Elevated levels of serum creatinine

Guidelines for management and referral

Canadian Society of Nephrology

A paradigm shift in management of progressive renal failure before dialysis has taken place. We now realize that it is necessary to:

- identify and treat reversible causes of renal failure, thereby preventing some cases of end-stage renal disease (ESRD);
- slow the rate of decline of progressive renal insufficiency and manage the many comorbid conditions associated with chronic renal failure; and
- facilitate efficient entry into dialysis or transplant programs of all patients who might benefit. The high mortality rate of patients using dialysis might be reduced through optimal pre-ESRD care. The best care will require close teamwork and cooperation between nephrologists and family physicians.

Working with the College of Family Physicians of Canada, the Canadian Society of Nephrology created a referral subcommittee, which has recently published guidelines endorsed by both organizations.[1] This summary is intended to highlight conclusions important to busy family physicians.

Refer patients earlier

Earlier referral of patients with elevated creatinine levels to nephrologists is expected to lead to better outcomes and lower costs for both patients and health care systems.

Late referral. Evidence suggests that late referral to nephrologists is a problem in Canada,[2] the United States, Scotland, England, France, and Brazil. Patients referred shortly before they need dialysis have higher rates of major complications, longer and more frequent hospital stays with associated increased costs, worse homeostatic parameters at the start of dialysis, suboptimal vascular access, and worse survival rates than patients referred early.

Three prospective studies have looked at multidisciplinary, intensive interventions applied to patients referred early. These studies demonstrate improved vocational outcomes, delay in onset of ESRD, better homeostatic parameters, reduced use of temporary dialysis access, and lower consumption of hospital resources.

Nonreferral. Nonreferral for dialysis is also a known problem in Canada. The incidence of ESRD in Canada is less than half that reported in the United States (Canada had 118 per million in 1997, United States 294 per million). A survey of Ontario family physicians and community internists showed that some patients are not referred for dialysis. The decision is influenced by age and comorbid disease.[2] Indeed, most physicians believed that dialysis was being rationed at the time of the survey (1994). Therefore, at least part of the reason for the difference in incidence between Canada and the United States is that many Canadian patients who could benefit from dialysis are not referred. Nonreferral has also been observed in the United Kingdom and South America.

Reasons to refer. The literature supports the notion that earlier referral has great potential to:

- affect comorbid diseases that begin in the predialysis stage;
- delay the onset of ESRD;
- improve patient survival;
- reduce use of temporary vascular access devices;
- increase use of native arteriovenous fistulae instead of inferior synthetic grafts;
- optimize biochemical, physical, and psychological state on initiation of dialysis
- improve vocational outcomes; and
- reduce health care costs.

Newly discovered renal insufficiency requires investigations

All patients with newly discovered renal insufficiency (elevated serum creatinine levels above the laboratory's pre-set upper limit [adjusted for age and height in pediatric patients]) require investigation to determine potential reversibility of disease, evaluate prognosis, and optimize care planning. Most patients with even mildly elevated

serum creatinine levels have lost about 50% of renal filtration function. Preliminary investigations to determine whether reversible factors can be identified are ultrasound and complete blood count, electrolyte, bicarbonate, urea, creatinine, calcium, phosphorus, glucose, and total protein assessment. Albumin, serum protein electrophoresis, urinalysis, and 24-hour urine sample for protein and creatinine clearance measurements should be included in the workup (**Figure 1**). A kidney biopsy can diagnose inflammatory renal disease that might be treated with immunotherapy if irreversible scarring has not yet occurred.

The upper limits of normal for serum creatinine levels for infants and children are considerably lower than for adults. The normal range of serum creatinine levels below 5 years of age is 26 to 45 μmol/L. Levels gradually increase from age 5 to adulthood.

It is important to note that elevated serum creatinine levels are not a normal feature of aging, nor is advanced age a contraindication to referral. Patients with rapidly increasing serum creatinine levels (eg, 20% increase over days, weeks, or months) require particularly urgent investigations, usually including kidney biopsy, and should be referred promptly. For this reason it is important to repeat testing for any newly discovered increase in serum creatinine levels to determine whether it is stable or rising progressively. If rising, 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.

All children with elevated serum creatinine levels should be evaluated by a pediatric nephrologist. This is required because of special issues related to growth, nutrition, bone, and metabolic disorders among children with even mild renal insufficiency.

Progressively rising serum creatinine levels

All patients with established progressively rising serum creatinine levels should be followed up by a nephrologist. Even when specific therapy for renal disease is unavailable, many nonspecific therapies can slow the rate of progression to ESRD or affect various comorbid diseases associated with progressive kidney disease (**Figure 1**). These modifiable conditions include left ventricular hypertrophy, accelerated atherosclerosis, malnutrition, renal osteodystrophy, and (in children) growth retardation. Therapeutic possibilities include blood pressure control, consideration of angiotensin-converting enzyme inhibition and other renal protective strategies, dietary modification, lipid evaluation, calcium phosphate control, anemia management with erythropoietin therapy, and (for children) recombinant human growth hormone (rhGH). A detailed, recent review for family physicians on this subject has been published.[3]

Preparation for dialysis or transplantation

Adequate preparation for dialysis or transplantation requires at least 12 months of relatively frequent contact with a renal care team. Many tasks must be completed to prepare patients for a lifetime of renal replacement therapy. A year of relatively frequent visits will allow time to provide adequate education about dialysis and transplantation, to help patients choose the most suitable ESRD treatment, to plan elective dialysis access, and to plan efficient entry into a dialysis program for those who choose that option (**Figure 1**). For example, recent guidelines stress that native arteriovenous fistulae are superior to all other access for hemodialysis. Because they take many months to mature, they should be created 1 year before anticipated need. Some patients can consider living donor transplants, and transplant can pre-empt the need for dialysis. To accomplish these goals, referral should occur, at the latest, when the serum creatinine level is 300 μmol/L or higher (or when creatinine clearance is below 30 mL/min [0.5 mL/s], whichever is worse), and sooner if it is increasing rapidly.

For children, referral should occur at much lower levels of creatinine. Growth failure has been documented in children with glomerular filtration rates below 70 mL/min for every 1.73 m^2. This might be improved by sodium chloride supplementation, correction of acidosis, nutritional supplements, and rhGH treatment.

Improvements in dialysis technology mean that no technical reasons exist any longer to prevent competent, informed patients who might benefit from dialysis from being referred. For example, most elderly dialysis patients perceive their quality of life to be good, and their life expectancy is often quite reasonable. Many primary care physicians are aware that dialysis facilities' expansion in Canada has not always kept up with demonstrated need.[4] No Canadian provincial ministry of health, however, has ever called for rationing ESRD therapy. Ontario, Quebec, and British Columbia have publicly affirmed the importance of accessibility to ESRD therapy. Certainly, perceived resource constraints must not be used by physicians as an excuse to justify nonreferral of suitable dialysis candidates.

Consultation and advice

Nephrologists should provide consultation for any patients with elevated serum creatinine levels in a timely manner. In addition, they should provide advice about what parameters require particularly urgent or emergency assessment.

Nephrologists are well aware that, unfortunately, patients sometimes have to wait several months for elective consultation appointments. This is because there are only

332 practising nephrologists in Canada. A large portion of their collective time is spent caring for dialysis and transplant patients. As the number of ESRD patients increases, human resource issues are a vexing problem.

Being given an elective appointment several months away can be troublesome for patients with elevated creatinine levels. There are definite indications for urgent or emergency consultations. For example, rising creatinine levels require urgent consultation, as do newly discovered creatinine levels above 300 μmol/L.

If a timely appointment cannot be given, nephrologists should communicate information to referring physicians, setting out clearly the parameters that might create cause for alarm and obligate early assessment. The Canadian Society of Nephrology has created a fax-back sheet to alert referring physicians to these parameters.

Although rural settings pose unique challenges, distance from a nephrologist or dialysis centre is not a reason to withhold referral. Rural physicians should establish links with nephrologists, who might perform preliminary chart reviews to determine whether or when rural patients with elevated creatinine levels should travel for a formal consultation, and to give interim advice. Many rural patients, however, can be successfully accommodated with satellite-based or home hemodialysis, or home-based peritoneal dialysis.

These guidelines represent a joint initiative by family physicians and nephrologists to define a general approach to management and referral of patients with chronic renal failure. An implementation strategy has been developed in hopes that improved and more cost-effective care of these patients will ensue.

This clinical practice guideline is endorsed by the College of Family Physicians of Canada.

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Figure 1. Approach to diagnosis and treatment of patients with elevated serum creatinine levels: *Creatinine values and time course are hypothetical, for illustrative purposes only.*