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ORIGINAL ARTICLE

Characteristics of outpatients referred for a first consultation with a nephrologist: impact of different guidelines

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Abstract

Introduction Chronic kidney disease (CKD) affects > 10% of the population but not all CKD patients require referral to a nephrologist. Various recommendations for referral to nephrologists are proposed worldwide. We examined the profile of French patients consulting a nephrologist for the first time and compared these characteristics with the recommendations of the International Kidney Disease: Improving Global Outcomes (KDIGO), the French "Haute Autorité de Santé" (HAS), and the Canadian Kidney Failure Risk Equation (KFRE).

Methods University Hospital electronic medical records were used to study patients referred for consultation with a nephrologist for the first time from 2016 to 2018. Patient characteristics (age, sex, diabetic status, estimated glomerular filtration rate (eGFR) and urine protein-to-creatinine ratio (PCR), etiology reported by the nephrologist) and 1-year patient follow-up were analyzed and compared with the KDIGO, HAS and Canadian-KFRE recommendations for referral to a nephrologist. The stages were defined according to the KDIGO classification, based upon kidney function and proteinuria.

Results The 1,547 included patients had a median age of 71 [61–79] years with 56% males and 37% with diabetes. The main nephropathies were vascular (40%) and glomerular (20%). The KDIGO classification revealed 30%, 47%, 19%, 4% stages G1-2 to G5, and 50%, 22%, 28% stages A1-A3, respectively. According to KDIGO, HAS and KFRE scores, nephrologist referral was indicated for 42%, 57% and 80% of patients respectively, with poor agreement between recommendations. Furthermore, we observed 890 (57%) patients with an eGFR> 30 ml/min and a urine protein to creatinine ratio 0.5 g/g, mostly aged over 65 years (67%); 40% were diabetic, and 57% had a eGFR > 45 ml/min/1.73m^2, 56% were diagnosed as vascular nephropathy and 11% with unknown nephropathy.

Conclusion These results underline the importance of better identifying patients for referral to a nephrologist and informing general practitioners. Other referral criteria (age and etiology of the nephropathy) are debatable.

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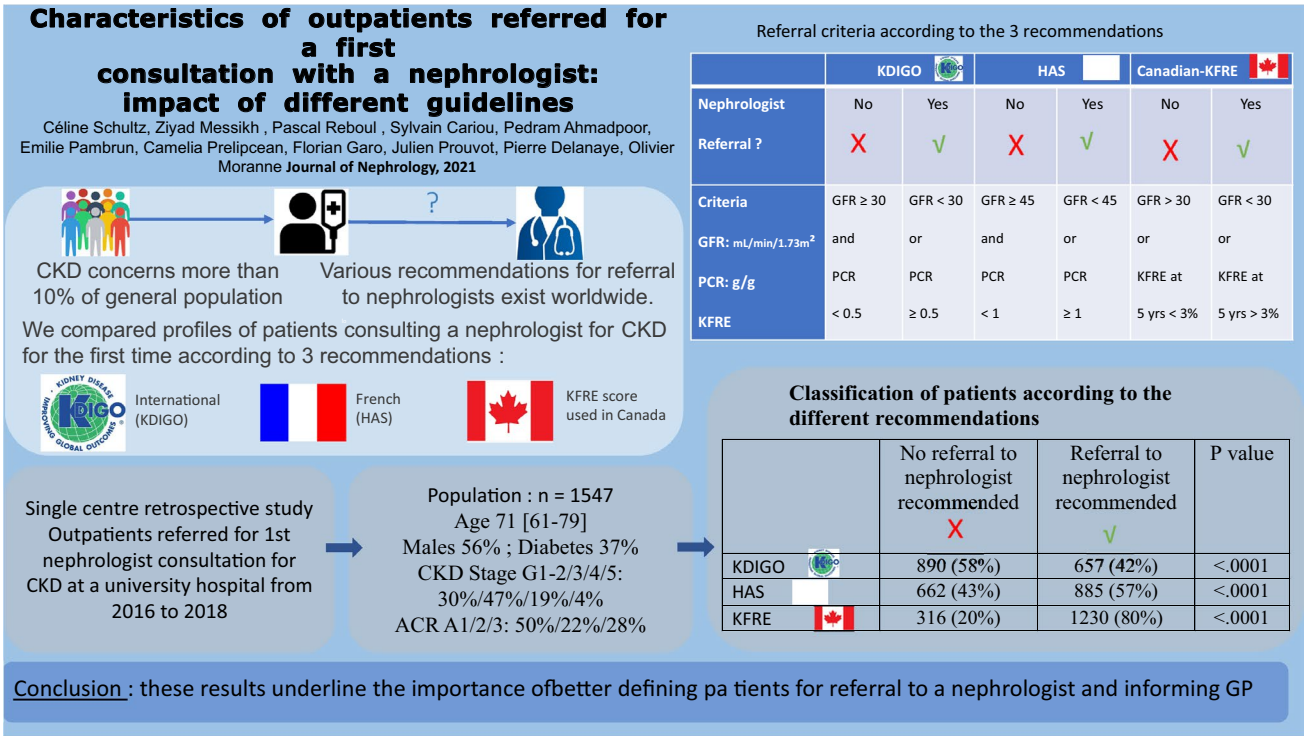
Graphical abstract



Keywords CKD · Nephrologist · Outpatient · Recommendations · Referral

Introduction

Chronic kidney disease (CKD) is defined by the kidney disease: improving global outcomes (KDIGO) organization as a reduction in glomerular filtration rate (GFR) below 60 ml/min/1.73 m^2 or the presence of marker(s) of renal damage (histological, morphological or abnormal blood or urine composition) for more than three months [1]. This definition corresponds to ~ 10% of the general population [2]. The nephrologist is a key player in the care of these patients, but the number of nephrologists is insufficient to provide specialized consultations for all CKD patients [2]. According to a survey by the International Society of Nephrology, the average number of nephrologists in the world is 8.8 per one million inhabitants, i.e. one nephrologist for every 14,773 patients with CKD, considering the 10% prevalence rate [3]. There are wide disparities in the number of nephrologists worldwide, with very low numbers in developing countries (3.64 and 1.17 per million inhabitants in Africa and South Asia, respectively) and higher numbers in the most developed countries, with a peak in Japan (78.79 per million inhabitants). In 2017, there were 1,730 active nephrologists in France, or 26 per million inhabitants [4]. Thus in France, this means that one nephrologist should potentially care for 3,846 CKD patients.

However, not all CKD patients require follow-up by a nephrologist, and it is essential to define which patients require referral. Many recommendations have been published by scientific societies based on different criteria: estimated glomerular filtration rate (eGFR), proteinuria (with different thresholds), eGFR slope, uncontrolled hypertension, and other criteria [1, 5–7]. The KDIGO guidelines recommend referral to a nephrologist when GFR is < 30 ml/min/1.73 m^2 or urine protein-to-creatinine ratio (PCR) > 500 mg/g or 500 mg/24 h (or urine albumin-to-creatinine ratio (ACR) > 300 mg/g or 300 mg/24 h). Other criteria include acute renal failure, rapidly progressive CKD (defined as a decline in eGFR > 5 mL/min/1.73 m^2/year),

Table 1 Guidelines for referral to the nephrologist

	KDIGO [1]		HAS [5]		Canadian-KFRE [9]	
Nephrologist referral	Group 1 No	Group 2 Yes	Group 1 No	Group 2 Yes	Group 1 No	Group 2 Yes
Criteria GFR: mL/min/1.73 m^2 PCR: g/g	GFR ≥ 30 and PCR < 0.5	GFR < 30 or PCR ≥ 0.5	GFR < 45 or PCR ≥ 1	GFR ≥ 45 and PCR < 1	GFR > 30 or KFRE at 5 years < 3%	GFR < 30 or KFRE at 5 years > 3%

Formula: the KFRE formula 5 years risk adapted for the non-North American population is as follows: 1 − 0.9365**exp(− 0.2201 * ((*age*)/10 − 7.036) + 0.2467 * ((1 if *male*, 0 *if female*) − 0.5642) − 0.5567 * (*CKD-EPI*/5 − 7.222) + 0.4510 * (log(*albuminuria, mg/g*) − 5.137)) (11)

Equations for the conversion of urine protein-to-creatinine (PCR) to urine albumin-to-creatinine (ACR) in mg/g [10]: ckdpcrisk.org/pcr2acr

hematuria, refractory hypertension, persistent abnormalities of serum potassium, persistent or extensive nephrolithiasis or hereditary kidney disease [1]. In France, the reference is the "Haute Autorité de Santé" (HAS) i.e. the French health authorities, who recommend referral for a GFR < 45 ml/min/1.73 m^2 or ACR > 0.7 g/g. Other criteria include a rapid decline in renal function, uncontrolled hypertension, the presence of complications, or doubts about the etiology of CKD [8]. A CKD management guide including these criteria is published for general practitioners (GPs) and is available from the HAS online.

The Canadian Society of Nephrology mostly agrees with KDIGO on the GFR threshold at 30 ml/min/1.73 m^2 but the threshold for ACR is 0.6 g/g. GPs are also invited to refer to nephrologists if there is a rapid deterioration in renal function, hydro-electrolytic disorder, hematuria, uncontrolled hypertension or, more recently, risk of end-stage renal disease at 5 years ≥ 3% according to the Kidney Failure Risk Equation (KFRE) score. This KFRE score is based on eGFR, sex and ACR. Hingwala et al. proposed a model for nephrology referral using the KFRE score for patients who did not meet the other referral criteria including GFR < 30 ml/min/1.73 m^2 or nephrotic proteinuria.

Since the introduction of these recommendations and the automatic reporting of eGFR by laboratories, consultations with nephrologists have exploded, lengthening the waiting time for a nephrology consultation. Like many other centers, our university hospital experiences long waiting lists for nephrology consultations.

The aim of our study was to examine the profile and care of patients seen in consultation with a nephrologist for CKD for the first time (i.e. incident patients), and to compare the patient's characteristics with international (KDIGO), French (HAS) and Hingwala's model using KFRE score recommendations [1, 8, 9]

Materials and methods

Population

Our study, conducted at the nephrology department of Nîmes University Hospital, France, from January 2016 to December 2018, identified patients referred to a nephrologist for CKD for the first time. Only outpatients were considered. Ten senior nephrologists work in this department where outpatients come in for consultation. There is no particular protocol for their referral and the nephrologists decide on what kind of follow-up is indicated. The secretaries take appointments for consultation based on requests from the patient's GP, other specialist or the patients themselves, but with no particular triage process according to CKD stage.

Patients seen for any other reasons (acute renal failure, kidney transplant follow-up, high blood pressure, fluid and electrolyte disorders, nephrolithiasis, nephro-obstetrics or other) or already followed for CKD between 2006 and 2015 (i.e. prevalent patients) were excluded. Patients with missing proteinuria data were also excluded from the analysis.

At our institution, the nephrologists systematically report the following data at each consultation: date, reason for consultation, age, sex, diabetic status, eGFR estimated by the creatinine-based Chronic Kidney Disease-Epidemiology (CKD-EPI) equation and PCR. We used a dedicated formula to convert PCR to ACR [10]. If the PCR was not reported at the time of consultation, we considered the first available result after consultation.

The type of nephropathy was defined as: vascular, diabetic, glomerular, tubulo-interstitial, genetic or undetermined. In the year after the first consultation, the following data were collected: number of consultations over the year, kidney biopsy, and the type of management. The type of management was defined as follows: no further follow-up by the nephrologist, sustained follow-up by the nephrologist,

Table 2 Description of incident patients for CKD referral according to classification of KDIGO including GFR and PCR

Criteria	Total	Stage G1 N = 168 (11%)			Stage G2 N = 297 (19%)			Stage G3a N = 301 (19%)			Stage G3b N = 426 (28%)			Stage G4 N = 291 (19%)			Stage G5 N = 64 (4%)		
PCR	**N**	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3
N	1547	95 56%	31 18%	42 26%	195 66%	52 17%	50 17%	180 60%	66 22%	55 18%	196 46%	118 28%	112 26%	92 32%	70 24%	129 44%	12 19%	9 14%	43 67%
Median age (years)	71 [61; 79]	50	44	44.5	65	61	62.5	73	70.5	66	76	73.5	70	79	77	76	76	72	70
Sex (male)	874 (56%)	21 22%	10 32%	9 21%	62 32%	20 38%	26 52%	93 52%	41 62%	38 69%	128 65%	86 73%	85 76%	72 78%	51 73%	85 66%	9 75%	5 55%	33 77%
Diabetes	561 (36%)	20	5	10	48	14	23	68	24	29	73	43	55	31	32	59	3	5	19
Nephropathy																			
Vascular	615 (40%)	13	7	6	63	17	7	104	32	11	126	56	33	49	39	37	5	4	6
Glomerular	305 (20%)	16	13	29	7	14	25	9	11	26	11	20	45	8	4	49	1	1	16
Interstitial	274 (18%)	5	2	0	56	10	8	35	9	8	31	22	14	16	14	22	5	1	6
Diabetic	120 (8%)	3	2	1	14	1	7	8	9	6	8	8	14	7	8	14	1	1	8
Genetic	56 (4%)	18	0	2	8	3	0	6	0	1	2	2	2	3	3	1	0	2	3
Unknown	177 (11%)	30	7	4	47	7	3	18	5	3	18	10	4	9	2	6	0	0	4
Kidney biopsy	169 (11%)	9 9%	9 29%	16 38%	3 1.5%	7 13%	14 28%	9 5%	1 1.5%	15 27%	11 6%	10 8%	24 21%	7 8%	7 10%	19 15%	2 15%	0 0%	6 7%

Definition: Group GFR: G1 = GFR ≥ 90 ml/min/1.73 m^2 G2 = GFR 60–89 ml/min/1.73 m^2 G3a = GFR 45–64 ml/min/1.73 m^2 G3b = GFR 30–44 ml/min/1.73 m^2 G4 = GFR 15–29 ml/min/1.73 m^2 G5 = GFR < 15 ml/min/1.73 m^2; Group Albuminuria: A1 = 0–150 mg/g A2 = 150–500 mg/g A3 = > 500 mg

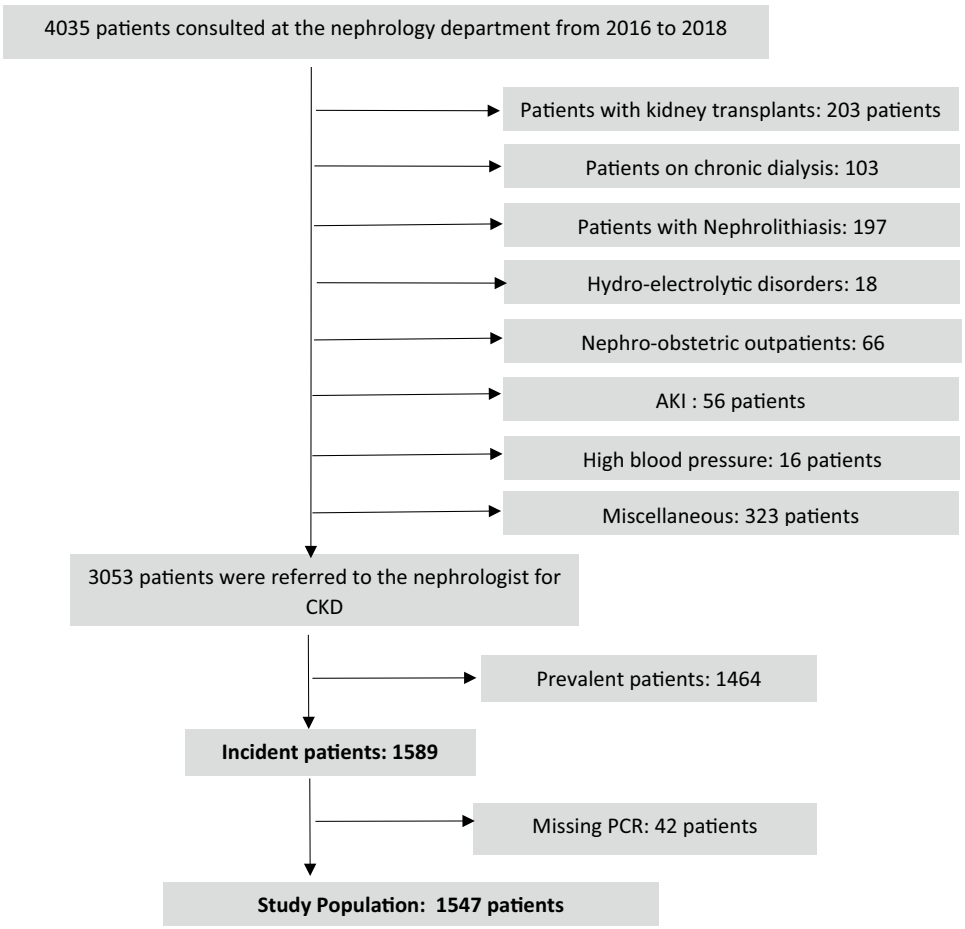


Fig. 1 Flow diagram of patients seen in consultation from 2016 to 2018

initiation of dialysis, conservative treatment, lost to follow-up and death.

Outcome measures

The objective of the study was the description, agreement and comparison of patient characteristics and a posteriori care displaying criteria described by three different guidelines for referral to nephrologists (Group 1: no referral needed, Group 2: to be referred to the nephrologist) (Table 1). We focused on eGFR and urine PCR criteria because these are the most frequently used in clinical research and practice, applying the cut-offs as recommended by the guidelines in Table 2.

Furthermore, as the different guidelines for referral are discordant for patients with a GFR > 30 ml/min/1.73 m^2 and PCR < 0.5 g/g, we described the characteristics and management of this population in an additional analysis.

Statistical analysis

Quantitative variables with a normal distribution are described with their means ± standard deviations and compared with Student's T-test. Variables with a non-Gaussian distribution are presented as medians with their interquartile ranges and compared with a non-parametric Wilcoxon-type test. Qualitative variables are presented in numbers and percentages and compared with a Chi^2 test. Concordance was tested by the kappa coefficient, classified as follows: 0–0.4 slight to fair; 0.41–0.6 moderate; 0.61–0.80: substantial; 0.81–1.0 perfect. A difference was considered statistically significant if p was < 0.05. Analyses were performed using SAS software version 9.3 (SAS Institute Inc.).

Ethical section

This study was approved by the local ethics committee and our internal review board under the no. 191004. Patients were informed of the study by letter and were included if they were unopposed to the use of their data from electronic records.

Table 3 Characteristics and care in patients with eGFR > 30 ml/min/1.73 m^2 and PCR < 0.5 g/g and according age

	Total N = 890	Age < 65 years N = 295 (33%)	65–74 years N = 295 (33%)	≥ 75 years N = 300 (34%)	p value
Age (years)	70 [59; 77]	52 [41; 59]	70 [67; 72]	81 [77; 84]	
Sex (male)	442 (49%)	131 (44%)	171 (58%)	140 (47%)	.002
Diabetic	277(31%)	43 (15%)	117 (40%)	117 (39%)	< 0.0001
Nephropathy					< 0.0001
Vascular	400 (45%)	66 (22%)	137 (46%)	197 (66%)	
Glomerulopathy	88 (10%)	41 (14%)	30 (10%)	17 (6%)	
Interstitial	174 (19%)	70 (24%)	69 (24%)	35 (12%)	
Diabetic	51 (6%)	12 (4%)	23 (8%)	16 (5%)	
Genetic	38 (4%)	36 (12%)	1 (0%)	1 (0%)	
Unknown	139 (15%)	70 (24%)	35 (12%)	34 (11%)	
CKD group					< 0.0001
G 1	122 (14%)	96 (33%)	19 (6%)	7 (2%)	
G 2	240 (27%)	118 (40%)	72 (24%)	50 (17%)	
G 3a	238 (27%)	46 (16%)	94 (32%)	98 (33%)	
G 3b	290 (32%)	35 (12%)	110 (37%)	145 (48%)	
Number of consultations with a nephrologist in the year following inclusion					
No consultation in the year	391 (44%)	128 (43%)	128 (43%)	135 (45%)	0.63
2 consultations in the year	321 (36%)	100 (34%)	113 (38%)	108 (36%)	
> 2 consultations in the year	178 (20%)	67 (23%)	54 (18%)	57 (19%)	
Reasons for no nephrology follow-up in the year N = 391					
No need for FU according to nephrologist advice	132 (34%)	52 (41%)	38 (30%)	43 (32%)	
New consultation after 1 year	136 (35%)	37 (29%)	50 (39%)	49 (36%)	
LTF	10 (2.5%)	3 (2%)	5 (4%)	2 (1%)	
Dialysis or transplant	74 (19%)	30 (23%)	22 (17%)	22 (17%)	
Palliative FU or death	17 (4%)	1 (1%)	7 (5%)	9 (7%)	
Kidney Biopsy	53 (6%)	32 (11%)	15 (5%)	6 (2%)	< 0.001

FU = Follow-up; LTF = Lost to Follow-up

Results

Over the inclusion period, 4,035 outpatients were seen at the hospital's nephrology department, for a total of 10,613 consultations (Fig. 1). Of these patients, 3,053 had been referred to a nephrologist for CKD, of whom 1,464 were prevalent patients and 1,589 were incident. We excluded 42 incident patients with missing proteinuria data. The final sample considered in the current analysis is thus of 1,547 patients. The median age of the population was 71 [61; 79] years, 56% were male, 36% were diabetic and the two main nephropathies reported were of vascular (40%) and glomerular (20%) origin. The distribution and characteristics of the 1,547 incident patients according to the KDIGO classification are presented in Table 2. Most patients were in stage G3 (47%) (eGFR between 45 and 60 ml/min/1.73m^2), with a predominance of low albuminuria [52% of stage G3 patients had ACR < 30 mg/g (stage A1)]. A third of the population was in stages 1 (G1) (eGFR > 90 ml/min/1.73 m^2) and 2 (G2) (eGFR between 60 and 90 ml/min/1.73 m^2), 19% in stage G4 and 4% in stage G5. Patients in first stages of the disease had lower albuminuria, whereas patients in stages 4 and 5 had ACR > 300 mg/g (stage A3) or ACR between 30 and 300 mg/g (stage A2) (22%). The percentage of males increased with stages G1–5, as did the median age and the prevalence of diabetes mellitus. Nephroangiosclerosis was the most frequently reported nephropathy for late stages of the disease, whereas glomerulopathy was the most frequent in stage G1. A kidney biopsy was performed in 11% of patients, mostly in early glomerular stages, and especially patients in stage A3.

In the year following the consultation, 61% of patients were still being followed by a nephrologist, including 27% who had at least two follow-up consultations within the year. Reasons for no follow-up consultations in the year (n = 606, 39%) were as follows: 33% (n = 204) had a new consultation more than a year after the first one, 28% (n = 144) were lost to follow-up, 3% (n = 19) were treated by dialysis or kidney transplant, 3% (n = 19) were being followed elsewhere, 9% (n = 54) had palliative follow-up or had died, and for 27% (n = 162) there was no follow-up indication according to the nephrologist.

Table 4 Patient characteristics according to indication for referral to a nephrologist (Group 2) or not (Group 1) according to the different recommendations (KDIGO, HAS and Canadian KFRE prognosis score)

Recommendations	KDIGO		HAS		Canada and KFRE	
Characteristics	Group 1 (GFR ≥ 30 and PCR < 0.5)	Group 2 (GFR < 30 or PCR ≥ 0.5)	Group 1 (GFR ≥ 45 and PCR < 1)	Group 2 (GFR < 45 or PCR ≥ 1)	Group 1 (KFRE at 5 years < 3% and GFR ≥ 30)	Group 2 (KFRE at 5 years ≥ 3% or GFR < 30)
N	890 (58%)	657 (42%)	662 (43%)	885 (57%)	316 (20%)	1230 (80%)
Age (year)	70 [59; 77]	72 [62; 81]**	67 [52; 75]	73 [65; 81]**	56 [41; 69]	73 [65;81]**
Sex (male)	442 (50%)	432 (66%)**	267 (40%)	607 (69%)**	82 (26%)	792 (64%)**
Diabetes	277 (31%)	284 (43%) **	198 (30%)	363 (41%)**	74 (23%)	486 (40%)**
Nephropathy		**		**		
Vascular	400 (45%)	215 (33%)	247 (37%)	368 (42%)	71 (22%)	544 (44%)
Glomerular	88 (10%)	217 (33%)	85 (13%)	220 (25%)	72 (23%)	232 (19%)
Interstitial	174 (20%)	100 (15%)	135 (20%)	139 (16%)	53 (17%)	221 (18%)
Diabetic	51 (6%)	69 (11%)	42 (6%)	78 (9%)	16 (5%)	104 (8%)
Genetic	38 (4%)	18 (3%)	36 (5%)	20 (2%)	26 (8%)	30 (2%)
Undetermined	139 (16%)	38 (6%)	117 (18%)	60 (7%)	78 (25%)	99 (8%)
Kidney biopsy performed	53 (6%)	116 (18%) **	46 (7%)	123 (14%)**	41 (13%)	128 (10%)
Consultation with a nephrologist in the year following inclusion						
No consultation in the year	391 (44%)	215 (33%) **	307 (46%)	299 (34%)**	153 (48%)	453 (37%)*
2 consultations in the year	321 (36%)	199 (30%)	244 (37%)	276 (31%)	103 (33%)	416 (34%)
> 2 consultations in the year	178 (20%)	243 (37%)	111 (17%)	310 (35%)	60 (19%)	361 (29%)
Reasons for no nephrology follow-up consultation in the year						
No nephrology FU indication	133 (34%)	29 (13%) **	123 (40%)	39 (13%) **	68 (44%)	94 (20%)**
Consultation after 1 year	136 (35%)	68 (31%)	104 (33%)	100 (33%)	42 (27%)	162 (36%)
Followed up elsewhere	10 (2.5%)	9 (4%)	5 (1%)	14 (4%)	0	19 (4)
LTF	94 (34%)	54 (25%)	69 (22%)	79 (26%)	41 (27%)	107 (23%)
Dialysis or transplant	1 (0%)	18 (8%)	0 (0%)	19 (6%)	0 (0%)	19 (4%)
Palliative FU/death	17 (13%)	37 (17%)	6 (2%)	48 (16%)	2 (1%)	52 (11%)

G1 vs G2 *p < 0.05; **p < 0.001; FU: follow-up; LTF: lost to follow-up;

Table 5 Classification of patients into two groups according to the different recommendations

	Group 1: no referral to nephrologist recommended	Group 2: referral to nephrologist recommended	p value
KDIGO	890 (58%)	657 (42%)	< 0.0001
HAS	662 (43%)	885 (57%)	< 0.0001
KFRE	316 (20%)	1230 (80%)	< 0.0001

Furthermore, we observed 890 (57%) patients with GFR > 30 ml/min and PCR < 0.5 g/g, mostly over 65 years old (n = 595, 67%), including 295 (33%) between 65 and 74 years old and 300 (34%) > 75 years old. Patients > 65 years were more often diabetic (40%), with higher eGFR > 45 ml/min/1.73 m^2 (57%) and more vascular nephropathies (56%) and unknown nephropathies (11%), and had undergone fewer kidney biopsies, while patients < 65 years had more genetic glomerulopathies and nephropathies of unknown etiology (Table 3). Moreover, for more than 30% of patients not seen again by the nephrologist in the year, the decision not to pursue with follow-up had been made by the nephrologist (Table 3).

The numbers and characteristics of patients according to the KDIGO, HAS and Canadian-KFRE recommendations for referral to the nephrologist are detailed in Table 4. According to KDIGO, the majority of patients were classified in Group 1 (no referral needed) (58%). Patients in Group 2 (to be referred) were older (70 vs 72 years, p < 0.001), more likely to be male (66% vs. 50%, p < 0.001) and diabetic

(43% vs. 31%, p < 0.001). The most frequent nephropathy in Group 1 was vascular followed by interstitial and undetermined nephropathy, while it was glomerular and vascular in Group 2. As expected, patients in Group 2 were significantly more often followed in consultation and underwent biopsies.

According to HAS recommendations, the majority of patients were in Group 2 (57%). Patients in Group 1 were younger (67 vs 73 years, p < 0.001) and more often female (60% vs 31%, p < 0.001). The most common nephropathies were vascular, interstitial and undetermined in Group 1 versus vascular and glomerular in Group 2. In Group 1, 46% of the patients were not seen in consultation within a year, and kidney biopsy was performed less often (7% vs 14%, p < 0.001).

According to the Canadian-KFRE prognostic score, the vast majority of patients were in Group 2 (80%). Patients in Group 1 were younger, (56 vs 73 years, p < 0.001), more often female (74% vs 36%, p < 0.001) and less often diabetic (23% vs 40%, p < 0.001). Nephropathy was mostly undetermined in Group 1 and vascular in Group 2. In the year following consultation, a kidney biopsy was more often performed in Group 1, but these patients were less frequently seen with significantly fewer indications for a nephrology consultation. Finally, concordance was slight-to-fair between KFRE and KDIGO (κ = 0.17, 95% CI 0.14–0.21) and between KFRE and HAS (κ = 0.40, 95% CI 0.36–0.44). The concordance between KDIGO and HAS was moderate (κ = 0.55, 95%CI: 0.52–0.59) (Table 5).

Discussion

Our population study included 1,547 patients with a median age of 70 years, 56% males, 36% with diabetes, with vascular and glomerular nephropathies as the main causes of CKD.

The number of patients meeting the recommendations to consult a nephrologist was very different according to the KDIGO, HAS and Canadian model using KFRE risk score with 42, 57 and 80% of the population, respectively. Many patients were still referred to nephrologists at our center without a referral indication according to the KDIGO or HAS guidelines. Indeed, 162 (10%) patients in our population had not been not recommended for follow-up according to the nephrologist's advice. These 162 patients identified by the nephrologist "as not requiring specific nephrology follow-up" were more often identified as such by the KDIGO (n = 133, 82%) and HAS (n = 123, 76%) than by Canadian guidelines using KFRE risk score (n = 68, 42%). Moreover, 81% of patients not recommended for follow-up according to the nephrologist's advice had an eGFR > 30 ml/min/1.73 m^2 and a PCR < 0.5 g/g.

Some patients were seen too late, with 4% of patients seen for the first time in stage 5, whereas earlier nephrological follow-up is known to be beneficial before reaching the terminal stage [11–14]. Implementing the recommendations for referring patients has led to a marked increase in the number of requests for consultations in certain countries [15, 16], opening up the debate on their relevance [17, 18, 19, 20]. The Canadian study by Akbari et al., describing patients seen by a nephrologist for the first time, reported approximately 60% of patients seen in stage G3, 20% in stages G1–2 and 20% in stages G4–5, in accordance with our practice [17]. In addition, the French study by Prévot et al. [21] reported 70% of patients with CKD as the reason for first nephrology consultations. This was similar to our population, but about 20% of these patients had a GFR > 45 ml/min and a PCR < 0.5 g/g, and 16% were classified as having no CKD, thus 36% had no theoretical indication for consultation, which was less than in our population. Moreover, only 0.9% were in stage G5 at the first consultation in their study.

Our data complete those found in a previous review [7], showing the difference in patient profiles according to the recommendations used. Indeed, our study found moderate classification concordance between KDIGO and HAS and slight-to-fair concordance between KFRE and KDIGO or HAS. The Canadian model using the KFRE score on top of GFR and ACR appeared to be of poor relevance to our study because the score gives a high weight to age, resulting in a systematically high score among the oldest age groups, unlike KDIGO and HAS. This heterogeneity between recommendations highlights the need to define more accurately which patients require a nephrology consultation to optimize the organization of consultations and prioritize high-risk patients with criteria that remain to be better defined. Moreover, evaluation of guidelines with impact studies seems necessary. One such study is currently under way in the UK, but only to evaluate the benefit of selecting consultations using the KFRE on the model of Hingwala et al. versus the NICE (National Institute for Health and care Excellence) recommendations [22].

Primary health care in France is centralized with the GP but, unlike in the UK, this is not an obligation. Patients are free to go directly to a nephrologist on their own initiative or be referred to one by their GP. There are no sanctions if the recommendations for good practices are not respected. Lastly, all consultation fees are covered by the Health care system and doctors working at university or at public hospitals get a fixed salary, regardless of the number of consultations they do.

GPs and other specialists must be made more aware of the recommendations for screening and referral to the nephrologist. Indeed, qualitative studies have reported that cooperation with the GP is frequently suboptimal and GPs are unsure of their place in the management of CKD and

report unsatisfactory communication [23–25]. Both Canadian [26] and American [27] studies have suggested that GPs be provided with tools to raise awareness of screening and encourage joint management of CKD with the nephrologist. Finally, consensually identifying the characteristics of this population referred to the nephrology department would develop better cohesion between nephrologists and other specialists to pinpoint those patients who would most benefit from a nephrology referral according to shared recommendations, and improve the delivery of care to the CKD population. Indeed, for this population we must improve the frequency of proteinuria or albuminuria dosage on spot urine to better identify patients who need nephrologist follow-up. The study by Stengel et al. [28] reported that in nephrology centers in Germany, Brazil and the US, only 30–40% of patients had proteinuria or albuminuria measurements.

Surprisingly, although 58% of referred patients did not meet the referral criteria, we observed that only 27% of patients were discharged by the nephrologist. It should be noted that, in France, the nephrologist has a regular salary from the hospital regardless of the volume of work or choosing to follow patients or not and there is no financial gain related to the number of consultations.

These results suggest several hypotheses which need to be documented in future studies, such as a possible lack of knowledge regarding referral criteria, GPs confusing the screening thresholds, difficulties in discharging patients without proper protocols or unknown guidelines for patients with chronic diseases such as diabetes and inappropriate guidelines.

Indeed, Torreggiani et al. found that several patients were referred whereas they would have been "outside/overdue" according to the guidelines and put this down to a possible lack of knowledge about referral criteria and GPs' screening thresholds particularly for diabetic and elderly patients.

Moreover, the problem of developing these guidelines is to find the right balance between over-referring and late delayed referral as observed in our study. This has also been discussed by others, showing that we will need more nephrologists to offer outpatient evaluations for all these people [29].

Considering our results, we suggest issuing consensual recommendations for referring patients to nephrologists for an indication of CKD after improving the algorithm to include other criteria, such as the etiology of the nephropathy and age, which need to be validated in prospective studies. With respect to age, the definition of CKD is controversial for people over 65 years of age without proteinuria, who demonstrate physiological aging of the kidneys, which is not predictive of progression to advanced renal failure. It is therefore proposed to reduce the GFR threshold for defining CKD in patients over 65 years old [30], especially as the benefits of nephrological follow-up for these patients has yet to be proven [31]. Thus, the question is raised about whether to refer patients over 65 years of age with an eGFR between 45 and 60 ml/min/1.73 m^2 and without proteinuria in the absence of a consensus on a diagnosis of CKD [32]. The study by Jonsson et al. [33] showed a lower prevalence of CKD in Iceland, using age-adapted thresholds (GFR < 75 ml/min/1.73 m^2 before 45 years, GFR < 60 ml/min/1.73 m^2 between 45–65 years and GFR < 45 ml/min/1.73 m^2 after 65 years). In our population, patients with an eGFR > 30 ml/min/1.73 m^2 and PCR < 0.5 g/g were predominantly over 65 years of age with eGFR > 45 ml/min/1.73 m^2 and vascular nephropathies.

The etiology of the nephropathies is included in the definition but not in the CKD prognostic score. Notably, in the no-indication/low-risk groups, vascular and interstitial nephropathies predominate, whereas they are less at risk of rapid progression and their management does not usually include specific treatments. Genetic nephropathies concern younger patients and are more often found in the group without indication for referral according to eGFR and PCR, but incur specific recommendations for consultation according to the KDIGO and HAS. However, the use of causal nephropathy as an indication for consultation is complicated because this diagnosis is often made by the nephrologist during consultation, and therefore is not always known by the physician before referral. Thus, the semiology of CKD syndrome could be more useful than the etiology of the nephropathy in primary care according to the presence of proteinuria, hematuria, or leukocyturia without urinary tract infection when discussing nephrology referral.

The study has several strengths. It includes a large population in a catchment area of 750,000 inhabitants, with exhaustive data collection over two years on patients referred to the nephrologist for CKD for the first time. It also analyzes the care organization of these patients over one year at the main nephrologist consultation site. As these outpatients had regular tests during their appointments with the nephrologist, few patients were excluded from the study for missing PCR data. However, the study does have certain limitations. First, it is a retrospective, single-center study relying solely on eGFR and proteinuria reported by nephrologists with no information about the decline in GFR, the physician who referred the patient or details about the indication. Nephropathy typing was based on the nephrologist's declaration, with few kidney biopsies performed to confirm the etiology.

There are also limitations in classifying the type of nephropathy in Type 2 diabetic patients who were reported as having a diabetic, glomerular or vascular nephropathy. Besides, although not stipulated in the recommendations, information about major comorbidities or the origin of the referral (GP, other practitioner or the patients themselves) were not available.

Finally, our results illustrate the situation at a university hospital in a developed European country with an efficient healthcare system, with referrals from both urban and rural areas. Results may be quite different in developing countries and/or in countries with poorer health coverage.

Lastly, we only compared three recommendations: the international KDIGO recommendations, the recommendations of the country where the consultations were carried out and the Canadian recommendations which propose the use of the Canadian-KFRE prognosis tool.

Conclusion

The results of our study emphasize the frequency of patients being referred to nephrologists for an indication of CKD without the guidelines being applied. It also suggests the necessity to issue homogeneous guidelines for GPs and specialists and to discuss ways of improving the referral algorithm so as to better select those patients who would benefit from referral. We also suggest discussing and evaluating the benefit of including age and/or etiology of the nephropathy into the usual aforementioned referral criteria to improve patient referral.

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Declarations

Conflict of interest The authors declare that they have no conflicts of interest.

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