

## Age and mortality after injury: is the association linear?

R. S. Friese · J. Wynne · B. Joseph ·  
A. Hashmi · C. Diven · V. Pandit · T. O’Keeffe ·  
B. Zangbar · N. Kulvatunyou · P. Rhee

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### Abstract

**Introduction** Multiple studies have demonstrated a linear association between advancing age and mortality after injury. An inflection point, or an age at which outcomes begin to differ, has not been previously described. We hypothesized that the relationship between age and mortality after injury is non-linear and an inflection point exists.

**Methods** We performed a retrospective cohort analysis at our urban level I center from 2007 through 2009. All patients aged 65 years and older with the admission diagnosis of injury were included. Non-parametric logistic regression was used to identify the functional form between mortality and age. Multivariate logistic regression was utilized to explore the association between age and mortality. Age 65 years was used as the reference. Significance was defined as  $p < 0.05$ .

**Results** A total of 1,107 patients were included in the analysis. One-third required intensive care unit (ICU) admission and 48 % had traumatic brain injury. 229 patients (20.6 %) were 84 years of age or older. The overall mortality was 7.2 %. Our model indicates that mortality is a quadratic function of age. After controlling for confounders, age is associated with mortality with a regression coefficient of 1.08 for the linear term ( $p = 0.02$ ) and a regression coefficient of  $-0.006$  for the quadratic term ( $p = 0.03$ ). The model identified 84.4 years of age as the inflection point at which mortality rates begin to decline.

**Conclusions** The risk of death after injury varies linearly with age until 84 years. After 84 years of age, the mortality rates decline. These findings may reflect the varying severity of comorbidities and differences in baseline functional status in elderly trauma patients. Specifically, a proportion of our injured patient population less than 84 years old may be more frail, contributing to increased mortality after trauma, whereas a larger proportion of our injured patients over 84 years old, by virtue of reaching this advanced age, may, in fact, be less frail, contributing to less risk of death.

**Keywords** Geriatric trauma · Outcome is elderly trauma patients · Old age and mortality · Intensive care unit admission and old age

### Introduction

In 2009, the Department of Health and Human Services Administration on Aging reported that 39.6 million persons, about one in every eight Americans, were aged 65 years or older. As the demographic transition progresses, this group of elderly Americans is expected to number 72 million and constitute 19 % of the population by the year 2030 [1]. An associated increase in geriatric admissions to trauma centers is expected to accompany the expansion of this age group [2, 3]. Additionally, unintentional injury is currently the ninth leading cause of mortality in persons aged 65 years and older [4].

However, the effect of this expected increase in the proportion of elderly in the population on mortality rates after injury remains unclear. Multiple studies have demonstrated that advanced age negatively impacts outcome after injury. Specifically, injured patients aged over 40–45 years have been reported to have higher complication and mortality

R. S. Friese · J. Wynne · B. Joseph (✉) · A. Hashmi ·  
C. Diven · V. Pandit · T. O’Keeffe · B. Zangbar ·  
N. Kulvatunyou · P. Rhee  
Division of Trauma, Critical Care, Burn and Emergency  
Surgery, Department of Surgery, University of Arizona College  
of Medicine, 1501 N. Campbell Ave., Room 5411,  
P.O. Box 245063, Tucson, AZ 85727, USA  
e-mail: b joseph@surgery.arizona.edu

rates [5–7]. In fact, several studies have described a linear relationship between advancing age and mortality after injury, with the oldest patients experiencing the highest mortality rates [3, 7–9].

The etiology for the observed increase in mortality with advancing age after injury remains poorly defined. Elderly trauma patients tend to have more clinically significant pre-existing conditions and less physiologic reserve than younger injured patients [10]. However, several authors have demonstrated that the presence of pre-existing conditions and the degree of injury, as measured by the Injury Severity Score (ISS), may not contribute to the observed increased mortality rate in this population [7, 11, 12]. In contrast, several other investigators have described specific pre-existing conditions that are associated with an increased risk of death and higher complication rates after injury in elderly patients [3, 13, 14]. These conflicting findings may indicate that an inflection point, or an age at which outcomes begin to differ, exists in this elderly cohort of injured patients. Furthermore, most studies of elderly trauma patients include patients of all ages in the analysis, potentially masking any effect of advancing age within the elderly cohort. The purpose of this study was to identify predictors of outcome after injury in elderly patients. We hypothesized that age is a strong predictor of mortality after injury and that this relationship is non-linear.

## Methods

This study is a retrospective, observational cohort analysis of patients treated at the University of Arizona Medical Center (UAMC), an urban level I trauma center, over a 24-month period. The trauma registry was queried for all geriatric patients (aged 65 years and over) who were seen and evaluated in our emergency department (ED) with the diagnosis of injury. All patients meeting these criteria were enrolled. Patients for whom an exact age could not be established were excluded. The Institutional Review Board for the University of Arizona College of Medicine and the site review authority for the UAMC approved this study.

Data extracted from the trauma registry included age, gender, ISS, heart rate on arrival to the ED, systolic blood pressure on arrival to the ED, Abbreviated Injury Score (AIS) head, mechanism of injury, arrival Glasgow Coma Scale (GCS) score, and need for mechanical ventilation in the ED. Additional variables collected were disposition from the ED, need for any operative procedure, intensive care unit (ICU) and hospital length of stay (LOS), in-hospital mortality, and disposition at hospital discharge. Patients were grouped according to age and assigned to either the elderly (age 65–79 years) or super-elderly (age >80 years) groups. Student's *t*-test for independent samples was utilized to

explore for differences in continuous variables between groups, Chi-square analysis was utilized to explore for differences in categorical variables, and non-parametric analysis (Mann–Whitney *U*-test) was utilized for between-group comparisons of ordinal variables. After excluding those patients discharged home from the ED, multivariate logistic regression analysis controlling for age, gender, ISS, arrival GCS score, injury mechanism, initial vital signs, AIS head, hospital LOS, need for ICU admission, and the need for any operative procedure was performed to identify variables predictive of outcome (discharge home and mortality). This regression analysis was performed on the overall dataset as well as each individual group (elderly and super-elderly). Lastly, utilizing the overall dataset, we performed non-parametric logistic regression by fitting a generalized additive model using a smoothing spline to identify the functional form of the relationship between mortality and age [15]. Multivariate logistic regression was then utilized to define the association between age and mortality controlling for injury mechanism, ISS, initial blood pressure, AIS head, hospital LOS, arrival GCS score, need for any operative procedure, and need for ICU admission. Age 65 years was used as the reference.

Data are reported as mean  $\pm$  standard deviation (SD) for continuous variables, as proportions for categorical variables, and as median and interquartile range for ordinal variables. Data storage and management were performed with the Microsoft Excel software package (Redmond, WA, USA). Statistical analysis was performed using the IBM SPSS 19.0 statistical software package (Armonk, NY, USA) and The R Project for Statistical Computing (free-ware, <http://www.r-project.org>).

## Results

We retrospectively identified 1,107 patients aged 65 years and over who were evaluated at our level I trauma center with a diagnosis of injury over the 24-month study period. Based on age, 708 patients were assigned to the elderly group (aged 65–79 years) and 399 patients were assigned to the super-elderly group (aged >80 years). Overall, the majority of patients were male (52 %), sustaining a blunt injury mechanism (97 %), with a median ISS of 9 [4, 16] and a mean age of 76.3  $\pm$  8.1 years. Approximately one-third of patients required ICU admission from the ED and 48 % of patients suffered some degree of head injury. Furthermore, of those patients with head injury, 55 % had severe head injury (AIS >3). Subgroup analysis revealed no between-group differences, with the exception of mean age (elderly 71.1  $\pm$  4.3, super-elderly 85.4  $\pm$  4.6;  $p < 0.001$ ) and proportion of males in the super-elderly group (elderly 57 %, super-elderly 44 %;  $p < 0.001$ ) (Table 1).

**Table 1** Patient characteristics

	All patients ( <i>n</i> = 1,107)	Elderly ( <i>n</i> = 708)	Super-elderly ( <i>n</i> = 399)	<i>p</i> value
Age (years) (mean ± SD)	76.3 ± 8.1	71.1 ± 4.3	85.4 ± 4.6	<0.001
Male	576 (52 %)	402 (57 %)	174 (44 %)	<0.001
ISS (median [IQR])	9 [4, 16]	9 [4, 16]	9 [4, 13.5]	0.813
Initial HR (bpm) (mean ± SD)	84.8 ± 18.6	85.4 ± 17.8	83.7 ± 19.8	0.158
Initial SBP (mmHg) (mean ± SD)	148 ± 30.5	148 ± 29.8	149 ± 31.8	0.538
ICU admission	377 (34 %)	237 (34 %)	140 (35 %)	0.633
Mechanical ventilation (ED)	34 (3.1 %)	27 (3.8 %)	7 (1.8 %)	0.085
Any head injury	534 (48 %)	341 (48 %)	193 (48 %)	0.997
AIS head ≥3	291/534 (55 %)	175/341 (51 %)	116/193 (60 %)	0.062
Blunt mechanism	1,069 (97 %)	683 (97 %)	386 (97 %)	0.942

*SD* standard deviation, *IQR* interquartile range, *ISS* Injury Severity Score, *HR* heart rate, *bpm* beats per minute, *SBP* systolic blood pressure, *ICU* intensive care unit, *ED* emergency department

The overall in-hospital mortality was 7.2 %, with a mean hospital LOS of 6.15 + 12.1 days and a mean ICU LOS of 3.84 + 6.10 days. Twenty-five percent of all patients underwent some type of operative procedure. Over a half (57 %) of all patients were eventually discharged home, with 20 % (*n* = 218) actually discharged home from the ED. Subgroup analysis revealed no differences in the in-hospital mortality or mean hospital and ICU LOS. Patients in the elderly group were more likely to undergo an operative procedure (*p* = 0.021) and were more likely to be discharged home from the ED (*p* = 0.016) or the hospital (*p* < 0.001). Patients in the super-elderly group were more likely to be admitted to the ICU from the ED (*p* = 0.016) (Table 2).

Multivariate logistic regression analysis of the overall dataset found that age [odds ratio (OR) 1.07; 95 % confidence interval (CI) 1.01–1.12], initial GCS (OR 0.75; 95 % CI 0.66–0.86), and the need for ICU admission from the ED (OR 8.47; 95 % CI 1.51–47.7) were independent predictors for mortality, while age (OR 0.91; 95 % CI 0.87–0.94), hospital LOS (OR 0.70; 95 % CI 0.63–0.78), and presence of severe head injury (AIS 3–6) (OR 0.45; 95 % CI 0.22–0.91) were independent predictors for discharge home. Independent predictors for mortality in the elderly group included age (OR 1.29; 95 % CI 1.09–1.52), initial GCS (OR 0.69; 95 % CI 0.56–0.87), hospital LOS (OR 0.85; 95 % CI 0.74–0.97), and the need for an operative procedure (OR 5.38; 95 % CI 1.16–24.9), whereas age (OR 0.90; 95 % CI 0.82–0.99), hospital LOS (OR 0.71; 95 % CI 0.62–0.81), and severe head injury (AIS 3–6) (OR 0.36; 95 % CI 0.13–0.99) were independent predictors for discharge home. Independent predictors of mortality in the super-elderly group included initial GCS (OR 0.65; 95 % CI 0.50–0.84) and the need for ICU admission (OR 24.6; 95 % CI 1.26–475), whereas age (OR 0.90; 95 % CI

**Table 2** Length of stay, operative procedures, and disposition

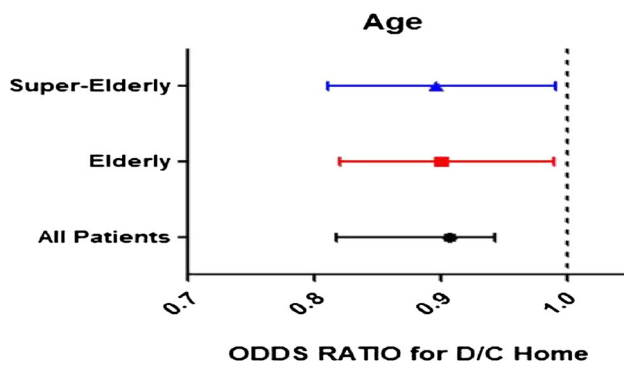
	All patients ( <i>n</i> = 1,107)	Elderly ( <i>n</i> = 708)	Super-elderly ( <i>n</i> = 399)	<i>p</i> value
ED disposition				
Floor	320 (29 %)	195 (28 %)	125 (31 %)	0.016
ICU	293 (27 %)	177 (25 %)	116 (29 %)	
Home	218 (20 %)	164 (23 %)	54 (14 %)	
Tele	43 (4 %)	22 (3 %)	21 (5 %)	
Obs	97 (9 %)	56 (8 %)	41 (10 %)	
ICU LOS (mean ± SD)	3.84 ± 6.10	3.99 ± 6.31	3.58 ± 5.64	0.457
Hospital LOS (mean ± SD)	6.15 ± 12.1	6.41 ± 14.7	5.73 ± 5.99	0.362
Any operation	277 (25 %)	193 (27 %)	84 (21 %)	0.021
In-hospital mortality	80 (7.2 %)	46 (6.5 %)	34 (8.5 %)	0.259
D/C home after admission	630 (57 %)	454 (64 %)	176 (44 %)	<0.001

*ED* emergency department, *ICU* intensive care unit, *Tele* telemetry, *Obs* observation, *SD* standard deviation, *LOS* length of stay, *D/C* discharge

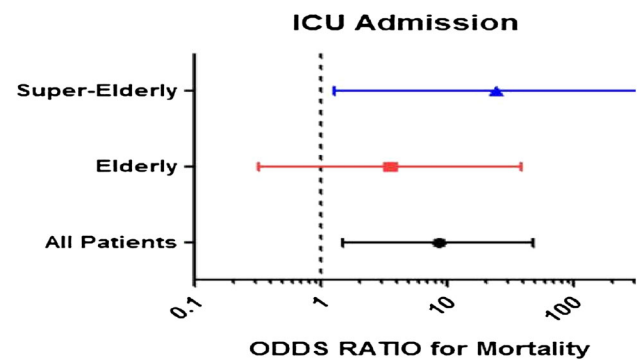
0.81–0.99) and hospital LOS (OR 0.66; 95 % CI 0.54–0.82) were independent predictors for discharge home (Figs. 1, 2, 3, and 4).

Neither gender nor ISS were found to be independent predictors of outcome (mortality or discharge home).

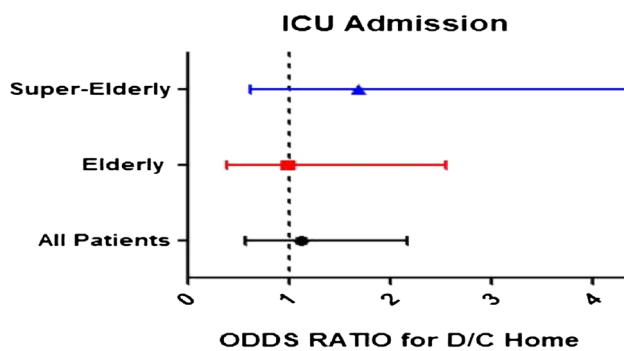
Lastly, our overall model found that mortality is a quadratic function of age. Specifically, after controlling for confounders, age is associated with mortality with a regression coefficient of 1.08 for the linear term (*p* = 0.02) and a regression coefficient of −0.006 for the quadratic term (*p* = 0.03). The model identified 84.4 years as the inflection point at which mortality rates begin to decrease.



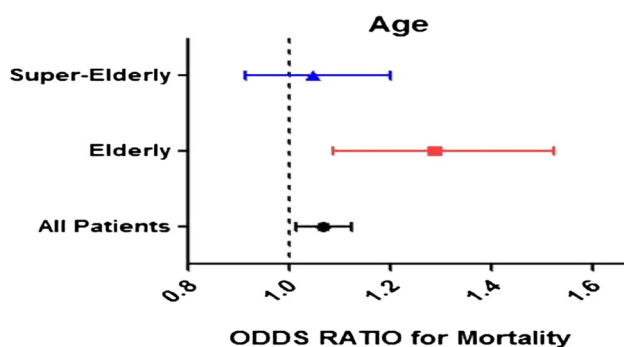
**Fig. 1** Odds ratio for age and discharge home



**Fig. 4** Odds ratio for ICU admission and mortality



**Fig. 2** Odds ratio for intensive care unit (ICU) admission and discharge home



**Fig. 3** Odds ratio for age and mortality

The OR for death at 65 years of age was 1.0 (reference); for 70 years, 2.99 (1.34–6.34); for 84.4 years, 11.78 (2.25–54.57); and for 90 years, 9.24 (1.96–43.58).

## Discussion

This study demonstrates that age becomes a much less important predictor of mortality for patients over the age of 84 years sustaining either blunt or penetrating trauma.

However, the need for ICU admission from the ED is highly predictive of mortality in this same group. Furthermore, this study confirms that advancing age is associated with a decreasing likelihood of discharge home from the hospital. We found no association between mortality after injury and gender or ISS in our cohort of patients aged 65 years and over. Finally, our model demonstrates that the association between mortality and age is non-linear, with those over 84 years old experiencing decreased mortality rates compared to those aged 65–83 years.

The injured geriatric patient is unique within the trauma patient population for several reasons. First, the reported mortality rates are high (9–15%), with significant increases when patients present with occult hypoperfusion or shock [3, 12, 16]. Additionally, the initial evaluation of the multiply injured geriatric patient can be misleading. These patients may present with fewer signs and symptoms after injury and may have a delayed presentation of shock. Several authors have described improved morbidity and mortality with protocols requiring higher levels of trauma team activation, as well as earlier and more invasive monitoring for elderly trauma patients [17–20]. Finally, injured elderly patients are more likely to have comorbidities on presentation. The effect of these comorbidities on outcome after injury is confounding and difficult to quantify due to significant variation in the number and severity of pre-existing disease processes between patients. Interestingly, the impact of the development of complications on outcome after injury in the geriatric patient admitted to the hospital may, in fact, be more profound than the presence of comorbidities. Several authors have reported that in-hospital complications during treatment for injury contribute to poor outcomes [3, 6, 14].

The definition of elderly for the purpose of exploring outcomes after injury has varied from 45 to 80 years of age [6, 21]. We chose age 65 years or greater to represent the geriatric population because the Centers for Disease Control and Prevention (CDC) uses 65 years of age and over as the oldest cohort in reporting causes of death by age group.

Additionally, this is the commonly used cutoff to define ‘geriatric’ used by several other studies [22–24]. We defined super-elderly patients based on age  $\geq 80$  years. Most influential in this decision was the tendency in the literature of identifying octogenarians as a unique subgroup of the elderly population [25–27]. Two important studies examining the relationship between comorbidities and outcomes after trauma in elderly patients warrant discussion. Milzman et al. examined over 7,000 trauma patients and found that 16 % had at least one pre-existing disease. The most common were hypertension, pulmonary disease, cardiac disease, and diabetes. This group did note a higher mortality for those patients with pre-existing disease, but the greatest increases in mortality were found among patients younger than 55 years of age with an ISS of less than 20 [9, 27]. A second study from MacKenzie et al. evaluated over 27,000 trauma admissions and described an association between the number of pre-existing conditions and hospital LOS. They found that hospital LOS was longer for those with pre-existing conditions versus those without pre-existing conditions.

Additionally, this group also noted that the effect of the presence of a pre-existing condition on hospital LOS was greater among younger patients [9, 28]. These findings may indicate that comorbidities in patients admitted following trauma play a larger role in influencing outcome for the elderly patient rather than the super-elderly patient. Indeed, chronological age may not be the best predictor of outcomes, given the inhomogeneity of the elderly population. Good functional status and absence of chronic health conditions characterizes some elderly, while others of a similar or even younger age have several significant chronic health conditions and disabilities. A better predictor would focus more on the processes of aging, which involve losses in multiple domains of function as well as the presence of chronic conditions [29, 30].

The age-related differences among elderly and super-elderly patients can be explained based on the concept of frailty. Frailty is a well-defined concept in the geriatric literature, defined as a state of increased vulnerability to health-related stressors, and can be measured by summing the number of frailty characteristics present in an individual [31–33]. Although in our study we did not assess the frailty among geriatric patients included in our cohort, we believe that the non-linear relationship between age and mortality in the elderly injured population found in our study can be explained based on the differences in frailty characteristics among the study patients. Studies have shown that frailty and not age is a significant predictor for worse outcomes in trauma patients [2, 3]. The overly frail patient may, in fact, not belong to the oldest age cohort, negatively influencing the outcome for this younger cohort, whereas an injured patient in our oldest cohort (over

80 years of age) may be less frail, having reached this age due to robustness, and, therefore, have a more favorable outcome. Understanding the frail state can help to risk-stratify patients and allocate hospital resources [22–24].

Several authors have reported results discordant with ours and describe a persistent linear relationship between age and mortality after injury. Most of these studies include all ages in the analysis, which may allow the stronger negative effect of age on mortality in ‘younger’ elderly patients to mask any less negative effect potentially present in the extremely aged [7–9]. However, one study examined a similar subset of patients, grouping their patients into those who were 65–74, 75–84, and  $>85$  years old. These authors then explored for predictors of mortality after injury. They found that increasing age continued to negatively impact survival with a greater magnitude for each cohort [3]. Their findings may differ from ours because they used as a reference the entire group aged 65–74 years, whereas we used as our reference group only those patients aged 65 years. It is possible that, by using the entire youngest cohort as a reference, these authors failed to take into account the influence of frailty on mortality outcomes.

The findings of our study must be interpreted within the context of its limitations. First, our study utilized in-hospital mortality as a measure of outcome in the regression analysis. Most older injured adults die shortly after discharge, with a much lower proportion experiencing in-hospital death after injury [34]. Second, we did not control for comorbidities, anticoagulation and antiplatelet status, and indicators of measures of frailty [10, 35]. Frailty measures are best captured in a prospective cohort. Assessing the patient’s frailty characteristics soon after injury by interviewing the patient and their family will assure a more accurate frailty assessment. Lastly, we did not find that gender or ISS was associated with outcome after injury.

The lack of identifying an improved outcome in our female patient cohort is inconsistent with other studies of injured patients. However, the benefit noted in female patients is potentially due to sex hormone differences. Our population of female patients were postmenopausal, eliminating or greatly reducing the sex hormone differences with the male cohort. We did not stratify our data by ISS but controlled for it in the regression model, and we had very similar distributions of ISS within both the elderly and the super-elderly groups.

## Conclusions

The relationship between advancing age and mortality after trauma is complicated and likely highly influenced by pre-existing and comorbid conditions, as well as the level of pre-injury functional status. Additionally, admission to the

intensive care unit (ICU) from the emergency department (ED) after injury may be a better predictor of the in-hospital mortality than age. Need for ICU admission in the oldest cohort of patients may be a surrogate maker for poor level of functional status rather than a marker of severity of injury. Further studies examining the impact of frailty on outcome after injury are warranted.

**Conflict of interest** There are no identifiable conflicts of interest to report. R. S. Friese, J. Wynne, B. Joseph, A. Hashmi, C. Diven, V. Pandit, T. O'Keeffe, B. Zangbar, N. Kulvatunyou and P. Rhee have no financial or proprietary interest in the subject matter or materials discussed in the manuscript.

**Compliance with Ethics Guidelines** This article does not contain any studies with human or animal subjects performed by any of the authors. The Institutional Review Board for the University of Arizona College of Medicine and the site review authority for the UAMC approved this study.

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