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#### Review

# The influence of sex on outcomes in trauma patients: a meta-analysis



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#### **KEYWORDS:**

Sex; Sex hormone; Trauma; Prognosis

#### **Abstract**

**BACKGROUND:** This study aims to assess the influence of sex on outcomes among trauma patients, including injury severity, medical resource utility, complications, and mortality.

**METHODS:** A systematic review of the literature was conducted by internet search. Data were extracted from selected studies and analyzed using Stata to compare outcomes between male and female injured patients.

**RESULTS:** Eventually, 19 studies met our inclusion criteria with 100,566 men and 39,762 women. Pooled data revealed that male sex was associated with increased risk of mortality, hospital length of stay, and higher incidence of complications. No difference was detected in injury severity between male and female patients.

**CONCLUSION:** Evidence of this meta-analysis strongly supports the sex dimorphism in the prognosis of trauma patients and further work should be done to decipher potential mechanism. © 2015 Elsevier Inc. All rights reserved.

Despite tremendous advances in management and prevention, traumatic injury still sweeps across the world nowadays. One factor that has received increasing attention recently for its potential role in affecting the prognosis of trauma patients is that of sex dimorphism. Laboratory studies based on the animal model of trauma and

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hemorrhage have provided substantial evidence for sexrelated outcome differences. 1-4 Sex hormone was a possible explanation, as a high ratio of estrogen-to-androgen appears to be protective both in immunologic and inflammatory responses to traumatic injuries. 5,6 Estrogen was even considered as a new therapeutic target for trauma. However, clinical studies failed to consistently reproduce these laboratory findings. Although some investigators reported improved outcomes in female patients, 8-16 some demonstrated no substantial differences 17-22 and others even provided opposing evidences. 23-25 Therefore, we conducted a quantitative meta-analysis of previous literatures in an effort to address the issue: does sex affect injury severity, medical resource utility, complications, and mortality in trauma patients?

#### **Patients and Methods**

### Search strategy

This study was conducted by the guideline from the meta-analysis of observational studies in epidemiology group. <sup>26</sup> English language literatures published in PubMed, Web of Science, and Cochrane Library up to October 6, 2013 were searched using a combination of Medical Subject Heading and keyword terms with synonyms: "gender or sex" and "trauma or injury." References cited by chosen articles and recent reviews were checked manually for any other potential study.

#### Study selection and data extraction

Studies that fulfilled the following inclusion criteria were chosen for further analysis: (1) population: patients were 14 years of age or older with either blunt or penetrating trauma; (2) comparability: results were reported separately for men and women; and (3) outcomes: the primary outcome was mortality, while injury severity score (ISS), length of stay in hospital (HLOS) or intensive care unit (ILOS), and incidence of major complications were measured as the secondary outcomes. At least one outcome was reported. (4) Study design: randomized controlled trial, prospective observational or retrospective cohort study, and case—control study.

Descriptive studies without comparative data such as reviews were excluded. For studies with overlapping population, only the study with the longest time of observation and the largest sample size were included.

Two investigators independently reviewed the title and abstract of all potential articles and selected ones that met our inclusion requirements for full-text analysis. Data

extracted from these articles included the name of first author, publication year, study design, inclusion/exclusion criteria, number of male and female patients, stratification methods, adjusted variables, and major conclusions.

#### Study quality assessment

Because it was not appropriate to carry out the randomized controlled trial to evaluate the effect of sex on trauma, all included studies were observational studies. Well-designed criteria by Taggart et al<sup>27</sup> were used to assess the quality of these kinds of studies in 5 aspects: participant selection, comparability groups, outcomes, sample size, and cohort design. Description for each component of the quality assessment is outlined in Table 1. Studies with lowest score in every category were considered as low quality and excluded.

# Statistical analysis

Statistical analysis was performed with Stata/SE 11.0 (Stata Corporation, College Station, TX). A kappa statistic was calculated for measuring agreement between 2 authors in articles selection and quality assessment. The pooled effect of binary variables including mortality and incidence of complications was evaluated as risk ratios (RRs) with 95% confidence intervals (CIs), whereas weighted mean differences with 95% CI were used for continuous outcomes including ISS, HLOS, and ILOS. Heterogeneity across studies was evaluated with *I*<sup>2</sup> statistic, which defined *I*<sup>2</sup> as greater than 50.0%. The combined effects were computed using either fixed-effects models or in the presence of heterogeneity, random-effects models. Subgroup analyses, meta-regression, and sensitivity analysis were performed to explore the possible resources of clinical,

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Table 1
          Quality assessment of nonrandomized studies
Participant selection
   Selected cohort was representative of the general injured population (1)
   Cohort was a selected group or the selection was not described (0)
Comparability of groups
   No differences between the groups explicitly reported (especially in terms of age, injury extent and mechanism, pre-existing disease)
      unless it was the variable under investigation, or such differences were adjusted for (2)
   Differences between groups were not recorded (1)
   Groups differed (0)
   Referenced definition of clinical outcome including mortality, ISS, HLOS, ILOS, and complications (2)
   Explicit definition that included trauma mechanism and patterns (1)
   Outcome of trauma not defined (0)
   >100 participants in each group (2)
   <100 participants in each group (1)
Cohort design
   Prospective cohort design (2)
   Retrospective design (1)
   HLOS = length of stay in hospital; ILOS = length of stay in intensive care unit; ISS = injury severity score.
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