ORIGINAL ARTICLES

CONTINUOUS AMBULATORY PERITONEAL DIALYSIS IN LIMPOPO PROVINCE, SOUTH AFRICA: PREDICTORS OF PATIENT AND TECHNIQUE SURVIVAL

Ramon A. Tamayo Isla,¹ Darlington Mapiye,² Charles R. Swanepoel,³ Nadiya Rozumyk,¹
Jerome E. Hubahib,¹ and Ikechi G. Okpechi³

Polokwane Kidney and Dialysis Centre,¹ Pietersburg Provincial Hospital, Polokwane, Limpopo, South Africa; South African National Bioinformatics Institute/Medical Research Council of South Africa Bioinformatics Unit,² University of the Western Cape; and Division of Nephrology and Hypertension,³ Groote Schuur Hospital and University of Cape Town, South Africa

◆ **Introduction and aim:** Continuous ambulatory peritoneal dialysis (CAPD) is not a frequently used modality of dialysis in many parts of Africa due to several socio-economic factors. Available studies from Africa have shown a strong association between outcome and socio-demographic variables. We sought to assess the outcome of patients treated with CAPD in Limpopo, South Africa.

◆ **Methods:** This was a retrospective study of 152 patients treated with CAPD at the Polokwane Kidney and Dialysis Centre (PKDC) from 2007 to 2012. We collected relevant demographic and biochemical data for all patients included in the study. A composite outcome of death while still on peritoneal dialysis (PD) or CAPD technique failure from any cause requiring a change of modality to hemodialysis (HD) was selected. The peritonitis rate and causes of peritonitis were assessed from 2008 when all related data could be obtained.

◆ **Results:** There were 52% males in the study and the average age of the patients was 36.8 ± 11.4 years. Unemployment rate was high (71.1%), 41.1% had tap water at home, the average distance travelled to the dialysis center was 122.9 ± 78.2 kilometres and half the patients had a total income less than USD (\$)180 per month. Level of education, having electricity at home, having tap water at home, body mass index (BMI), serum albumin and hemoglobin were significantly different between those reaching the composite outcome

and those not reaching it ($p < 0.05$). The overall peritonitis rate was 0.82/year with 1-year, 2-year and 5-year survival found to be 86.7%, 78.7% and 65.3% (patient survival) and 83.3%, 71.7% and 62.1% (technique survival). Predictors of the composite outcome were BMI ($p = 0.011$), serum albumin ($p = 0.030$), hemoglobin ($p = 0.002$) and more than 1 episode of peritonitis ($p = 0.038$).

◆ **Conclusion:** Treatment of anemia and malnutrition as well as training and re-training of CAPD patients and staff to prevent recurrence of peritonitis can have positive impacts on CAPD outcomes in this population.

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KEY WORDS: CAPD; Africans; outcome; peritonitis; socio-economic status; anemia.

The prevalence of end-stage renal disease (ESRD) continues to escalate world-wide including in many developing countries struggling to cope with the double burden of non-communicable and communicable diseases like tuberculosis, malaria, HIV/AIDS and diarrheal illnesses. The utilization of continuous ambulatory peritoneal dialysis (CAPD) as a renal replacement therapy (RRT) modality has been declining world-wide (1–3) but this is even more so in many developing countries, especially those in Africa where utilization of peritoneal dialysis (PD) has historically been low (4,5). Although there are many reasons for the reduced use of PD as an

Correspondence to: Ramon Tamayo Isla, Polokwane Kidney and Dialysis Centre, Pietersburg Provincial Hospital, Polokwane, Limpopo, South Africa.

tamayoisla@gmail.com

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RRT modality, it would appear that a major reason is the lack of facilities for local manufacturing of PD fluids leading to the prohibitive cost of buying fluids from other manufacturing countries (6–8). Other reasons include socio-economic and socio-demographic factors resulting from poverty like lack of transportation to dialysis centers, lack of running water and electricity and lack of manpower (trained nephrologists and nurses) at the local hospitals. In developed countries, increasing age, obesity, and associated comorbidities account for the decline in utilization of PD (1); other developing countries cite financial constraints, lack of patient enthusiasm, doubtful patient compliance and lack of an organized PD program as the factors limiting widespread use of PD (9).

Many studies have shown that long-term outcome in PD is not as favorable as that in hemodialysis (HD) although the cost utility ratio is more favorable for PD than HD in patients eligible for both modalities (10–12). One study from South Africa has reported a strong association between socio-demographic factors with outcome in 132 PD patients followed up in Cape Town (13). As there are few studies in Africa reporting on patient survival in CAPD, the objectives of this study included (i) reporting on the outcome of CAPD patients in the Limpopo province of South Africa; (ii) identifying factors associated with outcome of CAPD patients in Limpopo and (iii) assessing the rate of peritonitis in this group of patients.

MATERIALS AND METHODS

Limpopo is the northernmost province of South Africa, named after the Limpopo River that flows through it (Figure 1). It has an estimated population of about

Figure 1 — Map of Limpopo Province, South Africa. Inset is the map of South Africa showing the location of Limpopo (white). Polokwane can be seen in the middle of Limpopo.

5,518,000 with 97.3% of its racial demographic being black Africans according to 2013 data from Statistics South Africa (14). Although there are a few private dialysis units in Limpopo, the Polokwane Kidney and Dialysis Centre (PKDC) is the only dialysis unit in the public sector in the province. The PKDC, part of the Pietersburg Provincial Hospital Limpopo, was officially opened in 2007 and offers HD and PD. Due to the South African government's policy on rationing of dialysis (15,16), only 80 HD and 50 PD patients are currently permitted to be on the RRT programme in Polokwane. However, as the unit is currently run as a public private initiative in collaboration with Fresenius Medical Care, allowance is given to exceed this number. This partnership also means that imported PD fluids and locally produced PD fluids are equally used in the unit. Most patients start with 4 exchanges of 2-litre bags (1.5% solution) daily. The prescription may be changed from time to time to allow for better exchanges and fluid removal for patients who are volume overloaded. There is currently no capacity in the province for renal transplantation and all the patients in the dialysis unit are currently looked after by a specialist general physician (RT); there are no nephrologists in the Limpopo province.

This study received ethical approval from the Pietersburg Provincial Hospital Ethics Committee and was designed to retrospectively assess the outcomes of patients who commenced CAPD at the PKDC in Limpopo from 2007 to 2012. Patients who had commenced PD from other provinces and later joined the unit after settling in Limpopo were not included in the study. The study population therefore included a total of 152 patients. Relevant socio-demographic data recorded at time of initiation of CAPD were collected and included date of birth, gender, marital status, race, address (distance to PD unit), total household income, cause of ESRD, level of education, employment status, type of accommodation and availability of electricity and tap water at home. Houses were considered to be brick houses if they were predominantly made of bricks while shacks were considered as any informal houses built predominantly using old or discarded zinc (a tin-like material used for roofing). Clinical and biochemical data recorded on every patient visit were also collected. Patients were evaluated at the clinic every 4–6 weeks.

DEFINITIONS

1. Composite outcome: The composite outcome was death while still on PD or technique failure from any cause (peritonitis or catheter malfunction/extrusion) leading to a change in modality to HD.

2. Peritonitis: Peritonitis was adjudged to have occurred if a patient presented with typical clinical features (i.e. fever, abdominal pain, vomiting) or if there was a cloudy PD effluent observed or an effluent cell count with white blood cells (WBC) more than 100/ μ L (after a dwell time of at least 2 hours), with at least 50% polymorphonuclear neutrophilic cells (17). Peritoneal fluid for microbiology was often taken by the trained PD nurse and peritonitis was always treated using the International Society of Peritoneal Dialysis (ISPD) guidelines (17).

3. Peritonitis rate: Data on peritonitis were only available from January 2008. The peritonitis rate was calculated as number of infections by organism for a time period, divided by dialysis-years' time at risk, and expressed as episodes per year (17).

4. Clinic Attendance: This was calculated as a percentage of the total number of clinic visits attended by an individual to the number of clinic sessions scheduled for that individual.

STATISTICS

The data were analyzed using the IBM SPSS statistical software (version 21) (SPSS, Chicago, IL, USA). Continuous variable results were presented as means and standard deviation (SD) while categorical variables were presented as frequencies and percentages for exploratory analysis. Univariate analysis was performed using the independent student's *t*-test, chi-squared test or the Wilcoxon rank sum test as appropriate. Death or technique failure requiring transfer to HD was the composite outcome of interest in this study. The Kaplan-Meier estimate was used to determine survival of patients on PD and the log rank test was used to compare the significance of survival between subgroups. Univariate correlation analysis was first performed to investigate potential predictors of the outcome. Significant factors in the univariate model were then used to perform a multivariate regression analysis using the Cox proportional hazard regression model to establish predictors of the composite outcome. The Hosmer-Lemeshow test was used to assess the adequacy of this model. A *p*-value < 0.05 was considered statistically significant.

RESULTS

(1) DEMOGRAPHIC AND CLINICAL FEATURES OF THE PATIENTS

One hundred and fifty two (152) patients on CAPD were included in the analysis of this study. The average age

was 36.8 ± 11.4 years with male patients accounting for 52% of the study population. Most of the patients were black Africans (92.8%), many were unemployed (71.1%) and the average distance the patients travelled to reach the dialysis center was 122.9 ± 78.2 kilometres. Half of the patients (50%) earned less than \$180 per month and although only 2.6% of the patients were known to live in a shack, electricity and tap water were available in the homes of 86.2% and 41.4% of patients, respectively (Table 1). Table 2 summarizes key clinical features of the patients. The cause of ESRD was unknown in 47.4% of the patients, many of whom presented for the first time in ESRD needing urgent dialysis. However, hypertension was the most common known cause of ESRD (23.0%). Other causes were diabetes mellitus (9.9%), obstructive uropathy (5.9%), chronic glomerulonephritis (8.6%) and autosomal dominant polycystic kidney disease

TABLE 1
Demographic Features of the Patients

Variable	Value (n=152)
Age (years)	36.8 $\pm$ 11.4
Gender: male/female (%)	79/73 [52.0/48.0]
Distance travelled to the PKDC (n=135) (km)	122.9 $\pm$ 78.2
Race: Black Africans/Indians/Whites (%)	92.8/2.6/4.6
Employment status (%)	
Unemployed	71.1
Employed	15.1
Student	5.9
Unknown	7.9
Level of education (%)	
Primary	13.8
Secondary	66.4
Tertiary	9.2
None/unknown	10.6
Type of accommodation (%)	
Brick house	87.5
Shack	2.6
Unknown	9.9
Tap water present (%)	41.4
Electricity present (%)	86.2
Marital status (%)	
Single	52.0
Married	38.2
Others	9.8
Level of income per month (%)	
<\$180	50.0
\$180-\$900	37.5
>\$900	12.5

PKDC = Polokwane kidney and dialysis centre; km = kilometres; \$ = United States dollar.

TABLE 2
Important Clinical Features of the Patients
During Follow-Up

Variable	Value (n=152)
Cause of ESRD (%)	
Hypertension	23.0
Diabetes mellitus	9.9
Obstructive uropathy	5.9
Chronic glomerulonephritis	8.6
ADPKD	5.3
Unknown	47.4
Overall attendance to PD clinic (compliance) ^a (%)	94.4±11.3
Duration on peritoneal dialysis (months)	21.0±17.8
Systolic blood pressure ^b (mmHg)	140.5±20.1
Diastolic blood pressure ^b (mmHg)	85.8±13.5
Body mass index ^b (kg/m ²)	24.3±5.2

ESRD = end-stage kidney disease; ADPKD = autosomal dominant polycystic kidney disease; PD = peritoneal dialysis.

^a Overall attendance to clinic was calculated as a ratio of clinics attended to clinics scheduled for every patient.

^b This represents the mean of all the values obtained from each patient during follow-up visits.

(5.3%). Compliance to clinic attendance was good at 94.4 ± 11.3%. The average duration on CAPD was 21.0 ± 17.7 months.

(2) COMPARISON OF FEATURES BETWEEN PATIENTS REACHING THE COMPOSITE OUTCOME AND THOSE NOT REACHING THE COMPOSITE OUTCOME

Overall, 71 patients (46.7%) reached the composite outcome of death or technique failure requiring a change of modality to HD. There was no significant difference in age, gender, racial distribution, marital status, employment status, type of accommodation or total household income below \$180 per month between those patients who reached the composite outcome and those who did not reach the composite outcome (Table 3). However, important differences observed between patients reaching composite outcome and those not reaching the composite outcome, respectively, included level of education (50.7% vs 80.2% for secondary education; $p = 0.004$), presence of electricity at home (76.1% vs 95.1%; $p = 0.001$), presence of tap water at home (31.0% vs 50.6%; $p = 0.021$), BMI (22.8 ± 4.5 kg/m² vs 25.5 ± 5.4 kg/m²; $p = 0.002$), serum albumin (26.6 ± 5.5 vs 29.8 ± 4.7 ; $p < 0.0001$) and mean hemoglobin (10.3 ± 2.1 vs 11.3 ± 1.6 ; $p = 0.001$) (Table 3). Although the average number of episodes of peritonitis per year were higher in those

reaching the composite outcome, it was not significantly different between the two groups.

(3) PERITONITIS RATE AND ETIOLOGY OF PERITONITIS IN THE STUDY GROUP

Overall, there were 210 infections reported between January 2008 and December 2012 with a trend to reducing frequency of infections in that period. The overall peritonitis rate was 0.82/year and the frequency of peritonitis was observed to have decreased from 1.11/year in 2008 to 0.65/year in 2012. Overall, culture-negative peritonitis (CNP) was diagnosed in 62.3%. Organisms responsible for culture-positive peritonitis were gram-positive in 50.6%, gram-negative in 38.0%, fungi in 3.8% and tuberculous in 7.6%.

(4) SURVIVAL ANALYSIS

At the end of December 2012, 66 patients (43.4%) were still active on CAPD, 32 deaths (21.1%) had been recorded and 39 patients (25.7%) had been transferred to HD due to technique failure. Of those transferred to HD due to technique failure, 76.9% was due to peritonitis, 10.3% was due to catheter malfunction and 12.8% due to patients who reported not to be coping with PD. Six patients (3.9%) abandoned CAPD for various reasons, 3 patients (2.0%) were transferred to a different CAPD unit outside of Limpopo and 6 patients (3.9%) with ESRD due to malignant hypertension had recovered sufficient renal function to stop CAPD and are still being followed up at the clinic. Survival on CAPD based on the composite outcome of death or transfer to HD was 72.2%, 56.4% and 39.1% at 1 year, 2 years and 5 years, respectively. Patient survival at 1 year, 2 years and 5 years was 86.7%, 78.7% and 65.3%, respectively, while technique survival was 83.3%, 71.7% and 62.1%, respectively. Kaplan-Meier survival analysis for serum albumin, hemoglobin and occurrence of peritonitis are shown in Figure 2. The mean duration before transfer to HD (technique survival) was 49.2 ± 2.7 (95% confidence interval [CI] 43.9 – 54.6) months while the mean duration of patient survival on CAPD was 51.2 ± 2.7 (95% CI 45.7 – 56.6) months.

(5) MULTIVARIATE REGRESSION ANALYSIS

Factors that were significantly correlated with the composite outcome on univariate analysis were entered into a Cox multivariate regression analysis. Factors that were found to predict the composite outcome were BMI (hazard ratio [HR] 0.92, 95% CI 0.86 – 0.98; $p = 0.011$), serum albumin (HR 0.93, 95% CI 0.87 – 0.99; $p = 0.030$),

TABLE 3
Comparison of Selected Demographic and Clinical Features of Patients Reaching the Composite Outcome and Patients Not Reaching This Outcome

Variable	Composite outcome		P-value
	Yes (n=71)	No (n=81)	
Age	37.5±12.4	36.1±10.3	0.465
Gender (males) (%)	52.1	51.9	0.974
Duration on CAPD (months)	13.2±10.7	27.8±19.6	<0.0001
Race/ethnicity (%):			0.658
Black Africans	94.4	91.4	
Indians	1.4	3.7	
Whites	4.2	4.9	
Marital status: married (%)	42.3	34.6	0.120
Secondary school education (%)	50.7	80.2	0.001
Employment status (%)			0.145
Employed	12.7	17.3	
Unemployed	63.4	77.8	
Students	8.5	3.7	
Accommodation (brick house) (%)	80.3	93.8	0.778
Electricity at home (yes) (%)	76.1	95.1	0.001
Water at home (yes) (%)	31.0	50.6	0.021
Distance to dialysis center (km)	136.9±77.4	112.4±77.7	0.071
Level of income <\$180/month (%)	50.7	49.4	0.871
Episodes of peritonitis/yr	1.4±1.3	1.2±1.4	0.382
BMI* (kg/m ²)	22.8±4.5	25.5±5.4	0.002
Average SBP* (mmHg)	136.8±21.3	143.7±18.6	0.038
Average DBP* (mmHg)	82.3±14.2	89.0±12.1	0.002
Serum albumin* (g/L)	26.6±5.5	29.8±4.7	<0.0001
Hemoglobin* (g/dl)	10.3±2.1	11.3±1.6	0.001

CAPD = continuous ambulatory peritoneal dialysis; \$ = United States dollar; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure.

*These values represent the averages of all values obtained from each clinic visit during follow-up visits.

hemoglobin (HR 0.72, 95% CI 0.58 – 0.88; $p = 0.002$) and more than 1 episode of peritonitis (HR 1.90, 95% CI 1.04 – 3.47; $p = 0.038$) (Table 4).

DISCUSSION

This study is one of only a few studies published from South Africa and the entire sub-Saharan Africa region describing the outcome and factors associated with outcome in ESRD patients treated with CAPD. Over the years, PD utilization has continued to decline world-wide (1–3), and even more so in countries of Africa (for various reasons but usually due to cost), making it difficult to be able to report on the outcome of patients treated with this modality. Hence, an important aspect of this study is our observation that the patient and technique survival on CAPD from a poor province in South Africa (a

developing country) can match the outcomes reported from more developed countries (18,19). This point becomes even more relevant when one considers that the entire population of Limpopo in South Africa (over 5 million) is not serviced by a nephrologist. This, therefore, strengthens a point we have previously made that PD may be the preferred option of RRT in Africa given the frequent unavailability of health care resources if only the cost of PD fluids can be drastically reduced (6).

Surprisingly, we observed that the predictors of outcome in this study were not the prevalent adverse socio-demographic or socio-economic factors like long distances travelled to get to the dialysis unit, absence of tap water or electricity at home or poverty due to unemployment and lack of income. Instead we found that BMI, serum albumin, hemoglobin concentration and having more than 1 episode of peritonitis were the

Figure 2 — Kaplan-Meier survival curves for (A) serum albumin, (B) hemoglobin, (C) any episode of peritonitis and (D) more than 1 episode of peritonitis.

factors that predicted the composite outcome (Table 4). Using predetermined biomedical, socio-economic, and psychosocial factors, Zent *et al.* in Cape Town had previously investigated the relationship between episodes of peritonitis and exit-site infection with these factors (13). They reported that high occupant-to-bedroom ratio, absence of electricity at home, informal housing, alcohol abuse and previous psychiatric history were predictors of poor outcome (peritonitis). This led the authors to a conclusion that patients from poor backgrounds are unlikely to do well on CAPD, and race should be regarded as a proxy for poor outcomes for PD in South Africa (13). However, it should be noted that the CAPD systems and techniques used now are far more sophisticated than when Zent *et al.* (13) published their paper, with consequently less opportunity to become infected.

Poverty continues to be rife in South Africa especially among the indigenous black African population. This is evident from this study with an overwhelming black

African population (92.8%) that had a high unemployment rate (71.1%), low level of income (50.0% earning less than \$180 per month), poor access to tap water (41.4%) and poor access to health care services (average distance travelled to dialysis center = 122.9 ± 78.2 km) (Table 1). That these factors did not play a role in patients' outcome could therefore suggest that for the rest of Africa, utilization of CAPD can be possible even in the face of a poor socio-economic environment.

The role of inflammation, nutrition, anemia and peritonitis in patients' outcomes in PD has been extensively studied and reported by various authors. A high peritoneal protein clearance (leading to hypoalbuminemia) has been shown to correlate strongly with cardiovascular events in PD patients (20). In one large Chinese study, among independent risk factors of mortality in CAPD patients with diabetes were lower hemoglobin (HR 0.978, 95% CI 0.964 – 0.992, $p = 0.003$) and lower serum albumin (HR 0.924, 95% CI 0.876 – 0.976, $p = 0.004$)

TABLE 4
Predictors of the Composite Outcome by the
Cox Multivariate Regression Analysis

	HR	95% CI	P-value
BMI (kg/m ²)	0.92	0.86–0.98	0.011
Systolic BP (mmHg)	0.99	0.97–1.02	0.563
Diastolic BP (mmHg)	1.00	0.96–1.04	0.858
Albumin (g/L)	0.93	0.87–0.99	0.030
Hemoglobin (g/dl)	0.72	0.58–0.88	0.002
Electricity	2.08	0.73–5.90	0.172
Tap water	0.81	0.42–1.52	0.507
Peritonitis (>1 episode)	1.90	1.04–3.47	0.038

HR = hazard ratio; CI = confidence interval; BMI = body mass index; BP = blood pressure.

at initiation of CAPD (21). Also, the BRAZPD study, a large cohort of PD patients in Brazil, reported anemia (hemoglobin [Hb] < 11 g/dl) to be present in 57% of CAPD patients at baseline and to be an independent predictor of mortality (22). Although an attempt is often made for all CAPD patients treated at the PKDC unit in Limpopo to receive adequate anemia treatment according to guidelines, the role of nutritional status in these patients, which was not assessed in this study, could have contributed to anemia. Hence, other than peritoneal protein loss leading to hypoalbuminemia, poor nutrition may be invoked as a unified explanatory factor for low BMI, hypoalbuminemia, and anemia seen in this study.

Poor nutrition may also explain the high peritonitis rate observed in this study. One study in India has shown that the mean peritonitis rate per patient per year is significantly higher in patients with malnutrition (0.99 ± 1.07) compared to patients with normal nutritional status (0.18 ± 0.42) ($p = 0.007$) and that malnutrition was significantly correlated with peritonitis (23). The overall peritonitis rate in this study was 0.82/year (higher than 0.67/year recommended by the ISPD) (17). However, the peritonitis rate decreased year-on-year from 2008 to 2012 possibly due to the introduction of home visits, increasing the number of nurses who run the PD unit (1 in 2007 to 3 from 2009 onwards), and training of PKDC site staff by visiting nephrologists from Cape Town. Although the high rate of peritonitis is a challenge to adequate patient care, it provides an opportunity for training and re-training of patients on PD and the introduction of simple patient information leaflets to further educate them on the complications of PD.

The high frequency of culture-negative peritonitis seen in this study could be due to prior antibiotic therapy

before reaching the hospital or possibly due to poor sample collection technique. This pattern persisted from 2008 to the end of 2012. Also, the organisms isolated in culture-positive peritonitis were similar to those reported from other centers with gram-positive organisms (commonly staphylococcal) frequently isolated. We also observed that episodes of peritonitis, although they were higher in those patients who reached the composite outcome, were not significantly different between the two groups (Table 3). Although having 1 episode of peritonitis was not predictive of outcome on multivariate analysis, we observed that having more than 1 episode of peritonitis was significantly associated with the outcome (HR 1.90; 95% CI 1.04 – 3.47; $p = 0.038$) (Table 4).

This study has some limitations, including the retrospective design, which meant that there were gaps in the amount and type of data that could be collected. Also, data on residual renal function, PD adequacy and peritoneal membrane transporter status could not be obtained. This would have shed light on outcome and peritoneal membrane status as well as the effect of maintaining residual renal function on patient outcome. Finally, data on the cause of death could not be obtained as many of the patients died at home. Hence, although death was assessed as outcome, we could not assess if this was of cardiovascular or infectious origin. Despite these limitations, we still firmly believe that the outcome of patients on PD in Limpopo is reasonably good given the numerous socio-demographic challenges in the population.

CONCLUSIONS

Peritoneal dialysis is a viable option for RRT and can yield good outcomes even in an environment with numerous socio-economic challenges. Correctable factors like the treatment of anemia and prevention of malnutrition as well as training and re-training of CAPD patients and staff to prevent recurrence of peritonitis can have positive impacts on CAPD outcomes in this population.

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