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Comparative survival in hemodialysis and peritoneal dialysis

P. G. Blake

Director Peritoneal Dialysis. Associate Professor Medicine. Optimal Dialysis Research Unit. London Health Sciences Centre. University of Western Ontario. London. Ontario. Canada.

INTRODUCTION

With the spread in popularity of PD, and particularly of CAPD, in the 1980's, it was inevitable that comparisons would be made between the success of the modality and that of conventional HD. Such comparisons can be done on the basis of quality of life, hospitalization, technique survival and cost effectiveness. But the most critical «hard» end point is, of course, patient survival.

Initial studies addressing this issue from a variety of centres in North America and Western Europe were published between 1985 and 1995 and, in general, showed no consistent survival advantage for either [modality-6]. However, in 1995, Bloembergen y cols., using the US Registry (USRDS), described an excess mortality in PD patients which was most marked in females, diabetics and older patients[7]. This publication gave rise to concern about the viability of PD as a long term renal replacement therapy and may have contributed to the recent decrease in the percentage of patients managed with PD in North America[8]. In 1997, however, Fenton y cols. on behalf of the Canadian Registry described very different results in that they showed an excess mortality on HD which was most marked in the young and in non diabetics[9]. These apparently contrasting results have given rise to confusion. More recent studies, however, are helping to clarify this complex area.

METHODOLOGIC ISSUES

Before reviewing these important studies, it is essential to consider the problems that arise with comparative mortality analyses[10, 11]. These include, in particular, some of the following:

1. A large number of patients are required to show a significant survival difference between the two modalities and so such studies are typically based on national or regional registry data. However, even the best registries have limitations in terms of the completeness of data collection and the availability of information on baseline patient characteristics, such as comorbidity.

2. Such studies are, by their nature, retrospective and should not be interpreted as if they are prospective randomized control trials.

3. Most of the studies are based on incident patients, but some, including that by Bloembergen y cols., are prevalent based[7]. In general, incident-based studies are preferable as they avoid the bias that may result from an excess of early events on one or other modality.

4. Some studies use «intention to treat» (ITT) methodology, some use «treatment received» (TR) and others use both. Neither method is inherently superior as each attempts to answer a different question. ITT studies are most useful clinically in that they determine whether the initial modality selection influences ultimate survival. TR studies, however, may be more likely to detect any real difference that may exist between the two modalities.

5. Almost all studies adjust for age, sex, and diabetic status. Ideally, they should also correct for the number and severity of baseline comorbid conditions as well as functional status. This is not always the case in practice because, as already noted, registry-based studies rarely have more than limited comorbidity data. This is particularly important because it is a common observation that patients who present late, or in a critically ill state with end stage renal disease, tend to be initially treated with HD. This may introduce a bias in favour of PD if correction for this baseline comorbidity is not adequate. To minimize this,

Correspondencia: Dr. Peter G. Blake
Division of Nephrology
London Health Sciences Centre
375 South Street
London, Ontario, Canada

data from the first 90 days on dialysis are typically omitted in these studies, but this may not be sufficient.

6. The statistical technique used to compare survival on the two modalities is typically the Cox Proportional Hazards model which presumes that the relative risks (or hazards) between the two modalities stay constant with the time. This is clearly not the case in practice. A number of studies have noted that the death rate in the first 1-2 years is relatively higher on HD than PD, but that the opposite tends to be the case in subsequent years[9,12]. This disproportionality is the fundamental cause underlying much of the confusion in the literature and explains why PD looks better in studies based on incident as compared to prevalent patients.

7. Modality switches from PD to HD are much commoner than those in the opposite direction. In a pure ITT analysis, this is not an issue, but, in TR analyses or in ITT analyses that are modified by censoring at the time of a modality switch, it is a potential problem and there is a concern that mortality occurring on the second modality may unfairly be attributed to the first modality. This is typically dealt with by using a «period of grace» of 60-90 days after a modality switch. During this time, any deaths are attributed to the previous modality. In practice, this tends to have less effect on the outcome of studies than might be expected.

8. Practices are continually changing in both PD and HD; ideally, comparative studies should deal with a contemporary period, or else the results will be very out of date and may not be applicable to present day patients.

9. As already stated, correction for baseline comorbidity is important. Correction for ongoing comorbidity or for laboratory variables measured subsequent to initiation of dialysis is not appropriate, however, as these may be a consequence of the therapies being compared. For example, ongoing adjustment for residual renal function might correct away one of the advantages of PD while ongoing adjustment for serum albumin would be similarly unfair to HD.

CONTEMPORARY STUDIES

Against this background, some of the apparently contrasting outcomes in recent studies can be explained. The Bloembergen study has some weaknesses. It was a point prevalent one and so omitted a lot of early time on dialysis[7]. Because of the disproportionate hazards issue mentioned above, this makes HD look better relative to PD. It also did not correct for comorbidity and dealt with a period that is more than a decade ago.

The Fenton study was methodologically superior in that it was based on incident patients and used both ITT and TR analyses which gave similar results[9,13]. It included correction for comorbid conditions, but this was inevitably limited and there is concern that PD patients in Canada may be significantly more healthy at baseline.

Newer studies have clarified these issues somewhat. Vonesh y cols. have repeated the Bloembergen type analysis on more recent cohorts of US dialysis patients with a switch from a point prevalent to a period prevalent methodology in more recent years[14]. The advantage of HD over PD has decreased in successive cohorts to the point of being statistically and clinically insignificant, although an excess mortality persists in older diabetics and in black patients. These results may be explained by the fact that a period prevalent analysis includes a greater proportion of data from the early years on PD and so gives correspondingly better results for PD. An additional explanation may be that there has been an actual improvement in relative outcomes on PD over the past decade.

Collins y cols., using an ITT methodology with censoring after modality switches on over 100,000 incident US patients from the period 1994 to 1998, have shown that non diabetic patients have better survival on PD, while older female diabetics, in particular, do better on HD[15]. This again, emphasizes how incident studies which are generally preferred, are associated with better results for PD, relative to HD.

Recently, Murphy y cols. have presented detailed comorbidity data on a contemporary incident Canadian dialysis cohort[16]. They have shown that there is no difference in outcome between PD and HD patients in Canada when correction for baseline comorbidity and functional status is very detailed.

It thus appears that the methodology used has an enormous influence on the result of comparative mortality studies. It is desirable that incident patients be studied and when this is done, the advantage for HD seen in the US is no longer as marked as is the case in the Bloembergen study. Indeed, it may not be present at all as suggested by the recent data from Collins y cols. and Vonesh y cols.

When correction for comorbidity is comprehensive, the advantage for PD in Canada that was noted in the Fenton study is no longer found. Thus, the differences between the two modalities in the two countries are not as marked as initially appeared to be the case.

DATA OUTSIDE NORTH AMERICA

All these data come from North American studies. Much less published information is, unfortunately, available from elsewhere. Australian data on incident patients using ITT show an advantage for HD, but a more contemporary study in prevalent patients, showed no difference[16-18]. In the Lombardy Registry from Northern Italy, HD had a significant survival advantage, but there was a significant excess of baseline comorbidity in PD patients[8,19]. The opposite trend was seen in studies by Maiorca y cols. from an adjacent region of Northern Italy, and so it is difficult to draw comprehensive conclusions[3]. European Registry data addressing comparative mortality has not been published in recent years, but new information becoming available suggests that mortality on PD was historically higher, but that the gap has closed steadily over the past 20 years.

CONCLUSION

In conclusion, these analyses are very complex and much influenced by the methodology used. PD, in general, appears to do well early on, but less so later, perhaps due to better retention of residual renal function in the early years and also perhaps due to less unmeasured baseline comorbidity. HD, in many studies, seems to do better in later years and may be relatively superior in older diabetics, while PD may have the advantage in younger diabetics. Results to date, do not reflect recent radical changes in PD prescription practices and these may impact on results that become available in the future.

None of these data come from prospective randomized control studies and there is no justification for directing different sub groups to a particular modality. For now, modality selection should depend on individual patient issues and, most notably, patient preference.

Patients who are doing poorly on a given modality, despite optimal practices, should be considered for early modality switch. However, the two modalities should be considered as complementary rather than competitive and many patients may well require both during their time of dialysis.

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