Evidence of absence of effect was not a prespecified separate primary end point; thus, it was clear from the start that the study was underpowered to detect a difference in mortality alone. In this case, the proper comment seems to be that ‘absence of evidence does not mean evidence of absence of effect’. The FHN trial demonstrated among other a significantly greater regression in the left ventricular mass in favour of SDHD; at least this effect cannot be neglected, as it clearly affects survival in haemodialysis patients [3].

With regard to observational studies, improved survival of 15–45% with enhanced-frequency dialysis (i.e. home NHD) was previously noted in several studies [4, 5]. We agree with Labriola et al. [1] that this outcome could be influenced by selection bias, higher dialysis dose, setting and other factors.
However, among observational studies, only the International Quotidian Dialysis Registry (IQDR) study showed elevated mortality risk with frequent dialysis [6]. This study also had many limitations and met important criticism [7]. At best, it was a case–control study including patients from different databases. The study design was possibly subjected to biases related to incomparability of groups at study initiation, as data regarding the presence of comorbidities, BP control, type of dialysis access, residual diuresis and socio-economic status of patients were not available during the matching procedure. Importantly, analysis was not adjusted for the specific indications that led patients of the SDHD group to be assigned in a more aggressive dialysis schedule. It is therefore possible that patients in the SDHD group had much more comorbidities, resulting in worsened prognosis regardless of the assigned dialysis regimen.

Other arguments of investigators who oppose the benefits of enhanced-frequency dialysis are the increased risk of dialysis access complications, worsened residual renal function (RRF) and higher rates of method discontinuation among patients receiving SDHD or frequent NHD [1]. Vascular access problems appear to be the major issue; hence, we could similarly argue that current evidence is inconclusive, as in only one of the two randomized trials in the field vascular events were significantly higher with frequent dialysis [1, 8], obviously due to reduced power. Worsening of RRF was evident in post hoc analyses [9], but not in the main FHN trial [2], while perceived disease burden and quality of life will always represent ‘softer’ end points affected by numerous factors.

We believe that available evidence is at least suggestive of benefit with frequent modalities and clearly calls for proper randomized trials studying mortality, intermediate end points and all relevant complications. Among different strategies, alternate day dialytic modality should be specifically examined, as it possibly offer benefits through elimination of the long interdialytic intervals without aggravating the risk of complications related to the increased burden of therapy [10].

REFERENCES


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