Early referral and selection of peritoneal dialysis as a treatment modality

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The time of patient referral to a nephrologist in relation to residual renal function (RRF) is an important topic of discussion due to its potential impact on clinical outcome and total cost of renal replacement therapy to society. The present discussion is intended to outline the interrelation between early referral to a nephrologist, selection of dialytic modality, clinical outcomes and economic impact. Intuitively, we are prone to assume that early referral has beneficial medical and economic impact. Several recent studies also support this thesis.

The available evidence strongly suggests that early referral can improve the short- and long-term survival of uraemic patients; facilitate the management of comorbid conditions; provide the time necessary for patient education, creation of dialytic access and appropriate initiation of dialysis; help preserve adequate nutrition and biochemical parameters; reduce hospitalizations; and influence the selection of dialysis modality. Less compelling, but interesting reports also suggest that early referral may reduce the rate of progression of renal failure and the total cost associated with therapy. Cost analysis is complicated by the lack of complete data files, our inability to quantify the numerous and far reaching economic consequences of renal disease and replacement therapy on the patient and society, and the various sources of payment.

Arora et al. [1] have studied the prevalence, predictors and consequences of late nephrology referrals. Early referral was defined as a first visit to the nephrologist 4 months before initiation of dialysis. In their multivariate analysis, patients covered by health maintenance organizations were more likely to be referred late with odds ratio of 4.5 times that of patients covered by Medicare. Late referrals were more likely to suffer from hypoalbuminaemia, more severe anaemia, lower RRF at the start of dialysis and were less likely to receive erythropoietin or to have a permanent vascular access prior to dialysis.

Obrador et al. conducted an extensive analysis of the literature on the effects of early nephrological referral [2]. These data provide compelling evidence that early referral is associated with timely initiation of dialysis, an informed selection of dialysis modality, less frequent and shorter hospitalizations, better rehabilitation, lower costs, and most important, lower mortality. In addition, the long-term experience of Bonomini et al. has shown that early initiation of dialysis is associated with a 40% improvement in survival, a 35% decrease in morbidity and 24% cost savings [3]. In order to adjust for the lead time among patients starting dialysis early, these investigators compared 32 patients in the early dialysis group with 57 patients in the late start group, matching RRF, severity of comorbid factors and length of follow-up. They observed a slower rate of decline of RRF, better control of lipid profiles, glucose tolerance, bone resorption and fewer vascular calcifications among the early start group [2].

The evidence that malnutrition is a predictor of morbidity and mortality among dialysis patients is robust [3]. Various studies have demonstrated those baseline parameters reflective of malnutrition, such as hypoalbuminaemia and low body mass index, remain powerful risk factors many years after initiation of dialysis regardless of dose or other interventions. Although the precise mediators of the increased risk are not well characterized, the possibilities of progressive vascular disease or other metabolic abnormalities, mediated by cytokine activation or alternative immunological responses resulting in a chronic systemic inflammatory state has been suggested.

If indeed malnutrition is associated with advanced uraemia and carries a permanent negative prognosis,
then it is pertinent to define whether dialysis affects the nutritional status of the uraemic patient. There is extensive evidence that the decline in renal function is associated with a spontaneous reduction in protein intake and the eventual development of malnutrition in many patients and that uraemia is associated with abnormal protein metabolism [2–4]. Furthermore, it is well known that one of the first benefits of initiation of dialysis is the restoration of appetite. However, the evidence that dialysis alters or reverses malnutrition is weaker, but nonetheless available. McCusker et al. demonstrated an improvement in nutritional status 6 months after initiation of peritoneal dialysis among patients in the CANUSA Study [5]. Lindsay and Spanner also reported an increase in both protein catabolic rate and protein intake in two patients treated with peritoneal dialysis whose dose was increased or supplemented by additional haemodialytic therapy [6]. While more rigorous studies correlating initiation of dialysis with nutritional status are needed, the data suggest that a timely start of dialysis is required to prevent malnutrition, a well-established negative prognosticator among patients with renal insufficiency.

Early referral also has been shown to empower the patient to make therapeutic decisions based on pertinent information and to affect the selection of specific dialytic modalities. Many reports have indicated that early referral to a nephrologist, combined with a responsible, well-balanced presentation of all therapeutic options is associated with a higher selection of peritoneal dialysis as initial therapy [2, 7–10]. More significantly, among patients referred to a nephrologist with no specific medical indications for peritoneal or haemodialysis, after an impartial introduction to both therapies, 50% selected peritoneal dialysis [11]. The USRDS Dialysis Morbidity and Mortality Study Wave II has also shown that among patients seen by a nephrologist earlier, a higher proportion selected peritoneal dialysis and participated actively in the decision process [12]. Early referral provides the time for education before frank uraemia ensues, allows the patient to participate in choosing the modality of therapy that best suits his or her individual lifestyle and promotes self therapy, all of which should have a significant impact on quality of life and the cost of treatment.

Conceivably, early referral and adequate pre-dialytic care could influence the progression of renal insufficiency through control of arterial hypertension and fluid balance, correction of metabolic acidosis, abstention of potentially nephrotoxic drugs and dietary counselling, among others. In fact, Bergstrom et al. observed a significant reduction in the rate of progression of renal failure among patients who entered a prospective study that included monthly visits to a nephrologist as compared to less frequent monitoring during the preceding 2 years [13]. There was no dietary intervention during the study period, leading the authors to conclude that the frequency and the quality of care, including treatment of hypertension, may favourably influence the progression of renal failure. Early referral and the appropriate selection of therapeutic modality are also associated with a higher rate of rehabilitation, improved quality of life and better preservation of employment [2].

The higher rate of selection of peritoneal dialysis among patients referred earlier may have significant medical and economic consequences [14] in addition to the cost-benefit advantages of pre-dialytic education [15]. Peritoneal dialysis allows more freedom and time for education, recreation and the pursuit of gainful employment; eases the delivery of gradual increments in dose and preserves RRF better than haemodialysis [16]. The latter can reduce the initial cost of dialysis, if a gradual increment in dose is used. By reducing comorbid conditions and complications [17] through better elimination of uraemic toxins, autoregulation of arterial blood pressure and volume and by avoiding costly hospitalizations [10] and procedures associated with the creation and maintenance of vascular access, preservation of RRF further contributes to cost containment.

Despite the recent interest and general consensus that early referral and appropriate nephrologic intervention are beneficial, few if any incentives have been developed to promote this practice by governmental or private payers of health care. In fact, in the US, where the current incidence of treated end-stage renal disease is the highest in the world, exceeding 280 patients/100,000 population, as many as 75% of patients are not seen by a nephrologist until immediately before starting dialysis. In view of the many apparent advantages of early referral, why then the resistance to its adoption? The most common reasons for late referral are: advanced age of the patient, severe comorbidity, economic incentives and disincentives, lack of symptoms, delayed diagnosis and patient anxiety and refusal to see a nephrologist [2]. The study of these root causes should provide a solid framework to solve the problem. The available data in support of early referral and appropriate initiation of dialysis should stimulate a multidisciplinary effort by nephrologist, patients, private health organizations and governmental agencies to provide the education necessary to promote better referral patterns.

References
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rate is dependent upon the type and amount of treatment in dialyzed uremic patients. *Am J Kidney Dis* 1989; 13: 382–389

Fig. 1. Photomicrograph of a renal transplant removed because of chronic rejection. There is extensive intimal thickening with narrowing of the vascular lumen, glomerulosclerosis with expansion of the mesangial matrix, interstitial fibrosis, and tubular atrophy. Trichrome staining. (Courtesy Dr H. Benediktsson, Calgary, Canada.)