Fatigue in advanced kidney disease

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Fatigue is commonly experienced in patients with advanced kidney disease and associated with poor outcomes. The prevalence of fatigue ranges from 42% to as high as 89% according to treatment modality and the measurement instruments used. This paper reviews studies examining sociodemographic, biological, and psychological factors associated with fatigue in advanced kidney disease. The association between fatigue and psychological factors, such as depression and anxiety, behavioral factors, such as sleep and nutrition, and cytokines, such as IL-6 and CRP corroborates the view of fatigue as a multidimensional and multifactorial problem. Although depression and fatigue are related, the relationship is typically moderate in size, thus fatigue should not simply be seen as a symptom of distress. Accordingly, it is important for treatment plans to address the complex etiology of fatigue through pharmacological and nonpharmacological interventions. To date, results of nonpharmacological interventions are promising, with physical exercise and cognitive-behavioral therapy showing beneficial results. Work conducted in other patient populations highlights the importance of cognitions and behaviors in the prediction and maintenance of fatigue. Such work could be applied to advanced kidney disease allowing a model of fatigue to be developed from which to base suitable interventions in this setting.

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Fatigue is a common symptom in patients with advanced kidney disease, with implications for quality of life (QoL) and clinical outcomes. Fatigue is a complex, multidimensional, and multifactorial phenomenon, which has been defined as 'extreme and persistent tiredness, weakness or exhaustion-mental, physical or both'.[1,2] Common symptoms also include reduced motivation and physical activity, in addition to general lethargy. Renal patients adjust the timing and intensity of their daily activities in order to accommodate their fatigue.[3,4] For example, some dialysis patients who suffer from post-treatment fatigue require more than 3 h of rest after each session to recover,[5] which is a considerable burden on top of the treatment regimen. Accordingly, the management of fatigue is an important clinical priority for enhancing the patients' QoL.[6]

In addition to recognizing fatigue and its severity, it is important to consider the sociodemographic, physiological, and psychological correlates of fatigue in chronic kidney disease (CKD), end-stage renal disease, and transplantation[7] in order to develop and test treatment models specific to these settings.[8] The purpose of this review is to discuss the assessment methods, prevalence, correlates, and the main outcomes associated with fatigue in patients with kidney disease. This review also examines possible interventions to improve fatigue and concludes by defining some future research directions.

ASSESSMENT OF FATIGUE IN CKD

Fatigue assessment tools are generally self-report measures, which are either evaluative, assessing the severity of fatigue, or discriminative, which have the purpose of differentiating fatigued from nonfatigued individuals.[9] Discriminative tools use cutoffs, which are used to indicate fatigue 'caseness'. Several fatigue measures have been shown to hold good psychometric properties in patients with chronic illness.[10] When choosing a fatigue instrument it is important to consider the particular aspect of fatigue intended for study (i.e. unidimensional/multidimensional measure), the psychometric properties of the measure, and the population in which the scale has been used previously.[10] Many of the widely used scales are not specific for kidney patients but have been applied to a variety of other conditions. Although most fatigue instruments measure the overall experience of fatigue during a period of weeks or months, dialysis patients also experience day-to-day and diurnal variation in fatigue.

Ecological momentary assessment procedures have been used to measure fatigue in patients receiving intensive cancer therapy[11] and could be used in the dialysis population to improve our understanding of fatigue and its variation over time, particularly over the interdialytic period. Listed below are some of the most frequently used scales for measuring fatigue in renal patients. For a more detailed review on the assessment of fatigue in chronic illness, see Dittner *et al.*[12]

SF-36 vitality subscale

The four-item SF-36 vitality subscale is often used as a measure of fatigue. Scores range from 0 to 100, with higher scores reflecting higher energy levels.[13,14] The concept of vitality is considered to be at the opposite pole to fatigue on a fatigue–vitality continuum.[15] However, the vitality construct captures the reduction in energy level but fails to reflect other aspects of fatigue such as lack of motivation and weakness.[7]

Fatigue severity scale

The fatigue severity scale is a nine-item unidimensional questionnaire[16] scored on a seven-point Likert scale, with high sum scores indicating greater fatigue. The scale's psychometric properties have been corroborated by studies in multiple diseases, including fibromyalgia,[17] multiple sclerosis,[18,19] chronic hepatitis,[20] and Parkinson's disease.[21,22] Overall, the fatigue severity scale has been shown to have a good test-retest reliability and a high internal consistency.[12]

Visual analog scale to evaluate fatigue severity

The visual analog scale is a unidimensional scale in which a 100-mm line is anchored at either end: by 'no tiredness at all' at the left end and 'complete exhaustion' at the other. The intensity of fatigue is measured in millimeters from the low (left) end of the scale with, again, a higher score indicating an increased level of fatigue. Studies have suggested that the descriptiveness of the visual analog scale to evaluate fatigue severity is considerably lower compared with other measures.[23] Furthermore, the scale might fail to differentiate between sleepiness and fatigue.[24]

Multidimensional fatigue inventory

The multidimensional fatigue inventory[25] contains 20 statements that are organized into five dimensions of fatigue (general fatigue, physical fatigue, mental fatigue, reduced activity, and reduced motivation). A global fatigue score combining results from the five dimensions ranges from 20 to 100, with higher scores indicating higher levels of fatigue. However, the hemodialysis (HD) population has shown difficulty in understanding the instrument.[26]

Although the above scales have generally shown adequate psychometric properties, future work needs to evaluate their performance in patients with kidney disease. Currently there are no robust data specific for CKD to recommend a particular measure. For use in routine clinical practice, a simple visual analog scale may provide a useful and quick assessment. Although not widely used in the renal literature, the Chalder fatigue scale[27] measures both mental and physical fatigue, thus evaluation of this measure in CKD would be of interest.

PREVALENCE OF FATIGUE IN RENAL PATIENTS

Fatigue is one of the most frequently reported symptoms in renal disease patients.[28–30] Compared with the general population,[31,32] dialysis patients report far higher fatigue levels.[33–38] A significant proportion of patients with renal disease report problematic levels of fatigue (Figure 1),[28,29,37–45] at rates comparable to other physical conditions.[46] However, the exact prevalence remains contentious as most of the research has focused on the HD population, neglecting transplant and peritoneal dialysis (PD) patients. The estimated prevalence of fatigue ranges between 42 and 89% according to treatment modality and the instruments used to measure the presence of fatigue. A recent investigation using visual analog scale reported that 81.5% of HD patients experienced fatigue.[29] A similarly high prevalence of fatigue in the HD population (77.9%) is reported elsewhere,[43] although lower rates are seen when using the SF-36 vitality subscale (41.9%, Figure 1).[39]

CORRELATES OF FATIGUE IN CKD

Sociodemographic factors

CKD fatigue has a complex multifactorial etiology (Figure 2). Studies indicate that women report significantly higher levels of fatigue than men,[29,35,37,38,47–49] although others report no gender association.[34,39,47,50] Gender differences could reflect greater symptom reporting in females compared with males.[51–54] Age is also fairly consistently associated with higher fatigue levels in renal patients[35,37–39,42,48,55–59] with those over 60 years of age reporting higher levels of fatigue.[55] The age–fatigue relationship might be explained by differences in dialysis vintage, physical activity, malnutrition

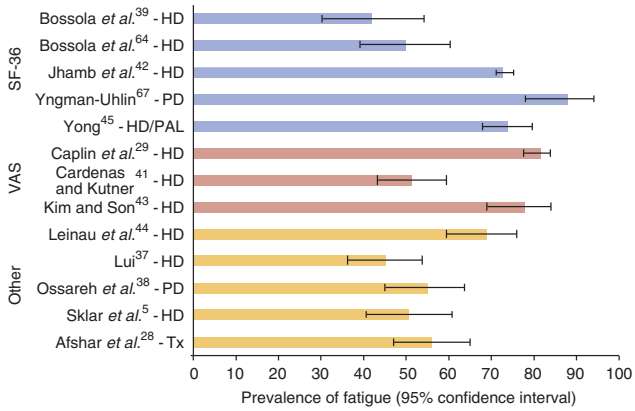

Figure 1 | Prevalence estimates of fatigue in advanced kidney disease (%). HD, hemodialysis; PAL, palliative care; PD, peritoneal dialysis; SF-36, Medical Outcome Study SF-36; Tx, transplant recipients; VAS, visual analogue scale - Fatigue.