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Why patients with progressing kidney disease are referred late to the nephrologist: on causes and proposals for improvement

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The adverse effects arising from late referral (LR) have been reported by nephrologists over the past 20 years from several countries [1–10]: not only does LR delay the introduction of measures to attenuate the progressive loss of kidney function and prevent uraemic complications [11], but LR has also numerous short and long-term deleterious effects on clinical outcome [1–8]. The only study that did not confirm the long-term harmful effects of LR is the study of Roubicek *et al*. [12]. It appears, however, that their definition of LR was longer (4 months before dialysis), patients were younger, with less co-morbidities and relatively long hospitalization times in both patient groups, and a shorter mean survival time of the early referral group than in most other patient series.

While a recent review analyzed the relationships between LR, mortality and morbidity, and the potential positive effects of early referral [10], the present editorial comment identifies and analyzes the different causes responsible for LR and suggests some

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actions which could reduce LR and improve the outcome of patients with progressive kidney failure.

Some facts about late referral

According to Eadington, referral is late 'when management could have been improved by earlier contact with renal services' [13]. This has often been defined as referral of a patient with progressive kidney failure to a nephrologist less than 3 months before the need to start dialysis, but definitions of LR vary largely and time limits ranging between immediate dialysis and <6 months have been used [1–10,12–22].

LR usually leads to emergency dialysis for acute complications such as fluid overload, arterial hypertension, pericarditis or gastro-intestinal complications of uraemia; such dialysis is usually haemodialysis and usually requires to be undertaken with a temporary vascular access which is prone to infective and/or other complications [23]. LR has many undesirable consequences which have been reviewed in detail and are summarized in Table 1.

In several European and North-American series, and despite the different definitions, LR is frequent and varies between 30 and 64% of the patients initiating dialysis. This does not seem to have changed over the last 20 years (see Table 2).

A retrospective analysis in a single unit even showed that LR is not diminishing but may in fact increase: it occurred in 13 out of 44 consecutive new dialysis patients in 1985 (31%), and in 18 out of 44 consecutive patients (41%) 10 years later – within the same unit, the same catchment area, the same social security system and an unchanged socio-economic background [15].

Table 1. Deleterious effects of late referral to the nephrologist [1–10]

Increased mortality at short term
Increased mortality at long term
Increased morbidity
Increased costs of initial hospitalisation
Emergency dialysis and acute dialysis access
Prolonged disruption to employment
Preferential choice of center hemodialysis vs peritoneal dialysis and transplantation

Table 2. Incidence – frequency of late referral

Year of observation	Late referral[a]	Country	Source
1981	23/55 (42%)	UK	Ratcliffe *et al.* [1]
1982–1987	274/585 (47%)	USA	Campbell *et al.* [14]
1985–1986	13/44 (31%)	Switzerland	Halabi *et al.* [15]
1989–1990	195/304 (64%)	Scotland	Khan *et al.* [16]
1989–1991	65/218 (30%)	France	Jungers *et al.* [2]
1991	24/60 (40%)	Canada	Levin *et al.* [17]
1992–1997	48/153 (32%)	USA	Arora *et al.* [5]
1994–1996	91/268 (34%)	Belgium	Lameire *et al.* [4]
1995	18/44 (41%)	Switzerland	Halabi *et al.* [15]
1997–1998	96/250 (38%)	UK	Roderick *et al.* [18]
1999–2000	502 (52%)	France	Kessler *et al.* [19]
1998–2001	137/280 (49%)	Germany	Schwenger *et al.* [20]

[a]Definition of late referral varied among the different studies from <1 month to <6 months before the start of dialysis.

Reasons for late referral

At least 4 different reasons may explain why LR remains a continuing problem (see Table 3).

Disease-related reasons

In some cases, LR may be unavoidable due to the pathogenesis and mode of onset of the kidney disease, such as irreversible acute renal failure or superimposed acute on chronic kidney disease. De novo acute diseases such as rapidly progressive glomerulonephritis or systemic vasculitis may lead to referral that is unavoidably late and at the stage of irreversible kidney damage. On the other hand, some kidney diseases may progress so slowly that the development of symptoms of uraemia go almost unnoticed. Overall, such disease-related causes do not account for more than 15–20% of the presently observed LR cases [2,18].

Patient-related reasons

When a patient is faced with the diagnosis of progressive kidney disease and the prospect of (ESRD) therapy, psychological factors may play an important role: lack of understanding of the process, denial of the progressing disease state, fear of the unknown, refusal to face therapeutic implications [16,24]. The patient might even refuse the referral proposed by the primary care physician (PCP), but this

Table 3. Reasons for late referral of patients with chronic kidney disease

1. Disease-related
acute illness
super-imposed acute on chronic kidney failure
asymptomatic disease
2. Patient-related
psychological factors (denial)
co-morbid conditions
distance to the center
low socio-economic status
3. Physician-related
primary care physician related
nephrologist related
dialysis center structure related
education and communication related
4. Health care system-related
limited access to care
limited access to specialized care
effects of managed care

eventuality seems to occur only in a very small minority of cases. In contrast, co-morbid conditions, in particular, an advanced age and/or cardio-vascular disease, have been identified as playing an additional role [7,16].

The distance to the centre might also be a potential reason for LR, but in two independent studies, one concerning an inner city population [25] and another a rural population [26], the distance to the dialysis centre was not a determinant factor. In contrast, it appears that within the same Australian region, patients living within a low socio-economic status area were more often referred late [27].

Physician-related reasons

Causes related to the PCP and/or the nephrologist certainly explain a large proportion of the LR pattern.

On the one hand, kidney diseases are infrequent and complex; therefore it is difficult for each PCP to accumulate enough clinical experience for an optimal follow-up of those patients. On the other hand, the present debate on LR prevention is not to increase the workload of the nephrologist, but to improve the CKD patient care by a more integrated approach provided by a consultation network.

Primary care physician. The PCP may directly apply to his patients selection criteria for ESRD therapy: non-referral is often practiced for reasons of age and/or existing co-morbidity by the PCP [16,28,29]. This planned conservative care may then be acutely changed when the occurrence of advanced uraemia alarms the patient and/or the family.

PCPs frequently fail to appreciate the benefit derived from nephrological care prior to the start of dialysis: nephrologists are often perceived as being only concerned with the technicalities of dialysis.

There is also a lack of appreciation of the utility of a nephrological consultation during the early stages of kidney failure: since no sophisticated technical procedures are used before the initiation of dialysis, many PCPs are of the opinion that the prescription of phosphate binding agents or antihypertensive drugs can be done as well by themselves as by the nephrologist.

Of the various medical specialities with which PCPs come in contact, nephrology is relatively rare; nephrologists are much less numerous than cardiologists or gastro-enterologists, and therefore are less likely to be known on a personal and regular basis.

Finally, the fear of losing clinical responsibility for a chronic patient is an additional factor that might play an important role, particularly in countries with a high medical density, when care for chronic patients on a regular basis is a source of financial income [30].

Nephrologist. The nephrologist is also to blame: patient appointments may be fixed late, delayed or postponed; insufficient time might be devoted to the patient at the right moment; the contact with the patient and his relatives may not be satisfactory; the information or the care delivered may not be optimal; communication concerning therapeutic strategies may be non-existent or conveyed to the PCP in a useless manner; and the nephrologist might even not return the patient to the primary physician and assume with or without the nursing staff a direct and often exclusive role in the choice of the ESRF treatment modality [31].

Later, once the patient starts dialysis therapy, the PCP may continue to be informed on the clinical evolution only by the patient's family members and may often remain without any medical information from the dialysis unit.

Many of those observations are favoured by the fact that insufficient numbers of nephrologists are available, indicating again that consultation networks instead of definitive referrals should be organised (see below).

Dialysis centre-related. In a recent survey of a cohort of incident dialysis patients in 4 adjacent Alpine regions in France, Italy and Switzerland, it appeared that LR was almost identical within the three countries, but much more frequent in the large city reference centers than in the regional units in each country [32]. This observation suggests that larger nephrological teams are usually not known on a personal basis by the PCP and this factor might also favour LR. Medical plethora in the large cities could also play a role.

Furthermore, in certain countries, PCPs may be reluctant to refer patients to a service which is perceived as lacking in facilities and being under resourced.

Education and communication. Campbell *et al*. [14] have shown that 91% of PCPs felt they had not received adequate training regarding time or indications for referral of patients with progressive kidney failure.

In a survey conducted by Mendelssohn in Canada [3], 54% of general practitioners felt that rationing of dialysis was appropriate; 50% of the PCPs recommended better communication and feedback from nephrologists. Should a patient be referred to a specialist for a diagnostic and therapeutic work-up of microscopic haematuria? 79% of the PCP's responded no, for proteinuria it was 69% and for an elevation of the serum creatinine concentration between 1.4–1.7 mg%, 83% responded no. In addition, there were 60% non-responders and it would be surprising if the non-responders to the questionnaire would refer patients more readily than the responders.

In a survey of Belgian dialysis units in Flanders, Van Biesen *et al*. found that the following medical specialties accounted for LR: generalists 20% of their referred patients, internists 60%, urologists 25%, endocrinologists 35% and cardiologists 40% [33].

Those percentages should be taken with caution as the majority of patients are referred by generalists and with respect to the cardiologists, a hyper-hydrated uraemic patient might have been referred to the cardiologist instead of being sent directly to the nephrologist. Nevertheless, the Diamant Alpin study also indicated that other specialists are much more responsible for LR than generalists [32].

In Switzerland, 850–950 new patients with terminal kidney failure start dialysis each year. According to the statistics of the Swiss Medical Association, there were 9710 PCPs practicing in the country in December 2002: internal medicine 4304, diabetology 117, cardiology 402, general medicine 3262, paediatrics 932 and 693 physicians without official specialist recognition [34]. That means that one patient with terminal kidney failure is seen by a PCP at an average rate of one patient every 11 years. This frequency certainly does not allow PCPs to gain enough experience in the care of patients with progressing kidney disease.

In a recent survey conducted by the St Vincent Declaration of Nephropathy Working Group among over 7000 European specialists on the optimal first referral of diabetic patients with evidence of kidney disease, it appears that 84% of the nephrologists would like to see a patient once microalbuminuria has been established, while only 36% of the diabetologists and internists share this opinion; in contrast, when the serum creatinine is >200 umol/l, these percentages are 1 and 34%, respectively [35]. Again, since only 1124 physicians responded, it would be surprising that those who did not respond have more homogeneous opinions.

Medical plethora could be an additional factor responsible for the increasing LR pattern. While the French speaking part of Belgium has one of the highest medical densities in Europe, the LR pattern (<3 months) remained at a high 50% between 1997 and 2000 [36]. Switzerland had 1 physician/600 inhabitants in 1985, and 1/284 inhabitants in 2002; it has been a common observation in the University hospitals that during the 1970s patients with progressing kidney disease were referred as soon as an abnormal serum creatinine had been noted; during the 1980s, those patients were referred for one single nephrological consultation only, while during the 1990s, a phone call asking for advice was all that was made when a progression of kidney failure was noted.

Health care system-related reasons

Finally, the health care system per se may either favour or impede the referral pattern.

Even in Western countries, some patients of poor socio-economic status may have no or only limited access to care [16,27]. Some health care plans restrict de facto referral to specialized care or consult. In a situation of managed care, a PCP penalizes himself when he refers a chronic patient to a specialist.

Regulated or deregulated reimbursement of drugs such as prescription or delivery of erythropoeitin (EPO), biological and radiological investigations may also play a role.

Taken globally, when Jungers *et al*. [2] investigated the reasons for LR in their patients, lack of symptoms from uraemia was responsible for 18%, physician related reasons for 40% and patient non-compliance for 42% of the late referrals.

Proposals to prevent late referral

Optimal referral is early referral. It allows for early diagnostic evaluation, delays progression and prevents the development of uraemic complications [11]. Furthermore, it allows for timely interventions to control co-morbid conditions, for adequately preparing the patient for renal replacement therapy (including preservation of the veins of forearm and arm) and to start dialysis at the optimum time [37].

Recent studies have shown that the cardio-vascular risk of CKD patients is dramatically increased not only at the stage of dialysis, but even at very moderate stages of kidney failure when the GFR is still at 80 ml/min [38]. Insufficient cardio-vascular risk management during this early phase of CKD might to, a large extent, account for the current poor dialysis outcomes.

Such a sophisticated therapeutic plan needs an interwoven collaboration between PCP and nephrologists.

Improved medical education and communication

While dialysis and transplantation have been routine therapy for almost 50 years, those domains are still not taught adequately in most of the pre- and post-graduate medical education programmes.

The fact that pre-dialysis care is presently not optimal is illustrated by the two following examples. Among 155 076 incident chronic dialysis patients within the US health care financing administration between April 1995 and June 1997, the mean serum albumin (a potent indicator of patient survival on dialysis) was only 3.3 g/dl and 60% of the patients had an albumin of less than 3.5 g/dl. The mean haematocrit was 28 vol% and only 23% received EPO during the pre-dialysis phase [39]. A survey among 4333 newly dialyzed patients in Europe led to similar results: 68% of the patients had an Hb <11 g/dl at their first visit to the dialysis unit [40]. These observations clearly illustrate that the care of pre-dialysis patients needs improvement.

In addition, therapeutic interventions have been demonstrated to be effective; for example, the use of EPO during the pre-dialysis phase has an impact on long-term mortality: among 4866 pre-dialysis patients with a median follow-up of 26.2 months,

EPO was given to 1107 (22.7%). After the start of dialysis, the adjusted relative risk of death was 0.80 in the EPO treated group and only 0.67 in the subgroup with the highest hematocrit [41].

In a 10 year study conducted at the Necker Hospital among 1152 patients (mean age 55 years, range 18–92), the length of the pre-dialysis care by the nephrological team had a significant beneficial effect on cardio-vascular morbidity and on 5 year survival on dialysis: patients followed for <6 months pre-dialysis had a cardio-vascular morbidity of 39.6% and a 5 year survival of 58%, while those followed >35 months pre-dialysis had a cardio-vascular morbidity of only 21% and a 5 year survival of 77% [21].

The role of guidelines

Different nephrological Societies have published guidelines to improve the delivery of care and collaboration between primary care physicians and nephrologists: NIH Consensus Statement, Canadian Society of Nephrology, British Renal Association, K-DOQI guidelines, etc. [42–45]. A worldwide coordinating group has even been recently set-up [46].

So far, however, this problem has received more attention from the nephrological community than from other physician groups. Our own experience clearly indicates that the initiation of this networking is not an easy task. Different attempts are presently planned to improve the collaboration between PCPs and nephrologists. To start this cooperation, an unified and clear definition of late referral is urgently needed.

An interwoven network

However, it has to be taken into account that PCPs are presently faced with (too) many guidelines in many medical fields.

It is important to stress that the referral concept does not mean a definitive transfer of the patient to the nephrologist; as a matter of fact there are not enough resources or nephrologists to take care of all those patients [47]. But since their present medical condition at the start of dialysis is not optimal and the vast majority of them are already identified and followed by other medical specialists, we may expect a substantial improvement of their medical condition by an interwoven and precisely timed collaboration of the concerned physicians: (1) patients at risk of developing progressive kidney disease (i.e. patients with arterial hypertension, diabetes mellitus, recurrent urinary tract infections, history of familial nephropathy, etc) should be screened by their PCP; (2) management of patients with CKD should be shared between the PCP and the nephrologist; the nephrologist should send the patient back to his PCP with a detailed report and also with a medium to long-term follow-up plan.

As a draft scheme, a time-table for work-up and follow-up is illustrated in Table 4. This plan implies a well-defined collaborative chart on mutual fast information and accurate data transmission.

Table 4. Proposed time-table for a nephrological consult in an interwoven network between primary care physicians and nephrologists

1	When a screening or diagnostic procedure has evidenced signs of a kidney disease to establish or confirm diagnosis (consider kidney biopsy, interventional radiology, etc) prognosis for general health and kidney function, genetic counseling, therapeutic and follow-up plan, including treatment of the underlying disease, prevention and treatment of uraemic complications in particular BP control (target 120/70 mmHg), osteodystrophy, proteinuria
2	Once per year, when a CKD has been diagnosed and does not progress towards ESRD to establish eventual treatment of the underlying disease prevention and treatment of uremic complications
3	When the estimated GFR declines by >20% diagnosis of an eventual superimposed deteriorating factor re-evaluation of the treatment of the underlying disease re-evaluation of the prevention and treatment of uremic complications in particular blockade of the renin-angiotensin axis, prevention of osteodystrophy, evaluation and correction of anemia (EPO and iron prescription), nutritional counseling, preservation of the arm and forearm veins, ... information on ESRD treatment possibilities
4	When the estimated GFR is <25–30 ml/min the nephrologist should take over the general management of the patient and establish complete information on ESRD therapies preparation of the dialysis access planning of the dialysis start

CKD, chronic kidney disease; ESRD, end-stage renal failure; estimated GFR, glomerular filtration rate in ml/min estimated through the Cockcroft–Gault formula [34,39–42].

In this context we point to the experience of A. Levin indicating that the quality of care for patients with progressing CKD delivered in the Vancouver region is gradually better according to the following order: no care, PCP, single nephrologist and multidisciplinary renal team [17]:

> Patient information should be improved. The patient and his relatives should receive detailed and empathic information at each stage of kidney failure. This information should be progressive, i.e. adapted to the patient's level of understanding, to the different stages of kidney failure and its progression rate.
> The advantages offered by a multidisciplinary team approach, including nursing staff, social worker, dietician, etc and providing clinical demonstrations, teaching material, and discussions groups have been emphasized [17]. Contacts with other ESRF patients and their relatives, patient's associations, and any written or electronic material to consult at home should become essential tools to help such patients cope with their deteriorating condition.
> In addition, regular information campaigns directed to the general population should make persons at risk aware of their condition and inform them on

the simple clinical and biological tests to perform in order to diagnose CKD.

Finally, health care system-related reasons could also be improved: the referral of a patient with progressive CKD should not penalize the patient or his PCP. We certainly have to convince health care administrators that simple measures which allow early detection and treatment of CKD are more cost-efficient than any expensive ESRD treatment.

Conclusions

In patients with progressing chronic kidney disease, the trend for late referral to the nephrologist is clearly detrimental to patients, the medical community, and the health care system. The present review has identified and systematically analyzed several factors that favour late referral. While some disease-related causes of late referral seem unavoidable, most other causes could be improved effectively and rapidly, but resolution of the problem calls for improved interdisciplinary cooperation. The setting-up of consultation networks at the regional or local level appears as one of the most urgent and effective steps.

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