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Caring for older people with chronic kidney disease—*primum non nocere*

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Screening people at risk for chronic kidney disease (CKD) in the community is increasingly recommended in order to slow the progression towards kidney failure. Algorithms have been developed for grading the risk of progression and referral to a specialist nephrology clinic [1]. These algorithms are based on the Kidney Disease: Improving Global Outcomes definitions using glomerular filtration rate (GFR) and albuminuria categories to evaluate the risk of progression [2]. Despite the fact that the number of nephrologists is limited, timely referral to a specialist clinic is an important part of adequate nephrology care as well as having positive implications for healthcare.

AGEING POPULATION

In the developed countries, the proportion of the population defined as old is growing. Many remain healthy for the better part of their lives, but there are a considerable number of people who are frail and suffer from several comorbidities. It is not easy to define when old age starts. Most studies use 65 years as a cut-off age, i.e. after the official retirement age in most countries. This is not a particularly adequate definition from a medical point of view, as many people remain healthy well past the age of 65 years. The Prepare for Kidney Care study, presented by Murphy *et al.* [3] in this issue, defines old age as 65–79 years of age with some degree of disability or ≥80 years. In order to allocate resources to where they are most useful, it is important to be able to distinguish between the effects of normal or healthy ageing and the effects of disease on the kidneys.

THE AGEING KIDNEY

There is a growing consensus among nephrologists that the decline in GFR usually observed with age is a sign of normal ageing rather than of disease. Delanaye *et al.* [4] propose that, given that there are no markers of kidney injury, including no albuminuria, an estimated GFR (eGFR) >45 mL/min/1.73 m^2 in people >65 years of age should not be classified as CKD. They show that mortality only starts to increase in these older age groups once eGFR is <45 mL/min/1.73 m^2. In a recent cross-sectional meta-analysis in a European population using measured GFR (mGFR), healthy ageing was associated with a higher mGFR compared with unhealthy ageing. However, mGFR was lower in healthy older people compared with healthy middle-aged people, suggesting that healthy ageing is not associated with preserved GFR [5].

CLINICAL CONSEQUENCES OF CKD IN OLDER PEOPLE

For older people with an eGFR >45 mL/min/1.73 m^2 without signs of kidney damage, some might say that the diagnosis of CKD could be deemed academic. But most would agree that there are clinical and healthcare consequences irrespective of age for people with an eGFR <45 mL/min/1.73 m^2. To address this issue, the European Renal Best Practice Guideline (ERBG) group developed a guideline to assist in the care of people >65 years of age with an eGFR <45 mL/min/1.73 m^2 [6]. An algorithm with a proposed pathway for shared decision-making in the management of older people was constructed based on the risk of progression to kidney failure, risk of death and frailty [7]. To date, >50% of all European patients on maintenance dialysis treatment are ≥65 years of age [8].

LOW CLEARANCE, PRE-DIALYSIS OR TRANSITION CLINICS

Many nephrology departments have specialized clinics for patients with CKD Stages 4 and 5 separate from those with an eGFR <20 mL/min/1.73 m^2. These clinics have a variety of names, including low clearance, pre-dialysis or transition clinics. I will use the term low clearance clinic, as it is descriptive of patients' uraemic status involving the complex therapeutic, preparatory and psychosocial needs of advanced CKD rather than pointing to a future direction of care. The traditional focus of the low clearance clinic has been pre-dialytic, i.e. on making the transition to kidney replacement therapy as smooth as possible.

Due to the complexity of the uraemic state, a multiprofessional and multidisciplinary approach is required. Initially, preparation and planning for kidney replacement therapy, including patient education and ensuring timely dialysis access surgery, were the main objectives. Subsequently the aims have expanded to comprise treatment targeting the slowing of the rate of uraemia progression in order to avoid or postpone dialysis for as long as possible and alleviating uraemic symptoms. Thus blood pressure control with a reduction in albuminuria, treatment of metabolic acidosis, protein-restricted diet together with other dietary adaptations, appropriate medication, exercise training and psychosocial support are all integrated into the objectives of the low clearance clinic. Currently, supportive care and palliative care have become recognized and feasible options for certain patients and integrated into the responsibilities of the low clearance clinic. However, this specialized and complex care is still undervalued by reimbursement systems.

EXISTENTIAL CRISIS WHEN FACED WITH KIDNEY FAILURE

Shared decision-making regarding therapy for kidney failure is a primary goal of the low clearance clinic. In a well-functioning clinic, there is close cooperation between the patient, the nephrologist and the renal failure nurse, as well as the patient's next of kin.

The first step towards shared decision-making regarding future therapy is for the patient to become aware of and accept the reality and the consequences of kidney failure. This insight usually triggers an existential crisis. Most patients are well able to solve this crisis with the help of their next of kin, some will find it helpful to talk to their nephrologist and/or renal failure nurse and some will need extra support from a clinical social worker or psychologist. Once the crisis is resolved, the patient is able to take in the necessary information concerning available therapies, risks and benefits and make an informed decision. The type of treatment and the patient's attitude towards the different options are dependent in part on where they are situated on the trajectory of life and in part on their philosophical attitude. In the old and frail, choosing supportive care can be a feasible option.

TIMELY REFERRAL

Early referral enables timely decision-making and allows for suitable dialysis access preparation before dialysis initiation. There is overwhelming evidence that this slows the progression of uraemia, reduces the number of in-hospital days around initiation of dialysis, decreases mortality and increases patient-reported quality of life after starting dialysis [9–12]. In a recent review, Evans and Lopau discussed the timing factor [13]. In general, early referral is categorized as at least 3–6 months prior to dialysis initiation. However, this period of time is too short to implement treatment for slowing progression rate. It can be too short to assess which patients will need kidney replacement therapy within 12 months and may not give patients enough time to make an initiated decision concerning their choice of therapy once they reach kidney failure. This poses a pivotal question concerning when patients should be referred to a specialist in nephrology. What is optimal referral time?

HOME-BASED OR INSTITUTIONAL DIALYSIS

Due to a strong awareness of the importance of timely planning, there is a marked focus on kidney replacement therapy in most low clearance clinics. For those who are eligible, a primary goal is to prepare the patient for a pre-emptive renal transplantation if there is a living donor available. A secondary goal is to encourage home dialysis. Choosing a home-based dialysis therapy is more common in patients who have participated in multiprofessional pre-dialysis education and reduces hospital stays and even mortality after dialysis initiation [14].

Home-based therapies are still not common in Europe. An important contributing factor is probably that institutional haemodialysis is favoured by most remuneration systems while home dialysis often receives a low rate of reimbursement. Only 13% of incident patients receiving dialysis at Day 91 after dialysis initiation, reported in the ERA-EDTA registry, were treated with peritoneal dialysis (PD) [8]. In the UK, 20% of all incident patients on dialysis start with PD [15], in Sweden, 35% have PD as their initial dialysis treatment [16]. In Sweden, ~15% of all patients treated with PD have assisted PD in their homes [16]. Assisted PD is usually chosen by elderly and frail people, who find visiting the dialysis clinic 3 times per week too arduous, who for medical reasons are deemed not to fare well on haemodialysis or who are not able to manage PD on their own. In Sweden, most municipalities will provide assisted PD in a patient's home, meaning that an assistant nurse will visit them 4 times a day to change the PD bags. Most patients on assisted PD appreciate the symptom alleviation and this form of treatment.

SUBOPTIMAL INITIATION OF DIALYSIS

There has fittingly been much focus on late referral as a negative factor, but there are other factors that also need to be taken into account. A recent multicentre observational study from nephrology clinics in the Scandinavian and Baltic countries reported that 40% of the patients included in the study had a suboptimal dialysis initiation [17]. The main reasons for this were acute progression of chronic uraemia (36% of all suboptimal initiations), acute uraemia (21%), late referral (12%), delayed planning (10%) and patient non-concordance (9%). A late referral was classified as <3 months before dialysis initiation and comprised 21% of all patients starting dialysis. Of these late referrals, 81% had a suboptimal dialysis initiation. Those patients with suboptimal initiation of dialysis had a steeper loss of eGFR during the 6 months preceding dialysis initiation compared with those with a timely dialysis initiation, showing that the level of eGFR was not a useful tool for timing dialysis requirement. In fact, the level of eGFR when dialysis information was given and planning for dialysis was started was similar for those patients who received timely dialysis initiation compared with those who had a suboptimal dialysis initiation. Patients

with suboptimal dialysis initiation suffered from hypoalbuminaemia and a high number of comorbidities [17].

APPLICABILITY OF RISK EQUATIONS

The ERBG for older people with an eGFR <45 mL/min/1.73 m^2 recommends using the Kidney Failure Risk Equation (KFRE) to find patients at risk for a high progression rate [6, 7]. Patients at risk for rapid progression of uraemia need to be referred at an earlier stage in order to prepare for the therapy of their choice after the onset of kidney failure.

In a recent observational study, Hallan *et al.* [18] applied the KFRE equation to a Norwegian population with an eGFR <45 mL/min/1.73 m^2 and >65 years of age. They found that over a 5-year period there was a good fit between the risk prediction of the KFRE equation and the observed progression to kidney failure. However, the number who progressed to kidney failure after 5 years was small, comprising a total of 42 of 1188 patients studied.

The ERBG for older people emphasizes that the risk of death before reaching kidney failure should also be taken into account when planning for kidney care in the elderly population. In a European population from Italy, the risk of death was higher than the risk of kidney failure for people >65 years of age with an eGFR <35 mL/min/1.73 m^2. Conversely, and independent of eGFR, the risk of kidney failure compared with death was higher for people <60 years of age [19].

Hallan *et al.* [18] applied an equation for older people called the Bansal equation in the ERBG and the Mortality Risk Equation for Kidney Disease (MREK) in their study. The MREK slightly underestimated mortality risk in people at lower risk due to a non-linear regression curve. They found that the 5-year average for death was 10-fold higher than the risk of kidney failure. However, for the small proportion of individuals who had a higher risk of kidney failure than death, the majority did in fact progress to kidney failure before dying. To complicate matters, kidney failure was much less frequent than death in all eGFR categories, except for those with an eGFR <15 mL/min/1.73 m^2 at baseline. For these patients with CKD Stage 5, approximately two-thirds progressed to kidney failure before death [18]. Thus, although useful on a population level, using an equation when facing an individual patient with an eGFR <15 mL/min/1.73 m^2 is not always straightforward. To conclude, these findings emphasize the importance of shared decision-making, taking available evidence of the various treatment options into account.

NEPHROLOGISTS' DILEMMA

In daily clinical practice, nephrologists are faced with how to best advise an elderly, frail and multimorbid patient with CKD Stage 4 or 5 concerning the choice of dialysis or supportive care. Despite the existence of well-constructed guidelines and evidence from observational studies, there is still a fear that a recommendation is not based on solid science. How to best adhere to *primum non nocere*?

PREPARE FOR KIDNEY CARE STUDY—A RANDOMIZED CONTROLLED STUDY IN OLDER PEOPLE

In this issue of *Nephrology Dialysis and Transplantation*, Murphy *et al.* [3] present an ongoing randomized controlled trial called the Prepare for Kidney Care study. Their aim is to provide solid evidence by constructing a randomized controlled trial to address the question of best practice in the treatment of frail and elderly patients with kidney failure. The Prepare for Kidney Care trial randomizes patients with an eGFR <15 mL/min/1.73 m^2 who are 65–79 years of age and have a World Health Organization performance status of 3+ or a Davies comorbidity score of 2+ or are ≥80 years of age to either preparation for dialysis or preparation for supportive management. The overall aim is to establish the effectiveness and cost-effectiveness between the two treatment arms in relation to quality and length of life in multimorbid, frail, older people with kidney failure. The primary outcome is the mean number of quality-adjusted life years observed in the two arms. There are secondary outcomes, which comprise survival-related, patient-reported outcome-related, physical functioning, relative-/caregiver- reported and health economic outcomes. The researchers have integrated qualitative and mixed methods throughout the trial to optimize its design and delivery. They also plan linkage to existing national healthcare databases in order to follow up commencement of dialysis, hospital admissions, date and cause of death [20].

This is a challenging, courageous and difficult study to perform. When completed, it should be able to provide new knowledge and address some important questions for people with kidney failure and the nephrology community.

CONFLICT OF INTEREST STATEMENT

None declared. This article has not been published previously in whole or part.

(See related article by Murphy *et al.* The Prepare for Kidney Care Study: prepare for renal dialysis versus responsive management in advanced chronic kidney disease. *Nephrol Dial Transplant* 2021; 36: 975–982)

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Striking new path(way)s—how a conceptual model of patient outcomes can help us advance outcomes that matter to patients

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In the field of nephrology there is a constant drive to improve therapies for patients, e.g. chronic kidney replacement therapy modalities. The establishment of haemodiafiltration (HDF) with its proven additional solute removal, has been one of the important advancements of the past decades [1]. While evidence is available that proves the superiority of HDF compared with haemodialysis (HD) in terms of clinical outcomes, i.e. blood values [2], the superiority in terms of mortality as one of the most important outcomes is still debated [3]. Moreover, evidence regarding the superiority of HDF related to outcomes that matter to patients is still scarce [4].

One important step taken by the Standardised Outcomes in Nephrology (SONG) Initiative is the development of an outcome set for HD using a multistakeholder approach, defining what outcomes (core outcomes, middle tier and outer tier) are important and thus should be measured in clinical trials [5]. Besides fatigue, as a critically important core outcome, mobility, as a sub-domain of physical functioning, has been identified as an important outcome for stakeholder groups [5]. Both outcomes are negatively correlated, i.e. with an increasing level of fatigue, physical functioning decreases [6]. One aspect of fatigue frequently reported by patients undergoing maintenance kidney replacement therapy is post-dialysis fatigue, resulting in hours of resting after dialysis and thus being physically inactive, which in turn increases general levels of fatigue. General fatigue is a core outcome for all stakeholders, while mobility and post-dialysis fatigue have been found to be critical only to some stakeholders in SONG and are therefore recommended to be reported in specific trials only [5].

These specific outcomes were reflected regarding online HDF and health-related quality of life (HRQOL) in the article by Pecoits-Filho *et al.* [7] published in this issue. They conducted a randomized controlled trial to investigate if HDF improves and preserves physical activity. The secondary