FATIGUE IN CHRONIC KIDNEY DISEASE

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FATIGUE IN CKD: EPIDEMIOLOGY, PATHOPHYSIOLOGY AND CONTRIBUTING FACTORS

In this section, we will define what is fatigue among CKD patients. We will also show some data on its prevalence among dialysis and non-dialysis-dependent CKD patients. We will also explore some mechanisms and factors associated with its occurrence.

ASSESSMENT AND MANAGEMENT OF FATIGUE IN CKD

We will discuss in this section some assessment tools that can be useful for measuring fatigue among CKD patients. We will also present potential treatment modalities that could be helpful to relieve this common condition among CKD patients. Lastly, we will present a study supported by our company that investigated the association of fatigue among incident peritoneal dialysis patients with mortality risk.

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FATIGUE IN CKD: EPIDEMIOLOGY, PATHOPHYSIOLOGY AND CONTRIBUTING FACTORS

Currently, there is no standardized definition for the term *fatigue*. Fatigue is a complex, multidimensional, subjective overwhelming feeling of tiredness at rest, exhaustion with activity, lack of energy that impedes daily tasks, lack of endurance, or a loss of vigor. Physical symptoms include muscle weakness or poor endurance, and psychologic symptoms include a sense of increased effort or diminished cognitive endurance. [1,2] Fatigue affects around 42%-89% of patients with advanced CKD depending on treatment modality and mode of measurement. [3] These numbers are much higher than the prevalence of fatigue reported in the general population (23.1%). [4] Moreover, a recent report from France using data from the French CKD-REIN cohort study (N=2,787) showed that 83% of non-dialysis dependent CKD patients experience fatigue. [5]

Multiple abnormalities present in CKD patients contribute to fatigue. Nutritional problems (including hyperphosphatemia), a state of chronic inflammation and acidosis both closely linked to CKD and protein energy wasting can result to fatigue. Anemia and chronic heart failure common among CKD patients result to impaired oxygen delivery with resultant physical fatigue. Psychologic manifestations such as depression and insomnia also contribute to fatigue in CKD patients. [2] (Figure 1)

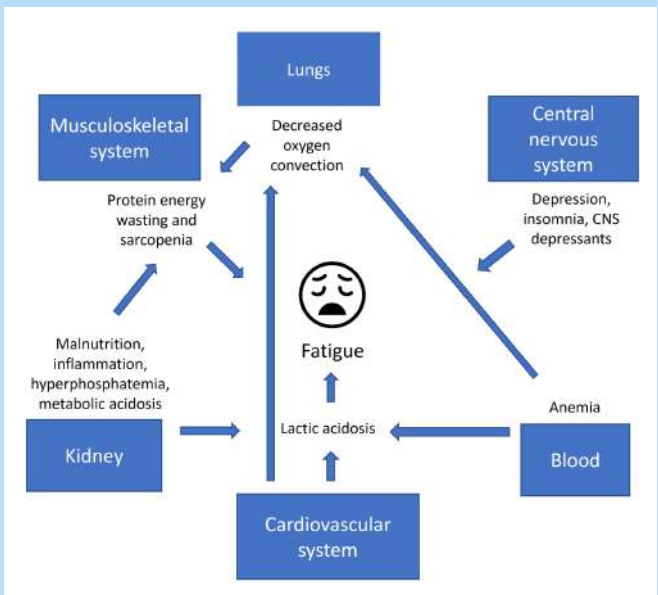

Figure 1. Pathophysiologic factors contributing to fatigue in CKD patients. Adapted from Clin J Am Soc Nephrol 2021;16(9):1445-1455.

ASSESSMENT AND MANAGEMENT OF FATIGUE IN CKD

There is currently no consensus about the best tools to measure fatigue in patients with CKD. A summary of available tools is provided below (Table 1). These scales are the most frequently used measurement tools for CKD and dialysis patients. Most of the measurement methods are single items embedded within longer questionnaires to rate depression, quality of life or disease burden. When choosing a fatigue instrument it is important to consider the particular aspect of fatigue intended (i.e. unidimensional/multidimensional measure), the psychometric properties of the measure, and the population in which the scale has been used previously. We also need to consider whether these measures have been validated so that they can be used in the clinical setting. [2,3]

After recognition and accurate measurement of fatigue, the next approach would be to look at interventions to reduce fatigue. Due to the complexity of fatigue, a multi-disciplinary approach to treatment should be adopted. (Table 2). [6]

A subanalysis of data from the ExTra CKD study (N=36) performed in the UK also reported that 12 weeks of supervised exercise had favourable effects on symptom burden and fatigue-related outcomes. [7]

Fatigue measurement tool
Functional Assessment of Chronic Illness Therapy- Fatigue (FACIT-F)
CKD Symptom Burden Index Fatigue Item*
Dialysis Symptom Index*
Quick Inventory of Depressive Symptomatology (QIDS-SR16) Fatigue Item
Patient Outcome Scale
Memorial Symptom Assessment Scale Short Form
Beck Depression Inventory (BDI) Fatigue Item
Edmonton Symptom Assessment Scale Fatigue Item
12-Item Short Form Health Survey (SF-12) vitality scale
36-Item Short Form Health Survey (SF-36) vitality scale
Fatigue Severity Scale
Visual Analog Scale to evaluate fatigue severity
Multidimensional Fatigue Inventory
*Scales specific for kidney patients

Table 1. Fatigue measurement tools available for CKD patients. Adapted from Clin J Am Soc Nephrol 2021;16 (9):1445-1455; Kidney Int 2014;86 (3):497-505.

Table 2. Potential multidisciplinary approaches to improve fatigue in CKD patients. Adapted from Am J Kidney Dis 2008;52(2):353-365.

Targeted area	Interventions
Increase health care provider awareness	• Education on prevalence, importance and severity of fatigue; training at identifying symptoms of fatigue
Improve measurement of fatigue	• Development of criteria for defining fatigue, improving fatigue scales specific for CKD population, assessment for measurement of day-to-day variation in fatigue, improved survey modalities (e.g., phone interview, computer-assisted interview, and proxy administration of interviews to reduce selection bias), frequent fatigue screening
Address gaps in understanding pathogenesis of fatigue	• Role of cytokines, mode of dialysis, frequency of dialysis, thermoneural hemodialysis
Test potential therapies for fatigue in CKD	• Non-pharmacological (nutritional therapy, sleep therapy and hygiene, exercise, stress management, cognitive behavioral therapy, energy conservation, acupressure, treatment of substance abuse/dependence) • Pharmacologic (hematopoietics, antidepressants, anxiolytics, levocarnitine, human growth hormone)
Improving social support for patients with fatigue	• Family members and care providers education and training • Addressing caregiver fatigue

COMPANY INITIATIVES

A real-world study on fatigue and mortality among incident PD patients

Analysis of real-world data in two cohorts of adult PD patients in Brazil (BRAZPD II) and the US (Fresenius Kidney Care) from 2004 to 2011 (N=4,285) was performed using the KDQOL-SF v1.3 survey using the vitality subscale. Patients who participated were those who started continuous ambulatory peritoneal dialysis (CAPD) or continuous cycling peritoneal dialysis (CCPD) within 90 days.

Results from the study showed that higher patient-reported fatigue in the first 90 days after the start of PD was associated with a increased risk of all-cause mortality. Also, the authors demonstrated that each 10-unit increase in vitality score was associated with lower risk of all-cause mortality in both cohorts (Brazil: hazard ratio [HR]=0.79; 95% confidence interval [CI], 0.70–0.90 and United States: HR=0.90; 95% CI, 0.88–0.93 and Pooled HR=0.86; 95% CI, 0.75–0.98). [8]

References:

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