Port J Nephrol Hypert 2011; 25(3): 191-193
Advance Access publication 24 May 2011

Early referral: still a challenge ten years after the millennium

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Received for publication: 28/03/2011
Accepted in revised form: 18/05/2011

Key-Words:
Chronic kidney disease; early referral.

Chronic kidney disease (CKD) is a growing problem worldwide. The past few years have seen an emergent interest in evaluating the timing of nephrology referral in the predialytic stage of CKD as an important variable related to prognosis[1]. A literature review shows the definition of early referral varies from author to author and also varies from 1 to 12 months prior to commencing renal replacement therapy (RRT)[2-4]. Kinchen *et al.*[3] and recently Mendelssohn *et al.*[4] defined early referral as referral to a nephrologist more than 12 months prior to initiation of RRT. This is the definition we favour. Overall, a patient is considered to have been referred late "when management could have been improved by earlier contact with renal services"[5].

In an attempt to address the risk determined by timing of referral, a number of guidelines have been developed recommending when patients with CKD should be referred to a nephrologist[6]. The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guideline 2 (Evaluation and Treatment) recommends consultation and/or co-management with a kidney disease care team during stage 3 and referral to a nephrologist in stage 4 of CKD[7].

Other professional national guidelines from UK[8], Canada[9] and Australia[10] also recommend referral of renal patients to the nephrology unit when the GFR decreases below 30 ml/min/1.73 m^2. The UK guidelines[8], the most complete, also include 3 urgency groups and not only describe the absolute GFR level but also a change in the GFR and include other criteria, such as proteinuria, electrolytes, hypertension, anaemia and systemic illness. They also recommend that patients should be routinely referred when the GFR is below 60 ml/min/1.73m^2. We know that many patients need specialised nephrology care previously, so we agree with Tzamaloukas and Raj[11], that referral of renal patients should be done earlier, at stage 3. Furthermore, a recent survey in Canada showed that two thirds of nephrologists would prefer referral while the patients were in stage 3[12].

Potential benefits of early referral include control of blood pressure and dyslipidaemia, slowing the progression of renal disease, attention to nutrition, treatment of anaemia and correction of metabolic abnormalities in the predialysis period[1]. Anaemia and its suboptimal correction have been associated with an increased prevalence of cardiovascular disease, which induces a higher morbidity and mortality in predialysis patients and in patients undergoing RRT[13]. Partial correction of anaemia with recombinant human erythropoietin (rHuEpo) has been shown to markedly improve the general condition, sense of well-being and quality of life of predialysis patients[14], although the correction of anaemia with rHuEpo has not been associated with increased survival and delay of the progression of renal failure in controlled studies[15]. However, previous studies using a lower target haemoglobin level showed a decreased progression of renal disease[14,16].

In terms of nutritional status and other systemic consequences of CKD, an early referral allows a better

control of the mineral abnormalities in the predialysis period and also nutritional support and advice by a dietician.

Regarding the major cause of morbidity and mortality, cardiovascular disease, an early intervention in cardiovascular risk factors such as hypertension, dislipidaemia and bone and mineral abnormalities will allow a decrease in the morbidity and mortality of kidney disease patients. Recently we showed the benefit of treating patients with statins and vitamin D in the predialysis period[17]. Moreover, timely measures such as smoking cessation, salt restriction and blood glucose level control will influence the morbidity and mortality of CKD patients.

Also, it is unarguable that earlier referral allows more time to prepare individuals for dialysis. Patients have additional time to choose the treatment modality and have earlier evaluation for transplantation[18]. Early referral also allows timely placement of a long-term vascular access, which correlates with the outcome of dialysis patients[19]. It has been shown that patients with arteriovenous fistula and referred in a timely fashion survived longer after initiation of dialysis treatment[20].

Despite the known advantages of early referral, 25% to 50% of patients worldwide who commence RRT are still referred late to a nephrology unit[6].

There is some inconsistency in reports examining factors that determine the timing of referral. However, late referral can be related to the kidney disease itself (asymptomatic or rapidly progressive), to the patient (denial, socioeconomic issues, comorbidities), to the doctors (training and lack of communication between general practitioners and nephrologists) or to the Medical Health Service[6]. The type of insurance is clearly related with the quality of medical assistance in the USA. Uninsured patients compared with those with insurance[3], and patients covered by health care maintenance organisations when compared with those covered by Medicaid[21] are referred later to nephrologists.

Consequences of late referral include increased morbidity and mortality, increased cost and duration of hospital stay, more temporary vascular access, increased need for urgent dialysis, suboptimal management of end-stage renal disease and its systemic consequences and reduced access to renal transplantation services[6].

In addition, timely referral to a nephrologist is associated with lower morbidity[22] and mortality on the initial[23] and long-term outcome of chronic dialysis patients[24]. The benefit of early referral on the mortality of dialysis patients seems irrespective of the presence of diabetes or older age[25].

In conclusion, timely referral to nephrology reduces mortality and morbidity related to chronic kidney disease, both in the short and long term.

However, the goal of earlier referral to a nephrologist is not yet achieved. In this respect, there are still a number of approaches that we can use. These include medical education, improved communication between the general practitioners and the nephrologists facilitating the access to the nephrology service, and adherence to the guidelines. Also, in our opinion, an outpatient "low-clearance" clinic with a multidisciplinary team (nephrologist, nurse, nutritionist and social worker), is of great importance, providing patients with information and preparing patients for RRT, focussing on CKD and all the systemic abnormalities that are invariably present.

To achieve the goal of a timely and appropriate referral to the nephrologist, much remains to be done, and surely this will save, not spend resources.

Conflict of interest statement. None declared.

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