Effectiveness of a multidisciplinary kidney disease clinic in achieving treatment guideline targets

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Abstract

Background. We have demonstrated previously that at referral most chronic kidney disease (CKD) patients have suboptimal metabolic and hypertension control. Although several studies suggest that CKD clinics improve patient outcome, in fact there are minimal published data describing the actual effect of such clinics on these parameters.

Methods. We performed a historical prospective review of a cohort of 340 CKD patients referred to our multidisciplinary clinic in 1998 or 1999, with estimated creatinine clearance (CrCl) < 60 ml/min. Data regarding blood pressure (BP) control, metabolic/anaemia parameters, medications, access planning and dialysis starts were collected.

Results. The number of patients followed was 234, 144, 100 and 70 at years 1–4 of follow-up, respectively. Twenty-five percent of the patients were diabetic, and 25% were suspected to have ischaemic nephropathy; mean age was 67 ± 15 years. Although phosphate control improved from referral, below a CrCl of 30 ml/min, 27% of visits showed hyperphosphataemia. Thirty-one percent of patients with CrCl < 15 ml/min had haemoglobin < 100 g/l at follow-up despite the availability of erythropoietin. BP improved from a mean of 151/80 mmHg at referral to 137/75 mmHg in subsequent visits. At follow-up visits, 62% of BPs were still > 130 mmHg systolic or 85 mmHg diastolic. For proteinuric patients (> 1 g/day), 75% of follow-up visits showed BP > 125/75 mmHg, despite angiotensin-converting enzyme inhibitor use increasing from 35% at referral to 79% at follow-up. Twenty-four percent of patients started renal replacement therapy, initially haemodialysis (HD) in 57%, peritoneal dialysis (PD) in 35% and pre-emptive transplant in 8%. Thirty-eight percent of dialysis starts occurred within 6 months of referral, but PD was the modality in half of these. Only half of the HD patients started using an arterio-venous fistula, and of those using a central catheter 11 of 24 had been followed > 6 months, but only four of them had attempted fistula creation.

Conclusions. CKD clinic attendance was associated with improvements in metabolic and BP control, and was able to facilitate the use of PD even for late referrals. However, even the multidisciplinary model with nephrologists, nurse educators and dietitians was unable to achieve guideline-recommended metabolic, anaemia, BP and access targets for a significant number of patients.

Keywords: chronic kidney disease; hyperphosphataemia; hypertension; multidisciplinary care; pre-dialysis

Introduction

An extensive literature currently exists supporting the referral of patients with chronic kidney disease (CKD) to nephrologists, and optimally to multidisciplinary clinics, in order to manage the complications of the disease and to prepare for therapies such as dialysis and transplantation (see for example [1–3]). More recently, specific guidelines have been promulgated outlining the details of such evaluation and management [4,5]. Although studies suggest that early pre-dialysis referral reduces mortality rates in dialysis patients and increases the selection of peritoneal dialysis (PD) as a modality and the use of native fistulae in haemodialysis (HD) patients [1,2,3,6], there are few specific data reported describing what nephrologists actually do while following such patients pre-dialysis.

We recently reported the status at referral of a large cohort of patients referred to our nephrology clinic with CKD [7]. We found that many aspects of their care before referral, such as blood pressure (BP) control and metabolic management, failed to meet generally accepted standards.

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We now report a 4 year follow-up of this cohort of patients after nephrologists working in a multidisciplinary clinic provided ongoing care. Although many aspects of renal care were improved as compared with that provided by primary care providers, achievement of care targets was by no means universal. Even in an optimal environment, it is difficult to meet current standards of care for BP, metabolic control and dialysis access placement.

Materials and methods

Previously, the quality of care pre-nephrology referral of patients with CKD was reported from our institution [7]. In that initial study, pre-referral care of all consecutive new patients seen in 1998 and 1999 by nephrologists at the Queen Elizabeth II Health Science Centre in Halifax, NS, the major tertiary care hospital for Atlantic Canada, with serum creatinine >140 µmol/l [1.6 mg/dl (men)] or 105 µmol/l [1.2 mg/dl (women)], was reported. These values correspond to a glomerular filtration rate (GFR) of ~60 ml/min, which has been suggested as an appropriate cut-off value for early renal insufficiency [8]. Patients were excluded if they had seen a nephrologist previously.

We subsequently decided to analyse the same cohort of patients in a historical prospective fashion to determine the adequacy of control of these same parameters by the kidney disease clinic, and also to determine how effective we were in achieving K/DOQI standards of care.

Ongoing care was provided in the setting of a tertiary care university multidisciplinary nephrology clinic, with ongoing involvement of nurses and nurse-educators, social workers, dietitians and full-time academic nephrologists. Patients were generally seen in the clinic annually for GFR 30–60 ml/min, every 6 months for GFR 15–30 ml/min and every 3 months for GFR <15 ml/min. No private practice fee-for-service remunerated physicians were involved, and the Canadian Medicare system provided all medical/surgical and ancillary care free of charge to the patients, including dialysis. Drug costs were also reimbursed for patients aged 65 or over, but erythropoietin was provided to all patients at no cost.

Care was not by protocol, but there was consensus in the clinic regarding the following principles: importance of tight BP control (<130/80 mmHg); using angiotensin-converting inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) whenever possible; metabolic control of calcium and phosphate within the normal laboratory range using dietary phosphate restriction, and calcium carbonate as the preferred phosphate binder; control of parathyroid hormone to be less than three times the laboratory upper limit of normal using calcium supplementation followed by vitamin D analogues; elimination of metabolic acidosis using supplemental sodium bicarbonate; and control of anaemia. Target haemoglobin was set at ≥10 g/l for this clinic, and erythropoietin was not initiated until ferritin was >100 µg/l and transferrin saturation (TSAT) was >20%. BP and weight were well documented in all patients. BP and weight were well documented in all patients. Medication lists were recorded carefully by nurses in a flow chart and were available for all visits. If laboratory data were not measured on the selected visit, then data from the closest date within 3 months in which these were measured were recorded. An exception was made for 24 h urine data and parathyroid hormone levels, for which data within 6 months of the indexed visit were recorded.

Aetiology of renal insufficiency as determined by the treating nephrologist, presence of diabetes, dietary education and whether the cause of anaemia was investigated were recorded.

Data regarding planning for renal replacement therapy (RRT) were also collected; date of referral to dialysis education, referral for access creation, date of access creation and start of dialysis were also recorded. For patients starting dialysis, access used at start of dialysis was also noted. Pre-emptive kidney transplantation dates were also recorded.

The reason for loss to follow-up was also determined where possible. Because of the centralized nature of the dialysis/transplant system in our region, ascertainment of patients receiving any form of RRT was complete. No further information after the start of any form of RRT or final discharge from the clinic was collected. There was no formal protocol for discharge from the clinic, but patients with stable GFR and satisfactory BP and metabolic status could be returned to their family practitioner for follow-up at the discretion of the attending nephrologist. Patients who were discharged and returned to the clinic were included in data collection. Death if documented from the chart or from the hospital medical records computer system was recorded, but we did not have access to registry of death information.
Effectiveness of multidisciplinary CKD care

Statistical analysis

Baseline and follow-up patient demographics were recorded as means and SDs for numeric variables and as frequencies and percentages for categorical and ordinal data. To test differences in numeric data across years (from baseline to 4 years of follow-up), analysis of variance (ANOVA) tests were used. Laboratory data were tested for correlation with creatinine clearance. Patients were then classified by level of creatinine clearance, and ANOVA tests were run to determine if differences of laboratory means existed across stages of kidney disease. Follow-up data were grouped, and differences in numeric variables from baseline to follow-up were calculated using paired t-tests.

In an attempt to identify possible bias introduced by variable follow-up duration due to patient drop-out, means for BP, serum calcium, phosphate, calcium–phosphate product, bicarbonate and haemoglobin at presentation were compared using ANOVA, with patients stratified by length of follow-up.

To examine RRT, demographics were calculated as above and compared between therapy types. Average time to RRT was recorded as date of RRT minus date of initial visit. For HD patients, differences in mean time to therapy were compared between fistula and catheter patients using Wilcoxon rank sum test.

Further analysis was conducted on RRT data. Kaplan–Meier curves were used to estimate time to RRT, stratified by level of creatinine clearance. χ² analyses were then used to evaluate certain possible associations with RRT.

All tests were two-sided and considered significant at an alpha level of 0.05. All analyses were conducted using SAS8.22 (SAS Institute, Cary, NC).

Results

Demographics

The number of patients analysed at the initial visit was 340 and subsequently 234 at 1 year, 144 at 2 years, 100 at 3 years and 70 at 4 years. At the initial visit, mean age was 66.6±15.2 years. There were 185 males and 155 females. The mean creatinine for each year of follow-up for the cohort remained statistically similar (ANOVA), with an overall mean of 274±160 μmol/l. Note that those starting dialysis were censored, so that this value cannot be used to gauge progression of renal failure within the cohort. Creatinine clearance was estimated by the Cockcroft–Gault equation [9], and in further analysis this clearance estimate was used to place patients within stages of kidney disease as described by K/DOQI [10]. At presentation, there were six patients with stage 1 disease, 31 with stage 2, 128 with stage 3, 105 with stage 4 and 70 with stage 5 disease. The mean creatinine clearance for each period of follow-up was similar, probably because of dropout of patients with advanced disease who started dialysis or died.

We collected documented reasons for loss to follow-up. Table 1 shows the various reasons for clinic drop-out. Ascertainment of patients receiving any form of RRT was complete. Details on cause of death could not be obtained from any external source; those patients refusing dialysis therapy and some of the patients listed in the ‘unknown’ group probably died. We did not have access to the registry of death data, so that we could not analyse survival. Of note, 15% of patients received some form of RRT and 17% were discharged to the care of their family physician having been judged as stable; demographic data for this group reveal that mean age was 70±11 years, with a mean creatinine clearance of 45 ml/min and mean BP of 138±18/77±10 mmHg. Eighty percent of these discharged patients had stage 3 or better kidney function. Eleven percent of all patients were lost to follow-up due to recurrent patient non-compliance with appointments. Because we do not have BP or metabolic data from those patients discharged or lost to follow-up, all subsequently reported follow-up data have the potential for unquantifiable bias in that the followed cohort is only a subset of the original patients.

The aetiology of chronic renal failure is noted in Table 2. Diabetes and atherosclerotic nephropathy accounted for about half of all cases.

Blood pressure

Tables 3, 4 and 5 describe BP control and antihypertensive therapy in patients. Control of BP appeared improved in those patients seen at subsequent visits compared with the full patient group seen at the initial visit. Despite mean BPs after the first annual visit of ~140/80 mmHg (Table 3), Table 4 reveals that at more
than half of the patient visits for those with stage 3 or worse disease, irrespective of follow-up period or stage of chronic kidney disease at presentation, systolic BP was >130 mmHg and/or diastolic pressure was >85 mmHg (Table 4). For the six stage 1 and 31 stage 2 patients followed in the clinic (data not shown in Table 4), initial and follow-up BPs were not different, both having means of 134/83 mmHg. There was a trend toward increasing numbers of medications being used over time in the subset of patients who continued to be followed in the clinic, and by the end of 4 years >60% of patients were taking either ACEIs or ARBs (Table 5). About half the patients were on diuretics at referral, and this fraction did not change over time.

Because variable follow-up times (patient drop-out from clinic) might have introduced bias to these findings, we also analysed mean systolic and diastolic BPs at initial visit, comparing patients followed for <1 year, 1 year only, 3 years only or 4 years only. Analysis by ANOVA revealed no differences in BPs between any of these groups, indicating that selection bias by follow-up time was unlikely to have influenced our findings.

The 24 h urine protein excretion was measured in 230 of 340 patients at first visit; 111 of these patients had proteinuria of >1000 mg/day. Mean proteinuria was 4358 ± 4822 mg. The mean BP in this subset of patients was 156 ± 28/83 ± 16 mmHg at first visit and 137 ± 22/83 ± 11 mmHg at follow-up visits. Since the usually recommended BP goal for this proteinuric subset of patients is more stringent than for non-proteinuric patients [4] at 125/75 mmHg, we examined the number of readings satisfying this target, and ACEI or ARB use in this subset of patients. The use of an ACEI or ARB increased from 35% of patients at initial visit to 79% after ≥2 years of follow-up, but even after ≥2 years of follow-up, 75% of proteinuric patients had BPs >125/75 mmHg.

### Metabolic parameters and anaemia

Only 40 follow-up visits did not have laboratory data measured within 3 months of clinic visit. There was a strong correlation between all metabolic parameters and estimated creatinine clearance, such that as creatinine clearance fell, serum calcium fell, while calcium–phosphate product and serum phosphorus rose, as did parathyroid hormone (P < 0.0001 for Pearson’s r statistic). We have therefore grouped results according to creatinine clearance/CKD stage at presentation, examining data at initial and follow-up visits. Patients whose kidney function deteriorated are considered within their presenting stage for the purposes of this analysis.

Table 4 shows the mean values for serum calcium, phosphorus, calcium–phosphate product, bicarbonate and haemoglobin. For the six stage 1 and 31 stage 2 patients (data not shown in the table), the mean values for all parameters were normal. Only 4% of follow-up visits for stage 2 patients revealed phosphorus concentrations >1.6 mM, and there were no other abnormalities. Initial visit calcium values did not differ for CKD stage 3 and 4 disease, but fell significantly in stage 5 patients (P < 0.05 by ANOVA). Phosphorus levels and calcium–phosphate product were significantly increased at reduced creatinine clearances, particularly in the subgroup of patients with stage 5 kidney disease (P < 0.05 by ANOVA). These parameters were significantly improved after clinic follow-up for stage 5 patients.

Haemoglobin levels fell progressively with creatinine clearance (P < 0.05 by ANOVA) and were significantly improved at follow-up in the patients with stage 5 kidney disease.

Because variable follow-up times (patient drop-out from clinic) might have introduced bias to these results, we also analysed the means of the parameters in Table 4 at initial visit, comparing patients followed for <1 year, 1 year only, 2 years only, 3 years only or 4 years only. The mean initial serum phosphorus concentration of the 105 patients followed for <1 year (1.37 mM) was statistically significantly higher (ANOVA P = 0.033) than initial phosphorus concentrations of those patients followed for 3 years (1.22 mM, n = 48) and

<table>
<thead>
<tr>
<th>Visit</th>
<th>n</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>340</td>
<td>151 ± 27*</td>
<td>80 ± 13*</td>
</tr>
<tr>
<td>1 year</td>
<td>234</td>
<td>140 ± 22</td>
<td>76 ± 12</td>
</tr>
<tr>
<td>2 years</td>
<td>144</td>
<td>139 ± 21</td>
<td>75 ± 12</td>
</tr>
<tr>
<td>3 years</td>
<td>100</td>
<td>135 ± 21</td>
<td>74 ± 12</td>
</tr>
<tr>
<td>4 years</td>
<td>70</td>
<td>135 ± 18</td>
<td>75 ± 11</td>
</tr>
</tbody>
</table>

*P < 0.0001 vs all subsequent years by ANOVA.

<table>
<thead>
<tr>
<th>Stage 3 (CrCl [a] 30–60 ml/min)</th>
<th>Stage 4 (CrCl [a] 15–30 ml/min)</th>
<th>Stage 5 (CrCl [a] &lt;15 ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial visit</td>
<td>Follow-up visits</td>
<td>Initial visit</td>
</tr>
<tr>
<td>Mean BP, mmHg (SD)</td>
<td>No. of readings</td>
<td></td>
</tr>
<tr>
<td>No. (%) &gt;130 mmHg systolic or &gt;85 mmHg diastolic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>151/82 (27/13)</td>
<td>128</td>
<td>152/80 (25/13)</td>
</tr>
<tr>
<td>37% (27/13)</td>
<td>258</td>
<td>140/73 (23/12)</td>
</tr>
<tr>
<td>80% (27/13)</td>
<td>102</td>
<td>87 (83%)</td>
</tr>
<tr>
<td>62% (27/13)</td>
<td>159</td>
<td>106 (64%)</td>
</tr>
</tbody>
</table>

[a] Estimated creatinine clearance by the Cockcroft–Gault method at initial presentation. Patients remain in this 'stage' category for further analysis, even if the GFR deteriorates over time.

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4 years (1.19 mM, \(n = 48\)). As a result, similar differences were noted in the calcium–phosphate product, although no differences were noted in serum calcium concentrations. Important differences were not detected in the other parameters.

We further examined the frequency of visits where patients’ metabolic and anaemia parameters fell outside generally accepted targets, to better evaluate clinic success. These data are also shown in Table 6. Abnormalities in serum calcium concentration were mainly noted in stage 4 and 5 patients. There was an apparent improvement at follow-up compared with the first visit in the group with stage 5 disease, but the potential bias effect of patients lost to follow-up must be remembered. However, \(\sim 10\%\) of stage 4 and 18\% of stage 5 patients continued to have hypocalcaemia at follow-up. Similar trends were noted for phosphorus concentrations and acidosis in stage 4 and 5 patients even after clinic follow-up, such that a substantial fraction of patients remained hyperphosphataemic and acidic despite nephrological care (Table 6). Hyperphosphataemia was present in spite of the use of phosphate binders (almost exclusively calcium carbonate) in 65\% of stage 5 patients, and in 80\% of such patients with any hyperphosphataemia.

A considerable number of patients had haemoglobin at follow-up below our agreed clinic target of 100 g/l (Table 6). Of those with stage 5 disease, almost one-third of patient visits manifested a haemoglobin < 100 g/l. Surprisingly, only 20 clinic patients were prescribed erythropoietin despite its availability without direct cost to patients. The clinic does have a policy of withholding this agent until iron stores were corrected to a ferritin of > 100 \(\text{mg/l}\) and TSAT of > 20\%, which may have accounted for some delay in erythropoietin institution.

### Renal replacement therapy

A total of 84 (24\%) patients, of whom 36 (44\%) were diabetics, had some form of RRT. The initial form of RRT was HD in 48 patients (57\%), PD in 29 (35\%) and pre-emptive transplantation in seven (8\%) patients. The average times from first visit to start of RRT were: HD 486±429 days, PD 420±488 days and pre-emptive transplant 672±282 days. Figure 1 displays the risk of a clinic patient starting RRT by Kaplan–Meier analysis, where patients are censored for death or any other cause for loss of follow-up, stratified by stage of kidney disease at initial presentation to the clinic. Patients with stage 3 disease experienced a low risk of such an event over 3 years, and only 40\% of stage 5 patients experienced such therapy. No stage 2 patients required initiation of RRT. Diabetic patients experienced a trend toward

### Table 5. Number (a) and type (b) of blood pressure medications

<table>
<thead>
<tr>
<th>Visit</th>
<th>All patients, no. of medications ± SD</th>
<th>Patients with BP &gt; 130/85 mmHg at specified visit, no. of medications ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>2.20 ± 1.37</td>
<td>2.37 ± 1.34</td>
</tr>
<tr>
<td>1 year</td>
<td>2.18 ± 1.32</td>
<td>2.39 ± 1.29</td>
</tr>
<tr>
<td>2 years</td>
<td>2.41 ± 1.34</td>
<td>2.64 ± 1.28</td>
</tr>
<tr>
<td>3 years</td>
<td>2.53 ± 1.25</td>
<td>2.76 ± 1.09</td>
</tr>
<tr>
<td>4 years</td>
<td>2.63 ± 1.28</td>
<td>2.78 ± 1.27</td>
</tr>
</tbody>
</table>

### Table 6. Metabolic parameters and anaemia control

<table>
<thead>
<tr>
<th></th>
<th>Stage 3 (CrCl(^\text{a}) 30–60 ml/min)</th>
<th>Stage 4 (CrCl 15–30 ml/min)</th>
<th>Stage 5 (CrCl &lt; 15 ml/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial visit</td>
<td>Follow-up visits</td>
<td>Initial visit</td>
</tr>
<tr>
<td>No. of observations</td>
<td>128</td>
<td>258</td>
<td>105</td>
</tr>
<tr>
<td>Mean calcium, mM(^b)</td>
<td>2.34 ± 0.12</td>
<td>2.30 ± 0.13</td>
<td>2.30 ± 0.16</td>
</tr>
<tr>
<td>% Calcium &lt; 2.1 mM</td>
<td>2</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Mean phosphorus, mM(^b)</td>
<td>1.17 ± 0.22</td>
<td>1.26 ± 0.30</td>
<td>1.36 ± 0.30</td>
</tr>
<tr>
<td>% Phosphorus &gt; 1.6 mM</td>
<td>3</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>Mean Ca×P, mM(^c)</td>
<td>2.74 ± 0.51</td>
<td>2.92 ± 0.69</td>
<td>3.10 ± 0.62</td>
</tr>
<tr>
<td>% Ca×P &gt; 4.44 m(^d)</td>
<td>1</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Mean HCO(_3) m(^c)</td>
<td>26.3 ± 3.0</td>
<td>25.6 ± 3.5</td>
<td>24.9 ± 3.5</td>
</tr>
<tr>
<td>% HCO(_3) &lt; 20 m(^c)</td>
<td>2</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Mean haemoglobin, g/l(^b)</td>
<td>124 ± 17</td>
<td>123 ± 16</td>
<td>117 ± 18</td>
</tr>
<tr>
<td>% Haemoglobin &lt; 100 g/l</td>
<td>4</td>
<td>7</td>
<td>20</td>
</tr>
</tbody>
</table>

\(^a\)Estimated creatinine clearance by the Cockcroft–Gault method at initial presentation. Patients remain in this 'stage' category for further analysis, even if the GFR deteriorates over time.

\(^b\)Mean ± SD.
increased risk of RRT ($P=0.06$), but there was no association of RRT with systolic or diastolic BP at follow-up visits. Younger patients were more likely than older patients to have RRT; mean age with RRT 62 years vs no RRT 68 years, $P<0.001$.

Patients starting HD with temporary catheters averaged $305\pm361$ days of clinic follow-up, a significantly shorter time than the mean of $668\pm421$ days for those starting HD with fistulae ($P<0.0024$ by Wilcoxon test). Of the 48 HD patients, 24 (50%) were started with a native fistula, earliest use 4.5 months after creation, and 24 (50%) with a central venous catheter. Of the catheter patients, 16 started dialysis within 6 months of referral to the clinic and could be regarded as late referrals. However, eight patients were followed for >6 months (average number of days of follow-up 734), but only four had an attempted AV access creation.

Of the 84 RRT patients, 32 (38%) were started on dialysis within 6 months of being referred to the clinic (late referrals). PD was the initial modality for 13 of these patients, earliest start date 1 month from first referral to clinic. PD was thus effected promptly even for some patients being referred late. Nineteen late referrals received HD; only three of these patients were started with a fistula, 4–5 months from referral.

Of the patients transplanted, one transplant took place 164 days from first clinic visit, but the average follow-up time was 672 days.

Discussion

This report is one of the few currently available which addresses the outcomes of care for CKD provided specifically by a nephrologist-supervised multidisciplinary clinic. Although Goldstein et al. [2] and Curtis et al. [6] recently reported the favourable effects of such a clinic upon mortality and morbidity of dialysis patients, their subjects were ascertained retrospectively from those already started on dialysis, and therefore do not represent the full range of CKD patients, many of whom have slow rates of disease progression and may not require dialysis [11]. Kausz et al. described the management of ~600 patients with chronic renal insufficiency by nephrologists in the Greater Boston area of the USA, but care was provided by a mixture of private practices and hospital clinics, so that differences between these two modes of care cannot be discerned [12]. Nonetheless, such studies do allow us to compare our experience with that of others.

We have chosen to categorize the stage of kidney disease of our patients using the Cockcroft–Gault equation, as permitted by the K/DOQI guidelines [10]. Although many centres employ the MDRD equation, which is also suggested in the guidelines, Cockcroft–Gault is very commonly used clinically in Canada. In fact, neither equation is optimally valid for this purpose, as recently demonstrated by Froissart et al., who reported misclassification rates of ~30% for both approaches [13].

It is interesting that ~17% of our patients remained sufficiently stable so that they were adjudged safe to return to their primary care physician for follow-up, with instructions to the family doctor regarding appropriate indications for re-referral. Unfortunately, we were unable to obtain further follow-up information on these patients to confirm the appropriateness of this decision. A recent report has noted that many patients with CKD do not experience significant disease progression [11], and after initial evaluation it seems sensible to concentrate necessarily limited clinic...
resources on those patients with observed hypertension resistant to control, progressive loss of renal function or high stage disease. Such an approach will only succeed if primary care physicians are given clear directives describing how to treat and follow such patients and under what circumstances to refer them back for further care. The fact that by 3 years of follow-up only those presenting with stage 4 and 5 kidney disease demonstrated a >20% risk of having RRT emphasizes the need to focus clinic efforts on such patients. Given the observational nature of this study, it is difficult to interpret the association of younger age with RRT, which might reflect either treatment bias, an age-dependent difference in progression rates or a higher death rate before RRT for older patients.

BP control is a major focus of efforts to improve outcome in patients with CKD. BP control was very poor at referral for our patients, and remained non-optimal during follow-up for many patients. Our analysis suggests that this was not caused by only following those patients with higher blood pressures at presentation (selection bias), since presentation BPs were similar for those patients followed for <1 year, 1 year, 2 years, 3 years or 4 years. Unfortunately, this experience is not unusual. In the NHANES III study, mean BP for patients with elevated creatinine was 157/82 and 150/76 mmHg for patients on and not on antihypertensive medications, respectively [14]. This was similar to our population at referral. In the NHANES III study, only 11% of patients with hypertension and elevated creatinine had BP <130/85 mmHg.

Mean BP at follow-up decreased from 150/80 to 137/75 mmHg, but this is still above the target suggested by K/DOQI [4]. Sixty percent of readings were above target at follow-up. Over time, the number of antihypertensive medications and the fraction of patients on ACEI/ARBs increased. These findings underscore the need for better BP control, and demonstrate the difficulty of achieving targets even in an optimal clinic environment with nephrologist supervision.

When proteinuria of >1 g/day was present, mean BP was also high at 156/83 mmHg initially and 137/83 mmHg during follow-up, and the number of readings with BP less than the recommended target of 125/75 mmHg [4] was only 14%.

ACEI and ARB use was increased by the clinic, but ~40% of patients were not treated with one of these agents. Problems with these medications of increases in serum creatinine and potassium occur in these patients, limiting their use even by nephrologists [15]. Additional studies are required to address how many patients in a non-trial routine practice setting can actually tolerate these agents.

Our experience is similar to that of others. Kausz et al. reported that in nephrologist-associated practices, only half of patients were treated with ACEIs, and that 65% of patients had two or more BP readings >140/90 mmHg [12]. Tonelli et al. [15] reported that in Canadian nephrology clinics, only half of patients with chronic renal insufficiency were prescribed an ACEI, and that only ~40% of patients had appropriate BP control. Schwenger and Ritz [16] reported that only 15% of their patients treated in a renal outpatient clinic in Germany achieved a target BP of 125/75 mmHg, and ~65% received ACEI or ARB agents. Seventy-seven percent were receiving diuretic agents. Goldstein et al. reported the status of their clinic patients at onset of dialysis, and the median BP was 152/78 mmHg with 25% of patients having a systolic pressure >166 mmHg and diastolic >90 mmHg. Only 60% of their patients were taking diuretics, and half were taking ACEIs or ARBs [2].

Clearly, even in specialist hands, it is difficult to control BP and to mandate the use of ACEIs/ARBs successfully. Only half of our patients were receiving diuretics, not an increase from status at referral, and even specialists are probably not applying these agents sufficiently frequently to renal patients, emphasizing the importance of recent guidelines encouraging their use [4]. It may well be that current BP targets are not achievable in many patients, given the problems of encouraging compliance with multidrug regimes and low salt diets, but obviously we are not yet using all of the available tools effectively.

Haemoglobin fell as the stage of CKD worsened, although for the subgroup continuing follow-up, clinic follow-up was associated with an improvement of anaemia as compared with the full cohort seen at the initial visit for all stages, as in Table 6. Thirty percent of follow-up visits for those with stage 5 disease had a haemoglobin <100 g/l, suggesting that more aggressive use of erythropoietin might be required. We believe that the use of erythropoietin in our clinic may have been delayed by attempts to correct inadequate iron stores before its initiation using oral iron supplements. Such an approach is cheaper and logistically simpler than use of parenteral iron, but certainly delays optimal correction of anaemia. Goldstein et al. [2] reported that at start of dialysis, their clinic patients had a median haemoglobin of 104 g/l as compared with mean haemoglobin of 107 g/l for our stage 5 patients at follow-up. It is interesting that 41% of the Goldstein clinic patients were receiving erythropoietin, compared with a quarter of our patients who started dialysis. Similarly, recent DOPPS data from Canada reveal that at dialysis initiation, 43% of patients were receiving erythropoietin, but the mean haemoglobin was 101 g/l, with 70% of patients having a haemoglobin <110 g/l [17]. Clearly clinic performance cannot be measured simply by frequency of use of erythropoietin.

Abnormalities in calcium, phosphorus, haemoglobin and bicarbonate correlated with creatinine clearance and were mainly noticed in stage 4 and 5 kidney disease. Similar observations are available from the NHANES data [18]. There were improvements in each parameter under multidisciplinary clinic care, but deficiencies persisted.

Calcium control was generally good, since only 8% of the subgroup of patients continuing follow-up had
hypocalcaemia during clinic follow-up, a reduction from the prevalence of 12% on initial visit. Most hypocalcaemia was detected in the subset of patients with creatinine clearance <15 ml/min. More vigilance should be exercised in this subset of patients, who may need to be seen more frequently. Patient compliance with the medications prescribed is a common problem with calcium carbonate. We did not look specifically at compliance or side effect profile.

Phosphorus control is more challenging, and almost half of patients at follow-up in the subgroup with creatinine clearance <15 ml/min had hyperphosphataemia. As in the analysis of Hsu and Chertow of the NHANES III data [19], abnormalities of serum calcium were less marked than those of phosphorus even in stage 4 and 5 CKD. Abnormalities of the calcium–phosphate product were seen mainly in this group of patients.

The possibility should be considered that patient drop-out resulting in variable follow-up times may have introduced a bias into these metabolic data. For example, if patients followed for the shortest times had lower phosphorus concentrations than those followed for longer, then the difficulty in achieving optimal control could be due to bias: more of those patients with a tendency to hyperphosphataemia would appear in the follow-up means of Table 6. In fact, our analysis (see Results) indicates that those patients followed for <1 year had higher initial mean serum phosphorus concentrations than those followed for 3 and 4 years, indicating that such a bias probably cannot explain problems in phosphorus control in stage 4 and 5 CKD in this population.

Goldstein et al. [2] noted that at dialysis start, median phosphorus was 1.8 mM, higher than the mean for our followed stage 5 patients of 1.5 mM. Forty-three percent of our stage 5 patient visits had phosphorus >1.6 mM, whereas Goldstein’s group reported that 75% of their cases had a phosphorus >1.5 mM at dialysis start. Evidently, even in a multidisciplinary clinic, setting phosphorus control is difficult to achieve. This difficulty mimics the experience reported for dialysis patients by DOPPS, where only ~40% of patients met K/DOQI targets [20].

Patients starting dialysis within 6 months of being referred are generally considered late referrals. In our cohort, 83 patients had stage 5 renal disease at referral and 125 stage 4 disease. Twenty-six patients were started on dialysis within 6 months of referral, but the total number of patients near dialysis at referral was probably larger since a number of patients declined dialysis. Temporary catheter use was more frequent in this group, indicating a need for earlier referral. One interesting observation was that we were able to perform PD in 13 of these patients, indicating that PD may be successfully performed more urgently than HD with fistula, due to the time required for fistula maturation. Our finding that half of the patients starting HD used a catheter is similar to the findings of Goldstein et al. from their clinic [2] and indicates that multidisciplinary clinics do not eliminate the problem of dialysis catheters, although their use may be reduced compared with solo nephrologist care.

The study methodology introduces significant limitations into data interpretation. Care was not fully by protocol, allowing practice variations within the clinic, which may have contributed to our failure to reach desired treatment targets. Of greater concern, the incomplete follow-up of our incident population implies that the patients followed over time necessarily represent only a subgroup of the full cohort, selected by unknown factors. Some stable well-controlled patients were discharged from clinic, whereas other sicker patients either did not attend the clinic or refused the offer of dialysis therapy and were lost to follow-up (Table 1). As a result, observed changes in BP and metabolic factors over time cannot be causally linked to clinic management. Certainly one cannot assume that our findings can be generalized to other populations. However, we believe that even these incomplete prospective data are helpful, when combined with recent retrospective data as ascertained from dialysis starts [2,6] in studies of the effect of multidisciplinary clinics. Both approaches fail to account completely for all incident patients followed in clinics.

This cohort study indicates that attendance at a multidisciplinary CKD clinic supervised by nephrologists was associated with apparent improvements in BP control, anaemia management and mineral metabolism over patient status at referral. Methodological limitations of the study as discussed above must be kept in mind. However, the data highlight the difficulty in achieving recommended targets for these parameters, even in such a care environment. Given our finding that metabolic abnormalities and anaemia are largely restricted to those patients with stage 4 and 5 disease, a case could be made that such patients should form the bulk of the workload of a multidisciplinary clinic. BP control remains a problem as well, and the high prevalence of hypertension at all stages of kidney disease suggests that efforts of both nephrology clinics and primary care physicians will be required. It may be that all aspects of care will require formal protocols, in order to increase further the number of patients achieving care targets. The setting of appropriate benchmarks for quality control in CKD care requires study of such cohorts in multiple settings and countries, so that we can determine what is actually achievable in large non-trial patient populations.

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