FROM THE EDITOR

Vascular dementia—a growing problem in renal disease

Dementia is a major public health challenge, with economic costs to society that are similar to heart disease and cancer, and set to rise markedly over the coming years (1). Its human cost cannot be understated. Where patients lack capacity, there are complex issues for family members, caregivers, and health care teams in relation to care-planning and decision making. Dementia is increasingly recognized as a political issue—the UK Prime Minister identified it as one of the key challenges facing the country in 2012 (2). It is also gaining prominence in popular culture, for example as the subject of a recent single by the Norwegian group Katzenjammer: “Lady Grey.”

In 2005, the Cardiovascular Health Cognition Study demonstrated a 37% increased risk among people with moderate renal impairment, noting a prominence of vascular-type rather than Alzheimer’s type dementia (3). Vascular risk factors are predictive of its development—indeed a dementia risk score that includes age, education, gender, blood pressure (BP), body mass index (BMI), cholesterol and physical activity predicts the development of dementia over 20 years in the general population (4). It is a frequent accompaniment to frailty, and treatment for kidney failure is also implicated in its progression. A recent randomized controlled trial from the UK reported that hemodialysis (HD) results in significant brain injury identified on magnetic resonance imaging (MRI), and that improvement in hemodynamic tolerability achieved by using cooled dialysate abrogated these effects (5). Thus, there is evidence that the dialysis population have an increased burden of dementia as a consequence of vascular injury.

In this issue of *Peritoneal Dialysis International* (PDI), Dawn Wolfgram and colleagues from Wisconsin examine Medicare claims data among 112,960 HD and 8,663 peritoneal dialysis (PD) starters from the 2006 – 2008 United States Renal Data System (USRDS) cohort. They identified risk factors for the new diagnosis of dementia, which included female gender, African-American race, and increasing age, as well as diabetes and hypertension as primary renal diagnoses. Utilising appropriate statistical methodology, including propensity matching, PD was associated with an approximately 25% lower risk of developing dementia than HD, with the fully adjusted risk for PD vs HD being hazard ratio (HR) 0.76, 95% confidence interval (CI) 0.64, 0.90. In keeping with an effect of dialysis modality *per se*, an increased risk of incident dementia was also seen in patients switching from PD to HD, with a reduction in risk when the switch was in the opposite direction. These data are

in keeping with the possibility that there is something about the HD process that increases the risk of dementia—possibly through recurrent cerebral ischemia—and underlines the importance of the assessment of cognitive function among dialysis patients. Clearly, potential sources of bias exist that the authors readily acknowledge—primarily, patients with subtle cognitive problems are unlikely to be allocated to PD.

The relationship between dialysis modality and dementia may echo the well-rehearsed debate around the impact of the type of dialysis on residual renal function (RRF), where most studies demonstrate a benefit for PD but epidemiological considerations leave room for doubters. Issues that are commonly cited include patient selection bias, the impact of late presentation, the relationship between co-morbidity and the rate of decline of RRF, the timing of dialysis start, as well as informative censoring, where patients with early loss of RRF disproportionately transfer to HD so that the rate of decline appears slower in those remaining on PD. Finally, there has not yet been an adequately powered randomized controlled trial examining the issue.

Pertinent to this discussion, 2 single-center studies in this issue of PDI examine risk factors for decline in RRF. The first (Yi-Hua Lu *et al.*) is a study of 295 incident continuous ambulatory peritoneal dialysis (CAPD) patients examining predictors of decline in glomerular filtration rate (GFR), defined as the “slope of the trend equation” of 6 monthly serial renal creatinine clearance measurements. Prior hemodialysis for more than 3 months and female sex were associated with anuria at CAPD initiation, whereas those in the rapid decline group were more likely to have higher co-morbidity, a higher starting GFR, a higher BMI, and male sex. In patients with low co-morbidity, a higher starting GFR was associated with better survival, but this was not seen in the presence of co-morbidity, leading the authors to hypothesize that patients in this group were possibly required to start PD earlier as a consequence of their higher co-morbidity.

The second (Szeto *et al.*) is a larger study of 645 incident Chinese CAPD patients from Hong Kong that permitted a detailed analysis of predictive factors. Proteinuria, baseline residual GFR, and the use of diuretics were independently related to the rate of decline of RRF; whereas proteinuria, baseline residual GFR, glucose exposure, and the number of peritonitis episodes were independent predictors for the development of anuria. Similar to the Yi-Hua Lu paper, higher baseline GFR was associated with a more rapid rate of decline of RRF, but not time to anuria. Of course, missing in these analyses is the role of predialysis care, unplanned presentation, and patient selection.

The impact of RRF on survival in PD is well known; however, among the factors that contribute to the rate of decline, greater co-morbidity is a clear adverse marker. Potentially, this group of patients have the most to gain from emerging evidence of the benefit of biocompatible solutions on RRF (6). It is tempting to anticipate that future well-designed studies will evaluate the impact that altering aspects of dialysis therapy associated with preservation of RRF will have on the risk of developing dementia.

ACKNOWLEDGMENTS

The author gratefully acknowledges Professor Simon Davies for commenting on the manuscript.

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