Continuous Mortality Risk Among Peritoneal Dialysis Patients

Conventional hemodialysis (CHD) administered thrice weekly for 3- to 4-hour sessions and peritoneal dialysis (PD) are the 2 most commonly delivered dialysis modalities. Patients treated with CHD are subject to short periods of rapid fluid and solute removal accompanied by brisk electrolyte shifts followed by long intervals when these substances reaccumulate. In contrast, PD uses the patient's peritoneal membrane to allow for continuous and gradual removal of fluid and uremic toxins.

A typical CHD schedule results in 2 one-day intervals and 1 two-day interval between dialysis sessions. The 2-day interval usually occurs from Saturday through Sunday or Sunday through Monday. Among CHD recipients, the period immediately following the 2-day interdialytic interval (either Monday or Tuesday) has recently been associated with an increased risk of death compared with other days of the week.[1] The increased mortality risk may be mediated via significant fluid gain and electrolyte disequilibrium that occurs during the 2-day hiatus from dialysis. Since PD occurs daily, we hypothesized that mortality rates should be stable across different days of the week among PD recipients compared with those receiving CHD.

Methods. We used the Canadian Organ Replacement Register (CORR),[2] a national registry that captures more than 95% of all dialysis and solid organ transplant recipients in Canada, to identify all incident patients receiving PD between 2001 and 2010.

We determined the number of deaths among PD patients for each day of the week and used a χ^2 test to compare differences between the observed number of deaths per day of the week and those expected in the absence of any weekly variation. Among patients receiving PD, deaths occurring after transfer to CHD or after kidney transplantation were excluded. This study was approved by the St Michael's Hospital research ethics board.

Results. Between 2001 and 2010, 8855 patients initiated PD, of whom 169 died during the PD course (24.5%); 1390 underwent kidney transplant (15.7%); and 2488 transferred to CHD (28.1%). Among PD patients who died, there was no difference in the observed and expected number of deaths by day of the week. (P=.16) (**Figure**).

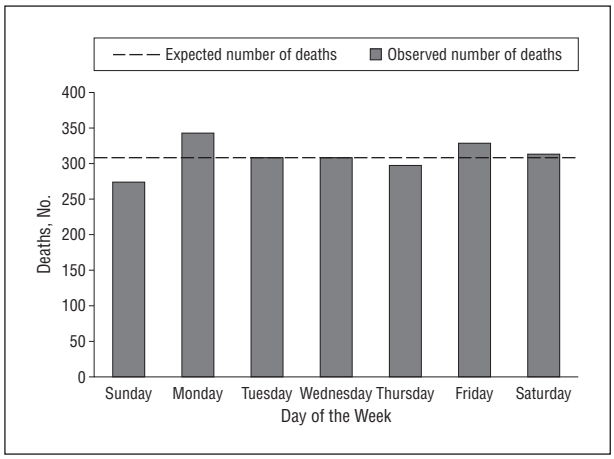

Figure. Number of deaths by day of the week among incident peritoneal dialysis patients in Canada from 2001 to 2010. P=.16 by the χ^2 test for equal proportions.

Comment. Our study of all patients undergoing PD in Canada over a 10-year period found no difference in the risk of all-cause mortality by day of the week during the PD course. These findings contrast with the results of Foley and colleagues,[1] who found a higher risk of death among CHD patients in the days immediately following the long intradialytic interval.

Although observational data would suggest that overall long-term survival among patients treated with either PD or CHD are similar, these studies have failed to account for potential differential risks of mortality according to the day of the week for patients receiving PD vs CHD.[3] Compared with CHD, PD might avoid extreme fluctuations in uremic toxin levels, electrolyte concentrations, and fluid accumulation. It is likely that these fluctuations are important contributors to the increased mortality observed after the long 2-day interval among those treated with CHD.[4]

Our work is limited to the Canadian setting and may not be generalizable to dialysis populations in other countries. However, the CORR registry is pan-Canadian, has been validated for cause and time of death, and performs similarly to other national administrative data sets, including The United States Renal Database.[2,5,6]

The variation in mortality risk by day of the week among CHD but not PD patients highlights an opportunity to improve survival among individuals receiving CHD. Further prospective study is needed to evaluate clinical outcomes using alternative hemodialysis strategies that eliminate the long interdialytic interval.

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1. Foley RN, Gilbertson DT, Murray T, Collins AJ. Long interdialytic interval and mortality among patients receiving hemodialysis. *N Engl J Med*. 2011; 365(12):1099-1107.
2. Moist LM, Richards HA, Miskulin D, et al. A validation study of the Canadian Organ Replacement Register. *Clin J Am Soc Nephrol*. 2011;6(4):813-818.
3. Chiu YW, Jiwakanon S, Lukowsky L, Duong U, Kalantar-Zadeh K, Mehrotra R. An update on the comparisons of mortality outcomes of hemodialysis and peritoneal dialysis patients. *Semin Nephrol*. 2011;31(2):152-158.
4. Foley RN. Why is mortality higher on certain dialysis shifts? *Semin Dial*. 2011; 24(4):415-417.
5. Karamadoukis L, Ansell D, Foley RN, et al. Towards case-mix-adjusted international renal registry comparisons: how can we improve data collection practice? *Nephrol Dial Transplant*. 2009;24(8):2306-2311.
6. Perl J, Wald R, McFarlane P, et al. Hemodialysis vascular access modifies the association between dialysis modality and survival. *J Am Soc Nephrol*. 2011; 22(6):1113-1121.

Mentholated Cigarettes and Cardiovascular and Pulmonary Diseases: A Population-Based Study

Cigarettes labeled as "mentholated" contain substantially higher levels of menthol than regular cigarettes, to produce a characteristic mint flavor and cooling sensation. Potential noncancer adverse health effects of added menthol to cigarettes are largely unknown. Epidemiologic data on the risks of cardiovascular and pulmonary diseases among smokers of mentholated vs nonmentholated cigarettes are extremely limited.[1,2] The purpose of this study was to determine if cardiovascular and pulmonary disease risk was different between mentholated cigarette smokers and nonmentholated cigarette smokers.

Methods. A multiyear, cross-sectional, population-based design was used. A total of 5167 current smokers at least 20 years old from the 2001-2008 US National Health and Nutrition Examination Surveys (NHANES)[3] formed the study group. Mentholation status of the cigarettes "usually" smoked was ascertained for 5028 individuals (97.3%). For 3791 individuals (75.4%), cigarette mentholation status was determined by survey administrator examination of smokers' usual cigarette packages. For 1237 individuals (24.6%), cigarette mentholation status was determined by asking participants whether cigarettes they usually smoked were mentholated. Health professional–diagnosed, self-reported hypertension, myocardial infarction, congestive heart failure, stroke, and chronic obstructive pulmonary disease (COPD) were the outcomes examined. Descriptive statistics and multiple logistic regression were use to examine the association between mentholated cigarette smoking and cardiovascular and pulmonary diseases. Given previously reported sex,[3,4] race,[3,5] and age group[3] discrepancies between mentholated and nonmentholated cigarette smokers, fully stratified analyses by sex (women vs men), race (African Americans vs non–African Americans), and age group (≥70 years vs < 70 years) were performed to look for potential differences in outcomes among subgroups of interest. To account for the complex sampling design of NHANES, all point estimates were appropriately weighted, and variance estimates were adjusted by Taylor linearization procedures.

Results. A total of 1286 of 5028 respondents (25.6%) usually smoked mentholated cigarettes, and 3742 of 5028 (74.4%) usually smoked nonmentholated cigarettes. After adjusting for sex, age, race, education level, total household income, body mass index, and smoking quantity and duration, mentholated cigarette smokers were found to have significantly increased odds of stroke compared with nonmentholated cigarette smokers (odds ratio [OR], 2.25; 95% CI, 1.33-3.78), and in particular women (OR, 3.28; 95% CI, 1.74-6.19) and non–African American smokers (OR, 3.48; 95% CI, 1.70-7.13) (**Table**). There were no significant associations between mentholated cigarette smoking and hypertension, myocardial infarction, congestive heart failure, and COPD. After also controlling for health professional–diagnosed, self-reported hypertension, diabetes mellitus, and dyslipidemia, the odds of stroke remained significantly increased among all (OR,

Table. Adjusted[a] Odds of Cardiovascular and Pulmonary Diseases Among Current Mentholated Cigarette Smokers vs Current Nonmentholated Cigarette Smokers From the 2001-2008 NHANES, Stratified by Race, Sex, and Age Group

	OR (95% CI)[a]						
Disease	All (n = 5028)	Women (n = 2289)	Men (n = 2739)	African Americans (n = 606)	Non–African Americans (n = 4422)	Age ≥70 y (n = 181)	Age <70 y (n = 4848)
Hypertension	1.17 (0.84-1.62)	1.28 (0.81-2.05)	1.04 (0.63-1.72)	1.61 (0.75-3.48)	1.03 (0.68-1.56)	1.52 (0.21-11.06)	1.09 (0.80-1.47)
MI	0.89 (0.40-1.99)	0.47 (0.15-1.44)	1.81 (0.59-5.49)	1.19 (0.42-3.41)	0.68 (0.20-2.39)	1.08 (0.20-5.74)	0.80 (0.26-1.79)
CHF	1.32 (0.56-3.15)	0.86 (0.26-2.83)	2.48 (0.73-8.44)	2.41 (0.38-15.37)	0.53 (0.12-2.44)	3.05 (0.11-84.59)	1.20 (0.45-3.18)
Stroke	2.25 (1.33-3.78)	3.28 (1.74-6.19)	0.92 (0.36-2.37)	0.60 (0.22-1.67)	3.48 (1.70-7.13)	5.82 (0.58-58.41)	1.90 (0.95-3.79)
COPD	1.06 (0.50-2.22)	1.16 (0.54-2.50)	0.78 (0.19-3.21)	0.37 (0.07-2.13)	1.29 (0.56-2.95)	1.82 (0.36-9.35)	0.92 (0.44-1.93)

Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NHANES, National Health and Nutrition Examination Surveys[3]; OR, odd ratio.

[a] Adjusted for age, sex, race, highest education level attained, total household income, body mass index, average number of cigarettes smoked in the past 30 days, average number of days respondent smoked in the past 30 days, and the age the respondent started smoking regularly.

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