Peritoneal Dialysis Peritonitis Outcomes: Getting to the Heart of the Matter

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See Clinical Research on Page 2388

Peritoneal dialysis (PD)-related peritonitis results in morbidity, higher treatment costs, and an increased risk of death, particularly in the early postperitonitis period.¹,² Despite advances in PD-related peritonitis preventive and treatment strategies, peritonitis remains the leading cause of transition to hemodialysis.³ Overall, peritonitis treatment failure rates resulting in relapse or recurrence of peritonitis or necessitating PD catheter removal and/or transition to hemodialysis have been shown to be as high as 35% of all episodes in a recent large international study of PD peritonitis outcomes.² PD-related peritonitis was identified as a core outcome of importance to patients, caregivers, and kidney health professionals in the multinational Standardized Outcomes in Nephrology PD initiative.⁴

Mortality rates following PD-related peritonitis vary substantially across studies, depending on the causative organism(s), the studied population, and the definitions employed. Although no uniform definition of peritonitis-related death exists, recent studies have used a “time limit,” defining mortality as death occurring within 30 or 50 days of a peritonitis episode.¹,² In a large case-crossover design study of peritonitis-related mortality among PD patients, it was suggested that peritonitis-related mortality be defined as any death occurring within 30 days of a peritonitis episode, where a significantly higher odds of peritonitis in the 30 days preceding death was seen.⁵ This definition, along with the inclusion of death during a hospitalization for PD peritonitis was recently employed as a proposed definition of peritonitis-related death in the updated 2022 International Society for Peritoneal Dialysis (ISPD) guidelines.⁶ Nevertheless, the long-term impact of a peritonitis episode(s) on mortality risk beyond the immediate short-term infection-related risks has not been well studied.

In this issue of KI reports, Cheikh Hassan et al.⁶ report an observational cohort study using data from The Australia and New Zealand Dialysis and Transplant registry to examine the association between PD-related peritonitis and cardiovascular (CV) mortality. This pan-Australian study included 9699 incident patients between 2003 and 2019, with a median follow-up time of 2.6 years. Individuals starting PD were divided into a peritonitis and a peritonitis-free group. The peritonitis group was further divided by the number (1 or ≥2) of peritonitis episodes to assess the impact of 1 versus repeated peritonitis episodes on the downstream risk of CV death. The definition of CV-related mortality in this study was death due to myocardial ischemia or infarction, heart failure, cardiac arrest, cerebrovascular accident, or aortic aneurysm rupture. Cox proportional hazards regression model was used to examine the association between peritonitis and CV death. A total of 3948 patients (41%) died, of which 1405 (36%) were CV-related. During the study period, at least 1 peritonitis episode occurred in 4353 patients (45%), while no peritonitis episodes occurred in the remaining 5346 patients (55%). In the peritonitis group, one-half had only 1 episode of peritonitis, and the other half had 2 or more episodes. CV mortality was higher among those who had a peritonitis episode compared to individuals who did not have a peritonitis episode (58.2 vs. 33.5 CV deaths per 1000 patient years, P < 0.001). In a multivariable model, having had an episode of peritonitis was associated with 31% higher independent risk of CV mortality and even a 69% higher independent risk among those with 2 or more episodes.

The findings that peritonitis is an independent risk factor for CV mortality and that these risks increase with increasing peritonitis
Given the nature of this registry-based retrospective analysis, no data were available on some of the additional important predictors of mortality among individuals receiving PD, such as residual kidney function, albumin levels, and inflammatory markers. C-reactive protein, which was also not available in the present study has been shown to be a marker of systemic inflammation and a predictor of CV mortality following PD peritonitis. Moreover, the impact of a peritonitis episode on subsequent peritoneal membrane ultrafiltration capacity and solute transport was also not evaluated in the present study. In addition, it would have been interesting if the authors examined the timing of CV deaths relative to the peritonitis episodes to quantify both early and late risks.

Building upon the authors important findings, certain details regarding the peritonitis episodes themselves would have been useful to better explore the relationship between PD-related peritonitis and CV mortality risks. For example, infection-related morbidity is higher in those with fungal, enteric, and polymicrobial peritonitis, compared to other more indolent organisms. It is not clear if certain organism groups would have conferred different CV mortality risks following a peritonitis episode. Relatedly, given the hypothesis that CV events are potentially driven by ongoing peritonitis-related inflammation, one can hypothesize that more severe episodes characterized by either prolonged effluent cell count elevation, and/or those that cannot be cured with antibiotics alone, thereby necessitating PD catheter removal or permanent hemodialysis transfer may be particularly higher risk episodes for CV death.

The authors employed robust use and analysis of registry data to demonstrate that peritonitis can increase CV mortality risks. However, classification of deaths as CV or non-CV related is not straightforward. This is particularly challenging because no standardized definition exists for causes of CV death among individuals receiving dialysis. Given the complex and multiple mechanisms underlying CV mortality in dialysis patients, CV deaths are a heterogenous group comprised of arrhythmias from electrolyte disturbances, deaths due to progressive vascular calcification and organ ischemia, deaths due to chronic volume overload leading to heart failure and impaired left ventricular function, and deaths due to athero-embolic causes. Additional details regarding CV hospitalization events in this cohort in addition to the recorded causes of CV deaths, may have allowed us to glean further insights into the details and patterns of CV events peritonitis puts patients at greatest risk of.

The authors of the present study are to be congratulated for their work and for providing critical insights into an important area in PD. Taken together, these findings further underscore the importance of optimizing peritonitis preventive strategies and prompt and effective peritonitis treatment strategies, which need to be further explored as a means of potentially reducing CV risks for patients receiving PD.

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