



EDITORIAL COMMENT

Improved nephrology referral of chronic kidney disease patients: potential role of smartphone apps

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ABSTRACT

In chronic kidney disease (CKD), referral to nephrology is based on Kidney Disease: Improving Global Outcomes 2012 guidelines and is generally indicated when the estimated glomerular filtration rate (eGFR) is <30 mL/min/1.73 m² or when there is a rapid decline of eGFR, elevated urinary albumin:creatinine ratio (>300 mg/g) or other 'alert' signs such as the presence of urinary red blood cell casts. Since eGFR declines with ageing in otherwise healthy individuals, we propose that the eGFR threshold for nephrology referral should be adjusted according to age. According to current recommendations, young patients without rapidly progressing CKD are referred more often to nephrology when CKD is more severe, compared with age-matched controls with normal eGFRs, than elderly CKD patients. In this commentary, we discuss the age factor and other specific situations not considered in current guidelines for nephrology referral of CKD patients.

Keywords: chronic kidney disease, nephrology referral, phone application, smartphone app

WHAT ARE THE CURRENT CRITERIA FOR NEPHROLOGY REFERRAL OF CKD PATIENTS?

Patients are considered to be correctly referred to nephrology when any of the following criteria are met, according to current Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guidelines [1]: estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m², a consistent finding of A3 albuminuria [urinary albumin:creatinine ratio (UACR) >300 mg/g], abrupt or progressive deterioration of kidney function, concurrent resistant hypertension and chronic kidney disease (CKD), presence of urinary red blood cell casts, persistent serum potassium abnormalities, CKD-associated anaemia and suspicion of hereditary CKD or polycystic kidney disease or the presence of recurrent/extensive nephrolithiasis (Table 1).

THE 'AGE FACTOR' IN CKD AND NEPHROLOGY REFERRAL

Surprisingly, based on the current criteria for referral to nephrology, a 20- or 50-year-old male with CKD and a stable serum creatinine level of 1.9 mg/dL and UACR of 290 mg/g (CKD categories G3a A2 and G3b A2, respectively) does not meet the criteria for referral to nephrology, whereas a 70-year-old woman with a serum creatinine level of 1.9 mg/dL and similar UACR (CKD category G4 A2) does. Additionally, a young 20-year-old woman with a serum creatinine level of 2.2 mg/dL and UACR of 290 mg/g (CKD category G3b A2) would not be referred to the nephrologist. Thus, according to current guidelines, younger patients, who have a long life ahead of them during which CKD may continue to progress to eventually reach end-stage renal disease,

Received: 25.4.2019. Editorial decision: 7.8.2019

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Table 1. Current criteria of nephrology referral in CKD (KDIGO 2012) [1]

Criteria
AKI with abrupt sustained decrease in GFR
GFR <30 mL/min/1.73 m ² (GFR categories G4–G5)
A consistent finding of significant albuminuria (ACR ≥300 mg/g or AER ≥300 mg/24 h, approximately equivalent to PCR ≥500 mg/g or PER ≥500 mg/24 h)
Progression of CKD
Urinary red cell casts, RBC >20 per high-power field sustained and not readily explained
CKD and hypertension refractory to treatment with four or more antihypertensive agents
Persistent abnormalities of serum potassium level
Recurrent or extensive nephrolithiasis
Hereditary kidney disease

ACR, albumin:creatinine ratio; AER, albumin excretion rate; PCR, protein:creatinine ratio; PER, protein excretion rate; RBC, red blood cell.

will not be referred to nephrology until the disease has reached a very advanced stage, thus depriving these patients of a specialist-driven diagnostic workup and/or early intervention. In our opinion, young patients with CKD, in whom a potentially treatable cause is more often found, cannot be equated to elderly patients in whom a cause is less often apparent, as the latter may represent patients with a lower range of age-associated loss of GFR. We believe that younger patients should be referred to nephrology in earlier stages of CKD rather than waiting until eGFR is <30 mL/min/1.73 m².

In non-albuminuric diabetic nephropathy, the factors responsible for progressive GFR decline are not fully understood. Patients with diabetes mellitus may have only a mild decrease in eGFR and UACR of <300 mg/g, which could delay referral to nephrology while kidney disease may be progressing [2]. Novel antidiabetic drugs, such as sodium–glucose cotransporter 2 inhibitors, reduce the risk of CKD progression in type 2 diabetes mellitus (T2DM) [3–5] and are particularly indicated for young T2DM patients, in whom they also reduce cardiovascular morbidity and mortality [6]. At present, these drugs are contraindicated in CKD category G4 [7], so late referral to nephrology may deprive CKD G4 patients of this nephroprotective intervention. Another example highlighting the importance of the ‘age factor’ in nephrology referral is young patients with CKD without a diagnosis (i.e. those who are not referred according to current criteria or whose diagnosis is delayed) could benefit from nephrological evaluation to determine the aetiology of CKD, thereby slowing its progression.

Landmark studies by Davies and Shock [8] demonstrated that in healthy non-CKD patients, GFR, based on inulin clearance, decreases with age. Normal GFR at age 30 years is 122 mL/min and at age 89 years is 65 mL/min. According to current criteria, referral to nephrology is made when eGFR is <30 mL/min/1.73 m². This means that CKD has reached relatively more severe stages at the time of referral in young than in elderly patients when compared with controls of similar ages (Figure 1). In our opinion, younger patients with CKD should be referred earlier to nephrology to assess whether therapy could slow CKD progression, and this issue could be considered in future guidelines. We propose referral to nephrology for patients <40 years of age when eGFR is <60 mL/min/1.73 m² and for those 40–60 years of age when eGFR is <45 mL/min/1.73 m², and to continue with the current criteria

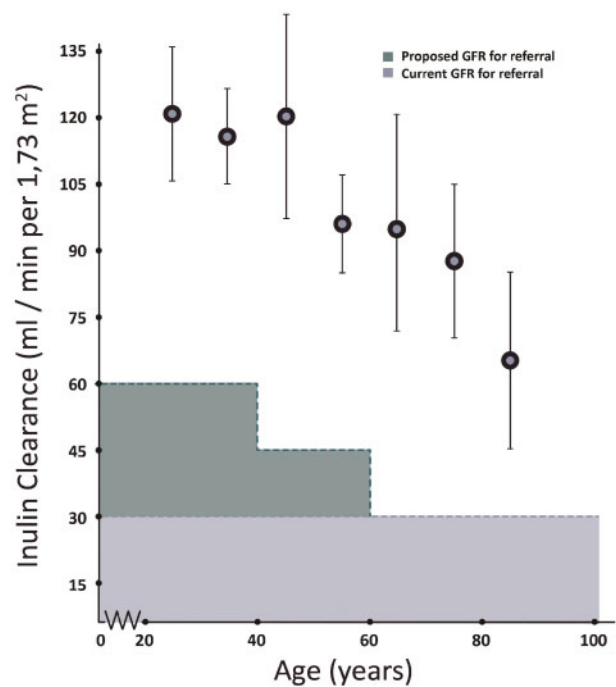


FIGURE 1: Normal age-related changes in GFR assessed by inulin clearance in the landmark studies by Davies and Shock [8]. Considering GFR as the reason for nephrology referral, current criteria, according to KDIGO guidelines, require eGFR of <30 mL/min/1.73 m² for referral in stable CKD patients. However, the relative loss of eGFR, compared with healthy age-matched controls, that would warrant referral is greater in young than in elderly CKD patients. We suggest adjusting eGFR thresholds for nephrology referral in younger individuals, which would match the relative loss of eGFR versus age-matched controls in current recommendations for elderly CKD patients. We propose new eGFR thresholds of <45 mL/min/1.73 m² for patients 40–60 years of age and <60 mL/min/1.73 m² for those <40 years of age.

for patients >60 years of age, that is, referral when eGFR is <30 mL/min/1.73 m² (Table 2).

OTHER SPECIFIC SITUATIONS IN WHICH TO CONSIDER EARLY REFERRAL IN CKD

Although considered safe, the long-term outcomes of nephrectomy for living kidney donors are not well understood. Living kidney donation, and thus nephrectomy, is associated with an increased risk of end-stage renal disease, as well as pre-eclampsia in female donors [9]. Removal of a kidney in patients with renal cell carcinoma may cause acute kidney injury (AKI) because of pre-existing kidney disease or decreased renal functional reserve. One-third of patients without CKD (eGFR ≥60 mL/min/1.73 m²) develop AKI after radical nephrectomy, which is associated with an increased risk of new-onset CKD at 1 year after surgery [10]. Patients with nephrectomy or kidney donors could benefit from early referral to nephrology. Early referral for loss of nephron mass could be particularly indicated for obese patients and those with hypertension or other cardiovascular risk factors, although this warrants research in prospective studies.

Patients with renal disorders such as tubulointerstitial nephritis of rheumatic causes characteristically can have low albuminuria and a mildly decreased eGFR [11], which can go unnoticed based on current referral criteria. The presence of CKD with extrarenal symptoms, such as uveitis, tubular proteinuria (that can be very low) or leucocyturia without bacteriuria, can guide the diagnostic workup to tubulointerstitial

Table 2. Proposed criteria for referral to nephrology in CKD

Criteria
AKI with abrupt sustained decrease in GFR
GFR <30 mL/min/1.73 m² (GFR categories G4–G5) for age >60 years
GFR <45 mL/min/1.73 m² (GFR categories G3b–G5) for age 40–60 years
GFR <60 mL/min/1.73 m² (GFR categories G3a–G5) for age <40 years
A consistent finding of significant albuminuria (ACR ≥300 mg/g or AER ≥300 mg/24 h, approximately equivalent to PCR ≥500 mg/g or PER ≥500 mg/24 h)
Progression of CKD
Urinary red cell casts, RBC >20 per high-power field sustained and not readily explained
CKD and hypertension refractory to treatment with four or more antihypertensive agents
Persistent abnormalities of serum potassium level
Recurrent or extensive nephrolithiasis
Hereditary kidney disease
Sterile pyuria with suspicion of tubulointerstitial nephritis
Nephrectomy or single kidney (specially in obese or hypertensive patients and patients with cardiovascular risk factors)

Changes proposed are highlighted in bold.

ACR, albumin:creatinine ratio; AER, albumin excretion rate; PCR, protein:creatinine ratio; PER, protein excretion rate; RBC, red blood cell.

nephritis. Suspected tubulointerstitial nephritis could also be considered as one of the criteria for early referral to nephrology.

WHAT IS NEFROCONSULTOR?

NefroConsultor is a software for smartphones (Figure 2), available in the App Store and on Google Play, based on the Spanish Society of Nephrology (SENEFRO) referral criteria to nephrology, which in turn are based on the KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease [1]. This app may be used as a decision-making tool for nephrology referral according to national and international guidelines. The app collects data on age, gender, serum creatinine level, UACR and race, as well as 'other reasons' for referral, featured in the current referral criteria (Table 1). Based on these data, the software indicates whether patients meet SENEFRO and KDIGO criteria for nephrology referral, as recently reported in the *Clinical Kidney Journal* (CKJ) [12]. In this CKJ report, NefroConsultor improved the rate of adequate referrals to nephrology by 28%. Interestingly, use of the app increased the rate of 'proteinuria' being cited as the reason for referral, as well as the number of referrals that also included urinalysis results and data on albuminuria at the time of referral. Although promising, the impact of smartphone apps used as a referral decision-making tool on outcomes should be investigated in randomized controlled trials.

CONCLUSIONS

Currently, and according to KDIGO guidelines, the decision of whether to refer CKD patients with similar serum creatinine levels to nephrology is based on age, and consequently on eGFR. Furthermore, there is delayed nephrology referral of young patients, thus depriving them of timely diagnostic workup and treatment by a specialist. In this regard, the severity of CKD and decline of eGFR upon referral is proportionally greater in young than in elderly patients as compared with healthy age-matched controls. Other particular clinical scenarios, such as loss of



FIGURE 2: The smartphone app NefroConsultor. Referral to nephrology can be impeded by numerous factors, including physicians' lack of knowledge of guideline recommendations for timing and indications of nephrology referral. Smartphone apps can overcome this hindering factor by providing user-friendly in-built calculators. Additionally, these apps allow exploration of multiple alternative patient scenarios and enable guideline developers to assess the real impact of guidelines being developed on different patient types.

nephron mass, or special situations characterized by low-grade proteinuria suggestive of tubulointerstitial nephritis could also benefit from early referral and are not included in the current criteria for referral to nephrology.

Unfortunately, referral guidelines cannot include all clinical situations. Therefore individualization and common sense should always prevail. Criteria for referral to nephrology have to be simple to facilitate the clinician's decision-making task of referring patients. Tools such as smartphone apps could complement the referral criteria and reduce the complexity for more accurate recommendations, making this decision easier for non-nephrologist clinicians, thus helping to minimize delayed referrals to nephrology.

ACKNOWLEDGEMENTS

The authors would like to thank the Spanish Society of Nephrology for endorsing this project and the NefroConsultor app.

CONFLICT OF INTEREST STATEMENT

None declared. E.O.-D., N.O.-D. and J.P. developed the app NefroConsultor, endorsed by the Spanish Society of Nephrology. The authors receive no financial gains from the app, which is available for free download on Google Play and in the App Store.

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