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Impact of Albumin-to-Creatinine Ratio Point-of-Care Testing on the Diagnosis and Management of Diabetic Kidney Disease

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Abstract

Background: For the diagnosis of diabetic kidney disease (DKD), quantitative albuminuria measurement using the albumin-to-creatinine ratio (ACR) is recommended according to various guidelines. It can be measured either in specialized laboratories or using ACR point-of-care testing (POCT). This observational study aims at evaluating the effect of ACR POCT utilization on the DKD diagnosis and treatment management for glycemic control and blood pressure.

Method: Data of 717 patients with diabetes (type 1 diabetes: n = 236; type 2 diabetes: n = 463; other diabetes forms: n = 18) were assessed in three centers. The impact of ACR POCT on DKD diagnosis and treatment management for glycemic control and blood pressure was assessed using a case report form. The assessment of ACR POCT utilization purpose and relevance for physicians was documented using a questionnaire.

Results: Of all participants (n = 717), 39.1% had a confirmed/suspected DKD diagnosis. Hereof, 8.6% were newly diagnosed with DKD, and 9.9% were suspected with DKD based on the actual ACR POCT values. Within the group of patients with confirmed/suspected DKD (n = 280), treatment modification was performed in 46.1% of participants. A drug initiation with GLP-1 receptor agonists or SGLT2 inhibitors was performed in 11.1% or 8.9% of patients with confirmed/suspected DKD, respectively. Regarding the utilization purposes of ACR POCT, 100% of the physicians (n = 8) indicated using it to examine patients with diabetes with or without hypertension; 75% considered it very important for patients with diabetes.

Conclusions: The implementation of ACR POCT may positively affect DKD diagnosis and subsequently allow better management of patients with diabetes.

Keywords

albumin-to-creatinine ratio, chronic kidney disease, diabetes, point-of-care testing

Introduction

Diabetes mellitus and hypertension are the most frequent causes of chronic kidney disease (CKD) worldwide.[1-3] In fact, approximately 20% to 40% of patients with diabetes develop diabetic kidney disease (DKD).[1,4]

The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines recommend a CKD classification based on cause, estimated glomerular filtration rate (eGFR) category, and albuminuria category, with either an eGFR < 60 mL/min/1.73 m^2, or an albuminuria $\geq$30 mg per 24 hours, or urine albumin-to-creatinine ratio (ACR) $\geq$30 mg/g (3 mg/mmol) defining CKD.[5] In DKD, albuminuria often represents the first sign of kidney damage and precedes a decline in GFR. The American Diabetes Association (ADA) and the International Diabetes Federation (IDF) recommend the assessment of urinary albumin (eg,

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ACR) and eGFR in patients with type 1 diabetes (T1D) with a duration of ≥5 years, in all patients with type 2 diabetes (T2D), and in all patients with comorbid hypertension at least once a year.[4,6]

The assessment of albuminuria via ACR can be performed either in specialized laboratories or directly in primary care offices using ACR point-of-care testing (POCT). The latter method delivers valid ACR results that compare well with values obtained using laboratory-based methods.[7] The utilization of POCT has some advantages. It allows time saving and high satisfaction and acceptability for the patient. Furthermore, it is likely cost-saving for the office/hospital.[8-12] Moreover, the implementation of POCT allows an optimization of the working processes,[9] and the immediate availability of POCT results is associated with the same or improved medication adherence compared with laboratory-provided test results.[13]

The aim of this observational study was to evaluate the influence of ACR POCT on the diagnosis of DKD and the subsequent implications for the management of glycemic control and blood pressure in patients with diabetes mellitus. Also, the utilization purpose and the relevance of ACR POCT were assessed by the physicians using a questionnaire.

Methods

This was an observational study concerning the ACR POCT implementation in one private diabetology outpatients' clinic and two hospital-based diabetology outpatients' clinics. Information on patients with diabetes was collected by their treating physician during their routine care. With the gathered data, a quantitative evaluation of the impact of ACR POCT on the DKD diagnosis and the management of glycemic control and blood pressure treatment was performed.

For the ACR testing, the Afinion 2 analyzer in combination with the Afinion ACR test cartridge was used. The manufacturer recommends the performance of quality controls for the first-time utilization of the Afinion 2 analyzer, each new shipment or batch of Afinion test kits, unexpected patient test results, after new training of new personnel, and if national or local regulations require more frequent quality control testing.[14]

The diagnosis of DKD was based on assessed laboratory values (ACR and creatinine-based eGFR) and the treating physician's judgment. Consequently, the diagnosis acuity may be affected by a certain extent of subjectivity. In accordance with the KDIGO clinical practice guidelines, three albuminuria categories were considered, depending on the investigated question or performed analysis: albuminuria category A1: normal to mildly increased (<3 mg/mmol); albuminuria category A2: moderately increased (3-30 mg/mmol); albuminuria category A3: severely increased 30 mg/mmol).[3]

One private diabetology outpatients' clinic and two hospital-based diabetology outpatients' clinics (Stoffwechselzentrum St. Gallen, Kantonsspital Frauenfeld, and Kantonsspital Olten) located in Switzerland participated in this seven-month study (March-September 2020). Data of 149, 187, and 381 patients with diabetes, who got an ACR POC test during routine care, were collected and evaluated in the three respective locations. In all, 236 patients had T1D, 463 had T2D, and 18 had other diabetes forms or were without any stated information about diabetes (a total of 717 participants). In the analyses, only patients with T1D or T2D were compared. The group of other forms of diabetes was not included in the comparisons. Consequently, the sum of the values of the T1D and T2D groups (shown in the tables) does not necessarily add up to the total.

At the participants' control appointment, the physician filled out a one-page personally non-attributable case report form. The first section was concerned with the general clinical characteristics of the participant (sex, age, weight, height, body mass index [BMI], ethnicity [black, non-black]). In the subsequent section, diabetes data were assessed, including the type of diabetes (type 1, type 2, or other types), date of first diagnosis (Table 1), and medication. Furthermore, different laboratory values (HbA1c, blood pressure, ACR value, creatinine in blood, eGFR) were assessed in the questionnaire if measured as per routine clinical practice.

To investigate the impact of ACR POCT on the diagnosis of DKD and the initiation or modification of treatment for glycemic control and blood pressure, the following methods were applied:

A. To determine the DKD diagnosis status (positive or negative) and the diagnosis time, the two following questions were asked: (1) "Has DKD been diagnosed?" (2) "If yes, when has DKD been diagnosed first time?" For this question, the three following categories were possible: (2.1) newly diagnosed DKD, based on actual ACR POCT values; (2.2) suspected DKD, based on actual ACR POCT values; and (2.3) previously known DKD.
B. For the assessment of diagnostic reasons for modification of treatment, the three following questions were asked: (1) "Has the medication been changed based on the actual ACR value?" (2) "Has the medication been changed based on the actual HbA1c value?" and (3) "Has the medication been changed based on the actual blood pressure?"
C. A differentiated evaluation of the modification of treatment in patients with a positive DKD diagnosis, based either on the time of DKD diagnosis (newly diagnosed DKD, suspected DKD, and previously diagnosed DKD based on ACR POCT), the HbA1c values, or the blood pressure values.
D. The medication modification for glycemic control and blood pressure was assessed according to the

Table 1. General Clinical Characteristics of the Examined Participants.

Clinical characteristics	Total	Type 1 diabetes	Type 2 diabetes	*P* value (T1D vs T2D)
Patients (n); male/female/NA	717 (415/300/2)	236 (134/101/1)	463 (269/193/1)	—
Median age (year) (IQR) Total: n = 704; T1D: n = 233; T2D: n = 453	60 (50-69)	52 (34-62)	63 (55-71)	$P < .001$
Median weight (kg) (IQR) Total: n = 694; T1D: n = 224; T2D: n = 454	87 (74-98)	80 (68-90)	90 (77-101)	$P < .001$
Median height (cm) (IQR) Total: n = 697; T1D: n = 226; T2D: n = 456	170 (163-178)	172 (165-180)	169 (162-176)	—
Median BMI (kg/m^2) (IQR) Total: n = 690; T1D: n = 221; T2D: n = 454	29 (26-34)	26 (24-29)	31 (28-35)	—
Median blood pressure (systolic/diastolic) (mm Hg) (IQR) Total: n = 679; T1D: n = 225; T2D: n = 436	137 (125-150)/81 (75-88)	134 (124-147)/80 (74-86)	139 (128-151)/82 (75-88)	$P < .001$
Median diabetes duration (years) (IQR) Total: n = 638; T1D: n = 223; T2D: n = 399	14 (6-21)	18 (9-30)	12 (5-20)	$P < .001$
Laboratory values	**Total**	**Type 1 diabetes**	**Type 2 diabetes**	***P* value (T1D vs T2D)**
Median HbA1c value (%) (at visit) (IQR) Total: n = 713; T1D: n = 235; T2D: n = 461	7.6 (6.8-8.5)	7.7 (6.9-8.4)	7.6 (6.7-8.6)	ns
Median ACR value (mg/mmol) (at visit) (IQR) Total: n = 709; T1D: n = 234; T2D: n = 457	1.9 (1.0-6.0)	1.5 (0.8-2.9)	2.5 (1.1-7.4)	$P < .001$
Subdivision of the ACR values into the albuminuria categories A1 to A3				
ACR < 3 mg/mmol	62.3% (n = 442)	75.2% (n = 176)	55.1% (n = 252)	$P < .0001$[a]
ACR 3-30 mg/mmol	32.9% (n = 233)	21.8% (n = 51)	39.2% (n = 179)	$P < .0001$[b]
ACR > 30 mg/mmol	4.8% (n = 34)	3.0% (n = 7)	5.7% (n = 26)	ns
Median blood creatinine value (µmol/l) (at date) (IQR) Total: n = 613; T1D: n = 212; T2D: n = 387	72.0 (61.0-86.0)	70.5 (60.0-80.3)	73.0 (62.0-91.0)	$P < .001$
eGFR (CKD-EPI) (mL/min/1.73 m^2) (at date) Total: n = 412; T1D: n = 168; T2D: n = 234				
eGFR < 30	1.2% (n = 5)	1.2% (n = 2)	1.3% (n = 3)	ns
eGFR 30-59	10.4% (n = 43)	4.2% (n = 7)	15.4% (n = 36)	$P < .0003$[c]
eGFR 60-89	30.6% (n = 126)	29.2% (n = 49)	31.6% (n = 74)	ns
eGFR > 90	57.8% (n = 238)	65.5% (n = 110)	51.7% (n = 121)	ns

Abbreviations: T1D, type 1 diabetes; T2D, type 2 diabetes; IQR, interquartile range; BMI, body mass index; ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; EPI, Epidemiology Collaboration.

[a] $\chi^2(1, N = 691) = 26.4$, $P < .00001$.

[b] $\chi^2(1, N = 691) = 21.0$, $P < .00001$.

[c] $\chi^2(1, N = 402) = 12.9$, $P < .0003$.

medication list on the case report form. First, the baseline medication of the entire group, patients without DKD, and patients with confirmed/suspected DKD was evaluated. Consequently, the medication modification performed in patients with confirmed/suspected DKD (dose increase or decrease and new drug initiation) was examined.

To investigate the utilization purpose and relevance of ACR POCT, physicians were asked to fill out a questionnaire with the two following questions: (1) "For what purpose do you use the ACR POCT value?" and (2) "How important is the ACR POCT value for you?" Multiple responses were possible.

For the statistical comparison of the general clinical characteristics and laboratory values between T1D and T2D groups, we performed the Mann-Whitney U Test. The percentage values of the T1D and T2D groups were compared using the chi-square test (χ^2).

As this observational study uses anonymously collected and irreversibly de-identified health-related data, it does not fall under the concept of research according to Article 2 (2c) of the law on human research (Humanforschungsgesetz [HFG]). Therefore, an evaluation by the Ethics Committee (Ethikkommission Ostschweiz [EKOS]) and collection of patient consent were declared as not being necessary.

Results

Patient Characteristics and Laboratory Values

First, we evaluated the general clinical characteristics and relevant laboratory values of the patients. Of the examined 717 participants with diabetes, nearly one-third had T1D and two-thirds T2D, whereas 18 patients (2.5%) had other diabetes types (eg, type 3C, gestational). The median diabetes duration was in patients with T1D significantly longer than in patients with T2D. It was noticeable that patients with T1D were significantly younger than patients with T2D. Furthermore, a significantly higher weight was observed in patients with T2D compared with those with T1D. Both systolic and diastolic blood pressure levels were slightly but statistically significantly higher in patients with T2D than in those with T1D. Further clinical characteristics are presented in Table 1.

Laboratory values for glycemic control (HbA1c) and kidney function (ACR, blood creatinine, and eGFR) were also assessed. The values for HbA1c were similar in the T1D and T2D groups. Concerning the diagnostic values of kidney function, ACR values and blood creatinine levels were significantly higher in the T2D group compared with the T1D group. The distribution of ACR values within the albuminuria categories A1 to A3 are also shown in Table 1. We further evaluated the distribution of eGFR in four categories. Concerning the entire group, nearly one-third of the participants had mildly reduced eGFR values (stage G2: 60-89 mL/min/1.73 m^2), and one-tenth had stage G3 (a or b) eGFR (30-59 mL/min/1.73 m^2). The percentage of participants with stage G3 eGFR was significantly lower among participants with T1D compared with participants with T2D. Also, the percentage of participants with normal eGFR (stage G1: $>$90 mL/min/1.73 m^2) was different among participants with T1D versus T2D.

Contribution of the ACR POCT to the Diagnosis of DKD

We next assessed the prevalence of DKD and whether DKD was diagnosed at a previous time point or was newly diagnosed or suspected based on the ACR POCT values at the present visit. Newly diagnosed DKD based on the actual ACR POCT refers to the confirmation of a previously detected albuminuria, whereas suspected DKD refers to a first-time detection of albuminuria at the current ACR testing (pending confirmation of albuminuria in a subsequent visit), as reported by the treating physicians on the questionnaire.

The entire group (n = 717) included 280 patients (39.1%) with a physician-reported diagnosis of DKD or suspected DKD. The proportion of patients with confirmed/suspected DKD was significantly higher in patients with T2D than in those with T1D (Table 2).

When specifically looking at the DKD diagnosis in the group of patients with confirmed/suspected DKD (n = 280), we observed that 51.8% (145 of 280) had a previous diagnosis of DKD, whereas 22.1% (62 of 280) were newly diagnosed with DKD based on the actual ACR POCT value, and 25.4% (71 of 280) had a suspected diagnosis of DKD based on the actual ACR POCT value. When excluding the latter group, that is, those without a definitive diagnosis of DKD, 30.0% were diagnosed based on the actual ACR POCT value. Thus, ACR POCT had a relevant impact on the detection of DKD.

Impact of Laboratory Testing and Blood Pressure on Medication Prescription

Modification of treatment based on the results of ACR POCT, HbA1c, and blood pressure was assessed. On the basis of the ACR POCT values, a change of prescribed medication was performed in 18.5% of the entire group (12.3% of all patients with T1D and in 21.6% of all patients with T2D), with the treatment modification in the T2D group being significantly higher in comparison with the T1D group. Treatment modification based on ACR POCT was most likely to be performed in those patients with an ACR in the range of $>$ 30 mg/mmol. In addition, treatment modification was assessed based on the time of DKD diagnosis (newly diagnosed DKD and suspected DKD based on ACR POCT and previously diagnosed DKD; Table 3).

Table 2. Assessment of Time Point of DKD Diagnosis.

Time of the diagnosis of DKD	Total n = 717	Type 1 diabetes n = 236	Type 2 diabetes n = 463	*P* value (T1D vs T2D)
Overall diagnosis of DKD	39.1% (n = 280)	23.3 % (n = 55)	47.5 % (n = 220)	$P < .00001$[a]
Newly diagnosed DKD, based on actual ACR POCT values	8.6% (n = 62)	4.7% (n = 11)	10.6% (n = 49)	$P = .004$[b]
Suspected DKD, based on actual ACR POCT values	9.9% (n = 71)	3.8% (n = 9)	13.4% (n = 62)	$P < .001$[c]
Previously known DKD	20.2% (n = 145)	14.8% (n = 35)	23.1% (n = 107)	$P = .006$[d]
Time of diagnosis not specified	0.3% (n = 2)	—	0.4% (n = 2)	—

Abbreviations: DKD, diabetic kidney disease; T1D, type 1 diabetes; T2D, type 2 diabetes; ACR, albumin-to-creatinine ratio; POCT, point-of-care testing.
[a]$\chi^2(1, N = 699) = 35.05$, $P < .00001$.
[b]$\chi^2(1, N = 699) = 8.15$, $P = .004$.
[c]$\chi^2(1, N = 699) = 16.23$, $P < .001$.
[d]$\chi^2(1, N = 699) = 7.46$, $P = .006$.

The modification of treatment based on HbA1c and blood pressure values was also investigated. Regarding the HbA1C values, the treatment modification was significantly higher in the T2D group than in the T1D group. Concerning the modification of treatment based on blood pressure values, also a significantly higher treatment modification was performed in the T2D group than the T1D group.

The investigation of treatment modification in patients with confirmed/suspected DKD (n = 280) showed that the proportion of treatment modifications based on the ACR POCT or HbA1c values were similar for patients with T1D or T2D and confirmed/suspected DKD. Also, on the basis of the blood pressure values, no noticeable differences in the treatment modification between patients with T1D or T2D and confirmed/suspected DKD were observable.

Assessment of Antidiabetic and Blood Pressure Baseline Medication and Treatment Modification

The highest rates of baseline antidiabetic medications related to the entire group, and patients with confirmed/suspected DKD were observed for basal insulin, metformin, and bolus insulin. Also, for GLP-1 receptor agonists (RAs) and SGLT2is, relatively high rates were observed. The rates of patients with baseline medication were, except for bolus insulin, higher in patients with DKD than in participants without DKD (Table 4). Of the patients with confirmed/suspected DKD, 31.4% had GLP-1 RAs, and 27.1% of them had SGLT2is as baseline medication. Regarding the modification of treatment, the highest dose increases were observed for basal insulin and bolus insulin. The rates of medication dose decrease were in general low. The highest new drug initiation rates were observed for GLP-1 RAs and SGLT2is (11.1% and 8.9% of patients with confirmed/suspected DKD, respectively). Metformin and basal insulin followed in the next position, with a new drug initiation in 3.6% and 3.2% of participants with confirmed/suspected DKD, respectively.

Concerning blood pressure medication, the highest rates for baseline medications regarding the entire group and to the group of patients with confirmed/suspected DKD were observed for diuretics and angiotensin II receptor blockers (ARBs). Also, high rates of baseline medication for angiotensin-converting enzyme inhibitors (ACEis), calcium channel blockers, and β-blockers were noticeable. The rates of patients with baseline medication were, except for the medication category "others," higher in patients with confirmed/suspected DKD than in those without DKD: 17.6% of all participants and 14.3% of patients with confirmed/suspected DKD had other baseline treatments not listed in the case report form (eg, acetylsalicylic acid, pantoprazole, insulin pump). An increase of the treatment dose was performed rather rarely, with the highest increase observable for ACEis. A medication dose decrease and new drug initiation were also performed seldom. The most commonly initiated drugs were ACEis.

Assessment of Utilization Purpose and Importance of ACR POCT

When asked about the utilization purpose of ACR POCT, all physicians (n = 8) answered that they use the ACR POCT value to examine patients with diabetes with or without hypertension. Most, seven of eight (87.5%), reported using it for screening purposes, and five of eight (62.5%) stated using ACR POCT to monitor and manage patients with existing kidney disease or generally for patients with hypertension. Further responses are shown in Table 5. Regarding the relevance of the ACR POCT, six of eight physicians (75%) considered the test as very important for people with diabetes, and two of eight (25%) rated it as important. The importance of ACR POCT for patients without diabetes was rated as important by six of eight physicians (75%) and as very important by one of eight (12.5%).

Discussion

The results of this observational study provide insights into the role of ACR POCT in the diagnosis of DKD and its impact on the initiation/modification of medications as well as its relevance for physicians. Patients with either T1D, T2D, or other diabetes forms participated in this study.

Table 3. Diagnostic Reasons for Modification of Treatment Regarding the Entire Group and the Group of Patients With Confirmed/Suspected DKD.

	Total n = 717	Type 1 diabetes n = 236	Type 2 diabetes n = 463	*P* value (T1D vs T2D)
Modification of treatment based on the actual ACR POCT value	18.5% (n = 133)	12.3% (n = 29)	21.6% (n = 100)	$P = .002$[a]
ACR < 3 mg/mmol (Total: n = 442; T1D: n = 176; T2D: n = 252)	2.3% (10/442)	1.1% (2/176)	2.8% (7/252)	—
ACR 3-30 mg/mmol (Total: n = 233; T1D: n = 51; T2D: n = 179)	44.2% (103/233)	47.1% (24/51)	43.0% (77/179)	—
ACR > 30 mg/mmol (Total: n = 34; T1D: n = 7; T2D: n = 26)	52.9% (18/34)	42.9% (3/7)	53.8% (14/26)	—
ACR not defined (Total: n = 8; T1D: n = 2; T2D: n = 6)	25% (2/8)	—	33.3% (2/6)	—
Modification of treatment based on the time of DKD diagnosis				
Medication change in patients with *newly* diagnosed DKD (Total: n = 62; T1D: n = 11; T2D: n = 49), based on current ACR POCT values	66.1% (41/62)	81.8% (9/11)	61.2% (30/49)	—
Medication change in patients with *suspected DKD* (Total: n = 71; T1D: n = 9; T2D: n = 62), based on current ACR POCT values	45.1% (32/71)	33.3% (3/9)	46.8% (29/62)	—
Medication change in patients with *previously known DKD* (Total: n = 145; T1D: n = 35; T2D: n = 107)	38.6% (56/145)	42.9% (n = 15/35)	36.4% (n = 39/107)	—
Modification of treatment based on the actual *HbA1c* value	37.0% (n = 265)	26.7 % (n = 63)	42.5 % (n = 197)	$P < .0001$[b]
Modification of treatment based on the actual *blood pressure*	8.2% (n = 59)	4.7% (n = 11)	9.9 % (n = 46)	$P < .02$[c]
	Total DKD (n = 280)	Type 1 diabetes and DKD (n = 55)	Type 2 diabetes and DKD (n = 220)	*P* value (T1D vs T2D)
Modification of treatment based on the actual ACR POCT value	46.1% (n = 129)	49.1% (n = 27)	44.5% (n = 98)	ns
Modification of treatment based on the actual *HbA1c* value	42.9% (n = 120)	41.8% (n = 23)	43.2% (n = 95)	ns
Modification of treatment based on the actual *blood pressure*	14.6% (n = 41)	10.9% (n = 6)	15.0% (n = 33)	ns

Five of the patients with diagnosed or suspected DKD had other/unspecified diabetes forms, or the information regarding diabetes was not assessed.
Abbreviations: DKD, diabetic kidney disease; T1D, type 1 diabetes; T2D, type 2 diabetes; ACR, albumin-to-creatinine ratio; POCT, point-of-care testing.
[a] $\chi^2(1, N = 699) = 9.37$, $P = .002$.
[b] $\chi^2(1, N = 699) = 16.81$, $P < .0001$.
[c] $\chi^2(1, N = 699) = 4.83$, $P < .02$.

Table 4. Baseline Medication and Modification of Antidiabetic and Blood Pressure Treatment.

	Baseline medication in the entire group (n = 717)	Baseline medication in patients without DKD (n = 437)	Baseline medication in patients with DKD (n = 280)	Modification of treatment in patients with DKD (n = 280)		
				Dose increase	Dose decrease	New drug initiation
Metformin	48.4% (n = 347)	44.2% (n = 193)	55.0% (n = 154)	3.6% (n = 10)	0.7% (n = 2)	3.6% (n = 10)
Glitazones	2.9% (n = 21)	1.6% (n = 7)	5.0% (n = 14)	0.4% (n = 1)	—	0.4% (n = 1)
Sulfonylurea	5.4% (n = 39)	4.8% (n = 21)	6.4% (n = 18)	0.7% (n = 2)	—	0.4% (n = 1)
GLP-1 receptor agonists	26.4% (n = 189) (T1D: n = 1; T2D: n = 187)	23.1% (n = 101) (T1D: n = 1; T2D: n = 99)	31.4% (n = 88) (T2D: n = 88)	5.4% (n = 15) (T2D: n = 15)	0.4% (n = 1) (T2D: n = 1)	11.1% (n = 31) (T2D: n = 31)
DPP-4 inhibitors	12.8% (n = 92)	9.4% (n = 41)	18.2% (n = 51)	0.4% (n = 1)	2.1% (n = 6)	0.7% (n = 2)
SGLT2 inhibitors	21.3% (n = 153) (T1D: n = 6; T2D: n = 144)	17.6% (n = 77) (T1D: n = 4; T2D: n = 70)	27.1% (n = 76) (T1D: n = 2; T2D: n = 74)	0.7% (n = 2) (T2D: n = 2)	1.1% (n = 3) (T2D: n = 3)	8.9% (n = 25) (T1D: n = 2; T2D: n = 21)
Basal insulin	58.2% (n = 417)	56.3% (n = 246)	61.1% (n = 171)	17.1% (n = 48)	3.6% (n = 10)	3.2% (n = 9)
Bolus insulin	44.2% (n = 317)	48.1% (n = 210)	38.2% (n = 107)	13.2% (n = 37)	2.1% (n = 6)	0.4% (n = 1)
Diuretics	22.0% (n = 158)	14.2% (n = 62)	34.3% (n = 96)	1.1% (n = 3)	—	—
Angiotensin-converting enzyme inhibitors	18.5% (n = 133)	14.0% (n = 61)	25.7% (n = 72)	4.3% (n = 12)	—	4.6% (n = 13)
Angiotensin II receptor blockers	20.5% (n = 147)	14.4% (n = 63)	30.0% (n = 84)	2.9% (n = 8)	0.4% (n = 1)	0.7% (n = 2)
Renin inhibitors	0.1% (n = 1)	—	0.4% (n = 1)	—	—	—
β-blockers	15.6% (n = 112)	9.8% (n = 43)	24.6% (n = 69)	0.4% (n = 1)	—	0.7% (n = 2)
Calcium channel blockers	16.3% (n = 117)	10.3% (n = 45)	25.7% (n = 72)	0.7% (n = 2)	0.4% (n = 1)	2.1% (n = 6)
Others	17.6% (n = 126)	19.7% (n = 86)	14.3% (n = 40)	—	—	0.7% (n = 2)

Abbreviation: DKD, diabetic kidney disease; T1D, type 1 diabetes; T2D, type 2 diabetes.

Table 5. Questionnaire for Physicians Regarding the ACR POCT.

Question	Responses		Total (n = 8), n (%)
For what purpose do you use the ACR POCT value?	a. I use it for monitoring and management of patients with existing kidney disease		5 (62.5%)
	b. I use it for screening		7 (87.5%)
	c. In patients with diabetes without hypertension		8 (100%)
	d. In patients with diabetes having hypertension		8 (100%)
	e. Generally for patients with hypertension		5 (62.5%)
	f. I only look after patients with diabetes		2 (25%)
	g. In patients with the following risk factors		
	• obesity, fatty liver		1 (12.5%)
	• in pregnant women with poorly controlled gestational diabetes and high risk of preeclampsia		1 (12.5%)
	• hypercholesterolemia		1 (12.5%)
How important is the ACR POCT value for you?	a. For patients with diabetes	• Very important	6 (75%)
		• Important	2 (25%)
		• Moderately important	—
		• Irrelevant	—
	b. For patients without diabetes	• Very important	1 (12.5%)
		• Important	6 (75%)
		• Moderately important	—
		• Irrelevant	—

Abbreviations: ACR, albumin-to-creatinine ratio; POCT, point-of-care testing.

The ratio of patients with confirmed/suspected DKD (39.1%) is comparable with rates given in the literature, varying between 20% and 40% for patients with T1D or T2D.[15] Significantly more participants with T2D were diagnosed to have DKD compared with those with T1D despite a considerably shorter median duration of diabetes in the former. This is likely due to the higher prevalence of hypertension and obesity in T2D patients, which both may contribute to the development of DKD.[16]

In this study, DKD was newly diagnosed at visit in 8.6% of the entire study population. Furthermore, DKD was suspected at visit in 9.9% of the participants based on the actual ACR POCT values. Thus, ACR POCT likely increased the detection rate of DKD in patients with diabetes. In 18.5% of the entire study population, ACR POCT led to a change in the medication. When looking specifically at the group of patients with confirmed/suspected DKD, ACR POCT testing led to a change in the medication in 46.1% of patients. This proportion was even slightly higher compared with patients in which HbA1c testing led to a change in the medication and considerably higher compared with the patients in which blood pressure readings led to a change in the medication in the DKD group. Therefore, the study demonstrated that ACR POCT has a considerable impact on patient management.

The distribution of treatment modification according to the three albuminuria categories stated in the KDIGO clinical practice guidelines[3] showed a frequent treatment adjustment in the albuminuria categories A2 (ACR of 3-30 mg/mmol) and A3 (ACR $>$ 30 mg/mmol). The markedly higher rates of treatment modification in the albuminuria category A2 and A3 compared with category A1 may be related to the fact that patients with category A1 may not have had DKD.

The assessment of baseline medication demonstrated high rates of baseline medication for the new medication classes GLP-1 RAs and SGLT2is in the entire group and participants with confirmed/suspected DKD. Besides, these two drug classes had the highest new prescription rates in participants with confirmed/suspected DKD, indicating an increasing acceptance and use. Almost only patients with T2D had GLP-1 RAs and SGLT2is as baseline medication. Also, the highest rates for treatment modification for these two drug classes were observable in this patients group. The increase in the application of these two drug classes is consistent with the albuminuria-reducing effect of SGLT2is and GLP-1 RAs, which has been investigated in several studies in patients with T2D.[17] It is to be noted that SGLT2is and GLP-1 RAs are not yet approved in Switzerland for T1D. The modification of blood pressure treatment was less prominent. In that regard, the highest treatment modification was observed for ACEis.

Looking at the numbers of newly diagnosed or suspected DKD and the high percentage of treatment adjustments in participants with DKD, the data underline the importance of the least annual assessment of the ACR value in patients with diabetes as recommended in guidelines[4,6] or even more often, if the ACR is already increased.

Albuminuria often represents the first sign of kidney damage in DKD and precedes a decline in GFR.[18,19] Another essential role of ACR is risk prediction for cardiovascular disease. The risk of cardiovascular disease is tripled in

patients with T2D and eGFR < 60 mL/min/1.73 m^2, compared with patients with diabetes only.[20,21] At any eGFR, the degree of albuminuria is associated with the risk of cardiovascular disease, CKD progression, and mortality.[4] Therefore, KDIGO recommends a comprehensive CKD staging that incorporates albuminuria at all stages of eGFR.[3] Even in patients without diabetes without any background disease, ACR predicts all-cause mortality and cardiovascular mortality in a Western population. Data of 5700 healthy patients collected from the Tromsø Health Surveys for ten years showed that those with a high ACR tend to have increased total mortality and also increased cardiovascular mortality over the ten years, even in those with a borderline ACR in the upper range.[22] A meta-analysis evaluating the data of 637 315 individuals without a history of cardiovascular disease over a period of more than four years confirmed the role of ACR for cardiovascular prediction. The authors concluded that eGFR and ACR should be taken into account for cardiovascular outcomes prediction, especially when they are already assessed for clinical purposes (eg, in individuals with CKD, diabetes, or hypertension), or when cardiovascular mortality and heart failure are the outcomes of interest. For the latter, ACR even outperformed eGFR. It was also found that Dipstick proteinuria showed a smaller improvement than ACR.[23]

Nevertheless, the frequency of ACR measurement has been found to be low. A Norwegian study assessed the status of T2D care in general practice and changes in the quality of care between 2005 and 2014. HbA1c, blood pressure, and cholesterol were measured by the physicians annually in 80% to 90% of the patients. The ACR measurements were only performed in 30% of the patients annually. Overall, diabetes management had not improved between 2005 and 2014.[24] A similar picture is obtained from a data set of more than 1 million individuals in Sweden.[25] The frequency of an annual albuminuria monitoring once every two years was found to be low, with 38% of patients with diabetes and 27% of CKD individuals undergoing albuminuria testing. Also, a newly published meta-analysis (data of > 1.3 million patients with diabetes) demonstrates similar results, with an ACR testing rate of 35.1% for patients with diabetes.[26]

Regarding the utilization purposes of the ACR POCT, all physicians (eight of eight) stated using it to examine patients with diabetes with or without hypertension. Although the questioned physicians group was small, these results indicate that ACR POCT is considered to be a relevant monitoring tool for patients with diabetes. Indeed, six of eight physicians (75%) considered it very important for this patients' group. Other high-rated utilization purposes for ACR POCT were screening as answered by seven of eight physicians (87.5%) and the monitoring/management of patients with existing kidney disease or in patients with hypertension (five of eight physicians [62.5%]). In this context, six of eight physicians (75%) reported that the utilization of ACR POCT in patients without diabetes is important. As indicated through the practitioners' answers, ACR POCT can be used as a screening tool for the early detection of kidney disease, as shown in an Australian study conducted by Shephard and colleagues.[27] In the screened 402 participants, 82 (20.4%) had results suggestive of CKD. Today, the ACR POCT offers comparable clinical effectiveness and performance to the laboratory-measured ACR.[28-30] In addition, the implementation of ACR POCT in general practices results in economic benefits and a lesser per-patient cost to the health care sector compared with ACR measured in a central laboratory.[9,10] The immediate accessibility to POCT results leads to a comparable/better medication adherence and compliance of the patients compared with obtaining results from testing laboratory.[13,31,32] Besides, the patient can discuss the obtained results and potential treatment decisions with his treating physician immediately after the POCT, eliminating the need for further examination appointments and telephone calls to arrange them.[33-35] Other positive aspects of the POCT implementation are time savings, workflow improvement, and process optimization in the practices.[9,33,36] Last, patients were highly motivated to manage their diabetes, and both practitioners and patients showed high satisfaction with the utilization of POCT.[11,12,33-35]

Our study has, however, some limitations. The patients' relatively small sample size is not representative of the population of patients with T1D or T2D. Also, the number of centers that evaluated the questionnaire was small. A further possible bias factor is that the examining physicians did know about the study. Consequently, the objectivity of the physicians filling out the case report form and the questionnaire may have been affected. Finally, our study only investigated the impact of ACR POCT on the diagnosis of DKD and the management of treatment. It is, however, unclear if these medication changes induced long-term benefits.

Conclusions

Summing up, the results presented in this study provide evidence that the implementation of ACR POCT in daily general practice can improve the diagnosis of DKD in diabetes, which may support improved management of CKD.

Abbreviations

ACR, albumin-to-creatinine ratio; ACEis, angiotensin-converting enzyme inhibitors; ADA, American Diabetes Association; ARB, angiotensin II receptor blocker; BMI, body mass index; CKD, chronic kidney disease; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; EKOS, Ethikkommission Ostschweiz; GLP-1 RA, GLP-1 receptor agonist; HbA1c, glycated hemoglobin A1c; HFG, Humanforschungsgesetz; IDF, International Diabetes Federation; IQR, interquartile range; KDIGO, Kidney Disease: Improving Global Outcomes; POCT, point-of-care testing; SGLT2i, SGLT2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes.

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