

## Meta-analysis

# Female geriatric patients with traumatic brain injury have better odds of survival compared to men-a meta-analysis and review of the literature

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## ABSTRACT

Geriatric trauma patients have worse outcomes compared to younger patients. Differences in trauma outcomes based on gender remain unproven. We sought to investigate the association of gender with outcomes among geriatric patients with traumatic brain injury (TBI) by performing a meta-analysis and review of the literature. A systematic review of published articles on outcomes of geriatric patients with TBI using PubMed was conducted. A total of 363 articles were identified, from these, 74 articles met the inclusion criteria of isolated TBI in geriatric patients. Upon review of the articles, only 5 met the specified criteria of the search which described male and female mortality amongst geriatric patients suffering isolated TBI. The data from these papers were combined into a master file and meta-analysis was performed using random-effect model with Rev Man 5.4 software. The total number of patients in these 5 papers was 23,893, of these 11,971 were men and 11,922 were women. The odds ratio for survival in these patients were 1.40, 2.40, 1.20, 1.28 and 1.15 with a combined final OR of 1.28 favoring women with a p value of less than 0.00001 and CI of 1.21-1.36. Female geriatric trauma patients sustaining TBI have better survival than men.

**Keywords:** Trauma, Geriatric, Female, Gender, TBI

## INTRODUCTION

Traumatic brain injuries (TBIs) have a devastating impact, with approximately 225,000 hospitalizations, and 60,000 deaths in the United States alone. The geriatric population is particularly susceptible to TBI, as adults greater than the age of 75 accounted for the highest proportion of all TBI-related hospitalizations and deaths in 2016 and 2017, with falls being the leading cause.<sup>1</sup> There are several pre-and post-injury factors that influence the prognosis, some pre-injury factors, including demographic features-such as age and gender play potentially conflicting roles while increased age in

associated with both increase incidence and worse outcomes of TBIs.<sup>5</sup>

Many studies have been conducted on TBI and related injuries in men, but findings in the female population remain relatively unstudied. Although studies have shown that the incidence of TBI in the geriatric population has increased among females, the incidence of TBI in both males and females in the geriatric population remains equal.<sup>3</sup> Within the geriatric population, differences exist between genders in factors of severity, complications, and mortality from TBI. Some studies report that females have decreased quality of life

following a TBI, increased self-awareness of their post-injury deficits, and less incidence of intracranial lesions compared to males.<sup>5-7</sup>

The relationship between gender and trauma outcomes is not clear, with recent publications citing age, education, physiologic factors, and severity of injury as modifiers of long-term outcomes after traumatic injuries.<sup>6,9-12</sup> Hormonal milieu has been postulated to improve trauma outcomes in females, potentially through modulation of multiple organ systems.<sup>10,12</sup> However, studies of both general traumatic injuries and specifically TBI implicate both male and female gender in prolonged hospitalizations and worse recovery.<sup>6,8,11,12</sup>

We sought to investigate the association of gender with outcomes among geriatric patients with TBI by performing a meta-analysis and review of the literature as clarification of the differences in relation to gender is necessary to properly treat TBI in the geriatric population and have better patient outcomes.

### METHODS

A systematic review of published articles on outcomes of geriatric patients with TBI using PubMed was conducted. A total of 363 articles were identified, from these, 74 articles met the inclusion criteria of isolated TBI in geriatric patients. Upon review of the articles, only 5 met the specified criteria of the search which described male and female mortality amongst geriatric patients suffering isolated TBI. The data from these papers were combined

into a master file and meta-analysis was performed using random effect model with Rev Man 5.4 software.

### RESULTS

The total number of patients in these 5 papers was 23,893, of these 11,971 were men and 11,922 were women. The odds ratio for survival in these patients were 1.40, 2.40, 1.20, 1.28 and 1.15 with a combined final OR of 1.28 favoring women with a p value of less than 0.00001 and CI of 1.21-1.36.

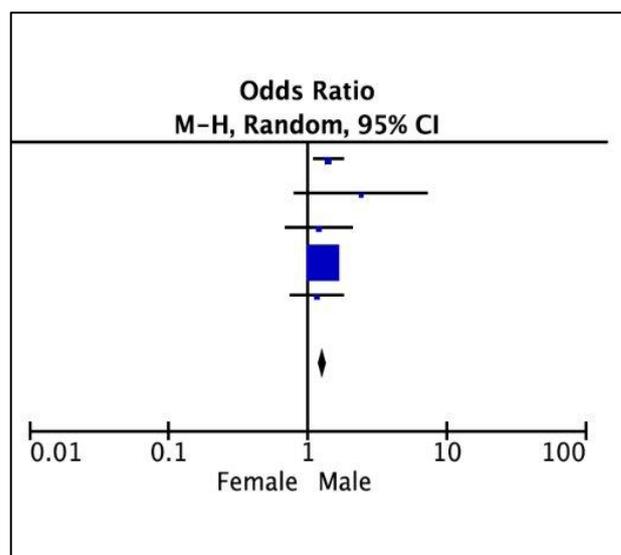


Figure 1: Odds ratio.

Table 1: Studies included in the meta-analysis.

Study (Years)	Male		Female		Weight (%)	Odds ratio
	Events	Total	Events	Total		
Albrecht (2017)	174	961	120	882	5.8	1.4 (1.09, 1.81)
Heydari (2019)	19	207	4	99	0.3	2.4 (0.79, 7.25)
Ki Seong (2019)	37	540	21	364	1.2	1.2 (0.69, 2.09)
Posti (2020)	2666	9893	2322	10366	90.8	1.28 (1.2, 1.36)
Wei-Ti Su (2021)	71	370	36	211	1.9	1.15 (0.74, 1.8)

### DISCUSSION

We found, on meta-analysis of published papers on geriatric trauma patients with TBI, that female patients had better survival compared to men. Although the role gender plays in outcomes after traumatic brain injuries has been mentioned, there is paucity of published studies in the geriatric population and it remains a subject of debate. Our findings shed more light on the subject and can have significant implications on the management of this group of injured patients.

The role gender plays in the outcomes of trauma patients have been studied before, though increased interest in the subject has been shown lately.<sup>13,15,16</sup> The role of gender probably extends beyond the sex of the patient and into the hormonal status of the patient, as Bosch et al argued

in a recent article. The prevailing hormonal milieu of the patient together with the estrus cycle might be the main determinants of the effect of these hormones on the outcomes of these patients.<sup>10</sup>

While published literature generally shows that male gender is associated with increased incidence and severity of traumatic injuries other authors have suggested that women have fewer complications following moderate to severe TBIs-which has been attributed to the neuroprotective effects of sex hormones in pre-menopausal women.<sup>3,9,11,12</sup> Roof et al in a study in rats, showed that estrogen provides neuroprotection in traumatic brain injuries by maintaining adequate cerebral perfusion after TBI and that this protective mechanism may explain the noted difference in outcome in their study.<sup>14</sup>

Gender, however, still has a less-straightforward association with outcomes, one major difference between males and females is the different sex hormones present—testosterone vs estrogen/progesterone, respectively.<sup>3</sup> Giordano et al while not focusing on geriatric patients, acknowledged the role hormone cycles play in the outcomes and argued that phasic differences within male and female populations affect these outcomes. The authors also called for incorporation of gender beyond the binary in TBI research. Although we did look into published articles on hormonal differences in geriatric patients, our review of the literature favored female gender in survival among geriatric trauma patients with TBI.<sup>13</sup>

There is mixed data on how this difference in sex hormones could affect outcomes, and whether this protective effect dissipates following menopause; other authors suggested that post-menopausal women have better outcomes compared to pre-menopausal women as well as men.<sup>3</sup> In a study in younger patients with traumatic brain injuries (TBIs), Yu et al demonstrated that ED systolic blood pressure and Glasgow coma scale (GCS) were associated with worse functional outcomes, but gender did not show significant association with functional outcome, they did not focus on survival.<sup>15</sup>

There is increased interest in the role gender plays in the outcomes of TBI, in 2014, academic emergency medicine, a global journal-held a consensus conference titled "gender-specific research in emergency care: investigate, understand, and translate how gender affects patient outcomes and a working group was formed, the goal is to guide TBI research, while this is an important step towards identifying that association, more work remains to be done to help bridge the existing gap in knowledge.<sup>16</sup>

Papers included in the meta-analysis generally showed higher rates of TBI-related hospitalizations and mortality in men (Albrecht, Posti, Heydari). A study of geriatric patients at a Maryland trauma center that treats 33% of all trauma cases in the state showed that on average, women were older and had shorter hospital stays Albrecht. Women in this study population were also less likely to have an ICU stay (65% of female patients compared to 73% of male patients) and decreased likelihood of death due to TBI (Albrecht). Additionally, men were more likely to have an abbreviated injury scale (AIS) score of 5 or above, indicating injuries of a more critical nature (Albrecht). A decade-long study of Finnish databases recording all geriatric admissions and deaths with a diagnosis of TBI echoed the findings described by Albrecht. This study found higher overall incidence rate of TBI related hospital admissions and in-hospital mortality in male patients in comparison to female patients (8.7% of male patients died while hospitalized due to TBI compared to 7.2% of female patients (Posti). Furthermore, 32% of male patients had acute neurosurgical operations (ANO) during their TBI-related

hospitalizations compared to 18% of female patients (Posti). Similarly, Heydari found that there was a higher incidence of TBIs in older male adults. The study found that higher rates of intracranial lesions were found in men as compared to women, with significant associations between intracranial lesions and the severity of head trauma. Subdural hematomas were the most common intracranial lesion found on CT (27.6%). Intracranial lesions were found in 14% of patients presenting to the ED. Overall, the severity of head trauma was associated with higher rates of mortality (Heydari). However, the association between gender and TBI in elderly adults remains conflicting in some of the literature. A multicenter study from Korea found that men are more likely to be exposed to TBI inducing injuries. It was found that the incidence of TBI between genders differs only from puberty to middle age, with similar rates of incidence in the other groups and no gender difference in the TBI ratio in elder patients. After the age of 75, a higher incidence of mild TBI was found in women due to a higher prevalence of falls in this demographic. This study found that surgical treatment was more common in men. This is thought to be because there is typically more conservative management in women because they have a higher proportion of concussions, as compared to men who have a higher rate of neurological symptoms (Ki Seong). Adding to the conflicting data, the study by Wei-Ti Su found no significant difference in gender between the mortality group and the survival group at all.

This study had limitations. Nearly 90% of the patients came from the Posti paper. This could present a bias in the information presented due to a majority of the review coming from one source. Relatedly, several of the other papers had very small sample size. Additionally, as the 5 papers included are retrospective analyses, this meta-analysis is then inherently subject to whatever selection biases were present in the original works.

## CONCLUSION

Ultimately, female geriatric trauma patients sustaining TBI have better survival than men. Our review illustrates that males have higher rates of TBI related hospitalizations, longer hospital stays, are more likely to require ICU admissions, are more likely to have an AIS score of 5 or above, are more likely to require acute neurosurgical operation, have higher rates of intracranial lesions, and have more serious complications from TBI. The exact cause as to why these differences exist have yet to be fully understood. However, our review demonstrates that there is a significant difference between male and female survival for TBI and these considerations should be taken into account during assessment and management.

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