Mortality predictor pattern in hemodialysis and peritoneal dialysis in diabetic patients

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
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Abstract

An excessive mortality in dialysis programs is the result of cardiovascular injuries and immune deficiency caused by uremic toxins. The vulnerability of dialysis patients is still increasing due to the growing number of diabetics, elderly and patients with a history of cardiovascular disease. Peritoneal dialysis (PD) and hemodialysis (HD) offer similar effectiveness during the first 2 years of the treatment. However, the survival advantage of HD subsequently appears. The problem of the factors responsible for the mortality during long-term PD and HD treatment was analyzed in our recently published investigation. A lower death risk for PD patients during the first several months was lessened over time, and, therefore, no survival advantage of PD was noticeable by the completion of the 2-year period. A sign of the diminishing benefit of PD was a high rate of modality switch – 57%, contrasting with 6% switched in the HD group. Longer observations confirmed that the extension of the treatment period above 2 years with HD was associated with improved survival among subgroups with cardiovascular disease and diabetes. A very relevant problem is the timely transfer of PD patients to the HD program, when an adequate nutritional intake cannot be ascertained and a decline of serum albumin level is observed. The aim of this overview was to compare the factors affecting the survival of diabetic patients in HD and PD patients.

Key words: hemodialysis, elderly, mortality, peritoneal dialysis, diabetics

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Introduction

The mortality in dialysis patients exceeds very significantly the rate observed in the general population, even exceeding the figures occurring in neoplastic disease. In addition to specific cardiovascular harm and immune deficiency caused by uremic toxicity, the pessimistic prognosis in the dialysis program is connected with the current clinical characteristics of dialysis patients, i.e., growing participation of the elderly carrying the frailty phenotype and a pronounced increase of type 2 diabetes. These features are evidenced by 46% rate of the 5-year survival in non-diabetic dialysis patients and barely 30% in type 2 diabetics.¹ The aim of this overview was to compare the factors affecting the survival of diabetic patients in hemodialysis (HD) and peritoneal dialysis (PD) patients.

Mortality comparison of the peritoneal dialysis and hemodialysis diabetic patients

In indirect comparisons using data from the Canada-USA Peritoneal Dialysis Study Group (CANUSA) study, encompassing PD and Regional Kidney Disease Program in Minneapolis for HD incident patients, the lack of disparity in the survival between both dialysis modalities was shown during the first 2 treatment years. It was also demonstrated that the same factors, i.e., lowering serum albumin level, older age, diabetes presence, and smaller dialysis dose measured by Kt/V negatively affected the outcome.²

In a large American cohort of incident dialysis patients (22360 HD and 1358 PD) undergoing dialysis treatment, examined on day 90 and followed for 24 months, no survival difference appeared between PD and HD patients after adjustment for diabetes mellitus, age, sex, and race.³ A lower death risk for PD patients during the first several months was lessened over time, and, therefore, no survival advantage of PD was noticeable by the completion of the 2-year period. A sign of the diminishing benefit of PD over time was a high rate of modality switch – 57%, contrasting with 6% switched in the HD group. The problem of the effectiveness of PD treatment, diminishing with the elapsed time in comparison with HD, was depicted clearly by recent observations of the Korean group (Lee et al.).⁴ They noticed in the prospective observations of the cohort of 1,000 dialysis patients that during 11 months, the risk of the PD technique failure was 10-fold higher than that of HD.

Longer observations by Weinhandl et al. confirmed that with the extension of the treatment period above 2 years, HD was associated with improved survival among subgroups with cardiovascular disease and diabetes.⁵ These results support the conclusions of the earlier Netherlands Cooperative Study on the Adequacy of Dialysis, in which no statistically significant differences in adjusted

mortality rates between HD and PD patients were observed during the first 2 years of dialysis.⁶ However, in the years thereafter (months 24 to 36), increases in mortality rates for PD patients and resulting decreases in a relative risk of death in favor of HD were noticed.

Collectively, this observational data indicates that PD and HD can be regarded as complementary modalities for incident end-stage kidney disease patients, bringing a comparable outcome during the first 2 years of treatment, but after that offering a consistent survival benefit associated with the HD therapy. The improvement accompanying long-term treatment with HD is particularly noticeable in high-risk groups: the elderly, patients with a cardiovascular disease history and diabetics. Such findings open the question of timely PD patient transfer to HD, when the threats of an ominous outcome appear during PD program. This issue will be discussed in the next part of the article, which is based on our study results.

Different mortality predictor pattern in hemodialysis and peritoneal dialysis diabetic patients in 4-year prospective observation

The problem of the factors responsible for the mortality during long-term PD and HD treatment was analyzed in our recently published investigation.⁷ It encompassed 61 prevalent diabetic subjects, treated with maintenance HD (35 persons) and PD (26 persons). The particular features of the cohort were as follows: longevity of dialysis therapy (median period: 17 months), retained urine excretion (median value: 500 mL/day) and elevated cardiovascular risk. All diabetic individuals included in the study group were older than 40 years. They carried Mönckeberg medial calcific arteriosclerosis on the forearm (proved by X-ray). Twenty-six subjects (43%) were older than 70 years. The cohort was prospectively followed for 4 years. Twenty-one individuals (12 treated by HD (34.3%) and 9 (34.6%) in the PD program) from the original set survived the entire 4-year follow-up. The survivors on HD were marked by lower interleukin (IL)-6 level ($p = 0.04$), higher albumin concentration ($p = 0.03$) and increased cholesterol concentration ($p = 0.004$). The only distinction in the PD program was the younger age of the survivors ($p = 0.05$). The younger age of PD survivors was also reflected in comparison with HD survivors (58.2 ± 10.5 years vs 69.8 ± 8.4 years; $p = 0.017$), even though at the study onset, HD and PD patients were of similar age. In addition, PD survivors displayed a significantly lower albumin concentration than HD survivors (3.4 ± 0.5 g/dL vs 4.0 ± 0.5 g/dL; $p = 0.012$). Cardiovascular diseases were the most common cause of mortality – 18 patients (45% of all deaths – 7 PD/11 HD), followed by infection – 12 patients (30% – 6 PD/6 HD), malignancy – 5 patients (12.5% – 1 PD/4 HD) and

Table 1. Cox's proportional hazard regression model. Dependent variable: survival time since the beginning of investigation

Variable	Parameter estimate	Wald test	p-value	HR	HR 95% lower	HR 95% upper
Serum albumin [g/dL]	−0.588	3.962	0.047*	0.556	0.311	0.991
HD patients (n = 35)						
Cholesterol [mmol/L]	−0.597	8.15	0.004*	0.551	0.365	0.829
PD patients (n = 26)						
Age [years]	0.050	3.93	0.047*	1.051	1.001	1.104

All patients (n = 61); HR – hazard ratio; HD – hemodialysis; PD – peritoneal dialysis; * statistical significance.

others reasons – 5 patients (12.5% – 3 PD/2 HD). Cox's proportional hazard regression analysis (Table 1) exhibited in respect to the entire diabetic study group that the lowering of serum albumin is the only variable with a significant negative impact on 4-year survival ($p = 0.047$).

This data is in agreement with long-term observations published by Browne et al.⁸ They showed that the patients who had died during 10 years of the dialysis program were marked by significantly lower albumin concentration at the start of the renal replacement therapy.

In creating a division for dialysis modality, the significant mortality predictor in HD patients was low cholesterol concentration ($p = 0.004$) and only older age ($p = 0.047$) in PD patients. There was a different tendency in the serum albumin behavior in the PD and HD programs during the 4-year follow-up. In the PD group, a significant decrease of albumin concentration was observed, but no changes occurred under HD treatment. This data indicates that the majority of diabetics in the PD program are not capable of restituting the peritoneal albumin loss, amounting to 6–8 g per day.

Summary: When peritoneal dialysis diabetic patient should be transferred to the hemodialysis program?

The key issue in approaching maintenance dialysis patients is the effective prevention of protein energy waste.^{9,10} Peritoneal dialysis patients require protein intake >1.2 g/kg/day with energy providing 30–35 kcal/kg/day. When an inadequate nutritional intake is noticed in PD patients, the dialysis dose should be increased, using 2.5 L exchanges for average-sized patients and 3.5 L exchanges for larger patients. An oral protein supplement can be also introduced. The lack of improvement during the subsequent 3-month observation with progressive serum albumin decline should be recognized as a warning signal, urging to shift from PD to HD modality. Particular attention should be given to high-risk patients: elderly, diabetics and with a cardiovascular disease history.

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