Center Effects and Peritoneal Dialysis Peritonitis Outcomes: Analysis of a National Registry

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Background: Peritonitis is a common cause of technique failure in peritoneal dialysis (PD). Dialysis center–level characteristics may influence PD peritonitis outcomes independent of patient-level characteristics.

Study Design: Retrospective cohort study.

Setting & Participants: Using Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data, all incident Australian PD patients who had peritonitis from 2004 through 2014 were included.

Predictors: Patient- (including demographic data, causal organisms, and comorbid conditions) and center- (including center size, proportion of patients treated with PD, and summary measures related to type, cause, and outcome of peritonitis episodes) level predictors.

Outcomes & Measurement: The primary outcome was cure of peritonitis with antibiotics. Secondary outcomes were peritonitis-related catheter removal, hemodialysis therapy transfer, peritonitis relapse/recurrence, hospitalization, and mortality. Outcomes were analyzed using multilevel mixed logistic regression.

Results: The study included 9,100 episodes of peritonitis among 4,428 patients across 51 centers. Cure with antibiotics was achieved in 6,285 (69%) peritonitis episodes and varied between 38% and 86% across centers. Centers with higher proportions of dialysis patients treated with PD (>29%) had significantly higher odds of peritonitis cure (adjusted OR, 1.21; 95% CI, 1.04-1.40) and lower odds of catheter removal (OR, 0.78; 95% CI, 0.62-0.97), hemodialysis therapy transfer (OR, 0.78; 95% CI, 0.62-0.97), and peritonitis relapse/recurrence (OR, 0.68; 95% CI, 0.48-0.98). Centers with higher proportions of peritonitis episodes receiving empirical antibiotics covering both Gram-positive and Gram-negative organisms had higher odds of cure with antibiotics (OR, 1.22; 95% CI, 1.06-1.42). Patient-level characteristics associated with higher odds of cure were younger age and less virulent causative organisms (coagulase-negative staphylococci, streptococci, and culture negative). The variation in odds of cure across centers was 9% higher after adjustment for patient-level characteristics, but 66% lower after adjustment for center-level characteristics.

Limitations: Retrospective study design using registry data.

Conclusions: These results suggest that center effects contribute substantially to the appreciable variation in PD peritonitis outcomes that exist across PD centers within Australia.

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Peritonitis is a serious complication in peritoneal dialysis (PD) patients and is one of the major reasons why patients discontinue PD therapy.[1-6] Following PD-related peritonitis, a significant proportion of PD patients will have severe adverse outcomes, including hospitalization, relapsed or recurrent peritonitis, PD catheter removal, permanent hemodialysis (HD) therapy transfer, and/or death.[2,4,7]

Previous studies have demonstrated marked variation across PD centers with respect to peritonitis rates[8,9] and technique survival[10-16] and have further observed that a considerable proportion of this variation is associated with center-level characteristics, such as PD experience (estimated by center size and/or proportion of dialysis patients treated with PD).[8-16] Because center variation in PD-related peritonitis outcomes and the relative contributions of center and patient effects have not been previously examined, the present study aimed to evaluate the associations of key peritonitis outcomes (cure, catheter removal, HD therapy transfer, relapsed/recurrent peritonitis, hospitalization, and mortality) with center-level characteristics, after adjusting for patient-level characteristics. The study also aimed to examine changes in the outcomes of peritonitis over time.

Methods

Study Population

The study included all incident PD patients in Australia who developed peritonitis from January 1, 2004, through December 31, 2014. The study used deidentified data from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA). ANZDATA collects data in accordance with the Australian Commonwealth Privacy Act and associated state legislations governing health data collection, and individual "opt-in" patient consent is not required for the registry data. The use of deidentified ANZDATA data for the purpose of analysis was approved

by the Princess Alexandra Hospital Human Research Ethics Committee (HREC/03/QPAH/032). Detailed information regarding data collection, analysis, and governance of ANZDATA is available eleswhere,[17] and permission to use data was granted by the ANZDATA executive.

Patient-Level Characteristics

Patient-level characteristics examined in the present study were age at PD therapy commencement; sex; race; body mass index (BMI); smoking status (current, former, or never); primary kidney disease; comorbid conditions including presence of diabetes, chronic lung disease, and cardiovascular disease (defined as a composite of coronary artery disease, peripheral vascular disease, and cerebrovascular disease); late referral to nephrologist (defined as <3 months before initiation of renal replacement therapy); initial renal replacement therapy modality; initial PD modality; and socioeconomic position (reported as Index of Relative Socioeconomic Advantage and Disadvantage scores[18]; higher scores reflect higher socioeconomic position, and scores were subcategorized into quartiles based on all incident PD patients during the study period [2004-2014] with the lowest quartile having been used as the reference group). BMI values were also categorized into 4 groups based on World Health Organization classification of BMI, and the normal BMI group (18.5-24.9 kg/m^2) was used as the reference group. Types of causative microorganisms were subcategorized into 3 groups according to the severity index related to the catheter removal rate, as published by Cho et al.[19] These groups were defined as low (coagulase-negative staphylococci, streptococci, and culture negative), moderate (corynebacteria, enterococci, *Staphylococcus aureus*, and non-*Pseudomonas* Gram-negative), and high risk (polymicrobial, fungi, and *Pseudomonas* species). The low-risk group was the reference group.

Center-Level Characteristics

Center-level characteristics examined in the present study were transplantation center (which was defined as whether at least 1 kidney transplantation was performed during the period of study), center size (calculated as mean annual number of incident PD patients in the center), PD proportion (estimated from the proportion of all dialysis patients in the center treated with PD), automated PD exposure (defined as the proportion of PD patients in the center exposed to automated PD at least once during the study period), peritoneal equilibration test performance (defined as the proportion of patients in the center who had a peritoneal equilibration test performed within the first 6 months of PD therapy initiation), and icodextrin exposure (defined as the proportion of patients in the center treated with icodextrin at least once). Peritonitis-related center characteristics were proportion of peritonitis episodes that were culture negative, proportion of peritonitis episodes requiring hospitalization for treatment, proportion of peritonitis episodes receiving complete empirical antibiotic therapy (ie, covering both Gram-positive and Gram-negative microorganisms at presentation), and proportion of peritonitis episodes concurrently treated with antifungal prophylaxis. The center for each patient was defined as the center at which PD therapy was initiated. All center-level characteristics except transplantation center status were subcategorized into quartiles based on all incident PD patients during the period of study (2004-2014), and the second and third quartiles were combined and used as a reference group.[16] Era of PD therapy initiation was subdivided into 2 periods, 2004 through 2009 and 2010 through 2014, with the earlier period used as the reference group.

Study Outcomes

The primary outcome of the study was cure of peritonitis with antibiotic therapy alone, which was defined as an episode that was not complicated by relapse or recurrent peritonitis, catheter removal, transfer to HD therapy for 30 days or longer, or death.[20-23] Secondary outcomes were relapse or recurrent peritonitis,[24,25] peritonitis-related catheter removal, transfer to HD therapy for 30 days or longer,[26] hospitalization, and mortality (defined as death occurring within 30 days of peritonitis onset).[27]

Statistical Analysis

Patient- and center-level characteristics are presented as frequency and percentage for categorical variables, mean ± standard deviation for normally distributed continuous variables, and median and interquartile range for non-normally distributed continuous variables. Primary and secondary outcomes were analyzed by multilevel mixed logistic regression models with patient- and center-level characteristics as fixed effects and patients and participating centers as random effects, such that peritonitis episodes were nested within patients and patients were nested within centers. Patient-level characteristics with $P < 0.2$ in univariate analyses were included in the multivariable analysis (first model). All covariates in the first model and center-level covariates with $P < 0.2$ in univariate analyses were included in a final model. There was no biologically meaningful first-order interaction between covariates. Because there was collinearity between center size and proportion of PD patients in a center with respect to the primary outcome, a separate analysis was performed with replacement of center size by proportion of PD patients in the center. Percentage reduction in variation in odds for peritonitis-associated outcomes across centers due to patient-level characteristics was calculated as the ratio of the difference in standard deviations (SDs) of center odds from a model adjusted for causative organisms and a patient characteristics model relative to the standard deviation of center odds for the model adjusted for causative organisms: $[(SD_{organism} - SD_{patient})/SD_{organism}] \times 100$. Percentage reduction in variation in odds for peritonitis-associated outcomes across centers due to center-level