Adverse outcomes among Aboriginal patients receiving peritoneal dialysis

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ABSTRACT

Background: The Aboriginal population in Canada experiences high rates of end-stage renal disease and need for dialytic therapies. Our objective was to examine rates of mortality, technique failure and peritonitis among adult aboriginal patients receiving peritoneal dialysis in the province of Manitoba. We also aimed to explore whether differences in these rates may be accounted for by location of residence (i.e., urban versus rural).

Methods: We included all adult patients residing in the province of Manitoba who received peritoneal dialysis during the period from 1997–2007 (*n* = 727). We extracted data from a local administrative database and from the Canadian Organ Replacement Registry and the Peritonitis Organism Exit-sites/Tunnel infections (POET) database. We used Cox and logistic regression models to determine the relationship between outcomes and Aboriginal ethnicity. We performed Kaplan–Meier analyses to examine the relationship between outcomes and urban (i.e., 50 km or less from the primary dialysis centre in Winnipeg) versus rural (i.e., more than 50 km from the centre) residency among patients who were aboriginal.

Results: One hundred sixty-one Aboriginal and 566 non-Aboriginal patients were included in the analyses. Adjusted hazard ratios for mortality (HR 1.476, CI 1.073–2.030) and adjusted time to peritonitis (HR 1.785, CI 1.352–2.357) were significantly higher among Aboriginal patients than among non-Aboriginal patients. We found no significant differences in mortality, technique failure or peritonitis between urban- or rural-residing Aboriginal patients.

Interpretation: Compared with non-Aboriginal patients receiving peritoneal dialysis, Aboriginal patients receiving peritoneal dialysis had higher mortality and faster time to peritonitis independent of comorbidities and demographic characteristics. This effect was not influenced by place of residence, whether rural or urban.

The Canadian Aboriginal population suffers from a high burden of illness,[1,2] low socio-economic status and geographic isolation.[3] A high prevalence of diabetes mellitus, obesity and hypertension in this population is resulting in rapid growth in rates of kidney disease and renal failure (i.e., end-stage renal disease).[4–6] The escalation in demand for dialytic services and care of patients with end-stage renal disease care will require appropriate planning and allocation of health care resources.

Hemodialysis is resource-intensive and requires residence in proximity to a dialysis centre. In Canada, roughly 18% of all dialysis patients are receiving peritoneal dialysis.[7] These patients are responsible for their own dialysis therapy and are seen periodically in an ambulatory clinic setting. No clear mortality-related benefit is associated with choice in modality of dialysis; each method has its own risks and benefits.[8–10] Complications of peritoneal dialysis include technique failure, which often requires conversion to hemodialysis and relocation of the patient, and peritonitis.

Dosage of peritoneal dialysis is determined by the combined clearance of solutes from the peritoneum (termed the peritoneal Kt/V) and, if applicable, by residual renal function (termed renal Kt/V). The peritoneal equilibration test is a marker of the peritoneal membranes solute transport characteristics and high peritoneal equilibration test values have been associated with inflammation, volume overload, technique failure and mortality.[11]

Compared with non-Aboriginal patients who have end-stage renal disease, Aboriginal patients with end-stage renal disease are younger on average and more likely to reside in geographically remote locations.[12] Use of home-based dialysis modalities, such as peritoneal dialysis, would be well suited to this population because it allows patients to continue to live in their communities. However, residing far from a dialysis centre or a patient's primary nephrologist is associated with increased mortality, poor compliance and impaired quality of life.[12,13] Previous studies have found that Aboriginal patients receiving peritoneal dialysis have similar mortality and rates of technique failure to patients of other ethnicities. But whether this is true in a contemporary cohort is not known.[14,15]

Our objective was to examine differences in mortality and in rates of technique failure and peritonitis among Aboriginal patients versus non-Aboriginal patients receiving peritoneal dialysis and to explore whether differences may be accounted for by urban versus rural residence.

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Methods

Study population and design

The study population (Figure 1) consisted of all adult patients in the province of Manitoba aged 18 years or older with end-stage renal disease who started peritoneal dialysis between Jan. 1, 1997, and Dec. 31, 2007, and were followed until June 30, 2009. Manitoba represents a catchment area of 1.2 million people.[16]

Sources of data

The Manitoba Renal Program supplies clinical care and captures prospective data on patient demographics, comorbid illness, date of initiation of dialysis, modality of dialysis, technique failure, peritonitis and deaths. There are roughly 1200 dialysis patients in Manitoba, with 20% receiving peritoneal dialysis.[7] Data on patients' modality of dialysis, demographic characteristics and outcomes were extracted from a database of the Manitoba Renal Program (Figures 1 and 2). Data related to comorbidities were obtained from the Canadian Organ Replacement Registry, a national database that collects information on patients in Canada with end-stage renal organ disease.[7] We obtained data related to peritonitis from the Peritonitis Organism Exit-sites/Tunnel infections (POET) database, a North American, industry-supported database that collects information on infections and transfers of modality related to peritoneal dialysis.[17] Multiple publications have been based on the Canadian Organ Replacement Registry[6,12,13,15,18,19] and on the POET database.[17,20–22]

We obtained ethics approval for our study from the Research Review Committee of St. Boniface General Hospital.

Cohort definitions

Aboriginal patients were identified by self-reporting. We categorized all other patients, the majority of whom were white, as non-Aboriginal. We defined comorbid diabetes mellitus as either diabetes type 1 or 2. We defined comorbid coronary artery disease as any of the following: the presence of significant stenosis as shown by angiography, a positive stress test, history of an acute coronary syndrome or coronary artery bypass surgery, congestive heart failure as evidenced by a history of pulmonary edema shown by imaging, peripheral vascular disease as shown by an ankle-brachial index of less than 1.0 or stenosis on angiography, or stroke with radiographic evidence of an ischemic event, hemorrhage or history of transient ischemic attack. Cigarette smoking and use of antihypertensive medications was determined at the time of dialysis initiation. We defined the date of initiation of peritoneal dialysis as the date of insertion of the peritoneal dialysis catheter. More than 95% of patients started peritoneal dialysis within 30 days of catheter insertion. Modality of dialysis was classified according to the first modality used and did not reflect changes in modality. For our analyses, we used the first peritoneal Kt/V value and renal Kt/V value recorded after patients initiated peritoneal dialysis.
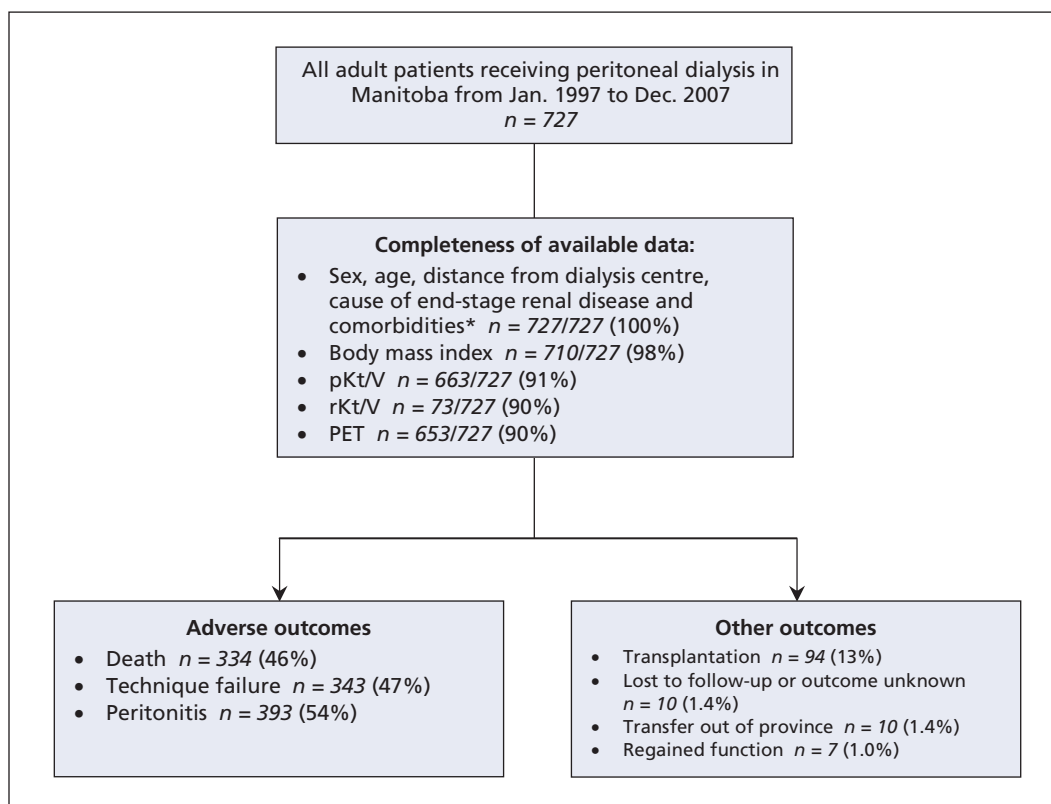

Figure 1: Patient inclusion, completeness of data and outcomes. *Comorbidities included diabetes mellitus, coronary artery disease, stroke, congestive heart failure, peripheral vascular disease, hypertension and smoking.

The distance from each patient's place of residence was defined as the direct linear distance from the patient's postal code to our major peritoneal dialysis hospital in Winnipeg, Manitoba, using Vincenty's formula.[23] We chose direct distance to our peritoneal dialysis hospital given the high level of variability in health care resources available rurally in northern communities. Furthermore, travel time is highly variable because many patients who live at great distances travel by medical air flights rather than by road.

Outcome measures

We examined the rates of mortality, technique failure and peritonitis. Technique failure was defined as discontinuation of peritoneal dialysis 14 days or more after initiation. Peritonitis was diagnosed by the presence of two out of three of the following: abdominal pain, a peritoneal fluid cell count greater than 100×10^6 cells/L and a white blood cell differential with greater than 50% neutrophils or a positive result on a peritoneal culture. Only the first episode of technique failure and peritonitis were included in the analysis.

Statistical analyses

Continuous variables of interest were summarized as means with standard deviations (SDs) or as medians with interquartile ranges (IQRs) as appropriate. Differences in baseline characteristics were determined using a student's t test for continuous variables and a χ^2 or Fischer exact test for dichotomous variables. We calculated the crude rates of mortality, technique failure and peritonitis per 100 patient-years of receipt of peritoneal dialysis.

To examine the association of Aboriginal ethnicity on time to event for mortality, technique failure and peritonitis, we performed univariate and multivariate analyses using Cox proportional hazards models. We selected variables for inclusion in the predefined models based on significance ($p \leq 0.05$) in univariate analyses and importance according to published results. To examine for consistency of association, we further analyzed the same models using multivariate logistic regression. Distance values in kilometers were log-transformed for analysis purposes. All results were considered significant at $p < 0.05$. We tested assumptions for the Cox and logistic regression models and examined the proportionality of the hazard ratios.

To examine the impact of location of residence, we classified patients living 50 km or less from the primary peritoneal dialysis centre in Winnipeg as urban and those 50 km or more as rural. We performed Kaplan–Meier analyses to assess outcomes as a factor of place of residence, with stratification by
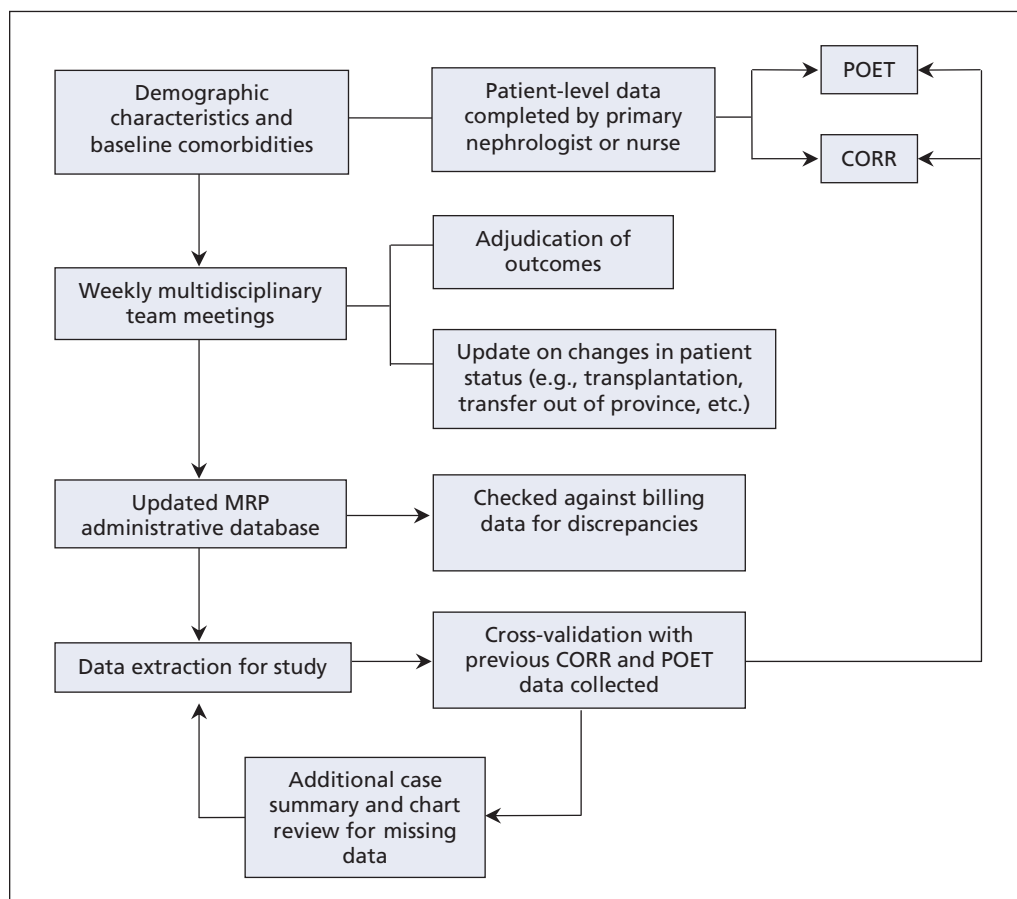

Figure 2: Extraction, consolidation and validation of data. Note: CORR = Canadian Organ Replacement Registry, MRP = Manitoba Renal Program, POET = Peritonitis Organism Exit-sites/Tunnel infections database.

Aboriginal ethnicity. Given that the distance defining urban from rural was based on previously reported results[14,24] and differed from the median distance in the Aboriginal population (250 km), we performed additional analyses using 100 km and 250 km.

Results

During the study period, 727 patients (161 Aboriginal, 480 white, 61 Asian, 30 African and 60 of other or unknown ethnicities) started peritoneal dialysis in Manitoba for a number of patient-years of dialysis of 382.7 for Aboriginal patients and 1353.9 for non-Aboriginal patients. A comparison of the baseline characteristics of the Aboriginal and non-Aboriginal cohorts is shown in Table 1. Aboriginal patients were more frequently women (54%), younger, obese and rural-residing compared with those from the non-Aboriginal cohort.

Among Aboriginal patients, the unadjusted mortality per 100 patient-years of receipt of peritoneal dialysis was 20.6; for technique failure the rate was 24.0 and for peritonitis it was 76.3. Among non-Aboriginal patients, the rates were 18.8 for mortality, 18.8 for technique failure and 51.6 for peritonitis.

Time-to-event analyses are summarized in Table 2. The median survival time was 40.1 (IQR 30.1–50.0) months for Aboriginal patients and 45.5 (IQR 41.3–49.7) months for non-Aboriginal patients ($p = 0.37$). Aboriginal patients had higher mortality in the model adjusted for baseline comorbidities (Model B: HR 1.587, CI 1.162–2.169) and baseline comorbidities plus peritoneal dialysis characteristics (Model D: HR 1.476, CI 1.073–2.030).

Adjustment for characteristics of peritoneal dialysis alone attenuated the increase in mortality (Model C: HR 1.002, CI 0.766–1.310). The median time to technique failure was shorter among Aboriginal patients but the difference was not significant (Aboriginal patients 976, IQR 754–1197 days; non-Aboriginal patients 1081, IQR 878–1283 days, $p = 0.096$). Aboriginal ethnicity was not associated (Models A, C, D) or was marginally associated (Model B: HR 1.341, CI 1.000–1.798) with earlier technique failure. The median time to peritonitis was 503 (IQR 354–702) among Aboriginal patients and 1126 (IQR 488–1763) among non-Aboriginal patients ($p < 0.001$ using a Mantel-Cox log-rank test). The hazard ratio for peritonitis was increased in all models (HR 1.546–1.912). Analyses using multivariate logistic regression yielded congruent findings (Table 3).

We performed two sensitivity analyses for ethnic classification. First, we performed multivariate modelling (i.e., Cox and logistic regressions), excluding all patients of African, Asian, and other or unknown ethnicities. In the second analysis, we examined the large number of patients who were classified as other or unknown ethnicities, reclassifying these 60 patients first as Aboriginal and then non-Aboriginal. No significant differences were evident for any outcome.

Table 1: Demographic characteristics, cause of end-stage renal disease, comorbidities and characteristics of peritoneal dialysis in Aboriginal and non-Aboriginal patients at baseline

Characteristic	Aboriginal patients, no. (%)* n = 161	Non-Aboriginal patients, no. (%)* n = 566	p value
Sex, female	87 (54.0)	238 (42.0)	0.009
Age, yr, mean (SD)	49.2 (13.1)	56.7 (15.3)	< 0.001
BMI, mean (SD)	28.19 (5.13)	26.57 (5.34)	0.001
Distance from centre, km, median (IQR)	249.5 (16.0–583.3)	7.4 (3.1–44.8)	< 0.001
Cause of ESRD			
Diabetes mellitus	105 (65.2)	219 (38.7)	< 0.001
Glomerulonephritis	28 (17.4)	102 (18.0)	0.91
Hypertension	11 (6.8)	67 (11.8)	0.083
Polycystic kidney disease	0	33 (5.8)	< 0.001
Obstruction	1 (0.1)	28 (4.9)	0.010
Other	4 (2.5)	58 (10.2)	0.001
Unknown	12 (7.5)	59 (10.4)	0.30
Comorbidities			
Diabetes mellitus	105 (65.2)	224 (39.6)	< 0.001
Coronary artery disease	32 (19.9)	116 (20.5)	0.91
Stroke	10 (6.2)	42 (7.4)	0.73
Congestive heart failure	15 (9.3)	70 (12.4)	0.33
Peripheral vascular disease	17 (10.6)	44 (7.8)	0.26
Taking antihypertensive medication(s)	130 (80.7)	401 (70.8)	0.012
Smoker	26 (16.1)	47 (8.3)	0.007
Peritoneal dialysis characteristics			
PET value, mean (SD)	0.730 (0.101)	0.677 (0.117)	< 0.001
Low	7 (4.3)	60 (10.6)	0.013
Low average	13 (8.1)	115 (20.3)	< 0.001
High average	342 (47.0)	117 (72.7)	0.005
High	49 (8.7)	24 (14.9)	0.025
pKt/V value, mean (SD)	1.65 (0.36)	1.64 (0.39)	0.78
rKt/V value, mean (SD)	0.66 (0.54)	0.72 (0.55)	0.26

*Unless otherwise indicated.
Note: BMI = Body mass index, km = kilometres, ESRD = end-stage renal disease, IQR = interquartile range, PET = peritoneal equilibration test, pKt/V = peritoneal Kt/V, rKt/V = renal Kt/V, SD = standard deviation.

Results of Kaplan–Meier analyses showed no significant differences in time to death, technique failure or peritonitis between urban and rural Aboriginal patients (Appendix 1, available at www.cmaj.ca/cgi/content/full/cmaj.100105 /DC1). Sensitivity analyses using distances of 100 km and 250 km from the primary dialysis centre did not significantly alter the results (data not shown).

Interpretation

In this large cohort of patients receiving peritoneal dialysis, Aboriginal ethnicity was associated with an increase in mortality and peritonitis after adjusting for baseline demographic characteristics, comorbidities and characteristics of peritoneal dialysis, and these findings were independent of patient residence in an urban or rural environment. Further, residence in a rural or urban environment had no impact on any outcome.

Outcome-based studies involving Aboriginal people with kidney disease have been reported from the United States,[25,26] Australia[27,28] and Canada.[12,15,18,24] Aboriginal people experience higher rates of kidney disease and renal failure,[4,27] poor access to renal transplantation[12,27] and poor achievement of quality indicators on hemodialysis.[8,25] Outcomes based on modality of dialysis have been difficult to interpret given that geographic location, availability of social supports and clinical comorbidities strongly influence the selection of modality.[15,29]

We found that mortality of Aboriginal patients was significantly increased (HR 1.476, CI 1.073–2.030) after adjusting for demographics and comorbid illnesses. Interestingly, adjustment for factors related to peritoneal dialysis attenuated the increase in mortality (Model C: HR 1.108 CI 0.853–1.439), suggesting this increase may be associated with dialysis clearance and membrane characteristics. Whether underlying inflammation or failure to remove fluid, with resultant left ventricular hypertrophy, is leading to the increase in mortality remains to be investigated.

In contrast to our findings, Tonelli and colleagues found no significant difference in mortality of Canadian Aboriginal patients receiving peritoneal dialysis.[15] In their model adjusted for case-mix, changes in modality of dialysis, dialysis centre, socio-economic characteristics and community size, the hazard ratio for Aboriginal patients was similar to that for patients who were white (HR 1.00, CI 0.71–1.4). Reasons for the discrepancy between those findings and our own may include the diversity of our sources of data (i.e., POET, the Canadian Organ Replacement Registry and the Manitoba Renal Program database), our use of a contemporary cohort (i.e., 1997–2009) or the lack of accounting for socio-economic factors in our analyses. Compared with national figures, Aboriginal people in Manitoba are more socio-economically disadvantaged, with higher unemployment, lower education and lower income.[16] Further studies examining the effects of these factors are required.

Peritonitis universally occurred more frequently among Aboriginal patients in all models. This observation is consistent with previous findings in Australia, where Aboriginal patients had an adjusted hazard ratio of 1.76 for developing peritonitis.[28] Rates of peritonitis in the Australian population

were higher at 115 episodes per 100 patient-years for Aboriginal patients (versus 76.3 in our study) and 60 for non-Aboriginal patients (versus 51.6 in our study). Variations and improvements in protocols for preventing and treating peritonitis likely account for these differences.

Causative organisms appear to differ in the Aboriginal population, given that streptococcus, pseudomonas and fungal peritonitis appear to be more common.[19,30,31] Our data show the shortened time to peritonitis persisted despite adjustment for factors associated with increased susceptibility to peritonitis (i.e., diabetes mellitus and high peritoneal equilibration test value). Reasons for this discrepancy may be intrinsic to the Aboriginal communities or genetic predisposition in individual patients. On a community level, the average number of residents per household is high in Aboriginal communities, so contact-based transmission and colonization could be more frequent.[16] Clustering of methicillin-resistant *Staphylococcus aureus* is known to occur frequently in Aboriginal families and communities.[32,33] Whether peritonitis events can be reduced by health-related interventions at the community level, such as eradication of *S. aureus* within entire families, remains unknown. Further discrepancies in sterile technique and hand-washing procedures may exist, with a need for retraining in sterile procedures.

Table 2: Association of Aboriginal ethnicity with mortality, technique failure and peritonitis using Cox proportional hazards models

Model	Hazard ratio (95% CIs)	p value
Mortality		
Univariate	1.04 (0.80–1.34)	0.80
Model A*	1.32 (1.00–1.76)	0.052
Model B†	1.59 (1.16–2.17)	0.004
Model C‡	1.00 (0.77–1.31)	0.99
Model D§	1.48 (1.07–2.03)	0.017
Technique failure		
Univariate	1.24 (0.96–1.59)	0.010
Model A*	1.19 (0.91–1.55)	0.20
Model B†	1.34 (1.00–1.80)	0.050
Model C‡	1.23 (0.95–1.60)	0.12
Model D§	1.31 (0.96–1.79)	0.08
Peritonitis		
Univariate	1.68 (1.34–2.11)	< 0.001
Model A*	1.87 (1.46–2.39)	< 0.001
Model B†	1.91 (1.45–2.52)	< 0.001
Model C‡	1.55 (1.23–1.95)	< 0.001
Model D§	1.79 (1.35–2.36)	< 0.001

Note: CI = confidence interval.
*Data from model A were adjusted for age, sex and diabetes mellitus.
†Data from model B were adjusted for age, sex, diabetes mellitus, coronary artery disease, congestive heart failure, stroke, peripheral vascular disease, antihypertensive medication(s), cigarette smoking and distance from dialysis centre.
‡Data from model C were adjusted for peritoneal equilibration test value, renal Kt/V value and peritoneal Kt/V value.
§Data from model D were adjusted for all of the factors adjusted for in models A thru C.

Table 3: Association of Aboriginal ethnicity with mortality, technique failure and peritonitis using logistic regression

Model	Hazard ratio (95% CIs)	p value
Mortality		
Univariate	1.15 (0.80–1.64)	0.45
Model A*	1.21 (0.85–1.72)	0.026
Model B†	1.78 (1.08–2.06)	0.012
Model C‡	0.95 (0.66–1.39)	0.81
Model D§	1.62 (0.99–2.64)	0.053
Technique failure		
Univariate	1.51 (1.06–2.16)	0.024
Model A*	1.32 (1.00–1.76)	0.052
Model B†	1.59 (1.16–2.17)	0.004
Model C‡	1.00 (0.77–1.31)	0.99
Model D§	1.48 (1.07–2.03)	0.017
Peritonitis		
Univariate	2.34 (1.60–3.43)	< 0.001
Model A*	2.54 (1.69–3.80)	< 0.001
Model B†	2.59 (1.69–3.80)	< 0.001
Model C‡	2.24 (1.51–3.32)	< 0.001
Model D§	2.44 (1.52–3.92)	< 0.001

Note: CI = confidence interval.
*Data from model A were adjusted for age, sex and diabetes mellitus.
†Data from model B were adjusted for age, sex, diabetes mellitus, coronary artery disease, congestive heart failure, stroke, peripheral vascular disease, antihypertensive medication(s), cigarette smoking and distance from dialysis centre.
‡Data from model C were adjusted for peritoneal equilibration test value, renal Kt/V value and peritoneal Kt/V value.
§Data from model D were adjusted for all of the factors adjusted for in models A thru C.

Geographic isolation and limitations in access to health care are known to be associated with increased mortality in the population of patients who have chronic kidney disease and receive dialysis.[13,14,29] As the capital city of Manitoba, Winnipeg has a very high urban Aboriginal population,[16] which allowed us to explore whether the above-mentioned association exists in the Aboriginal population. In our comparison of urban-residing Aboriginal patients (i.e., less than 50 km from the dialysis centre) to rural-residing (i.e., more than 50 km), we found no significant differences in mortality, technique failure or peritonitis. This finding suggests that geographic isolation did not measurably alter delivery of care and access to health-care resources, and is reassuring evidence that continuing to offer peritoneal dialysis to geographically isolated Aboriginal patients does not confer a worse outcome. This finding contrasts with those of earlier studies that suggested increasing distance from a patient's primary nephrologist was associated with increases in mortality.[14,24]

Limitations

Our study had several limitations. Our classifications of rural and urban residency were based on distance measurements from the dialysis centre at time of dialysis initiation and did not account for relocation of patients. The distance measure was a crude indicator intended only to capture isolation and distance from resources, and is not an accurate measure of transit time to medical care. Although attempts were made to cross-reference and validate data, the data we collected for many variables (e.g., ethnicity, smoking history) were based on self-reporting by physicians or patients and may be erroneous. Whether peritoneal dialysis is underutilized among Aboriginal patients could not be quantified in our study, leading to a selection bias; hence it is plausible that our findings are based on discrepancies in the Aboriginal population who select peritoneal dialysis. Our analyses did not adjust for other important variables for which data were not available, including socio-economic status, population health indicators and laboratory values such as hemoglobin and albumin.

Conclusion

We observed that Aboriginal patients receiving peritoneal dialysis are at increased risk for peritonitis and mortality. This effect was independent of whether patients resided in a rural or urban location. Further studies and strategies to improve outcomes of peritoneal dialysis in the Aboriginal population are required.

This article has been peer reviewed.

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