



Cross-Sectional Assessment of Achievement of Therapeutic Goals in a Canadian Multidisciplinary Clinic for Patients With Advanced Chronic Kidney Disease

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Abstract

Background: The implementation of advanced chronic kidney disease (CKD) multidisciplinary clinics has now demonstrated their effectiveness in delaying and even avoiding dialysis for patients with CKD. However, very little has been documented on the management and achievement of targets for a number of parameters in this context.

Objective: Our goal was to assess our multidisciplinary clinic therapy performance in relation to the targets for hypertension, anemia, and calcium phosphate assessment.

Methods

Design and setting: A cross-sectional descriptive study was conducted with a cohort including all patients followed up in our multidisciplinary clinic in July 2014.

Measurements: Comorbidity, laboratory, and clinical data were collected and compared with the recommendations of scientific organizations.

Results: The cohort included 128 patients, 37.5% of whom were women. Mean follow-up time was 26.6 ± 25.1 months and mean estimated glomerular filtration rate (eGFR) was 14.0 ± 4.7 mL/min/1.73 m². A total of 24.2% of patients with diabetes achieved blood pressure targets of <130/80 mm Hg, while 56.5% of patients without diabetes achieved targets of <140/90 mm Hg. Hemoglobin of patients treated with erythropoiesis-stimulating agents was 100 to 110 g/L in 36.2% of the patients, below 100 for 39.7% of them, and above 110 for 24.1%, whereas 67.2% were within the acceptable limits of 95 to 115 g/L. In addition, 63.4% of patients had a serum phosphate of <1.5 mmol/L, and 90.9% of patients had total serum calcium <2.5 mmol/L.

Limitations: Our study is a single center study with the majority of our patients being Caucasian. This limits the generalizability of our findings.

Conclusion: The control rates of various parameters were satisfactory given the difficult clinical context, but could be optimized. We publish these data in the hope that they are helpful to others engaged in quality improvement in their own programs or more generally.

Abrégé

Contexte: L'implantation de cliniques multidisciplinaires spécialisées en néphropathie chronique de stade avancé a prouvé leur efficacité à retarder — voire à éviter — le recours à la dialyse chez les patients atteints d'insuffisance rénale chronique (IRC). Cependant, il existe peu de littérature sur la gestion et l'atteinte d'objectifs propres à un tel contexte en regard de certains paramètres.

Objectif de l'étude: Nous avons voulu évaluer l'efficacité thérapeutique de notre clinique multidisciplinaire par rapport aux paramètres suivants : l'hypertension, l'anémie et le taux de phosphate de calcium.



Méthodologie

Cadre et type d'étude: Une étude descriptive transversale a été menée auprès d'une cohorte constituée de tous les patients suivis à notre clinique multidisciplinaire en juillet 2014.

Mesures: On a colligé les comorbidités, les résultats de laboratoire et les données cliniques des patients. Ces données ont ensuite été comparées aux valeurs recommandées par la communauté scientifique.

Résultats: La cohorte comptait 128 patients, 37,5 % étaient des femmes. La durée moyenne du suivi était de $26,6 \pm 25,1$ mois et le DFGe moyen des participants était de $14,0 \pm 4,7$ mL/min/1,73 m². Seuls 24,2 % des patients diabétiques présentaient une tension artérielle inférieure à 130/80 mm Hg, soit la valeur cible pour ce groupe de patients, alors que 56,5 % des non-diabétiques ont maintenu leur tension artérielle sous la valeur cible de 140/90 mm Hg. Le taux d'hémoglobine des patients traités avec des agents stimulant l'érythropoïèse se situait entre 100 et 110 g/L dans 36,2 % des cas; 39,7 % présentaient un taux d'hémoglobine inférieur à 100 g/L, et 24,1 % présentaient un taux supérieur à 110 g/L. Dans la majorité des cas (67,2 %), le taux d'hémoglobine se situait dans les limites acceptables, soit entre 95 et 115 g/L. Enfin, 63,4 % des participants à l'étude présentaient des valeurs de phosphate sérique inférieures à 1,5 mmol/L et un total de 90,9 % des patients présentaient des valeurs de calcium sérique inférieures à 2,5 mmol/L.

Limites de l'étude: Notre étude s'est tenue dans un seul établissement et auprès d'une population à majorité caucasienne, ce qui limite la généralisation de nos résultats.

Conclusion: Compte tenu du contexte clinique difficile, nous considérons les taux de contrôle pathologique atteints pour les paramètres étudiés comme satisfaisants, quoiqu'ils puissent encore être améliorés. Nous publions ces résultats dans l'espoir qu'ils serviront notamment à l'amélioration de programmes mis sur pied par d'autres équipes.

Keywords

anemia, arterial hypertension, chronic kidney disease, hyperphosphatemia, multidisciplinary care

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What was known before

Advanced chronic kidney disease (CKD) multidisciplinary clinics have grown in popularity for 2 decades. However, few studies have been published to serve as comparison for the achievement of therapeutic goals in these clinics.

What this adds

This study showed the difficulty of treating patients with advanced CKD and identified potential targets for interdisciplinary interventions.

Introduction

Chronic kidney disease (CKD) affects a large segment of the Canadian population: 12.5% have CKD stage 1 to 5, while 3.1% have stage 3 to 5.¹ Chronic kidney disease can lead to peripheral and pulmonary edema, arterial hypertension, electrolytic disorders such as hyperkalemia or metabolic acidosis, renal bone mineral disease, and anemia resulting in cardiovascular accidents. In addition, deterioration of kidney

function is associated with an increase in hospitalizations, cardiovascular accidents, and mortality.²

Advanced CKD multidisciplinary clinics usually include nephrologists, nurses, nutritionists, pharmacists, and sometimes psychologists and social workers. Studies have shown the effectiveness of this type of clinic in slowing down the deterioration of kidney function^{3,4} in the survival of patients before renal replacement therapy (RRT)³⁻⁵ and even when hemodialysis has already begun.⁶ Inadequate preparation has been associated with increased mortality among hemodialysis patients.⁷

In 2006, an advanced CKD multidisciplinary clinic was created at the Trois-Rivières Regional Affiliated University Hospital Centre (CHAUR) with the aim of preventing deterioration of kidney function in patients in the Québec regions of Mauricie and Centre-du-Québec. The clinic is composed of nephrologists, nurses, social workers, nutritionists, and psychologists if needed. There are no pharmacists in the multidisciplinary clinic due to lack of budget. This clinic manages patients when their estimated glomerular filtration rate (eGFR) is <20 mL/min/1.73 m². Patients are followed each month to each 6 months, depending on the severity of the

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Table 1. Target Values for Hypertension in Different Populations.

	CSN	CHEP ^a	KDIGO
Patients with diabetes	<130/80 mm Hg	<130/80 mm Hg (Grade A)	<140/90 mm Hg if <30 mg/24 h albuminuria (Grade 1B) <130/80 mm Hg if between 30 and 300 mg/24 h albuminuria (Grade 2D)
Patients without diabetes	<140/90 mm Hg	<140/90 mm Hg (Grade B)	<130/80 mm Hg if >300 mg/24 h albuminuria (Grade 2C)
Very elderly patients (age ≥ 80 years)		<150 mm Hg (Grade C)	

Note. CSN = Canadian Society of Nephrology; CHEP = Canadian Hypertension Education Program; KDIGO = Kidney Disease Improving Global Outcomes.

^aThe CHEP recommendations are the values that will be used for comparison with the clinic's values.

disease and the stability of their renal function. Bloodworks are done each month, even if no visit is scheduled this month. There is no clear management algorithm implemented in the clinic in hypertension, anemia, or phosphorus and calcium axis, although nephrologists refer to existent guidelines to treat their patients.

Through better management of parameters such as hypertension, phosphorus and calcium levels, and anemia, the clinic staff hopes to avoid or delay RRT. However, only few studies report the degree to which hypertension, calcium phosphate status, and anemia preset targets have been reached for patients with advanced CKD followed in multidisciplinary clinics. Thus, the data of multidisciplinary clinic patients were compared with the recommendations of specialty societies.

Methods

A cross-sectional cohort was selected for this study on July 16, 2014, and included all patients followed at the multidisciplinary clinic at that period. No patient followed on this date was excluded from the study. Patients are admitted in the clinic when their eGFR fell below 20 mL/min/1.73 m².

Sociodemographic characteristics and comorbidities of patients, as well as the major relevant metabolic parameters for monitoring renal failure, were collected in the patient records. Blood pressure (BP) was estimated with a single measure taken with a nonautomated oscillometric device. The proteinuria and albuminuria were measured only in a small number of patients (n = 10) and thus are not reported. History of neoplasia was not collected. To assess the effectiveness of the multidisciplinary clinic therapeutic approach, the values of clinic patients were compared with the recommended values. Authorization from the ethics committee and authorities concerned was obtained. It should be noted that the eGFR is calculated with the CKD-EPI method.

The main recommendations that are guiding the management of patients with CKD were examined. For hypertension, the recommendations of 3 different organizations were used: those of Kidney Disease Improving Global Outcomes (KDIGO),⁸ as well as the Canadian Society of Nephrology (CSN)⁹ and the Canadian Hypertension Education Program (CHEP).¹⁰ KDIGO adapts treatment based on proteinuria

without making a distinction between patients with diabetes and patients without, whereas the CHEP and CSN clearly differentiate the treatments for these 2 groups. There was an implicit consensus to follow the CHEP guidelines between nephrologists. Also, due to the frailty of the very elderly patients, CHEP recommends aiming for a BP below 150 mm Hg in these patients. A summary of the recommendations is presented in Table 1.

To control anemia, erythropoiesis-stimulating agents (ESA) are used in patients with CKD. The organizations recognize that a certain level of hemoglobin should not be exceeded and that therapy should be personalized according to the patient's medical history and quality of life.¹¹⁻¹³ When ESAs are used, the organizations differ on targets to be achieved. The CSN proposes keeping the hemoglobin level between 100 and 110 g/L, but it recognizes that 95 to 115 g/L remains within acceptable limits. However, these recommendations are not based on high-quality evidence. The reference values used for purposes of comparison with anemia were those of KDIGO.¹¹

While recognizing the importance of controlling phosphorus and serum calcium levels, the current recommendations for these parameters indicate primarily that they should be maintained within normal values.¹⁴⁻¹⁶ CHAUR's nephrologists consider that phosphorus and total calcium levels should remain below 1.5 mmol/L and 2.5 mmol/L, respectively. The calcium hospital reference values are between 2.20 and 2.55 mmol/L. The reference values for phosphorus are between 0.74 and 1.20 for men and between 0.90 and 1.32 for women.

Statistical analyses were conducted using SPSS software version 22. For the tests between the proportions, chi-squared tests or Fischer exact tests were conducted.

Results

Mean patients age was 71.6 ± 12.4 years. The main eGFR was 14.0 ± 4.7 mL/min. Other patients' characteristics of the patients are presented in Table 2. The population was in majority Caucasian. For the purposes of analysis, the cohort was stratified by diabetes status. The statistical analyses performed demonstrate that there is no statistically significant difference between patients with diabetes and patients

Table 2. Demographic and Clinical Characteristics.

	All	Patients with diabetes	Patients without diabetes
Sex (n = 128)			
Women (%)	48	30 (45.4)	18 (29.0)
Men (%)	80	36 (54.5)	44 (71.0)
Age (years) (n = 128)	71.6 ± 12.4	70.5 ± 11.9	72.9 ± 12.9
Follow-up (months) (n = 128)	26.6 ± 25.1	25.6 ± 24.4	27.6 ± 26.1
eGFR (mL/min/1.73 m ²)	14.0 ± 4.7	14.6 ± 4.6	13.28 ± 4.7
SBP (n = 127)	136.6 ± 15.9	138.6 ± 16.3	134.5 ± 15.3
DBP (n = 127)	70.2 ± 12.2	67.8 ± 11.6	72.7 ± 12.5
Antihypertensive medications (n = 128)	3.2 ± 1.7	3.6 ± 1.7	2.8 ± 1.6
ARBs use	28 (21.9)	17 (25.8)	11 (17.7)
ACEIs use	33 (25.8)	18 (27.3)	15 (24.2)
Hb (n = 127)	110.0 ± 14.2	108.3 ± 12.1	111.8 ± 16.0
Iron levels (g/L) (n = 65)	11.9 ± 4.0	11.6 ± 3.8	12.5 ± 4.4
Ferritin levels (µmol/L) (n = 72)	185.1 ± 130.7	210.4 ± 142.7	149.8 ± 104.2
Erythropoiesis-stimulating agents (%)	59 (46.1)	33 (50.0)	26 (41.9)
Use of iron supplementation (%)	46 (35.9)	28 (42.4)	18 (29.0)
Phosphorous (mmol/L) (n = 123)	1.44 ± 0.28	1.46 ± 0.28	1.43 ± 0.17
Calcium (mmol/L) (n = 121)	2.30 ± 0.19	2.30 ± 0.20	2.31 ± 0.17
Parathormone (pg/L) (n = 120)	20.7 ± 12.0	20.1 ± 10.7	21.3 ± 13.3
Hypertension (%)	117 (91.4)	63 (95.5)	54 (87.1)
Anemia ^a (%)	114 (89.1)	62 (93.9)	52 (85.2)
Coronary heart disease	22 (17.2)	12 (18.2)	10 (16.1)

Note. eGFR = estimated glomerular filtration rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; ARB = angiotensin receptor blocker; ACEI = angiotensin-converting enzyme inhibitor; Hb = hemoglobin.

^aFor this value, n = 127 for all, n = 66 for patients with diabetes, and n = 61 for patients without.

Table 3. Hypertension Targets Reached in Patients With and Without Diabetes.

	Patients with diabetes (n = 66)			Patients without diabetes (n = 62)		
	n (%)			n (%)		
	<130/80 mm Hg	<130 mm Hg	<80 mm Hg	<140/90 mm Hg	<140 mm Hg	<90 mm Hg
All patients	16 (24.2)	19 (28.8)	54 (81.8)	35 (56.5)	27 (59.7)	52 (83.9)
Age < 80 years	12 (23.1)	15 (28.8)	40 (76.9)	24 (58.5)	25 (61.0)	32 (78.0)
Age ≥ 80 years	4 (28.6)	4 (28.6)	14 (100)	11 (52.4)	12 (57.1)	20 (95.2)

without, except for a greater use of antihypertensive medications in patients with diabetes. There was a significant prevalence of atherosclerotic coronary heart disease, which impacts on the choice of treatments.

Concerning the BP control, the mean BP for all patients was 136.6 ± 15.9 / 70.2 ± 12.2 mm Hg. arterial hypertension (HTN) control of both systolic and diastolic BP was 24.2% in patients with diabetes and 56.5% in patients without, while control of systolic BP alone was somewhat better at 28.7% and 59.7% in each group. When using the <140/90 threshold for patients with diabetes, up to 38 patients (57.6%) had their BP controlled. Overall, the use of angiotensin receptor blockers (ARB) was 21.9% and was 25.8% for angiotensin-converting enzyme inhibitors (ACEI). Table 3 presents the hypertension targets that were reached based on the CHEP

and CSN guidelines. To assess whether old age could have had an influence, achievement of targets was also analyzed by dividing the population between those above and those below 80 years of age. We noted that the achievement of targets was substantially the same for these subgroups.

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Concerning the hemoglobin management, the mean hemoglobin level in all patients was 110.0 ± 14.2 g/L. Iron levels in our population were low, with a mean of 11.9 ± 4.0 g/L.

Table 4. Hemoglobin Targets Reached in Patients With and Without ESA.

Hemoglobin values (g/L)	Treated with ESA (n = 58)	Not treated with ESA (n = 69)
	n (%)	n (%)
<100	23 (39.7)	6 (8.7)
100-110	21 (36.2)	19 (27.5)
>110	14 (24.1)	44 (63.7)

Note. ESA = erythropoietin-stimulating agent.

Table 5. Calcium and Phosphorus Targets Reached.

Parameters	Hospital laboratory values		Nephrologists preset targets	
	References values	Control rates	References values	Control rates
Phosphorus (n = 123)	0.74-1.29 for men 0.90-1.32 for women	37 (30.1)	<1.5	78 (63.4)
Calcium (n = 121)	2.20-2.55	91 (75.2)	<2.5	110 (90.9)

However, the iron stores status was collected only in 65 of our patients. Among patients treated for anemia, 36.2% of patients were treated with ESAs reached the targets and about 36% were treated with iron supplementation. In addition, a subsequent analysis revealed that 67.2% of patients fell within the acceptable values of the CSN guidelines, that is, between 95 and 115 g/L. We also note in Table 4 that 8.7% of patients have not been treated with ESAs even if their hemoglobin was below 100.

Concerning the phosphorus and calcium axis management, mean phosphorus level in all patients was 1.44 ± 0.28 mmol/L. The results for achieving calcium and phosphorus targets are mainly dependent on the reference values. They are presented in Table 5. It should be noted that there is a statistically significant difference ($P < .001$) in target rates depending on whether one uses reference laboratory values or preset targets.

Discussion

The goal of our study was to describe our advanced CKD multidisciplinary clinic along with therapeutic performance concerning BP, hemoglobin levels, and phosphorus and calcium levels. Patients in our clinic are old, have a very low eGFR, and have multiple comorbidities. A good therapeutic performance is complex in these patients.

Hypertension is a known risk factor for deterioration of renal function. In our study, there was a significant deviation from guidelines. Another study has focused on hypertension management in patients with CKD.¹⁷ Although the authors did not stratified BP control based on diabetes, they achieved a BP control rate of 26.5% when aiming for a 130/80 threshold and 48.2% when aiming for a 140/90 mm Hg. Thus, when compared with this study, our therapeutic performance was equivalent if not slightly better. Multiple comorbidities of patients can be accounting for the gap between the

observed control rate and a perfect control rate. For instance, many patients in the present study had a history of peripheral artery disease, which could participate in isolated systolic hypertension.¹⁸ Finally, BP management was based on a single measure taken by a nonautomated oscillometric device. Blood pressure measurements taken with automated office BP devices, such as the Omron HEM 907 used in the Systolic Blood Pressure Intervention Trial (SPRINT),¹⁹ take several measurements to estimate BP. Blood pressure management based on a single oscillometric measure could have led to an underestimation of the hypertension control. Concerning the medication use in hypertension, ARBs and ACEIs were used in less than 50% of patients, even in patients with diabetes. Although ARBs and ACEIs have been shown to slow the course of diabetic nephropathy, nephrologists often suspend the use of ARBs and ACEIs to gain time during the initiation of an arteriovenous fistula. Finally, it is also important to mention that in addition to professional practices, patient compliance with their treatments probably plays a role in meeting targets, in terms of both taking medication and changing lifestyle habits.

Concerning the hemoglobin management, anemia was present in 89.1% of patients in the cohort without distinction made between mild and severe cases. Mean iron stores were low, with a mean around 12 g/L. Mean ferritin levels around 185 $\mu\text{mol/L}$ in the presence of low iron levels suggest that an inflammatory component participates in the anemia in this group of patients. However, iron store status was not collected in all of our patients. Thus, the iron stores and transferrin levels may reflect only the status of our sicker patients and may not reflect the tendency of all our patients. When analyzing the data of patients treated with ESAs, we noticed that 36.2% had hemoglobin values between 100 and 110, while 40% were below, and almost a quarter (24.1%) above. If one takes into account the CSN's comments stating that

values between 95 and 115 are acceptable, then 67.2% of patients achieved the targets. Another study on the achievement of targets in pharmacist-managed ESA clinics showed that 71.1% of the patients had a hemoglobin concentration between 100 and 120 g/L.²⁰ This other study cohort had a mean eGFR around 30 mL/min. Thus, our multidisciplinary clinic had similar control rate for hemoglobin levels when compared with other clinics with patients with less severe CKD. It should be noted that hemoglobin control threshold is based on low-quality evidence. Plausible hypotheses on the disparity in targets are hemoglobin variability, caused by multiple factors,²¹ such as hemoglobin fluctuations, hemodilution, and resistance to erythropoietin (EPO) response.

Management of phosphorus and calcium axis is challenging and is presently not based on high-quality evidence.²² For calcium, control rates were 75.2% when the hospital's values were taken into account and 90.9% for preset targets. Patients with serum calcium levels that were too low were very few and not considered in the laboratory targets. For phosphorus, control rates were 30.1% for the hospital's values and 63.4% if preset targets were used. The therapeutic performance of our clinic compares with what exists in the literature. Another study on mineral metabolism targets showed that 55% and 70% of patients in stage 5 CKD reached the targets for phosphorus and calcium, respectively.²³ However, these patients were followed at a general nephrology clinic, not a multidisciplinary clinic, and the targets to be met were those of the kidney disease outcomes quality initiative (KDOQI), which are much broader.²⁴ One way to explain the difference in targets could be patients' compliance with medication. It was also documented that the frequency of taking chelating agents, the size of the tablets, and their possible side effects represent barriers to treatment.²⁵ A diet low in protein and phosphorus may also have an impact on meeting the phosphorus and calcium targets.

Our study has several limitations. First, our study is a single center study with the majority of our patients being Caucasian. This limits the generalizability of our findings. Second, proteinuria was measured only in a small number of patients in the year preceding the date of the data collection. We recognize that proteinuria should have been measured in all patients yearly, and therapeutic action should have been taken to lower the proteinuria below 1 g/day and even lower in patients with diabetes, as this may also preserve renal function. Third, while BP control was based on high-quality evidence, the anemia control and phosphorus and calcium axis control were not. Clinicians in our clinics may be aware of this and thus may not have sought to achieve these guidelines aggressively. Finally, one must remember that clinical practice should be tailored to the patient. Achieving target values in a certain patient may be an indicator of good quality care, but in another patient with several comorbidities, it may not.

The results of this study help to draw a portrait of the therapeutic effectiveness of patient management in our

advanced CKD multidisciplinary clinics and, hopefully, in similar clinics. This would appear worthwhile because, to our knowledge, only a few studies evaluating the effects of the organization of multidisciplinary care have been published. The overall finding is that this type of management is effective, but the deviations noted from the recommendations suggest that it could be optimized. The gaps may be explained in part by a number of existing comorbidities, potentially poor compliance with treatment, a certain clinical caution, and targets based on low-quality evidence. Another consideration is that professional practices may vary and influence treatment decisions. By publishing this study, we wished to share our experience and help improve programs in other multidisciplinary clinics. Finally, it would also be beneficial to verify, by subsequent studies, if the achievement of therapeutic targets results in slowing down the deterioration in kidney function.

Ethics Approval and Consent to Participate

Research ethic board review was not required for this research since it relies exclusively on secondary use of anonymous information, according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans. However, authorizations from hospital authorities were obtained. Participant informed consent was not required for this study.

Consent for Publication

All authors consent to the publication of this study.

Availability of Data and Materials

Not available

Declaration of Conflicting Interests

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