



## End-stage renal disease

### *Timely, appropriate treatment is crucial*

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All patients with end-stage renal disease (ESRD) deserve access to the life-sustaining therapies now available for treating kidney failure: dialysis and renal transplant. A country that holds equity as a principle of its health care system must ensure that timely, appropriate referral for ESRD therapy is accessible to those who can benefit, so that informed decisions can be made about which therapy, if any, patients choose for this severe condition. The authors of the clinical practice guideline published in abbreviation in this issue (page 661) have this need in mind. These guidelines state that physicians must check:

... for any newly discovered increase in serum creatinine to determine whether it is stable or rising progressively. If rising, then this is an urgent (not elective) referral. One possible caveat is that patients with known stable mild renal insufficiency documented with serial creatinine tests over a few years, especially if dipstick testing shows no hematuria or proteinuria, may be followed carefully, with particular attention to serial monitoring of blood pressure, protein excretion rate, and kidney function, without referral.

This guideline is very reasonable and is most likely already being followed in primary care. For example, a survey of Ontario family physicians by Mendelssohn et al<sup>1</sup> showed that only 2.5% of family physicians would not refer a patient with a creatinine level greater than 300 µmol/L. What is perhaps not recognized by the authors of this guideline is that most increases in serum creatinine levels in primary care fall into the “exception” situation where referral is not needed. Most elevations are either transient and due to reversible factors, such as medication use, transient disease, or dehydration, or they are “known stable mild renal insufficiency documented with serial creatinine tests over a few years.”

#### **More research is needed**

To compound the problem, no data are available on the true prevalence of elevated creatinine levels, nor of the natural history of individuals who have marginally elevated levels. For example, more men than women are consistently diagnosed with ESRD, yet there are no population studies available on the prevalence of elevated creatinine levels in men compared with women to indicate whether sex differences in prevalence are a result of an underlying natural prevalence or an artificial result due to differences in the way men and women are

treated by a health care system. Research is greatly needed on the natural history of elevated creatinine levels in primary care. The authors of the guideline do not give any information on this topic, and we were unable to find anything in the literature.

What proportion is transient and reverts to normal? What proportion is chronic and stable and needs only monitoring? What proportion needs referral? The authors of the guideline seem to believe that most are progressive and require referral, yet any seasoned family physician knows these patients are in the minority. More objective evidence than our opinion is needed.

In Canada, family physicians are trained to deal with the various situations that lead to transient reversible causes of elevated creatinine levels. They are able to monitor and follow and refer at the appropriate time, if at all, those patients with chronic, stable elevated creatinine levels. The guideline should stress that family physicians need to be educated on the importance of dealing with early reversible causes of mild elevations in serum creatinine levels; on the importance of monitoring chronic, stable situations; and on recognizing situations where referral is needed. Saying that we should refer everyone with a creatinine level above 120 µmol/L with one exception is not useful because that exception constitutes most of what we see.

#### **When is referral a must?**

We agree with the authors of the guidelines that late referrals for dialysis are disadvantageous to patients and that situation should be avoided whenever possible.<sup>2</sup> Those referred just before needing dialysis do not do as well as those referred early. What evidence is there of a problem in delayed referral for ESRD? Incidence and prevalence rates of ESRD vary markedly by country, with richer countries having higher rates than poorer countries. It is likely, therefore, that underdiagnosis and underreferral for ESRD both contribute to the variation in rates. However, no studies indicate which parts of the system are more of a problem. Are low rates of therapy for ESRD in poorer countries a result of limitations in the primary care system either in initial diagnosis or delay in referral, or are they the result of few resources available to treat ESRD, and a subsequent self-imposed limitation on referral by primary care practitioners?

### Circumstances of referral

The issue of late or lack of referral of patients with ESRD, discussed in detail in the guidelines, is not the same as “what are the circumstances under which a patient with an elevated serum creatinine level should be referred?” If a person has ESRD, it is already too late, and the patient should have been referred long ago—providing the patient would agree to the referral. Certain criteria need to be met before a referral is made from primary care to secondary or tertiary care.

- The patient must agree to the referral.
- The referring physician should have the skill or facilities to diagnose or manage the condition better than the primary care physician.
- The patient should benefit from the referral because the disease will progress if it is not made but will be curtailed or cured if the referral is made.

The first criterion is based on an informed decision made by patients. Criteria 2 and 3 are met for acute or chronic progressive creatinine elevations but are not true for transient or chronic, stable situations.

Many possible reasons exist for late referral: diagnosis might not have been made until late in the course of the disease; the physician or patient might have chosen to delay referral; or the patient might not have agreed to referral until he or she was feeling ill.

Further, it is unknown whether delays in diagnosing ESRD are due to delay in diagnosis in the first instance at the primary care level, or due to delay in referral to nephrologists, although likely both occur. The studies cited in the guidelines to support the notion that family physicians delay referral are unable to distinguish between delays in diagnosis of elevated creatinine levels by family physicians or delays in referral. Even the prospective study cited suffers from this limitation.<sup>1</sup> Why would family physicians choose not to refer patients with rising creatinine levels? Patients might demur because of barriers, such as distance, family responsibilities, or other more pressing problems. The wait to see a nephrologist might be a disincentive, as the number of nephrologists in Canada is low compared with the potential demand for their services. Family physicians might choose to wait and see whether other conditions explain the rise in creatinine levels.

One possible explanation for the responses to surveys about the levels at which patients should be referred is a difference in perception. The nephrologists conducting the surveys are asking questions about what they see as the most

common cause for elevation of creatinine levels, chronic progressive renal disease, while the primary care physicians are answering in terms of what they see as the most common causes of elevated creatinine levels: transient or stable disease. Family physicians should continue to remind patients of their options, take into account patients' wishes, and make a decision about referral.

These new guidelines lack information about the natural history of elevated creatinine levels, including knowledge of what the true prevalence of ESRD is. They also fail to acknowledge the role family physicians can play in optimizing therapy for comorbid conditions, such as atherosclerosis and diabetes; referral to nephrology for management of these conditions is an inappropriate use of scarce resources.

### Benefits from early referral

The guidelines fail to acknowledge that delaying referral could reflect a late diagnosis at the primary care level, because of either patient or physician factors, rather than a conscious decision against referral.

These guidelines do, however, emphasize the improvement in morbidity and mortality that dialysis and transplant can bring to patients of any age, either sex, all races, and all socioeconomic conditions in Canada. They remind us of how important early referral of rapidly progressive disease is and inform us of the time required for optimal preparation for ESRD therapies. Some of this work can be done by family physicians and some, such as initiating erythropoietin therapy, by nephrologists. Together we can work toward early identification of patients with developing ESRD who will benefit from intervention, and together we can advocate for the resources required to support such patients. ♦

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