Adverse health effects of frailty among chronic kidney disease (CKD) patients: A systematic review

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A B S T R A C T

*Aim*: Frailty is associated with increased susceptibility to adverse health outcomes. This systematic review uncovers the adverse health effects of frailty in patients with chronic kidney disease (CKD); we also deliberate the causes and prevalence of the comorbidities of frailty.

*Study design*: PubMed, Medline, CINAHL, Web of Science, Google Scholar, and Cochrane were used to identify the articles.

*Data synthesis*: Articles available online before the 17th of February 2019 which mentioned adverse effects of frailty in patients with CKD was qualified for the systematic review.

*Results*: The literature search yielded 537 articles, of which 64 met the criteria and were included. Several biological (cardiovascular, renal, immunological, cognitive, endocrinologic, etc.) and psychological effects are attributed to ‘frailty’ in CKD patients, who also present with worse quality of life and increased risk of health-care utilization.

*Conclusions*: Frailty in patients with CKD is associated with an increased risk of adverse health outcomes, with a considerable amount of evidence showing causality between frailty and worsened health.

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1. Introduction

Frailty, as a syndrome of decreased physiological reserve, characterized by increased susceptibility to stressors and adverse outcomes 1. There are two most acknowledged conceptualizations of frailty and approaches to its measurement, as described below. Fried phenotype, developed by Linda Fried, featuring a set of symptoms as criteria of frailty: slowness, weakness, low physical activity, exhaustion and shrinkage 1. Frailty is described a syndrome with sarcopenia as the key pathophysiological factor 1. Fried phenotype is lately developed into simple FRAIL scale, which measures fatigue, resistance, ambulation, illnesses and loss of weight.

The second approach is frailty index approach, and by quantifying deficits among multiple organ systems, it manifests that frailty is a state of accumulation of cellular deficits leading to a loss of redundancy in organ systems. Regardless of measurements, frail patients experience a declined physical function and have higher risk to develop adverse health outcomes.

The link between chronic kidney disease (CKD) and frailty is not completely understood, however, patients with inflammation is predisposed to frailty 2,3 , Shlipak et al. also demonstrated that pro-inflammatory cytokines in CKD patients are risk factor to frailty 4.

A previous systematic review summarized the relationship between frailty in patients with CKD and falls, hospitalizations, and mortality 5.

1. Method
   1. Search strategy

The following search terms were used to identify articles that assessed adverse health outcomes associated with frailty among patients with CKD: (‘frail’ OR ‘frailty’ OR ‘frail phenotype’ OR ‘frailty index’) AND (‘chronic kidney disease’ OR ‘chronic renal disease’ OR ‘chronic renal insufficiency’ OR ‘kidney transplant’ OR ‘renal transplant’ OR ‘end-stage kidney disease’ OR ‘end-stage renal disease’ OR ‘dialysis’) AND (‘frail’ OR ‘complication’ OR ‘cause’ OR ‘etiology’ OR ‘aetiology’).

This review intends to find out the adverse health outcomes caused by frailty among patients with CKD. Thus, we limited the search criteria to find out results including causality. To make the search less strict, we add ‘frail’ after the second AND operator to look for articles in which ‘complication’, ‘cause’, ‘etiology’ or ‘aetiology’ are not used but covers the adverse effects of frailty.

* 1. Selection criteria

We include primary research articles and case series which analyzed the prevalence of comorbidities, or causal relationship between frailty and adverse health outcomes. All studies deal with the effects of frailty in patients with CKD, end-stage renal disease (ESRD), on dialysis, or have gone through kidney transplantation published before 17th February 2019 are eligible for the inclusion. We excluded articles if they were not available in English, Spanish, Portugese, or German languages. If over one article approached the same study population with various analyses, the articles that meet the aim of the systematic review were selected and presented in combination.

1. Data analysis
   1. Data extraction

Abstracts were examined for relevance to the study criteria. We recorded, when available, information about the demographics of the study population, adverse health effect, and data for severity of CKD, frailty assessment method, and risk differences of complications caused by frailty among patients with CKD.

1. Results

Our search produces 1223 (w/o GS and embase) (w/ GS and embase 1891) references. We removed 686 (w/o GS and embase) (w/ GS and embase 592) redundant articles, leaving 537 (w/o GS and embase) (w/ GS and embase 1299) reports for abstract examination. After the examination, 473 results were removed from further analysis for the following reasons: discussed the causes of frailty: 17; abstract unavailable: 4; did not measure frailty in patients with CKD: 266; did not measure the effects of frailty in patients with CKD: 175. Within the included, 3 references in review articles which measure the causes or effects of frailty in patients with CKD were collected manually. 64 full texts met the inclusion criteria and were selected for review, in which \_\_\_ studies (\_\_\_ %) were primary prospective analysis and \_\_\_ studies (\_\_\_ %) were secondary analysis.

* 1. Demographics of the study population

Twenty nine studies studied frailty in dialysis patients with CKD, elevan studies focus on frailty in patients who had renal transplantation or on a waitlist, and others examined pre-dialysis patients. Out of 20555 participants with CKD, 64.16% (n = 13189) are at stage 5D. The study characteristics and population demographics are presented in Table \_.

* 1. Method of frailty assessment

Frailty status was mostly assessed with the Fried frailty phenotypes (n = \_\_\_, \_\_\_ %), whereas interpretations of the five characteristics differ between studies and from the original definition of purposed by Fried et al. (Table \_) 1.

There were \_\_\_ studies (\_\_\_ %) that modified the Fried criteria for frailty and substituted the measurement of grip strength and gait speed for questionnaire based assessments of physical function.

\_\_\_ studies (\_\_\_ %) employed different measures to the Fried phenotype for frailty assessment. The most common of these, used in \_\_\_ studies, was \_\_\_. \_\_\_, which \_\_\_, was used and has been shown to be \_\_\_. [cite] used \_\_\_, which is \_\_\_. Other measures used in the studies include \_\_\_, \_\_\_, \_\_\_ and \_\_\_.

* 1. Causes and risk factors for frailty

Nine studies demonstrated a positive correlation, increased prevalence, or a significant increased odds ratio (OR), relative risk (RR) toward frailty when certain biological factors exist 67891011121314. Yadla et al. found that patients with CKD and hypertension (HTN), peripheral vascular disease, or left ventricular dysfunction bear a slightly higher risk for frailty, with RR from 1.18 to 1.68 6. Mansur et al. suggested endothelial dysfunction a potential mechanism underlying frailty in patients with CKD, having a high OR 3.8 8.

* 1. Biological complications
  2. Psychological complications
  3. Sociological complications
  4. Quality of life and independence
  5. Health-care utilization and death

1. Frailty and the kidney transplantation (post-transplantation complications and prognosis)
2. Discussion

In this systematic review of the adverse effects of frailty in patients with CKD, frailty was a significant predictor of adverse health outcomes, particularly in those with severe CKD stages.

1. Conclusion

Conflicts of interest

None.

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