International Urology and Nephrology (2019) 51:461–465
https://doi.org/10.1007/s11255-018-2061-0

NEPHROLOGY - REVIEW

Usefulness of frailty evaluation for handling chronic kidney disease elderly patients: a review and original proposal

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Received: 15 April 2018 / Accepted: 12 December 2018 / Published online: 2 January 2019

Abstract
There is interdependence between chronic kidney disease (CKD) and ageing whereby CKD makes ageing more accelerated and pronounced, whereas ageing accelerates chronic nephropathy's progression. Frailty status catalyzes this spiral, with renal and systemic negative consequences, and this condition can currently be documented by applying already validated clinical scores (frailty phenotype) or physical test (gate speed). Although, nephroprevention strategies are similar between young adult and senior CKD patients, standard targets should be adequate to very old and frail elderly individuals. For this purpose, an original algorithm is here proposed to adjust the conventional nephroprevention strategies to the condition of CKD frail patient (more relaxed targets and tighter control), as well as to prescribe anti-frailty interventions to slow patient's functional decline, hospitalization and mortality.

Keywords Chronic kidney disease · Nephroprevention · Elderly · Frailty

Introduction

Chronic kidney disease (CKD) is a condition characterized by progressive and irreversible renal function decline for a period of at least 3 months, requiring its diagnose the presence of at least one of the following parameters: reduction in the glomerular filtration rate (GFR), altered urinalysis (renal haematuria and/or albuminuria–proteinuria), and kidney structural abnormalities, detected by a biopsy or imaging [1]. The prevalence of CKD is approximately 10% in the general population, and it increases with age, affecting over 30% of people older than 65 [2]. Moreover, a reduced GFR represents a significant mortality risk factor in the elderly when its value is lower than the expected for their age ($\leq$45 mL/min/1.73 m^2) [2, 3]. Frailty is a condition usually found in elderly people, and it is the opposite of fit or robust status (where old people are freely ambulant and live independently at home). This frailty status is characterized by weakness, motility and balance issues, and a diminished capability to resist stressors, all of which lead to increased risks of falls, fracture, institutionalization, hospitalization, dementia, dependence, poor quality of life, and death [2, 4]. The prevalence of frailty among community-dwelling people rises with age, being roughly 4–7% in old people, and 9–26% in very old people. Moreover, female gender and chronic diseases also increase the frailty phenotype prevalence, including 14% of the non-dialysis CKD elderly patients, having these individuals higher risk of hospitalization and mortality [4, 5]. There is a considerable difference between ageing with and without frailty, characteristically presenting the former a reduced homeostatic capability which makes the elderly individual much more vulnerable to stressors [6–8].

Frailty evaluation

Based on two different conceptual models of frailty, two main frailty assessment tools have emerged: the fragility phenotype coined by Fried et al. [10], and the Fragility Index (FI) coined by Jones et al. [11]. Nevertheless, other diagnostic criteria, such as fatigue, resistance, ambulance, illnesses, loss of weight (FRAIL) and SHARE-FI (Frailty Instrument for Primary Care of the Survey of Health, Aging and Retirement in Europe) have similarly been validated [9–11]. Fried et al. [10] coined the concept of "frailty phenotype", which

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is based on the evaluation of five clinical domains that include: shrinking, weakness, poor endurance and energy, slowness, and low physical activity. Those patients with three or more of these domains are considered to have a frail phenotype, those with one or two domains are classified as vulnerable individuals (pre-frail), and those with no domains as fit or robust elderly people [4, 10, 12–14]. Some authors consider the presence of sarcopenia (generalized muscle mass and strength reduction secondary to ageing) as part of the "shrinking domain" of the frailty phenotype [10, 12]. Sarcopenia diagnosis is based on muscle mass assessment by body imaging techniques, bioimpedance analysis, muscle strength, and clinical scores [15]. However, frailty is more multifaceted than sarcopenia alone, since the former goes beyond physical factors to encompass physiological and social dimensions. Furthermore, the frailty phenotype is usually accompanied by insulin resistance and insufficiently regulated inflammatory response that enhance sarcopenia and loss of muscle strength [2, 5]. CKD is one of the multiple diseases that may be involved in the onset and progression of sarcopenia owing to several mechanisms such as malnutrition, low vitamin D levels, hormonal decline, and metabolic acidosis [1, 2, 5]. Moreover, sarcopenia explains why when kidney function is assessed in elderly people using an estimating glomerular filtration rate equation based on serum creatinine levels (eGFR-Cr), those individuals with the lowest and highest eGFR values were associated with the highest mortality. This U-shape is more prominent in octogenarians; probably owing to the fact that higher eGFR-Cr partly reflects those with lower muscle mass and malnutrition [16]. The FI is based on a multidimensional geriatric assessment, which evaluates the accumulation of deficits, including disease, physical and cognitive alterations, and psychosocial risk factors. In addition, it is a more sensitive predictor of adverse health effects. Rockwood et al. also designed a screening instrument based on clinical judgment: The Clinical Frailty Scale (CFS), which indicates the different stages of frailty in a patient. CFS is a validated tool for diagnosing frailty, and consists of an evaluation of seven to nine items indicating the overall clinical status of an elderly person based on the assessment of their state in the domains of mobility, energy, physical activity, function, and prognosis [17, 18]. Physical performance can also be measured. For this purpose, gait speed, also often referred to as walking speed, seems to be the most recommended test, since it has been associated with increased survival in the elderly [19].

Senescent nephropathy

There is interdependence between the inflammation process associated to CKD and the inflammation process associated to ageing (inflammaging), whereby CKD makes ageing more accelerated and pronounced, whereas ageing accelerates chronic nephropathy's progression. Additionally, when an elderly patient suffering from any cause of CKD presents a frailty phenotype, this new inflammatory condition catalyzes the above-mentioned vicious circle inducing renal and systemic negative consequences. This deleterious combination of CKD and frailty phenotype has been named "senescent nephropathy". This condition has different clinical complications, therapeutic needs and worse overall prognosis compared to CKD in robust elderly patients (Table 1) [20]. CKD is a condition associated with several changes such as: malnutrition, chronic inflammation, increased oxidative stress, etc. which can directly and indirectly contribute to accelerate and worsen the ageing process leading even to develop frailty phenotype [2, 4, 5]. Sarcopenia increases progressively, along with the loss of renal function in CKD patients. CKD-associated muscle mass loss justifies the high prevalence of low grip strength and slow gait speed in this population. Although CKD itself is a predictor of adverse health outcomes, coexistence of CKD and frailty has been shown to further increase risks of falls, fractures, hospitalization, and mortality [2, 4, 5]. Consequently, frailty must be evaluated to initiate adequate treatment in the CKD patient due to its important implication in morbid-mortality in this group [2]. It is of the utmost importance to examine frailty status in the ESRD population as they are at the highest risk among CKD patients [4, 21]. Although rehabilitation in these patients may be cost-effective and prevent institutionalization, these services are usually underutilized in this population. Even though, the treatment of frailty can

Table 1 Differences between chronic kidney disease (CKD) in fit elderly from senescent nephropathy (SN) patients

	CKD in fit elderly	CKD in frail elderly (SN)
CKD diagnosis	Positive	Positive
Frailty phenotype score	Negative	Positive
Treatment	Conventional CKD therapy	CKD therapy adjusted to frailty status + frail rehabilitation and home assistance
CKD follow-up	Conventional control rate	Tighter control rate
CKD prognosis	Usual	Worse

improve this condition, particularly in its initial stages, the impact of this treatment on CKD progression has not been studied yet [22–24]. Finally, the dialytic treatment seems to prolong survival in the elderly compared to conservative treatment, but not in the most seriously ill elderly patients [5, 22]. Some authors have reported a loss of independence in very old CKD patients who started dialysis treatment, observing that many patients suffer deterioration of their functional state 3 months from the beginning of dialysis, with a negative impact on their daily activities. In such cases, conservative treatment could be a better therapeutic alternative [2, 25].

Frailty phenotype and nephroprevention

An algorithm is hereby proposed for the management of CKD in elderly patients, based on the current evidence of the most suitable approach to different clinical scenarios (Fig. 1). When evaluating an old patient with CKD, we recommend assessing the presence of the frailty phenotype, applying any of the validated abovementioned scores. If the patient is classified as frail, then a diagnosis of senescent nephropathy is present. In such cases, frailty treatment should be initiated, targeting the frailty-inducing mechanism, for instance: if sarcopenia is detected as the patient's frailty-inducing factor, a normal diet (instead of a low-protein diet) and muscle exercise should be prescribed. Moreover, conventional CKD therapeutic measures, such as low sodium and protein diet, antihypertensive, antiproteinuric, hypoglicemic agents, immunosuppressants, dialysis, etc. should be implemented more carefully, lower doses and tighter control since they can be less tolerated in this group. If conventional targets cannot be achieved due to patient's intolerance to nephroprevention therapy, such as hypotension (anti-hypertensive drugs), hyponatremia (low sodium diet), malnutrition (low protein diet), hypoglycaemia (anti-diabetic medication), etc., lower nephroprevention targets should be sought. Conversely, the required erythropoietin dose could be higher in CKD frail elderly patients compared to CKD robust elderly patients (Table 2) [21, 26]. It is worth mentioning, that since there several degrees of frailty status, and the algorithm here proposed is just a general therapeutic guide, of course each CKD elderly patient should be evaluated to decide which would be the most adequate and complete therapy according to his/her frailty phenotype. On the other hand, if the patient is classified as fit or robust, the differentiation between old and very old patients should be further performed. In the former group, conventional nephroprevention strategies will be initiated, including dialysis prescription when indicated. The latter group, however, should be treated as though the frailty phenotype were present, with more caution when initiating conventional CKD therapies, as well as delaying the start of dialysis (conservative treatment). Although there is no frailty treatment recommended in this group, we strongly suggest running a periodic assessment of the frailty phenotype, to initiate the corresponding rehabilitation therapy as early as possible.

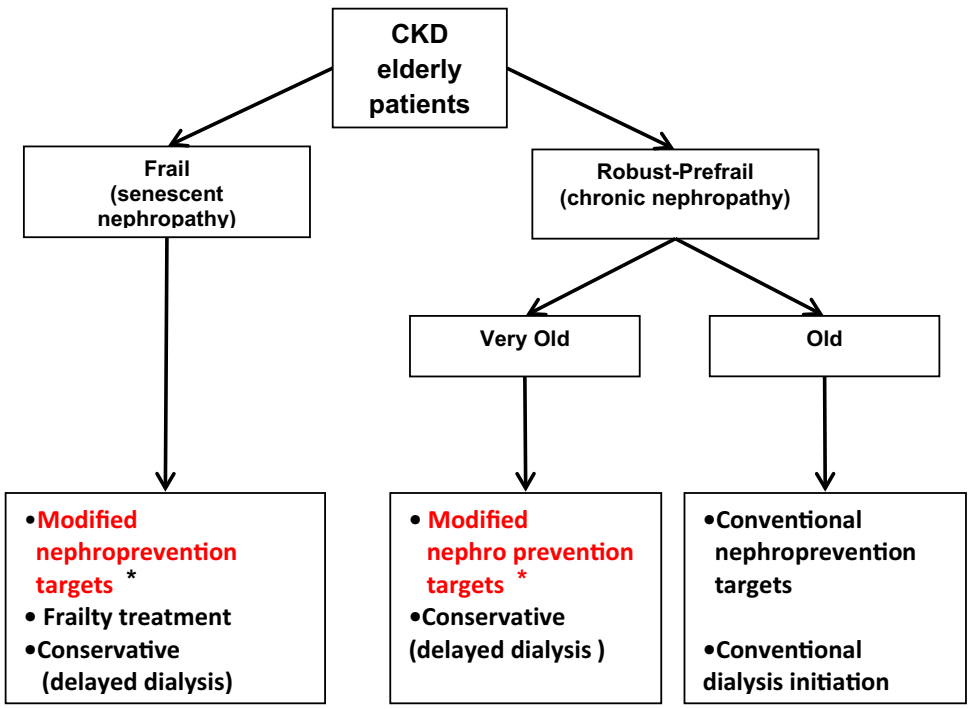

Fig. 1 Proposed nephroprevention algorithm in the elderly patients. *CKD* chronic kidney disease, *Old* 65–79 years of age, *Very old* ≥ 80 years of age. *Modified nephroprevention targets: This means that personal therapeutic targets should be seek depending on the patient's tolerance to CKD therapy, and level of frailty

Table 2 Differences in nephroprevention targets (estimative) between chronic kidney disease (CKD) and senescent nephropathy (SN) patients

Nephroprevention targets	CKD in fit elderly	CKD in frail elderly (SN)
Diet	Low sodium Low protein	Normal sodium Normal protein
Hemoglobin (g/dl)	11	11.5–12
Glycated hemoglobin (HbA_{1C}) (g/dl)	< 7%	7.5–8.5
Blood pressure (mmHg)	≤ 130–80	≤ 140/150–80 Diastolic < 60
Proteinuria (g/day)	< 0.5 g/day	< 1 g/day

Conclusion

Even though the nephroprevention strategies are similar between young adult and senior chronic kidney disease patients, standard therapeutic targets should be adjusted to very old and frail elderly individuals. Additionally, the diagnosis of senescent nephropathy in this population implies the need for prescribing anti-frailty interventions to slow patient's functional decline, hospitalization and mortality.

Compliance with ethical standards

Conflict of interest All the authors declare that they have no conflict of interest.

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