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To cite this article: Paraskevi Tseke & Emiliios Andrikos (2012) Studying Survival Studies in PD versus HD: Is There Something More to Know?, Renal Failure, 34:4, 536-537, DOI: [10.3109/0886022X.2011.653773](https://doi.org/10.3109/0886022X.2011.653773)

To link to this article: <https://doi.org/10.3109/0886022X.2011.653773>



Published online: 20 Jan 2012.



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BRIEF REPORT

Studying Survival Studies in PD versus HD: Is There Something More to Know?

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Abstract

Peritoneal dialysis (PD) has been introduced more than 25 years ago as an alternative to hemodialysis for the treatment of end-stage renal disease. However, after the peak of the number of PD patients, which was noted in the mid-1980s, and despite the fact that in some countries there is a tendency for PD first, the number of incident PD patients in Europe and the United States is constantly decreasing. A large number of studies comparing the effect of these two treatment modalities on patients' outcomes have yielded conflicting results, which raise confusing messages to nephrologists. Epidemiologic methods, survival analysis models, and interpretation of results are not always clear and understandable for the average nephrologist. This review will focus on the exploration of possible causes of discrepancy among survival studies and it will try to clarify the basic key points of survival analysis in order to make the results as clear as possible.

Keywords: peritoneal dialysis, hemodialysis, survival analysis, mortality, review

INTRODUCTION

End-stage renal disease population continues to evolve greatly every year and patients along with nephrologists come up with the dilemma of choice of dialysis modality. In-center hemodialysis (HD) and home peritoneal dialysis (PD) are the most common forms of renal replacement treatment. The percentage of PD patients is relatively low and it does not exceed 8% in the United States.¹ Concerns about better patient survival on HD in comparison with PD may have led nephrologists to select this type of dialysis for their patients, but is this a fact? Is there enough proof to conduct a safe conclusion about survival in PD compared with HD? Numerous survival studies have made comparisons between PD and HD.^{2–4} Their findings, however, are inconsistent. The Achilles heel of these studies is several statistical biases, which are introduced in almost every stage of analysis.

Survival analysis is a data analysis of a time series with a clear starting point and an end point. The starting point of the study is usually the initiation of dialysis, which implies that incident patients rather than prevalent patients are usually included. However, there are

studies in the literature that have involved prevalent patients, that is, the study by Bloembergen et al.⁵ Therefore, in a survival study which patients are included is important to be declared. Very often, when incident patients are involved, authors exclude patients who died within the first 90 days. This usually happens when Registry data are presented. When this inclusion criterion is used, the study is biased toward the modality that is more often used in critically ill patients who usually pass away within the first 3 months.

The end point of a survival study is usually death (of any or certain cause), technique failure, or both. When an object does not reach the end point, it is considered censored. We should realize here that if cardiovascular death is the end point, then a patient who died due to cancer complications should be noted as censored and not as dead. Censoring is a very important section in survival analysis, because it can often provide much information (informative censoring). For instance, censoring due to loss to follow-up could imply a change in patient's residence, which really means nothing when comparing treatment modalities. However, censoring due to kidney transplantation could imply a better health status.

From the statistical sight of view, the best way to compare these two modalities would be a randomized prospective trial. So far, the only randomized prospective trial in this era was designed by Korevaar et al.,⁶ but the study was terminated early due to low inclusion rate, as patients did not wish to be randomized. Furthermore, beyond patients' preferences there are certain contraindications in modality selection. It seems that any effort to compare these two modalities is actually an effort to compare the incomparable, as usually dialysis patients suffer from many comorbidities.⁷ Even when populations are comparable regarding the presence of comorbid situations,⁴ the severity of these should also be evaluated. In other words, when designing a survival study to compare dialysis modalities we must take into account that this would be by default a biased study, as there will always be enough selection bias. To address this problem several methods have been used by other authors, such as inclusion of patients awaiting kidney transplantation or patients who have been referred to nephrologists at least 4 months prior to dialysis initiation or have planned versus unplanned dialysis initiation.^{8–10} However, there are so many other parameters, that is, the effect of the center, the education of the nephrologists on PD, and other measured and unmeasured factors that affect the patients' allocation to HD and PD, that selection bias will always exist in such studies.

Additionally, most of these studies are retrospective and there is recall bias, as much information is difficult to be recalled. At the same time all these studies are observational, which means that they are subject to residual confounding and they cannot prove causation between treatment modality and mortality. The identification of confounding factors and the separation of them from the true effect modifiers (risk factors) are crucial for the data analysis, as adjustment in the first one is considered as a statistical pitfall.

The selection of the statistical model that should be used for the data analysis, the careful check of non-violation of the model's assumptions (i.e., proportionality for Cox models), and the evaluation of model's fit into data are of major importance for the conduction of a reliable survival study.

Finally, as with all studies, there is publication bias. The latter has to deal with the "potentiality" of the authors to publish a study in reliable scientific journals. This "potentiality" is sometimes subject to factors other

than the quality of the study, such as the origin of the authors and the center of the study.

Despite the experience and the knowledge that have been gained over the last years in the era of renal replacement therapies, it seems that the ideal mode of dialysis remains upon patients' and nephrologists' decisions and there are no safe guidelines for this choice. However, given the fact that PD remains a lower cost treatment in the sight of economic crisis we could possibly wait for its percentage to increase over the next years.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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