.22	<0.001	1.29	1.01–1.65	0.042
Penetrating mechanism	2.40	1.87–3.08	<0.001	1.51	1.07–2.14	0.020
Age (years)	1.046	1.041–1.051	<0.001	1.04	1.04–1.05	<0.001
Female sex	0.84	0.71–0.94	0.04	0.84	0.68–1.03	0.089
Admission hypotension SBP<90 mmHg	3.69	3.05–4.46	<0.001	1.30	0.93–1.81	0.122
				2.24	1.79–2.82	<0.001
Harrell's C concordance statistic = 0.9031			Harrell's C concordance statistic = 0.8613			

Table 3

Age 65, all mechanisms of injury: proportional hazards regression modeling to determine independent risk factors for in-hospital and post-discharge mortality

	In-hospital mortality			Post-discharge mortality		
	Hazard Ratio	95% Confidence Interval	p value	Hazard Ratio	95% Confidence Interval	p value
Age (years)	1.09	1.04–1.14	<0.001	1.04	1.03–1.05	<0.001
ICU admission	2.61	1.23–5.11	<0.001	1.62	1.41–1.87	<0.001
Admission GCS 8	5.26	2.27–12.2	<0.001	2.56	2.18–2.99	<0.001
ISS	1.09	1.05–1.14	<0.001	1.75	1.45–1.87	<0.001
Admission hypotension SBP<110mmHg	3.89	1.51–10.04	0.005	0.57	0.49–0.65	<0.001
Cervical spine fracture	2.58	1.30–5.10	0.038	2.09	1.63–2.68	<0.001
Harrell's C concordance statistic =0.8786			Harrell's C concordance statistic =0.7334			

Table 4

Age 65, mechanism of injury being a fall: proportional hazards regression modeling to determine independent risk factors for post-discharge mortality

	Hazard Ratio	95% Confidence Interval	p value
Sarcopenia	4.77	2.71–8.40	<0.001
Discharge to SNF	4.17	1.16–3.19	0.011
Admission from SNF	2.03	1.24–3.33	0.005
ICU admission	1.72	1.12–2.65	0.014
Age (years)	1.03	0.99–1.06	0.056
Harrell's C concordance statistic =0.788			