Commentary

Survival methods, including those using competing risk analysis, are not appropriate for intensive care unit outcome studies

David Schoenfeld

Professor of Medicine, Harvard Medical School, Massachusetts General Hospital Biostatistics Center, Staniford Street, Boston, MA 02114, USA

Corresponding author: David Schoenfeld, dschoenfeld@partners.org

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Abstract

The preferred analysis for studies of mortality among patients treated in an intensive care unit should compare the proportions of patients who died during hospitalization. Studies that look for prognostic covariates should use logistic regression. Survival methods, such as the proportional hazards model, or methods based on competing risk analysis are not appropriate because prolonged survival among patients that die during their hospitalization does not benefit the patient and, therefore, should not be measured in the statistical analysis.

Introduction

In *Evaluating Mortality in Intensive Care Units: Contribution of Competing Risks Analysis* [1], the authors introduce the use of the Fine and Grey regression model [2], based on the cumulative incidence function (CIF), to analyze data from outcome studies in the intensive care unit (ICU). They show that this model can be used to provide a valid analysis of hospital or ICU mortality. The authors prefer this model to analyzing mortality as a binary variable (lived versus died) using binary data analysis techniques such as logistic regression. I argue that mortality should be analyzed as a binary variable because patients who die in the ICU do not benefit if the duration of their survival is prolonged. Because survival methods, including those based on the CIF, measure this increase in survival, these methods can lead to inferences where a treatment is preferred that doesn't confer patient benefit. I conclude that logistic regression should be the preferred method of analyzing ICU data. First I compare total mortality and hospital mortality as outcomes for ICU studies. I explain which survival theory methods are appropriate for these outcomes. Then I show why these methods may lead to misleading results.

Total mortality as an outcome

Most medical studies use total mortality as their primary outcome variable. To capture this outcome patients must be followed after they leave the hospital to make sure that they do not die elsewhere. Survival analysis methods allow us to incorporate non-informative censoring in which a patient is known to be alive at a certain time. The authors correctly point out that when a patient is known to leave the hospital alive, survival methods that consider the patient as censored are not appropriate [1]. The CIF and the Fine and Grey models are also not appropriate when total mortality is the outcome because deaths after the patient leaves the hospital are not included in the CIF. In an analysis of total mortality, censoring is the last time the patient was contacted. Methods to incorporate information about whether or not a patient is in the ICU are available in the literature but would only be useful if many patients were still in the ICU at the time of analysis [3].

Total mortality is rarely used as an outcome in studies in the ICU because patients leaving the hospital alive are hard to follow and their death rate is very low. In a recent acute respiratory distress syndrome network study, we were requested by the FDA to follow patients 30 days after they left the hospital [4]; 1 of 235 patients died after returning home on unassisted breathing. Finally, deaths after the patient returns home may be unrelated to the disease that brought them to the ICU or the treatment they received there.

Hospital mortality as an outcome

Hospital mortality is defined as death within the study hospital. Patients who leave the hospital alive and subsequently die are not considered to be deaths. Hospital mortality as a function of follow up time is estimated by the cumulative incidence function or a cure model [5] and can be related to covariates using the Fine and Grey model. These estimates require special software. As an alternative, one can simply assign an arbitrarily large censoring time to all the patients who leave the hospital alive. This will give the same

CIF = cumulative incidence function; ICU = intensive care unit.

estimator as the CIF when there are no patients still alive in the hospital and will approximate it if there are only a few.

Why 'survival' and competing risk methods should not be used

The problem with these estimators is that they focus on when patients die in the hospital rather than whether they die. The quality of a patient's life in the ICU is very poor. Thus we should avoid any analysis that can confuse longer survival with better morality. The Proportional Hazards model estimated using the methods of Fine and Grey or by using standard software as defined above measures the difference in the survival curves over time. Treatments could have the exact same 30 day mortality and still show a significant benefit in one of these models [6]. Such an analysis would be seriously misleading. An example of such an analysis is [7], which showed a highly significant difference in survival with a much more modest significance level for a comparison of 30 day mortality. The only advantage of using survival methods is that they provide a small increase in power that translates to a smaller sample size. For instance, a trial using the log-rank test to test whether 28 day mortality goes from 40% to 30% would require 700 patients, whereas a trial using the Fisher exact test would require 750 patients [8]. This reduction in power requires, however, that the ratio of the hazard functions of the two treatments during the first 28 days is constant. Under other assumptions there might even be a decrease in power.

Conclusion

The preferred analysis of ICU outcome data should be hospital mortality after, say, 60 days, which should be analyzed using binary data analysis techniques such as the Fisher exact test or logistic models.

Competing interests

The author(s) declare that they have no competing interests.

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