The Frail Dialysis Population: A Growing Burden for the Dialysis Community

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Frailty · Dialysis · End-stage renal disease

Abstract
Background: The dialysis population is aging worldwide. It is well known that patients on dialysis have limited functional status, but only recently has frailty been considered.

Summary: The prevalence of frailty among patients on dialysis ranges from 3.4- to 10-fold higher than among community-dwelling elderly, depending on the method of assessing frailty and patient characteristics. Despite its high prevalence and the high overall mortality in the dialysis population, frailty is associated with higher mortality, independent of clinical and demographic characteristics and comorbidity. The prevalence of frailty among patients with non-dialysis-dependent chronic kidney disease (CKD) is also high, and cross-sectional data suggest that the prevalence may increase as CKD progresses. Thus, interventions to improve frailty have the potential to improve quality of life and mortality. Although interventions to improve physical dysfunction have been successful in the population with end-stage renal disease, no studies have specifically targeted frail individuals. Therefore, the extent to which exercise or physical activity interventions are feasible among frail patients and can improve frailty urgently needs to be examined. In the meantime, providers should refer frail patients to physical therapists and encourage them to be more active if possible. In addition, more attention should be focused on the possibility that rehabilitation among patients with earlier stages of CKD could improve dialysis outcomes. Key Messages: Frailty is extremely common among patients on dialysis and is independently associated with adverse outcomes. Providers should take advantage of available resources to improve functioning in this population, and research should address the optimal strategy for addressing frailty, including timing of intervention.

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Aging Dialysis Population

The mean age of the dialysis population has been increasing in Japan and the United States over the last decade (fig. 1) [1, 2]. Japan’s incident and prevalent dialysis populations (67.8 and 66.6 years at the end of 2011) are considerably older than the US dialysis population and likely the dialysis populations of most other countries in the world. Sixty-three percent of Japanese dialysis patients are 65 years or older, and 36% are 75 or above [2]. Therefore, it is becoming important for dialysis practitioners to understand syndromes common among the elderly.
What Is Frailty?

A recent consensus conference of European and American frailty experts defined frailty as a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death [3]. Aging and chronic diseases likely contribute to the development of frailty through mechanisms that include oxidative stress, inflammation, and reductions in anabolic hormones [4]. Thus, it is not surprising that chronic kidney disease (CKD), which itself can lead to all of these perturbations, is associated with a higher prevalence of frailty among community-dwelling elderly [5].

Operational definitions of frailty have incorporated the concepts of multiple contributing causes and multiple manifestations forming a syndrome. Fried et al. [6] developed a frailty phenotype consisting of three or more of: unintentional weight loss, exhaustion, physical inactivity, slow gait speed, and weak grip strength. According to this definition, approximately 7% of community-dwelling elders in a large US cohort study were frail, and frailty was associated with a higher prevalence of frailty among community-dwelling elderly [5].

Prevalence of Frailty in the Dialysis Population

Using such a self-report-based definition of frailty, we assessed the prevalence and significance of frailty among incident dialysis patients participating in the United States Renal Data Systems Dialysis Morbidity and Mortality Study [8]. Two-thirds of the patients were frail, including many who were under the age of 65 years. Older patients, women, and patients with diabetes mellitus were more likely to be frail. Frailty was associated with >3-fold higher risk of death in univariate analysis (hazard ratio [HR] 3.42, 95% confidence interval [CI] 2.45–4.76, p < 0.001) that persisted in multivariable analysis (HR 2.24, 95% CI 1.60–3.15, p < 0.001). Since then, the Fried frailty phenotype has been applied in prevalent dialysis populations in the US [9, 10]. The prevalence was lower by this method at 30–42%, but was still 4–6 times that of healthy elderly despite inclusion of all adults in these studies rather than only those older than age 65. The prevalence of frailty in patients with ESRD has varied across cohorts, likely as a result of differences in the method of assessing frailty (table 1). Differences in patient characteristics, such as dialysis vintage or degree of comorbidity probably also contribute to the variation. Nevertheless, all studies have shown a prevalence of frailty that is substantially higher than among community-dwelling elderly.

Given the high burden of comorbid illness among patients on dialysis and the high overall mortality, it is important to consider whether frailty provides prognostic information in this population. If comorbidity and markers of inflammation already in use in the dialysis population capture the risk associated with frailty, then frailty may not improve prediction of adverse outcomes. However, frailty was independently associated with higher mortality in all studies that have examined the association to date. Furthermore, frailty has also been found to be associated with higher risk of falls and fractures [11, 12]. There is ongoing debate about the value of frailty assessment in the dialysis population and the method by which frailty should be assessed [13, 14], and longitudinal studies are needed to address these questions.

Time Course of Development of Frailty among Patients with CKD

Although there have been no longitudinal reports of frailty among patients with CKD, cross-sectional studies suggest that frailty increases as eGFR declines (table 2). Dalrymple et al. [15] examined the association of stages...
of CKD defined using Cystatin C and frailty by the Fried phenotype and found a strong linear correlation, with a higher prevalence of frailty at more advanced stages of CKD. Similarly, Roshanravan et al. [16] found that the estimated glomerular filtration rate (eGFR) categories of <30 ml/min/1.73 m² and 30–44 ml/min/1.73 m² were associated with a 2.8-fold (95% CI 1.3–6.3) and 2.1-fold (95% CI 1.0–4.7) higher prevalence of frailty compared with eGFR ≥60 ml/min/1.73 m². In this study, frailty was associated with higher odds of death or initiation of di-

Table 1. Studies of frailty among patients with ESRD

<table>
<thead>
<tr>
<th>Reference</th>
<th>Population</th>
<th>Weight loss</th>
<th>Exhaustion</th>
<th>Physical activity</th>
<th>Gait speed</th>
<th>Grip strength</th>
<th>Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johansen, 2007 [34]</td>
<td>Incident dialysis</td>
<td>Malnourished according to provider assessment</td>
<td>SF-36 Vitality</td>
<td>Inactive (single question about frequency of activity)</td>
<td>SF-36 PF scale</td>
<td>SF-36 PF scale</td>
<td>67.7</td>
</tr>
<tr>
<td>Bao et al., 2012 [35]</td>
<td>Incident HD</td>
<td>No</td>
<td>SF-12 Vitality</td>
<td>Human Activity Profile</td>
<td>SF-12 PF</td>
<td>SF-12 PF</td>
<td>73</td>
</tr>
<tr>
<td>McAdams-DeMarco et al., 2013 [36]</td>
<td>Prevalent HD</td>
<td>Yes</td>
<td>CES-D</td>
<td>MMLTA</td>
<td>&gt;15 feet</td>
<td>Yes</td>
<td>41.8</td>
</tr>
<tr>
<td>Johansen et al., 2014 [37]</td>
<td>Prevalent HD</td>
<td>Yes</td>
<td>CES-D</td>
<td>MMLTA</td>
<td>&gt;15 feet</td>
<td>Yes</td>
<td>30</td>
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<tr>
<td>Johansen et al., 2014 [14]</td>
<td>Prevalent HD</td>
<td>Yes</td>
<td>SF-36 Vitality</td>
<td>MMLTA</td>
<td>SF-36 PF</td>
<td>SF-36 PF</td>
<td>53</td>
</tr>
<tr>
<td>Wilhelm-Leen et al., 2009 [39]</td>
<td>Community-dwelling elderly CHS participants with SCr ≥1.3 in women and ≥1.5 in men</td>
<td>Yes</td>
<td>CES-D</td>
<td>MMLTA</td>
<td>&gt;15 feet</td>
<td>Yes</td>
<td>15</td>
</tr>
<tr>
<td>Roshanravan et al., 2012 [16]</td>
<td>Stages 1–4 CKD (mean eGFR 51 ml/min/1.73 m²)</td>
<td>Yes</td>
<td>SF-36 Vitality</td>
<td>Self-reported exercise &lt;1 time/week</td>
<td>Yes</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Dalrymple et al., 2013 [15]</td>
<td>CHS participants with eGFR &lt;45 ml/min/1.73 m² by cystatin C</td>
<td>Yes</td>
<td>CES-D</td>
<td>MMLTA</td>
<td>&gt;15 feet</td>
<td>Yes</td>
<td>24</td>
</tr>
<tr>
<td>Reese et al., 2013 [17]</td>
<td>CRIC participants</td>
<td>Yes, &gt;5% in one year</td>
<td>CES-D</td>
<td>MESA questionnaire</td>
<td>&gt;15 feet</td>
<td>Yes</td>
<td>7</td>
</tr>
</tbody>
</table>

NHANES = National Health and Nutrition Examination Survey; CHS = Cardiovascular Health Study; CRIC = Chronic Renal Insufficiency Cohort; MESA = Multi-Ethnic Study of Atherosclerosis.

References:

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290

Johansen
Frailty in the Dialysis Population

Can Frailty Be Addressed?

We are aware of no published studies specifically designed to address frailty in the dialysis population. Unfortunately, recent studies suggest that functional status declines further after initiation of dialysis among frail and very elderly patients without intervention [18, 19], making it imperative that we consider treatments or interventions to reverse the downward trajectory. Since physical inactivity is a part of the definition of frailty, it is possible that interventions to increase activity could address frailty directly or indirectly if they also improve physical performance or symptoms of fatigue and exhaustion. Numerous studies have shown that patients on hemodialysis are extremely inactive [20–22] and that low physical activity is associated with worse physical performance [23] and with lower survival [22, 24, 25]. Few studies have focused on increasing habitual physical activity in the dialysis population [26, 27], but such a strategy seems promising and should be investigated. Even without solid evidence for a benefit in the dialysis population, patients should be encouraged to follow physical activity guidelines for older patients if possible.

There have been numerous studies of more vigorous exercise training programs designed to increase exercise capacity or physical performance [28], and although many studies are small and/or of low quality, the majority have led to improvements. Furthermore, patients with lower baseline functioning derived greater benefit in one of the largest exercise intervention studies [29]. Therefore, aerobic exercise training would seem to have the potential to improve frailty. However, the vigorous nature of such training programs has led to the exclusion of large numbers of patients on hemodialysis as ineligible, and frail patients would more likely have factors that lead to exclusion. In addition, there has been a high rate of patient refusal to participate in such programs when offered [30], suggesting that fear or reluctance to do vigorous activity is a barrier for patients’ adoption of exercise programs. Thus, the extent to which aerobic exercise training during dialysis or at another time will be able to reverse frailty remains to be seen.

Because weakness is part of frailty and muscle atrophy is a key underlying mechanism [10, 31], resistance exercise or other anabolic interventions might be logical choices to ameliorate frailty in the dialysis population [32]. Indeed, resistance training has been shown to increase muscle strength among patients on hemodialysis [32] as well as among institutionalized nonagenarians [33], proving that such programs are possible even among patients with extremely low functioning and can be beneficial. Therefore, referral of frail individuals for physical therapy and strength training should be strongly considered when weakness or frailty is detected.

Conclusion

Frailty is common in the aging dialysis population and is associated with adverse outcomes including death, hospitalization, falls, and fractures. Frailty is also more common among individuals with CKD than those without and appears to progress as CKD progresses. Studies are needed to determine whether interventions can improve frailty, which interventions are most successful, and when such interventions should be applied. The frequent onset of frailty in CKD before dialysis and the potential association of frailty with higher risk of ESRD would suggest that intervention in predialysis stages of CKD may be of most benefit, but it is also important to consider the dialysis population whose functioning is currently extremely impaired.

Conflicts of Interest

The author declares no conflicts of interest in relation to this work.

References
