Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

# The effect of early goal-directed therapy on mortality in patients with severe sepsis and septic shock: a meta-analysis

*Jun Lu, PhD,*[a] *Xing Wang, PhD,*[a] *Qiuhua Chen, PhD,*[a] *Mingqi Chen, MM,*[a] *Lu Cheng, MM,*[a] *Linfeng Dai, MM,*[a] *Hua Jiang, MD,*[a] *and Zhiguang Sun, PhD*[b,*]

[a] *Intensive Care Unit, Affiliated Hospital of Nanjing University of Traditional Chinese Medicine, Nanjing, Jiangsu, China*

[b] *The First Clinical College, Nanjing University of Traditional Chinese Medicine, Nanjing, Jiangsu, China*

ARTICLE INFO

*Article history:*
Received 27 August 2015
Received in revised form
29 November 2015
Accepted 10 December 2015
Available online 4 January 2016

*Keywords:*
Sepsis
Septic shock
Early goal-directed therapy
EGDT
Meta-analysis

ABSTRACT

*Background:* The Surviving Sepsis Campaign has recommended early goal-directed therapy (EGDT) as an essential strategy to decrease mortality among patients with severe sepsis and septic shock. However, three latest multicenter trials failed to show its benefit in the patients with severe sepsis and septic shock. This article was to evaluate the effect of EGDT on the mortality of patients with severe sepsis and septic shock.

*Methods:* Relevant studies from PubMed, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials were identified from January 1, 2001 to June 13, 2015. With both randomized controlled trials (RCTs) and non-RCTs selected, a meta-analysis on the effects of EGDT on all identified trials was performed. The primary outcome was the inhospital mortality. In subgroup, RCTs and non-RCTs were analyzed, respectively.

*Results:* A total of five RCTs and 10 non-RCTs involving 3285 patients in EGDT group and 3233 patients in the control group were identified. Pooled analyses of all studies showed significant difference in the inhospital mortality between the EGDT group and the control group (risk ratio [RR], 0.84; 95% confidence interval [CI], 0.74–0.94; $P = 0.003$) with substantial heterogeneity ($\chi 2 = 24.93$, $P = 0.04$, $I^2 = 44\%$). In subgroup analysis, there were no significant difference in inhospital mortality between the EGDT group and the control group (RR, 0.95; 95% CI, 0.83–1.10; $P = 0.51$) with no significant difference in heterogeneity ($\chi 2 = 6.62$, $P = 0.16$, $I^2 = 40\%$) in RCTs. In non-RCTs, EGDT significantly reduced inhospital mortality (RR, 0.75; 95% CI, 0.65–0.88; $P = 0.0003$) with no significant difference in heterogeneity ($\chi 2 = 11.96$, $P = 0.22$, $I^2 = 25\%$).

*Conclusions:* This meta-analysis suggests that EGDT can significantly reduce the mortality among patients with severe sepsis and septic shock.

© 2015 Elsevier Inc. All rights reserved.

* *Corresponding author*. Nanjing University of Traditional Chinese Medicine, 138 Xianlin Avenue, Nanjing, Jiangsu 210023, China. Tel.: +86 13260900001; fax: +86(250)85811006.

E-mail address: pr_zhiguangsun@163.com (Z. Sun).

0022-4804/$ – see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2015.12.048

## Introduction

Severe sepsis and septic shock are major health care problems, the latter of which can contribute to high mortality rate [1,2]. During the last 2 decades, the treatment of the disease has been improved significantly. In 2001, Rivers *et al.* [3] found that early goal-directed therapy (EGDT) provides significant benefits in regard to outcome in patients with severe sepsis and septic shock. After that, a series of studies demonstrated that implementing EGDT in patients with severe sepsis and septic shock was associated with significant reduction in mortality [4–7]. Subsequently, use of EGDT as a first-line strategy for patients presenting in severe sepsis and septic shock was incorporated into international guidelines. Since 2004, the Surviving Sepsis Campaign Guideline Committee has released the international guidelines for management of severe sepsis and septic shock that put implementing EGDT as one of the most important components [8,9]. In 2010, Barochia *et al.* [10] conducted a meta-analysis comparing the difference in survival rate, discovering that EDGT has consistent and observable improvement in survival rate for patients with septic shock. Nevertheless, three latest multicenter, randomized trials failed to demonstrate a similar positive relationship between protocol-based EDGT and patients with severe sepsis and septic shock [11–13]. Thus, it was our purpose in this designed meta-analysis to find out whether EGDT, compared with usual care, may decrease all-cause inhospital mortality in patients admitted to the emergency department or intensive care unit with severe sepsis and septic shock.

## Materials and methods

### *Search strategy and study selection*

We identified relevant studies by searching PubMed, Embase, Web of Science, and the Cochrane Central Register of Controlled Trials using the terms "sepsis," "severe sepsis," "septic shock," "bundle," "early goal-directed therapy," and "EGDT" from January 1, 2001 to June 13, 2015. The inclusion criteria were used as follows: (1) patients with severe sepsis and septic shock; (2) studies comparing EGDT or EGDT-based bundle therapy with usual care or other intervention, irrespective of randomized controlled trials (RCTs), observational studies or retrospective studies; (3) studies provided adequate information for meta-analysis; (4) published and full text available studies. The exclusion criteria were as follows: (1) nonhuman trials; (2) pediatric studies; (3) non-English studies; (4) case reports; (5) studies which enrolled patients less than 10 in each group. For studies with the same or overlapping data, the most appropriate studies with the original data were selected.

Two authors independently checked the title and abstract of the studies, which were identified by search strategy to evaluate whether the studies potentially met the inclusion criteria. One author was blinded to the whole information relevant to the identified studies such as author, institution, setting, study design, outcome, and publications. Two authors screened whether the study fit the inclusion criteria. If there were any disagreements between the two authors, the third author joined the discussion, and all of them reached a consensus. If there were significant heterogeneity in the meta-analysis, we performed subgroup analysis that assesses the effect of EGDT regarding RCT and non-RCT, respectively. We used inhospital mortality as the outcome of our meta-analysis. If the trials did not provide inhospital mortality rates, we selected 28-d, 60-d, or 1-y mortality rates for further analysis.

In our review, randomized and nonrandomized trials were all included. For randomized trials, we used the Cochrane Collaboration's Risk of Bias tool to assess the risk of bias [14]. The tool consists of seven domains: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; (7) other bias. Judgments as "low," "unclear," or "high" risk of bias were provided in each of the domains for each study. Studies with low risk of bias for all the domains were considered to be at low risk of bias. Studies with high risk of bias for one or more domains were considered to be at high risk of bias. The remaining studies were considered to be at unclear risk of bias. The Newcastle–Ottawa scale (NOS) was used to assess the risk of bias for each identified cohort study [15]. The NOS contains eight items, categorized into three domains including: (1) selection; (2) comparability; (3) outcome. A series of options for each item is provided. Stars system is used to allow an assessment of study quality. A maximum of one star is awarded in each item for the highest quality studies, with the exception of the two stars that are awarded for the comparability domain. The NOS ranges from zero up to nine stars. Two authors independently completed the assessment.

### *Characteristics of the identified studies*

Twenty studies were identified in accordance with the search strategy, as shown in Figure 1, of which there were three with abstract only, one not using inhospital morality as prime outcome, and another one with data overlapping, leaving us with 15 qualified ones in total, five RCTs and 10 non-RCTs included. In the 10 latter non-RCTs, there were five observational studies, two for before-and-after studies and three retrospective ones.

Table 1 summarizes the design of all identified studies. There were 3285 patients in EGDT group and 3233 patients in the control group. EGDT was used for the primary intervention in 10 trials [3–5,7,11–13,16–18], whereas sepsis bundle protocol was used in three trials [6,19,20]. The remaining two trials selected resuscitation bundle [21] and simplified severe sepsis protocol [22] as the interventional strategy, respectively. Of the 15 identified trials, there were seven selected applying the inhospital mortality as the primary outcome [3,6,11,16,18,21,22], which was used as the second outcome in six trials [4,12,13,17,19,20]. Only two trials did not analyze inhospital mortality, which were replaced with 28-d mortality [5] and 1-y mortality [7], respectively in this review. In one research, the authors divided the whole enrolled patients into three groups: protocol-based EGDT group, protocol-based standard

Download English Version:

https://daneshyari.com/en/article/4299242

Download Persian Version:

https://daneshyari.com/article/4299242

Daneshyari.com