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PREDICTORS OF LONG-TERM SURVIVAL ON PERITONEAL DIALYSIS IN SOUTH INDIA: A MULTICENTER STUDY

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♦♦ ***Background:*** **Little is known about survival on peritoneal dialysis (PD) in Indian patients since the initiation of continuous ambulatory PD (CAPD) in India in 1991. Survival data from single centers with small numbers have been published.**

♦♦ ***Objective:*** **A retrospective 4-center analysis for predictors of survival >3 years in south Indian chronic PD patients.**

♦♦ ***Methods:*** **A total of 309 patients were trained during the observation period (from 1999 to 2004) and were analyzed in a multicenter study (4 centers), including 150 patients (male:female 109:41) that survived ≥3 years and 59 patients that did not survive ≥3 years (nonsurvivors; male: female 43:16) that were taken as controls. The patients were on chronic PD, predominantly CAPD, using double-bag disconnect systems. They were supervised by 4 nephrologists. Mean age in the nonsurvival group was 56.6 ± 10.6 years. In the survival group, mean age was 50.9 ± 14.9 years; there were 92 (62%) nondiabetics and 58 (38%) diabetics; the majority were nonvegetarians; 148 patients were doing 6 – 8 L exchanges and 2 were doing >8 L exchanges daily; 93 of 102 patients were average transporters based on peritoneal equilibration testing. At the beginning, mean combined Kt/V was 2.31 and weekly creatinine clearance was 73 L. Patients making one lifetime payment were 46% and 21% belonged to the full reimbursement group.**

♦♦ ***Results:*** **Body mass index (BMI) was normal in 114 patients (76%). Ultrafiltration volume was 1377 ± 452 at the start and 1400 ± 461 mL/day after 3 years. Anuric patients at the start were 12% and after 3 years 44%; urine output decreased from 527 ± 26 to 253 ± 14 mL/day from the start to after 3 years. Peritonitis rate was 1 episode/75 patient-months at the beginning and after 3 years it was 1 episode/30 patient-months. Exit-site care was done daily by 88% and 3 times weekly by 12%. Nonsmokers were 92% and smokers were 8%. Those that lived in the city were 62% and rural areas were 38%. Mean blood pressure was 143 ± 16/88 ± 10 and 136 ± 18/85 ± 9 mmHg, calcium × phosphorus product 44.6 ± 15.6 and 45.9 ± 15.7 mg^2/dL^2, albumin 3.33 ± 0.5 and 3.25 ± 0.4 g/dL, hemoglobin 9.18 ± 2 and 9.48 ± 1.8 g/dL at the beginning and after 3 years, respectively. Statistical analysis showed a significant fall in both systolic ($p \leq 0.001$) and diastolic blood pressure ($p \leq 0.05$), an increase in BMI ($p \leq 0.01$), and a decrease in blood urea ($p \leq 0.001$) in the survival group. Those with Hb ≥11 g/dL survived longer ($p \leq 0.001$), those with serum albumin ≥3 g/dL had better survival ($p = 0.001$), and anuric patients survived longer ($p = 0.001$).**

♦♦ ***Conclusion:*** **This multicenter cohort study of prevalent continuous PD patients in south India showed nondiabetics, average transporters, nonsmokers with reasonable nutritional status, with Hb 11 g/dL, with low peritonitis rate, with over 1 L ultrafiltration volume per day, the great majority that joined the once per lifetime payment scheme, and the reimbursement group survived for 3 years or longer.**

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KEY WORDS: South Indian PD patients; survival > 3 years; predictors of survival.

Technique survival 3 years and longer on continuous peritoneal dialysis (CPD) is considered rare in South Asian regions (1–4). The dropout rate decreased to about 25% in 2006, compared to 51% a decade ago (1,2). The major causes of dropout, thereby reducing peritoneal dialysis (PD) survival to less than 3 years, were sudden cardiovascular death in diabetics, unresolved peritonitis, inadequate dialysis due to cost constraints, suboptimal ultrafiltration, and malnutrition (1,4). As diabetic nephropathy is the leading reason for renal replacement therapy including CPD, it is not surprising that

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comorbid conditions will lead to diminished patient survival (4).

By the year 2006, the nationwide penetration of continuous ambulatory PD (CAPD) reached over 15% and a recent publication showed 6500 prevalent patients on CPD in India (2). The treatment is catered to the more affluent patients in the society and those that get reimbursement from their employers due to lack of insurance coverage. There is hardly any health insurance coverage for CPD therapy. The initiation of a regular training program for nephrologists, renal nurses, and technologists enabled development of a pool of trained specialist personnel that facilitated the growth and expansion of PD in India. With the provision of clinical coordinators and a special once per lifetime payment to healthcare industries, some patients may acquire a loan from Commercial banks either by pledging property or other immovable assets for the cost of PD. Patients pay up front or in two to three installments to the dialysis fluid manufacturing industry and they are assured a lifetime supply of dialysis fluid and accessories. Up to 2003, for 3 and 4 exchanges per day, the lifetime scheme cost was US$8125 to US$10 000 respectively. Currently, in 2008 the cost is US$13 414. For those patients not in the lifetime scheme, the current monthly expense for CAPD therapy is approximately US$414 (3 daily exchanges). Once patients enroll in a CAPD scheme, they are provided the supply for 1 month; this includes fluid and accessories such as minicaps. If the patient switches over to hemodialysis, undergoes a renal transplantation, or dies, after a nonrefundable amount of US$1097 is deducted, the remaining credit amount is refunded back to the patient or family. A legal agreement is made between the patient and the industry as per the existing laws of the country. The supply of stocks is made anywhere within India and there is no extra transportation cost. All end-stage renal disease patients can take advantage of the once per lifetime scheme. This system of a once per lifetime payment enabled the growth of CAPD using the twin-bag system, as the cost of CPD for a lifetime is assured without any escalation, whereas, in other renal replacement modalities, there is escalation of the long-term cost. However, choice of treatment modality is a complicated topic in developing countries as there seems to be interaction between patient characteristics, reimbursement policies, wealth status, and mortality risks (5).

We compared and analyzed technique survival in a retrospective cohort of patients that survived on CPD ≥ 3 years and < 3 years from four leading centers in south India. We looked specifically at factors potentially influencing outcome of technique survival in patients that survived for more than 3 years.

MATERIALS AND METHODS

This retrospective multicenter randomized study included patients that started on the therapy from 1999 to 2004 analyzed predictors of technique survival in long-term CPD patients. A total of 309 patients were trained during the observation period (from 1999 to 2004), including 150 patients that survived 3 years and more and 59 that were taken as controls (nonsurvivors). Although 159 patients in the nonsurvival group were trained, baseline demographic characteristics, clinical parameters, and outcome details were available only in 59 patients for inclusion in the comparison. The other 100 patients were lost for follow-up and clinical details were not available. The analyzed population comprised 150 patients (male:female 109:41; mean age 50.9 ± 14.9 years) that survived ≥ 3 years on CPD (CAPD and automated PD). For the purpose of comparative analysis we included 59 patients (nonsurvivors) from all the four centers whose details regarding baseline demographic characteristics, clinical parameters, and outcome were available and who survived less than 3 years; they were doing 2 L 3 times daily. Table 1 shows the demographics and baseline characteristics of the retrospective cohort. Table 2 shows the details of therapy for the survival group.

Patients were stratified to the anuric group if urine output was less than 100 mL/day. Duration of diabetes, diet, socioeconomic status, employment, number of exchanges, reimbursement, lifetime payment scheme, residual renal function, hypertension, coronary artery disease, erythropoietin usage, peritoneal equilibration test (PET), Kt/V for urea, compliance and prescription, ultrafiltration status, peritonitis rate, technique failure, body mass index (BMI), serum albumin, calcium × phosphorus product, exit-site care, exchange procedure, and dwelling place (city/town/village) were considered.

TABLE 1
Demographics and Baseline Characteristics

Variable	Survival on PD ≥3 years	<3 years
Patients (*n*)	150	59
Males/females (*n*)	109/41	43/16
Mean age (years)	50.9±14.9	56.6±10.6
Lifetime payment/reimbursements (*n*)	68/32	3/2
Diabetes mellitus (*n*)	58	42
No diabetes mellitus (*n*)	92	17
Vegetarians/nonvegetarians (*n*)	22/128	14/45
Coronary artery disease (*n*)	5	10

PD = peritoneal dialysis.

TABLE 2
Therapy Details in the Survival Group (n=150)

Exchanges (n)	6–8 L: n=148; >8 L: n=2
Transport status by PET (n=102)	High: 6; high-average: 45; low-average: 48; low: 3
Kt/V; weekly creatinine clearance	2.31; 73 L/week
Mean ultrafiltration volume at start versus after 3 years (mL/day)	1377±452 vs 1400±461
Mean residual renal function at start versus after 3 years (mL/day)	527±26 vs 253±14
Peritonitis episodes ≤3 years versus >3 years (per patient-months)	1/75 vs 1/30
Noninfectious catheter-related episodes ≤3 years versus >3 years	6 vs 4

PET = peritoneal equilibration test.

The statistical methods used included logistic regression analysis to find the predominating factor that affects survival. Paired t-test was used to compare initial parameters to those after 3 years. Independent Student's t-test and chi-square test were used appropriately to determine any difference in age, gender, anuric versus nonanuric patients, hemoglobin levels, serum albumin, and ultrafiltration volume in the long-term survival group. A p value less than 0.05 was considered statistically significant.

RESULTS

At the start of therapy there were 92 (62%) nondiabetic patients and 58 (38%) diabetics. There was no conversion from nondiabetic status to diabetic status in the survival group. There were 32 (21%) patients receiving entire therapy reimbursement (eligible government employees, other reimbursement including multinational banks, industries), including medications; 68 (46%) patients had the lifetime PD scheme, 50 (33%) were self-paying, and 12 (8%) were noncompliant with their prescription. Changes in PD prescription were implemented (CAPD, daytime ambulatory PD) in 7% of the survival patients. There was a mean decline in ultrafiltration volume of 100 mL over 3 years in 63 (42%) patients. At the start there were 19 (12%) anuric patients; after ≥ 3 years there were 67 (44%) anuric patients. Survival was better in anuric patients. PET data revealed a change in transport characteristics in 2 patients: 1 patient changed from high to high-average and the other from low-average to low transporter status.

Peritonitis rate in patients that survived ≥ 3 years was 1 episode in 75 patient-months during the first 3 years and 1 episode in 30 patient-months subsequently. The descriptive statistics of the results are given in Figure 1. Fifty percent of the patients that survived ≥ 3 years did not develop any peritonitis. Figure 2 shows technique survival up to 50 months. The number of patients that survived up to 4 years was 94 and 40 survived 5 years, 10 survived 6 years, 4 survived 7 years, and 3 survived 8 years. There were no catheter-related problems for 141 (94%) patients. Inflow and outflow obstructions, infusion pain, and other difficulties were observed in 4% of patients during the first 3 years and in 2% after 3 years. Hypertension was prevalent in 101 (67%) patients. Mean hemoglobin level at the start was 9.18 ± 2 g/dL; mean Hb at study end 9.48 ± 1.8 g/dL. Those patients with Hb levels < 11 g/dL survived a shorter time (p < 0.001). Serum albumin level was < 3 g/dL in the nonsurvival group (p < 0.001). Daily exit-site care was done by 132 (88%) and 18 (12%) patients were doing exit-site care 3 times weekly.

Regarding BMI, 17 patients were below 19 kg/m^2, 17 were above 25 kg/m^2, and 2 were ≥ 30 kg/m^2; the rest were between 19 and 25 kg/m^2.

Attendants performed the exchange procedure for 64 (43%) patients and 86 (57%) patients did the exchanges for themselves. Ninety-three (62%) patients resided in the city and 57 (38%) resided in small towns and villages. Patients that were employed numbered 69 (46%) and 72 (48%) were unemployed. Of the 9 pediatric patients (6%), 3 attended school. All analyzed patients tested negative for hepatitis B, hepatitis C, and HIV. Among the 59 patients that did not survive, the major cause of dropout was cardiovascular death (59%) as 71.2% were diabetics. These patients were paying from their own pocket for medications and gradually became noncompliant with dialysis prescription and follow-up care due to inability to pay.

DISCUSSION

Our cohort study analyzed patient and treatment variables, socioeconomic status, treatment payment patterns, comorbid conditions, infective episodes, dietary habits, dwelling place, peritoneal membrane characteristics, adequacy of dialysis, residual renal function, and biochemical parameters as survival factors in a multicenter study in south Indian CPD patients. Renal

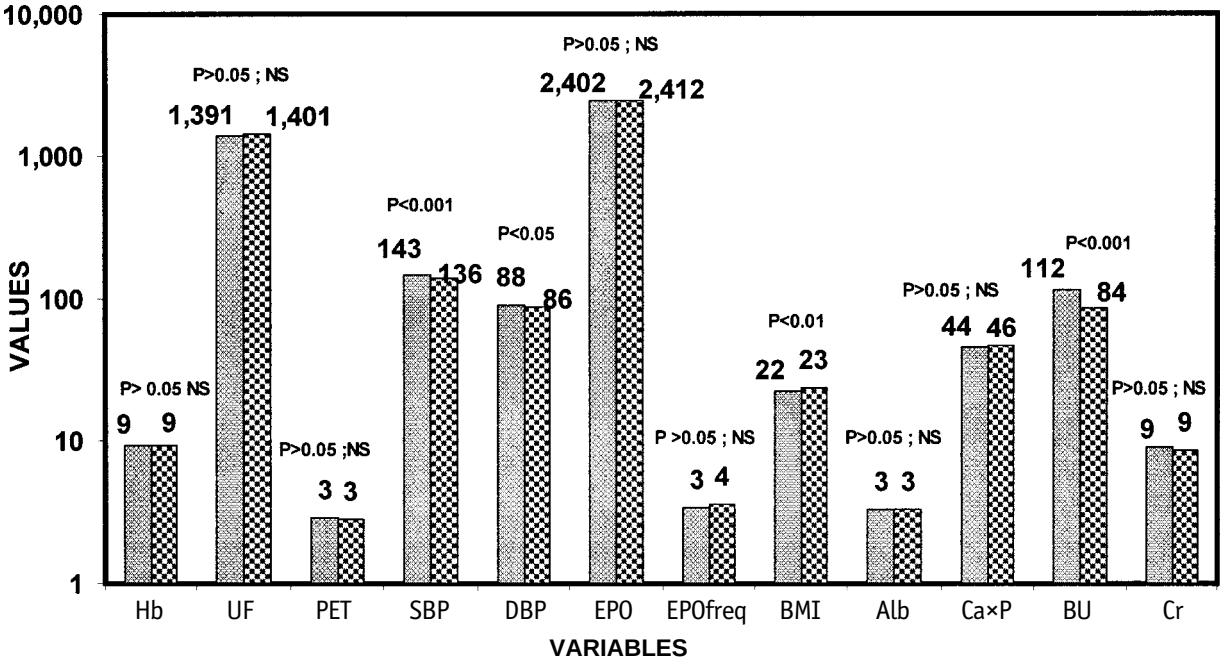

Figure 1 — Descriptive statistics of the various parameters compare changes in clinical and laboratory variables at the beginning (gray bars) and after 3 years (hatched bars) on peritoneal dialysis. Hb = hemoglobin (g/dL); UF = ultrafiltration (mL/day); PET = peritoneal equilibration test; SBP = systolic blood pressure (mmHg); DBP = diastolic blood pressure (mmHg); EPO = erythropoietin (units/week); EPOfreq = erythropoietin frequency/month; BMI = body mass index (kg/m^2); Alb = serum albumin (g/dL); Ca×P = calcium × phosphate product (mg^2/dL^2); BU = blood urea (mg/dL); Cr = serum creatinine (mg/dL); NS = not significant.

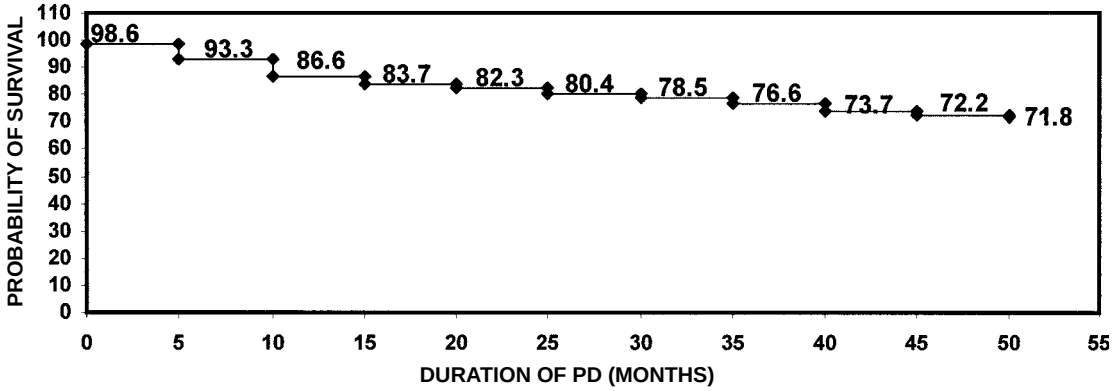

Figure 2 — Probability of technique survival in patients on peritoneal dialysis (PD; *n* = 209).

replacement therapy is affordable to only 3.5% of patients requiring dialysis, translating to an estimated 5000 – 9000 patients per year (3). This is the first study of its kind to look at long-term PD success in India using an integrated multicenter approach.

Lower rates of peritonitis led to better preservation of the peritoneal membrane, as shown by the ultrafiltration characteristics. Although there had been a mean decline of 100 mL in ultrafiltration volume in 42% of the patients, a prescription change enabled them to maintain enough fluid removal. Ultrafiltration volume was 1377 ± 452 mL/day at the start of the therapy and 1400 ± 461 mL/day after 3 years. This also had a positive impact on hypertension control as blood pressure at the start of therapy was 143/88 mmHg and after 3 years it was 136/85 mmHg. It was a significant survival factor. Several studies have shown a greater incidence of left ventricular hypertrophy in prevalent PD patients (6,7). The average PET characteristics (high-average and low-average transport status), which reflect beneficial peritoneal membrane properties, are in accordance with other studies showing technique survival. Anuric patients formed 44%; their survival was related to the maintenance of extracellular fluid volume by changing the dialysate concentration and volume either using hypertonic dialysate or increasing the volume of dialysis pre-

scription. Icodextrin-based solutions at cost-effective rates can prolong technique survival, which in turn translates into enhanced patient survival in developing countries. There was, however, a decrement in urine output, from 527 ± 26 mL/day at start to 253 ± 14 mL/day after 3 years of observation, implying a decline in residual renal function (8). However, anuric patients showed a survival advantage, which may be due to the optimal ultrafiltration volume.

Patients without diabetes mellitus (62%) survived longer; diabetes should not deter nephrologists from using PD as a renal replacement therapy (9). Previous epidemiologic studies attributed selection bias, center bias, small patient numbers, incomplete case-mix stratification, and the use of a prevalent instead of an incident patient database to differences in survival outcome of diabetic patients on CPD (10).

Adequacy parameters, as judged by solute clearance including Kt/V and weekly creatinine clearance, in our cohort of patients were above the minimum required (11,12). Our limitation is that this was a retrospective analysis: there are data missing and the amount of information available on clinical aspects of adequacy other than anemia status, hypertension, BMI, serum albumin level, ultrafiltration volume, and urine output, is limited.

In multivariate analysis, anemic patients with hemoglobin level ≤ 11 g/dL had mortality rates as high as 15.66 times, and patients with serum albumin ≤ 3.5 g/dL had mortality rates of 4.14 times compared to patients with serum albumin > 3.5 g/dL. This highlights the need for anemia treatment and periodic nutritional assessment and emphasizes their importance as elements in survival. Generic erythropoietin was used in 102 patients; over 15 generic forms of erythropoietin are available in India at a cost of US$9 – 20 per 2000 IU.

The majority of survivors had normal BMI (76%), were nonvegetarians, and had serum albumin ≥ 3 g/dL, which may reflect absence of inflammatory state and better nutritional status/eating habits (4). However, Indian nonvegetarians consume meat, fish, and eggs only 2 or 3 times per week on average. B complex vitamins and vitamin D analogs are regularly used by the patients, irrespective of their parathyroid status. In the first author's CPD program, a cross-sectional study showed mean intact parathyroid hormone level was 321.2 ± 501.5 pg/mL and 1,25(OH)2D3 level was 15.7 ± 11.86 ng/mL. Calcium × phosphorus product was 44.6 ± 15.6 mg^2/dL^2 at start and 45.9 ± 15.7 mg^2/dL^2 after 3 years, which is within acceptable limits according to DOQI guidelines ($p > 0.05$). There was a statistically significant increase in BMI in the survival group, which could be interpreted as an increase in lean body mass or fat mass due to use of more hypertonic glucose-based dialysis exchanges (12).

Cardiovascular mortality was less in the current cohort: 93% of the long-term survivors were nonsmokers, which highlights the importance of cardiovascular protection, contrary to previous observation (1,13).

In the survival group, 82% of patients were in the middle and old age group, which affirms the importance of utilization of PD as a renal replacement therapy in this age group.

There are challenges in running a CPD unit with increased utilization in India, where reimbursement policies and self-payment issues are major roadblocks. As shown in our study, special once in a lifetime payments and reimbursement of therapy are cost-effective plans that enable patients to live longer on PD. These systems of payment have a unique advantage where the cost of therapy for a lifetime is not influenced by escalation due to inflation and thereby ensures compliance to therapy (2,14). The majority of patients that survived belonged to the reimbursement group or the one lifetime payment group. This financial arrangement can be emulated in other developing regions of the world for the success of CPD.

An efficient and well-structured home visit by the clinical coordinators ensured patient well-being. This impacted technique survival, quality of life, and success of the PD program (14,15). It is very difficult to compare technique survival between countries because of differences in patient backgrounds, including age, gender, race, year, cause of CKD, and, especially, economic status/cost and reimbursement policies (14). Even after 3 years, 46% were employed; 6% were pediatric patients and 3 were attending school. Renal rehabilitation with an empowerment program enabled the patients to become experts in their own healthcare, with a goal of increased autonomy (16).

City dwellers seem to have better survival compared to those living in towns and villages as they had better access to medical care. Patients in the rural areas do not have access to proper microbiology services, well-stocked pharmacies, or medical care for comorbid conditions. However, this situation is changing due to the availability of clinical coordinators and telemedicine for visual and verbal communication with the patient for problems such as cloudy dialysis bags and exit-site infection.

The steady increase in the growth and expansion of PD in India in this decade is due to better-educated nephrologists, positive patient selection, the ease of the peritoneal dialysis technique, better patient training, economic growth, different ways of cost containment such as once per lifetime payment scheme and reimbursement,

and better training and retraining implemented by the teams, which consist of nephrologists, nurses, dieticians, and dedicated clinical coordinators.

DISCLOSURE

Authors V. Kumar, G. Srinivasan, M. Krishnamurthy, A. K. Prasath, and S. Kumar, are employed by Baxter Chennai, India.

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