

Peritoneal dialysis as first option: a successful choice

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Received for publication: 17/11/2010
Accepted in revised form: 07/02/2011

ABSTRACT

Mortality and morbidity in dialysis patients (haemodialysis or peritoneal) still remains high in spite of advances in both techniques in recent years. Differences in outcomes between the two modalities are not clear enough to support a modality choice based on survival. In this brief review, we focus on the analysis of current data that suggests peritoneal dialysis as an optimal first renal replacement therapy option until kidney transplantation is available, or even when kidney transplantation is not recommended at all.

Key-Words:

Dialysis modality; haemodialysis; peritoneal dialysis; survival

INTRODUCTION

Recent European data on survival of end-stage renal patients treated by dialysis therapy show us that the mean adult survival probability at five years after starting dialysis approaches 50%¹. American Registry of end-stage renal disease shows even worse results with mortality rates in dialysis patients reaching 20 to 30% per year². When kidney transplant, the best option to treat end-stage renal disease, is not immediately available, the patient has to make a choice of dialysis modality: haemodialysis or peritoneal dialysis.

The main question of the patient selecting a dialysis modality and the nephrologist advising him is to evaluate if the decision should be tempered by survival concerns or if this is only a life-style

choice. The perspective of an integrated managed care of end-stage renal disease could suggest that peritoneal dialysis, carefully selected, should stand out as a first dialysis option, before haemodialysis is needed. In this brief review we present arguments that peritoneal dialysis is the best first option when adapted to patient life-style and associated to preservation of residual kidney function.

When considering a dialysis modality, we evaluate medical and nonmedical factors. Survival is one of the more important medical factors. Depurative efficacy, infectious and cardiovascular risk, and effects on kidney transplant outcomes are other clinical relevant points to analyse. Quality of life related to health level, rehabilitation and active life integration, and finally, general costs are some of the nonmedical factors that are determinant to the final choice of dialysis modality. In this review, we give more importance to survival matter, even knowing that for a certain kind of patients this might be not the main factor to final decision.

“Not every choice in life has to be made to maximize survival or we would probably never leave the house, cross the street or drive on the freeway”³.

B. Piraino and J. Bargman

SURVIVAL

Randomised controlled trials

There have been three attempts of conducting a randomised controlled trial to compare survival

between peritoneal dialysis and haemodialysis. The first, published in 1984 by Gutman RA *et al.*, compared home haemodialysis (HD) and automatic peritoneal dialysis (PD) three times a week⁴. Data showed lower hospitalisation rate and better nutritional parameters in HD patients but the conclusion was not confident enough as PD patients did not attain Kt/V adequacy. The second attempt, in 1990, made by the Baxter Pharmaceutical company did not succeed because of the difficulties in recruiting patients, and data were never published. The third randomised study, published in 2003 by Korevaar J *et al.*, compared survival and quality of life of 700 ESRD patients randomised to PD or HD (Netherlands based NECOSAD study)⁵. The researchers only managed to recruit 38 patients (18 in HD and 20 in PD). Even with this small sample they published the results of five years' follow-up. It is stressed that 735 patients refused to enter the study because they had a modality preference (52% for HD, 48% for PD). Of the 38 patients analysed there was a significant difference in long-term survival which benefited PD modality, and no differences in quality of life year score between the two groups. Due to the small sample, the main conclusions of this study can not be generalised.

■ Observational trials

So far, we have had to rely on observational studies to conclude on the survival differences between PD and HD patients. This has to be done reflecting an analysis of the main recommendations for comparative studies that aim to evaluate survival differences between distinct forms of renal replacement therapy, as suggested by Quinn R *et al.*⁶. Some of these recommendations are inclusion of incident ESRD patients instead of prevalent patients, patients included should be eligible for all the therapies being compared, and choice of time zero of the study should reflect the point in time when patients really are making decisions about modality choice. With these kind of recommendations in mind, we analyse in this review different observational studies comparing outcomes between both modalities (PD and HD) grouped in three ways: those that showed best survival on PD versus HD, same survival, and worst survival.

■ Observational trials showing best survival on PD versus HD (first 12 to 24 months)

In a chronological order, the first report of best outcomes of PD compared to HD was based on the Canadian Registry and published in 1997 by Fenton A *et al.*⁷. They studied 10633 ESRD patients (7792 on HD and 2841 on PD) and compared incident CAPD/CCPD and incentre HD patients between 1990 and 1994 for a maximum of five years' follow-up. They showed evidence that CAPD/CCPD was not more associated with increased mortality rates than HD, and in the first two years of follow-up, outcomes were even better on PD. After Fenton's data, Collins AJ *et al.*⁸ published a similar study based on the American ESRD Registry with significantly more patients (117158 patients, 15% of them on PD and 85% on HD). They concluded that within the first two years of therapy, CAPD/CCPD appears to be associated with higher outcomes than HD. Based on the Danish terminal uraemia registry, Heaf JG *et al.* published data in 2002 that showed that PD mortality was significantly lower than HD, with this difference confined to the first two years of therapy⁹. The authors of this study lend support to the idea of an integrative care approach to uraemia, where patients are started on PD and transferred to HD when PD-related mortality increases.

In 2004 Vonesh EF *et al.*¹⁰ attempted to identify the factors with the greatest impact on modifying the effect of treatment modality on survival. They concluded that diabetes mellitus as cause of ESRD, age, and the presence or absence of one or more comorbid conditions had a significant impact on treatment modality and associated mortality. This study was based on the analysis of 398940 US Medicare patients followed between 1995 and 2000, 11.6% of them treated by PD. They found that outcomes were better in PD patients if they were not diabetic, and if they did not present any comorbidity. Those patients with diabetes mellitus showed better survival on PD than HD if they did not present other comorbidity and if younger than 44 years old.

In 2009 McDonald SP *et al.*¹¹ conducted a retrospective study on 27015 incident ESRD patients in the Australia and New Zealand Registry, between Oct 1991 and Dec 2005 (14733 on HD and 10544 on PD). The main advantage of this study was the high

number of PD patients included, as prevalence of PD in those countries ranges from 20 to 40%. The researchers found overall mortality rates significantly lower during the first 90 to 365-day period among those being treated with PD, but this survival advantage of PD in the first years turned out to be the opposite after this period of time. Data from the ERA/EDTA Registry showed that survival of incident HD and PD patients between 1998 and 2002 was better for PD than HD patients in the first years of treatment (adjusted for age, gender, and primary renal disease: 87% survival at 1 year on HD and 93% on PD; 77% survival at 2 years on HD and 82% on PD), although we highlight that point zero of this analysis is day 91, which favors HD outcomes, and strengthens the PD results¹².

The latest data from the USRDS Registry (2009) reproduces the European results, showing better survival on PD in the first and second year of treatment (150 deaths per 1000 pt years at risk in the first year on PD compared to 240 on HD)². Recently, a new retrospective study aiming to compare survival of incident HD and PD patients was published relative to 6337 matched pairs of patients who initiated dialysis in 2003 in the United States¹. Peritoneal dialysis was associated with improved survival compared to HD among subgroups with age <65 years, no cardiovascular disease and no diabetes. Cumulative survival probabilities for PD versus HD were 85.8% versus 80.7%

($p<0.01$), 71.1% versus 68% ($p<0.01$) at 12 and 24 months, respectively. The authors of this study suggest that increased use of PD may benefit incident ESRD patients.

■ Observational trials showing similar survival on PD versus HD

The more important observational studies that showed similar outcomes in terms of survival probability on PD versus HD are presented in a chronological order in Table I.

■ Observational trials showing worst survival on PD versus HD

All the observational studies available showing worst survival probability on PD patients versus HD patients have some kind of limitations that could question their results. The first and oldest of all, published by Gentil MA *et al.*¹⁷ in 1991, compared the survival of 842 patients on HD and 272 patients on CAPD and concluded that patient 3-year survival was higher in HD than in PD (80% survival probability versus 64% respectively). However, when accounting for the adjustment for risk factors (PD patients were older and had a greater comorbidity), no significant differences could be shown in the survival rates of the two treatment modalities.

Table I

Observational studies that showed similar outcomes in terms of survival probability on PD versus HD

Type of study, first author, year, reference	Number of patients, follow-up	Results	Main limitations of the study
Prospective cohort; Maiorca R. ¹³ 1991	480 incident patients on PD and 373 on HD between 1981 and 1987; 7 years of follow-up	No significant differences in patient survival between the two groups	No adjustment of comorbidity; PD group included comorbidity more severe
Historical prospective; Held P.J. ¹⁴ 1994	1725 diabetic and 2411 nondiabetic ESRD patients incident from 1986 to 1987; 2 to 4 years of follow-up	No significant difference in mortality risk among nondiabetic for CAPD versus HD but higher adjusted mortality among diabetic patients	Time zero is 30 day after onset of dialysis; historical prospective study
Prospective cohort; Jaar B.G. ¹⁵ 2005 Choice Study	747 incident patients on HD and 247 on PD; 7 years of follow-up	No significant differences for risk death among patients on PD versus HD in the first year; worst outcomes on PD after the first year	Time zero is 45 day after onset of dialysis; much higher proportion of HD enrolled; method of patient selection not described
Historical prospective; Sanabria M. ¹⁶ 2008	923 patients (53% on PD and 47% on HD) that started dialysis between Jan 2001 and Dec 2003; 2 to 4 years of follow-up	No significant differences in survival between PD and HD patients adjusting for covariates	Historical prospective study; 44.9% of the patients enrolled did not have residual renal function data at the start of therapy; lack of dialysis adequacy data

Bloembergen WE *et al.*¹⁸ compared the mortality rate and cause of death between PD and HD patients based on the USA Registry (a cohort of 170700 incident patients between 1987 and 1989 followed for one year). Comparing all patients in each modality, they found higher risk of mortality of PD patients versus HD patients. This difference was more severe in the diabetic population. The main limitations of this study are the analysis of prevalent patients and the lack of adjustment for other comorbidities apart from diabetes.

Ganesh SK *et al.*¹⁹ analysed mortality differences by dialysis modality among incident ESRD Medicare and Medicaid patients with and without coronary artery disease (CAD) in a more recent study. They showed the mortality risk for new ESRD patients was dependent on treatment modality: in both diabetic and nondiabetic patients treated with PD, the survival probability was lower than HD patients, and this difference was higher in patients with associated CAD. One of the shortcomings of this study is the lack of age adjustment.

The last study that revealed worst outcomes in PD patients than HD patients after one year of treatment was the designed Choice Study, already mentioned, with all its limitations (recruitment after 45 days of dialysis start; higher number of patients on HD than on PD; method of patients recruitment not clearly described)¹⁵.

In conclusion, based mainly on observational studies, we can assume that compared to HD, PD is associated with equivalent or better survival among nondiabetes mellitus patients and younger diabetes patients (under 45 years old) during the first 1-2 years of therapy. Diabetes mellitus, age and comorbidities such as cardiovascular disease all impact on the survival of PD patients, but the exact effect of these items deserves further clarification.

■ DEPURATIVE EFFICACY

Patient survival is highly influenced by delivered dialysis dose in both HD and PD. HD is an intermittent therapy with peaks and valleys of small solute concentration over the week. Peritoneal dialysis is

a continuous therapy without wide modifications of solute concentrations. Furthermore, there are significant differences in solute transport characteristics between peritoneal and haemodialysis membranes and also differences in protein losses across the membranes. All these differences between the two dialysis modalities could explain the paradox of clinically adequate CAPD at Kt/V urea levels that are considered inadequate for haemodialysis. Keshaviah PR *et al.*²⁰ showed evidence, based on the peak concentration approach, in the variable volume and single pool urea kinetic model, that a weekly CAPD Kt/V urea index of 1.7 is equivalent to an HD Kt/V of 2.6 per week or 0.86 per treatment.

At the same Kt/V of 1.7, the TAC urea for HD and the steady state BUN for CAPD are almost identical. However, due to the intermittent nature of HD, BUN levels on HD exceed the CAPD level for half the entire week. The same authors, in 2002, established that when the dose of dialysis is correctly matched, HD and PD provide comparable 2-year survival rates, independent of age, diabetic status and history of cardiovascular disease, which is an indirect confirmation of the peak concentration hypothesis²¹. In PD a Kt/V urea of 1.7 per week and a creatinine clearance of 50L are absolute minimal targets²².

The main conclusion is that if we carefully match delivered doses of Kt/V in each modality, we can achieve the same survival outcomes and the depurative efficacy factor should not be a decision parameter to influence the choice of a dialysis modality.

■ INFECTIOUS RISK

Infectious risk in uraemia is tightly linked to immune dysfunction and proinflammatory state²³. The immunosuppressed state in uraemia, not adequately improved by dialysis therapy, leads to increased susceptibility to infection and may also lead to chronic inflammation and cardiovascular risk. In addition, other external factors such as dialysis procedure, dialysis access (blood or peritoneal), medication, and protein-energy wasting may activate or inhibit the immune system. A prospective observational study into differences in infectious morbidity and mortality between HD and PD patients showed equivalence of both dialysis modalities²⁴.

The authors of this study concluded that dialysis modality was not an independent factor of infectious risk, as the global infection episodes rates were equivalent (0.77 episodes/year on HD *versus* 0.86/year on PD, $p=0.24$). Although there were no differences in global infectious risk, the type of infectious episode differed between the two modalities (only HD patients presented bacteraemia during the period of follow-up and only PD patients developed peritonitis, as expected).

The more recent USRDS Annual Data Report (2009) reported that there was a significant difference of infectious hospitalisation rates between PD and HD in the last 14 years (from 1993 until 2007)². The infectious hospitalisation rate increased 34.5% for HD and 4.7% for PD for the same period. This is mainly explained by increased admissions for HD vascular access infection and bacteraemia/septicaemia in the last decade, compared to a decrease of peritoneal dialysis peritonitis. The number of hospitalisations for pneumonia was also higher in HD patients than in PD patients.

■ CARDIOVASCULAR RISK

In dialysis patients, in addition to the traditional cardiovascular risk factors that are common to the general population, we have to deal with non-traditional risk factors such as oxidative stress, inflammation, disturbances of mineral metabolism, anaemia, fluid overload and uraemic toxicity. All of these contribute to potentiating the overall global cardiovascular risk in ESRD patients²⁵.

There is limited evidence that dialysis modality may influence cardiovascular risk. Bleyer AJ *et al.*²⁶ observed an increased risk of cardiac death in HD patients than PD, based on data of USRDS from 1977 to 1997. They associated this fact with the intermittent nature of HD therapy that contributes to an increased sudden and cardiac death rate on Monday and Tuesday for HD patients enrolled in USRDS.

In 2003, Stack AG *et al.*²⁷ showed contrary data to the assumed theory that ESRD patients with congestive heart failure benefit more from PD than from HD. Based on reports from 107922 new ESRD patients from the Center for Medicare and Medicaid

Services, they found that adjusted mortality risk was significantly higher for patients with congestive heart failure treated with PD than those treated with HD.

A recent study into cardiovascular risk and dialysis modality showed a worse outcome in PD patients when suffering from ischaemic heart disease or cardiac failure when starting dialysis treatment than in HD patients²⁸. This study, performed in Australia and New Zealand in 2007-8, showed that of the 24587 patients who started dialysis therapy (first treatment PD $n=6521$, first treatment HD $n=18066$), PD patients presented an increased risk of cardiovascular death than HD after 1 year of follow-up, due to an increased risk of myocardial infarction.

■ QUALITY OF LIFE ASSOCIATED TO HEALTH STATUS AND PERSONAL SATISFACTION WITH GLOBAL CARE

One of the nonmedical factors that can have a significant impact on dialysis modality choice is the lifestyle each modality could offer to the patient, and the quality of life and global satisfaction he/she can enjoy when selecting either HD or PD. In the light of conflicting evidence of the effect of medical factors on patient survival, patients can sustain their choice based on nonmedical factors.

In a recent and elegant analysis aiming to compare patient satisfaction with HD and PD in a cohort of patients who have recently begun dialysis, Rubin H *et al.*²⁹ concluded that patients receiving PD rated their care higher than those receiving HD therapy. This overall global evaluation of quality of dialysis care was related to all the satisfaction domains selected for this study (caring, concern, information brought by nephrologist and instructors, coordination with other physicians, interpersonal relationship with nurses and other staff, technical aspects). It overall indicates that PD could be a great modality in terms of patients overall satisfaction and quality of life associated to health status. Another recent study suggests that PD patients, in general, are more satisfied with their overall care, and believe that their treatment has less impact on their lives than do HD patients³⁰.

■ OUTCOMES AFTER KIDNEY TRANSPLANTATION

In a large retrospective cohort study of 92844 USRDS patients incident from January 1990 until December 1991, the effect of pretransplantation renal replacement therapy on allograft and recipient survival outcome was analysed³¹. The main conclusion was that compared with PD, HD as the modality immediately before transplantation or as a predominant dialysis modality during the ESRD course, was associated with increased risks of graft failure and recipient death. Van Biesen W *et al.*³² conducted a trial showing that compared to HD, PD as pretransplantation dialysis modality can reduce the incidence and the severity of delayed recovery of renal function after renal transplantation. This protective effect was independent from cold ischaemia time (CIT) and fluid status, two other major influencing factors. Some other retrospective studies could not demonstrate differences between HD and PD on kidney transplantation outcomes. One of them enrolled 345 patients followed up for 30±15 months and showed that the influence of PD and HD on complications after renal transplant at 1 year and 5 years and graft survival rates were similar³³. Another recent study concluded that as pre-transplant dialysis modality, neither HD nor PD affects the outcome of renal transplantation³⁴.

In summary, there are no studies showing better outcomes after kidney transplantation in HD patients. Some observational studies show similar or better outcomes (graft failure, patient survival, complications after kidney transplantation) on ESRD patients whose pretransplantation renal replacement therapy was PD.

■ GLOBAL COSTS

Financial issue is one of most important nonmedical factor in dialysis modality choice in different countries³⁵. As prevalence of ESRD in developed countries increases yearly, dialysis modality choice must be able to join adequately targets of therapy and financial savings for health providers (public or private). The considerations on financial costs would be a sharp force driving the final decision. Many cost comparisons of dialysis modalities have been conducted in the past^{35,36}. The main conclusion is dialysis therapy costs

vary widely from country to country according to many local market conditions, reimbursement models of payment, production and distribution factors.

Neil N *et al.*³⁷ published a recent study based on the 2007 Annual Data Report of the USRDS whose main goal was to evaluate a 5-year budget-impact analysis on total Medicare dialysis costs if different scenarios of PD share of total dialysis varied. The final conclusion was that increasing clinically appropriate use of PD would be associated with considerable savings to Medicare. As an example, if the PD share of total dialysis were to decrease from the current 8% to 5%, Medicare spending for dialysis would increase by an additional \$401 million over a 5-year period. Alternatively, if the PD share of total dialysis were to increase to 15%, Medicare could make potential savings of >\$1.1 billion over 5 years. In Hong Kong the development of a “peritoneal dialysis first” (PD-first) policy has contributed to a significant successful dialysis programme in Hong Kong since 1960³⁸. Currently in Hong Kong 80% of ESRD patients on maintenance dialysis are on PD, mainly CAPD; 20% are on haemodialysis.

Our personal evaluation, as we have had the opportunity to participate in a general hospital study in Portugal, leads us to conclude that the majority of expenses with dialysis therapy in PD modality concerns disposable solutions and other materials that make up almost 70% of the global cost. All other parts considered, such as medication, staff remunerations including physician fees, technology maintenance, laboratory and other diagnostic investigations, were significantly lower in PD therapy than in-centre HD therapy (*data not published*). The higher price of peritoneal solutions and other disposable materials in Portugal makes the technique less competitive, which could be modified by a more frequent use of this modality and simultaneously a decrease of global costs of peritoneal solutions.

In conclusion, data and experience currently available tells us that peritoneal dialysis is a successful first choice in survival, depurative efficacy, infectious risk, outcomes after a future kidney transplantation, quality of life and cost-effectiveness of therapy for the general candidate to renal replacement therapy. For the particular ESRD patient suffering from diabetes mellitus and cardiovascular diseases such as coronary heart disease, these two comorbidities having an

impact on the survival of PD patients, exact recommendation and adequacy of PD modality deserves special ponderation of risks and benefits.

Conflict of interest statement. None declared.

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