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Is albuminuria screening and treatment optimal in patients with type 2 diabetes in primary care? Observational data of the GIANTT cohort

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Abstract

Background. Failure of diagnosing and treatment of albuminuria play a role in morbidity and mortality in type 2 diabetes (T2DM). We evaluated guideline adherence and factors associated with albuminuria screening and treatment in T2DM patients in primary care.

Methods. Guidelines recommend annual measurement of albuminuria and, if increased, treatment with renin–angiotensin–aldosterone system (RAAS) blockers. We performed a cohort study of T2DM patients managed by 182 Dutch general practitioners (GPs; Groningen Initiative to Analyse Type 2 diabetes Treatment database), and evaluated guideline adherence in the years 2007–2009. We assessed whether demographic, clinical, organizational or provider factors determined guideline adherence with multilevel analyses.

Results. Data were available for 14 120 T2DM patients [47.6% male, mean age 67.3 ± 11.7 years, median diabetes duration 6 (IQR: 3–10) years]. The albumin–creatinine ratio (ACR) was measured in 45.2% in 2007, 57.4% in 2008 and 56.8% in 2009. Only 23.7% of all patients were measured every year and 21.4% were never measured. The ACR was more often measured in patients <75 years, with a previous ACR measurement, using anti-diabetic medication, and receiving additional care by a diabetes support facility. RAAS treatment was prescribed to 78.4% of patients with prevalent micro/macroalbuminuria, 66.5% with incident micro/macroalbuminuria, 59.3% with normoalbuminuria and 52.1% of those without ACR measurements. In those not treated with RAAS blockers, it was initiated in 14.3, 12.3, 3.0 and 2.3%, respectively. The presence of micro/macroalbuminuria, higher blood pressure, incidence of cardiovascular events and treatment with antihypertensive medication were the determinants of RAAS-treatment initiation.

Conclusions. Guideline implementation regarding the management of albuminuria in T2DM patients in primary care should be further improved.

Keywords: albuminuria; guidelines; primary care; type 2 diabetes

Introduction

Type 2 diabetes mellitus (T2DM) is an increasing public health problem due to the ageing population, an increasing trend in obesity and changes in lifestyle. In parallel, the costs associated with diabetes care and the disease burden for patients are increasing [1]. One of the major complications of diabetes is diabetic nephropathy. Microalbuminuria is one of the earliest signs of diabetic nephropathy, and is associated with increased risk of end-stage renal disease, cardiovascular disease and all-cause mortality [2, 3]. The agents blocking the renin–angiotensin–aldosterone system (RAAS) lower albuminuria and prevent worsening of albuminuria beyond their blood-pressure-lowering effect [4–6]. Because of the risks associated with increased albuminuria, clinical guidelines recommend screening for albuminuria in patients with T2DM with sufficient life expectancy [7, 8]. In patients with T2DM and confirmed elevated albuminuria, RAAS blockers are the preferred treatment option irrespective of concomitant blood pressure levels [7, 8].

Despite these therapeutic options, morbidity and mortality rates are still high in T2DM patients. This could be partly due to the fact that the current interventional protocol or strategies do not sufficiently take care of all the risks in these patients. Alternatively, the implementation of such strategies in practice may be difficult and partly failing. Discrepancies have been reported between recommended diabetes care by clinical guidelines and observed diabetes care in practice [9]. In this respect, much attention has been paid to the quality of risk factor monitoring and treatment of the conventional risk factors for diabetic renal and cardiovascular complications, such as blood glucose, blood pressure and cholesterol levels [10–18]. Few studies have focused on the quality of screening for and treatment of elevated albuminuria, even though this is one among the strongest cardio-renal risk factors [19].

Therefore, our aim was to assess adherence to clinical guideline recommendations with respect to albuminuria

management in Dutch primary care patients with T2DM, and to identify demographic, clinical or organizational factors associated with guideline adherence.

Subjects and methods

Study population and setting

For this observational study, we used data of patients with T2DM obtained from 182 general practitioners (GPs, 150 practices) who collaborated in the Groningen Initiative to ANalyse Type 2 diabetes Treatment (GIANTT) project. GIANTT provides quality assessments for most GPs in Groningen province, the Netherlands [11]. The included practices covered a total population of over 500 000 persons in 2008. The patient population for this study consisted of all those who had been diagnosed with T2DM for at least 1 year on 1 January 2007, were still alive on 1 July 2010, did not leave the practice before July 2010, did not object to the data collection (<1%) and were primarily managed by their GPs ($n = 14\,120$). In our study region, a regional diabetes facility offers support to GPs. Patients can be referred to this facility for laboratory tests and physical examination. The results are reported back to the GPs who remain responsible for further management and treatment decisions. Patients who were primarily managed by a specialist for their diabetes, as indicated by the GP, were excluded from this study ($n = 2933$).

Data collection

We used data on demographic characteristics, organizational factors, clinical characteristics, laboratory parameters and prescribed medication from the GIANTT database. This database contains anonymized data extracted from structured tables and free text parts of electronic medical records using an automated and validated method [20]. This is complemented by the GPs with information on their gender and years of practice experience. For research with anonymous medical record data, no ethics committee approval is required in the Netherlands.

Guideline recommendations

The Dutch primary care guideline recommends yearly albuminuria screening in all diabetes patients with sufficient life expectancy (at least 10 years) [8]. For the yearly albuminuria screening, measurement of the albumin–creatinine ratio (ACR) is favoured over urinary albumin concentration [21]. If the measurement indicates the presence of micro- or macroalbuminuria, this has to be confirmed by a repeat measurement within the next few months. According to the guidelines, all patients with confirmed micro- or macroalbuminuria should be prescribed RAAS treatment [angiotensin-converting-enzyme inhibitors (ACEi)/ angiotensin II receptor blockers (ARBs)] even if their blood pressure readings are in the normal range. For the treatment of hypertension in patients with normoalbuminuria, thiazide diuretics are first-choice antihypertensives, followed by RAAS treatment. When on RAAS treatment, yearly albuminuria testing is recommended to monitor response to treatment and disease progression.

Definitions

Patient ACR values were classified as normoalbuminuria, microalbuminuria or macroalbuminuria. Microalbuminuria was defined according to gender-specific cut-offs, being ACR >2.5 mg/mmol in men and >3.5 mg/mmol in women [22]. Macroalbuminuria was defined as ACR >25 mg/mmol in men and >35 mg/mmol in women. We clustered patients with micro- and macroalbuminuria for analyses on guideline adherence because the evaluated guideline recommendations are equal for micro- and macroalbuminuria. These patients are all denoted as having increased albuminuria.

Based on the most recent ACR measurement in the period 2007–2009 (index measurement), patients were classified into those without any measurements, those with normoalbuminuria and those with increased albuminuria. The patients with increased albuminuria were subdivided into those with incident increased albuminuria and those with prevalent increased albuminuria. Based on the prior ACR measurement, patients with repeated increased albuminuria were denoted as having prevalent increased albuminuria.

Treatment with RAAS blockers was defined as any prescription of an agent intervening in the RAAS system in the year before the index ACR measurement. A repeat ACR measurement was defined as a second measurement of ACR within 100 days from the index measurement. Initiation of RAAS treatment was defined as the start of RAAS treatment within 100 days after the index ACR measurement or within 100 days of the repeat measurement of ACR. RAAS treatment initiation was defined as a new prescription of any RAAS blocker, after not being treated with a RAAS blocker in the 12 months before the index ACR measurement.

Determinants of guideline adherence

As potential patient-level determinants of guideline adherence, we considered demographic characteristics (age and gender), organizational factors (additional care by a diabetes support facility), clinical characteristics [known duration of diabetes, having ACR measurements in the preceding 12 months, prior ACR status (unknown, normoalbuminuria, increased albuminuria), body mass index, systolic and diastolic blood pressure], laboratory parameters (glycosylated haemoglobin, serum creatinine estimated glomerular filtration rate according to the modification of diet in renal disease (MDRD)-study equation [23], low-density lipoprotein, high-density lipoprotein), diabetes-regulating medication use (none, use of oral antidiabetics, use of oral antidiabetics and insulin), use of antihypertensive agents in the 12 months before the index ACR measurement (number of antihypertensives used, use of RAAS). For the clinical and laboratory parameters, we used the most recent value in the 12 months before the index ACR measurement if available and the most recent value in the 12 months before a random date generated according to a similar date distribution otherwise. For analyses of the determinant of RAAS prescription, we also took incident cardiovascular comorbidity or events into account (chronic heart failure, myocardial infarction, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, stroke, transient cerebral ischaemia). Furthermore, we included the general practice as a possible determinant of guideline adherence, since diabetes care in the Netherlands is mainly organized at this level. In additional analyses, we included the provider level instead of the practice level, in which we considered the GP's gender and years of practice experience (≤5 years, 5 to <10 years, 10 to <20 years, ≥20 years) as potential determinants.

Statistical analysis

We performed the analyses using STATA version 11.2 (STATACorp LP, Texas, USA). We calculated in what proportion of patients an ACR measurement was recorded in each calendar year. The differences in patient characteristics between patients with and without ACR measurement in 2009 were compared with Student's *t*-test for continuous variables and the chi-squared test for categorical variables. For all groups of patients, we calculated what proportion of patients received RAAS treatment and in what proportion RAAS treatment was initiated and, if applicable, ACR measurement was repeated. The descriptive analyses are also presented stratified by age below and over 75 years, and repeated using longer time periods in which the ACR measurement could be documented or the RAAS treatment could be initiated. We used multilevel analyses adjusting for the clustering of patients within GP practices, taking into account the policy and organization structure may differ between practices and adjusting for these differences, to assess which patient-level factors were associated with ACR measurement. Intra-class correlation coefficients were calculated to estimate the variation at the practice level. We determined whether random slopes significantly improved model fit with the likelihood ratio test and used a forward selection procedure adding variables to the baseline model (containing age and sex) one at the time, based on the Wald statistic, using a P-value <0.1 as the acceptance level. To allow analyses with all available patients and to minimize bias, we used multiple imputation of missing values. We used the same multilevel modelling strategy to assess which patient-level factors were associated with RAAS-treatment initiation in all patients, including increased albuminuria (increased versus not increased or not determined) as the determinant, and in four subgroups divided by albuminuria status (without ACR measurement, with normoalbuminuria, with incident and with prevalent increased albuminuria). For all analyses, we considered a P-value of <0.05 to be statistically significant. Finally, we conducted multilevel analyses where patients are clustered at the provider level, that is, at the level of the individual GP instead of the practice. In these analyses, the gender and practice experience of the provider were included as provider-level factors.

Results

Data between 2007 and 2010 were available from 150 practices with 182 GPs with a total of 14 120 patients with T2DM. Of the 14 120 patients, 47.6% were male, the mean age was 67.3 ± 11.7 years and the median duration of diabetes was 6 (inter-quartile range 3–10) years (Table 1).

ACR measurement

The ACR was measured at least once in 6377 patients (45.2%) in 2007, in 8111 patients (57.4%) in 2008 and in 8025 patients (56.8%) in 2009. Extending the interval from 12 to 15 months increased these percentages to 53.9, 65.0 and 61.5%, respectively (Figure 1). In the 3-year period between 2007 and 2010, 11 106 patients (78.7%) had at least one measurement, 3351 patients (23.7%) had at least one ACR measurement in each consecutive year and 3014 patients (21.4%) did not have any ACR measurement.

The ACR was more frequently measured in patients below than above 75 years (58.9 versus 52.7% in 2009, $P < 0.001$), and in patients receiving care at the diabetes support facility when compared with those receiving routine diabetes care in the GP practice (64.7 versus 52.8%, $P < 0.001$). The differences in characteristics between patients with and without ACR measurement are shown in Table 1. In a multilevel model (Table 2), the most important determinants of ACR measurement were the patient's previous ACR measurement, use of antidiabetic medication and additional care by the diabetes support facility. The intraclass correlation coefficient at the level of GP practice was 0.17, indicating considerable variation across practices.

Prevalence of increased albuminuria

Based on the most recent ACR measurement before 2010 ($N = 11\,106$), 8823 patients (79.4%) had normoalbuminuria, 1970 patients (17.7%) had microalbuminuria and 313 patients (2.8%) had macroalbuminuria. The guideline makes a distinction between actions needed for incident and prevalent increased albuminuria, and we therefore used the prior albuminuria measurement to distinguish between incident and prevalent increased albuminuria. Of the patients with increased albuminuria (presence of micro- or macroalbuminuria, $N = 2283$), 1360 patients (59.6%) also had increased albuminuria on the prior ACR measurement, indicating prevalent increased albuminuria. A total of 923 patients (40.4%) did not have increased albuminuria on the prior ACR measurement or did not have a prior measurement, indicating incident increased albuminuria.

Repeat measurements and RAAS treatment

Of patients with prevalent increased albuminuria, 78.4% received RAAS treatment in the year up to the index measurement, compared with 66.5% of patients with incident increased albuminuria, 59.3% of patients with normoalbuminuria and 52.1% of patients without any ACR measurements.

In patients with incident and prevalent increased albuminuria not receiving RAAS treatment, the guidelines recommend further action. The appropriate steps differ between patients with incident increased albuminuria and patients with prevalent increased albuminuria (Figure 2).

Of the 294 patients with prevalent increased albuminuria not on RAAS treatment, RAAS treatment was initiated in 42 patients (14.3%; Figure 2). In patients with incident increased albuminuria, the albuminuria status merits confirmation by a repeat measurement. Of the 309 patients with incident increased albuminuria not on RAAS treatment, the ACR measurement was repeated in 41 (13.3%) patients and in 37 (12.0%) patients RAAS treatment was initiated without confirmatory ACR measurement. In 231 (74.8%) patients, no action was undertaken. Of the 41 confirmatory measurements, in 28 (68.3%) patients increased albuminuria status was confirmed and RAAS treatment was subsequently initiated in one patient (Figure 2). Overall, RAAS treatment was initiated in 38 patients (12.3%) with incident increased albuminuria. In total, appropriate action (i.e. repeat measurement performed and/or RAAS-treatment initiation) was undertaken in 51 patients (16.5%). In comparison, in patients with normoalbuminuria not receiving RAAS treatment, treatment was initiated in 108 patients (3.0%) after the most recent ACR measurement, and in patients without any ACR measurements RAAS treatment was initiated in 33 patients (2.3%). RAAS-treatment initiation was thus more common in patients with increased albuminuria versus patients without increased albuminuria (13.6 versus 2.8%, $P < 0.001$)

Extending the interval for initiation of RAAS treatment from 100 days after the index ACR measurement to 200 days of the index measurement did not substantially increase the number of new RAAS-prescriptions in patients with increased albuminuria (data not shown).

The proportion of patients receiving RAAS treatment was similar in patients with increased albuminuria below and above 75 years (73.3 versus 72.6%, $P = 0.13$), and appropriate action in patients with increased albuminuria was undertaken in similar numbers of patients 15.0 versus 13.3% ($P = 0.34$) below and above 75 years, respectively.

Determinants of RAAS-treatment initiation

In the overall multilevel analysis, increased albuminuria status, blood pressure and number of antihypertensives (other than those intervening in the RAAS) that were already used were important patient-level determinants of RAAS-treatment initiation (Table 2). Among patients without any ACR measurement, the most important determinant of RAAS-treatment initiation was increased blood pressure (Table 2). Among patients with normoalbuminuria, increased blood pressure, incident cardiovascular events, and the number of antihypertensive agents already used by the patient were associated with RAAS-treatment initiation (Table 2). The number of antihypertensive agents already used was also associated with RAAS-

Table 1. Baseline characteristics overall and stratified by ACR measurement

	Registration degree *N* (%)	Overall[a]	ACR measured 8025 (56.8%)	ACR not measured 6095 (43.2%)	P-value
Demographic characteristics					
Age, years	14 120 (100)	67.3 ± 11.7	66.5 ± 11.3	67.7 ± 12.5	<0.001
Age >75 years	14 120 (100)	4107 (29.1)	2166 (27.0)	1941 (31.9)	<0.001
Male sex	14 120 (100)	6722 (47.6)	3948 (49.2)	2774 (45.5)	<0.001
Organizational factors					
Support care by diabetes facility	14 120 (100)	4825 (34.2)	3120 (38.9)	1705 (28.0)	<0.001
Clinical characteristics					
Known duration of diabetes, years	14 120 (100)	6 [3–10]	6 [3–10]	6 [3–9]	<0.001
Body mass index, kg/m^2	9902 (70)	30.2 ± 5.5	30.2 ± 5.5	30.2 ± 5.6	ns
ACR measured previous 12 months	14 120 (100)	8111 (57.4)	5621 (70.0)	2490 (40.9)	<0.001
Blood pressure, mmHg					
Systolic	12 381 (88)	143 + 19	143 ± 19	142 ± 20	<0.001
Diastolic	12 381 (88)	79 ± 10	79 ± 10	78 ± 10	<0.001
Laboratory parameters					
Glycosylated haemoglobin - %	12 803 (91)	7.0 ± 1.0	7.0 ± 0.9	6.9 ± 1.0	<0.001
Serum creatinine, mmol/L	12 223 (87)	93 ± 30	92 ± 26	94 ± 35	<0.001
eGFR (MDRD), mL/min	12 223 (87)	60 ± 18	61 ± 17	60 ± 18	ns
Cholesterol, mg/dL					
Low-density lipoprotein	11 751 (83)	2.4 ± 0.9	2.3 ± 0.9	2.5 ± 0.9	<0.001
High-density lipoprotein	11 793 (84)	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	ns
Albumin-to-creatinine ratio, mg/mmol	8025 (57)	1.2 [0.5–2.7]	1.2 [0.5–2.7]	–	n/a
Medication					
Diabetes regulating medication	14 120 (100)	12 037 (85.3)	7175 (89.4)	4862 (79.8)	<0.001
Oral antidiabetics	14 120 (100)	11 165 (79.1)	6753 (84.2)	4412 (72.4)	<0.001
Insulin	14 120 (100)	2768 (19.6)	1539 (19.2)	1229 (20.2)	<0.001
Blood pressure regulating medication	14 120 (100)	10 882 (77.1)	6356 (79.2)	4526 (74.3)	
Number of antihypertensive agents	14 120 (100)	2 [1–2]	2 [1–2]	2 [0–2]	ns
RAAS treatment	14 120 (100)	8479 (60.0)	5028 (62.7)	3441 (56.5)	<0.001
Beta-blockers	14 120 (100)	5642 (40.0)	3271 (40.8)	2371 (38.9)	<0.001
Calcium antagonists	14 120 (100)	3088 (21.9)	1819 (22.7)	1269 (20.8)	<0.001
Diuretics	14 120 (100)	6607 (46.8)	3831 (47.7)	2776 (45.5)	<0.001
Other	14 120 (100)	319 (2.3)	181 (2.3)	138 (2.3)	ns

[a]Data are presented as *n*(%) or mean ± SD or median[iqr].
ACR, albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate; MDRD, modification of diet in renal disease study equation; ACEi: angiotensin-converting-enzyme inhibitors; ARB, angiotensin II receptor blockers; ns: not significant; n/a: not applicable.

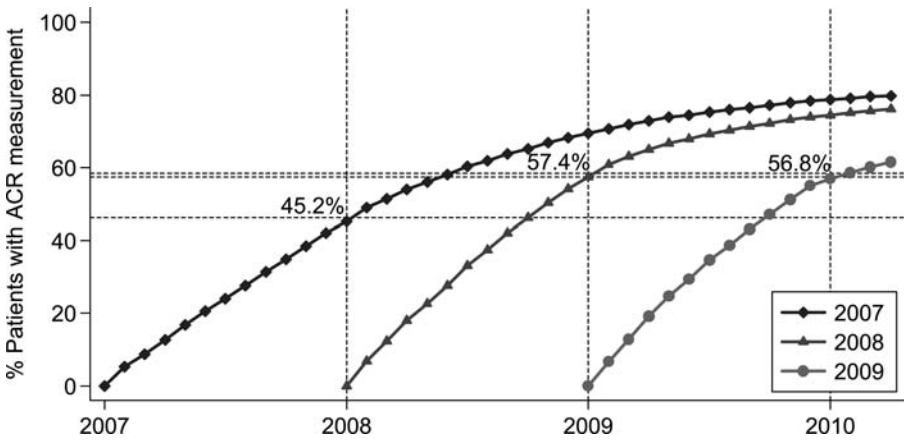

Fig. 1. Cumulative proportion of ACR measurements between 2007 and 2010 for each starting year independently. Horizontal dotted lines indicate the percentage of patients with at least one ACR measurement from beginning of 2007, 2008 and 2009, respectively. The population selected was stable ($N = 14\,120$) throughout this time-interval, the percentage of patients with at least one ACR measurement was calculated for each year independently.

treatment initiation in patients with incident increased albuminuria (Table 2). The estimated variation at the practice level was largest for RAAS-treatment initiation in patients with incident increased albuminuria (intraclass correlation coefficient 0.28), and smallest for treatment initiation in those without an ACR measurement

Table 2. Determinants of ACR measurement and RAAS-treatment initiation in all patients not yet treated with RAAS blockers and according to albuminuria classification

	ACR measurement				All patients				No ACR measurement				Normoalbuminuria				Incident increased albuminuria				Prevalent increased albuminuria			
N	14 120				5630				1434				3593				309				294			
Intraclass correlation coefficient	0.170				0.113				0.015				0.152				0.275				0.067			
Determinants	OR	95% CI		P	OR	95% CI		P	OR	95% CI		P	OR	95% CI		P	OR	95% CI		P	OR	95% CI		P
Demographic characteristics																								
Age 1 january 09 (5 years)	0.98	0.96	1.00	0.044	0.97	0.91	1.04	0.429	0.93	0.82	1.07	0.326	0.92	0.84	1.01	0.095	1.07	0.85	1.35	0.563	1.01	0.87	1.17	0.870
Female sex	0.86	0.80	0.94	0.000	0.63	0.47	0.84	0.002	0.76	0.37	1.56	0.449	0.87	0.58	1.32	0.512	0.27	0.10	0.71	0.008	0.41	0.20	0.86	0.019
Organizational factors																								
Support care by diabetes facility	1.83	1.58	2.11	0.000									0.53	0.32	0.87	0.013	0.30	0.10	0.86	0.025				
Clinical characteristics																								
Known duration of diabetes, years	0.98	0.98	0.99	0.000																				
Body mass index, kg/m^2					1.03	1.00	1.07	0.034									1.10	1.02	1.19	0.016				
ACR measured previous 12 months (yes/no)	3.63	3.30	4.00	0.000	NA				NA				NA				NA				NA			
Blood pressure, per 10 mmHg																								
Systolic	1.04	1.02	1.06	0.001	1.21	1.10	1.33	0.000	1.29	1.01	1.65	0.040	1.46	1.31	1.64	0.000								
Diastolic					1.17	0.97	1.42	0.095									1.05	1.00	1.10	0.056				
Laboratory parameters																								
Glycosylated haemoglobin %	1.09	1.04	1.14	0.000									1.21	0.98	1.49	0.071								
Serum creatinine mmol/L																								
eGFR (MDRD) - mL/min																	1.03	1.00	1.05	0.052				
Cholesterol, mg/dL																								
Low-density lipoprotein	0.87	0.83	0.91	0.000																				
High-density lipoprotein	1.10	0.97	1.25	0.122																				
Increased albuminuria (no or unknown/ yes)					5.14	3.75	7.03	0.000	NA				NA				NA				NA			
Medication																								
Diabetes regulating medication																								
None (reference)																								
Oral antidiabetics	1.69	1.50	1.90	0.000																				
Oral antidiabetics and insulin	1.34	1.15	1.55	0.000																				
RAAS treatment	1.12	1.00	1.26	0.046	NA				NA				NA				NA							
Number of antihypertensives																								
None (reference)																								
One antihypertensive[a]	1.10	0.97	1.25	0.147	1.62	1.13	2.32	0.009					2.20	1.35	3.59	0.002	1.78	0.60	5.28	0.297				
Two or more antihypertensives[a]	1.08	0.94	1.25	0.271	2.75	1.92	3.95	0.000					3.16	1.87	5.33	0.000	5.55	1.85	16.67	0.002				
Morbidity																								
Incident Cardiovascular Morbidity	NA												6.63	1.58	27.8	0.010								

These multivariate models are based on multilevel analyses adjusting for the clustering of patients within GP practices, taking into account the policy and organization structure may differ between practices and adjusting for these differences. Only the final models are reported. The models were selected using a forward selection procedure adding variables to the baseline model (containing age and sex) one at the time, based on the Wald statistic, using a P-value <0.1 as the acceptance level.

[a]Other than RAAS blockers. N/a: not applicable.

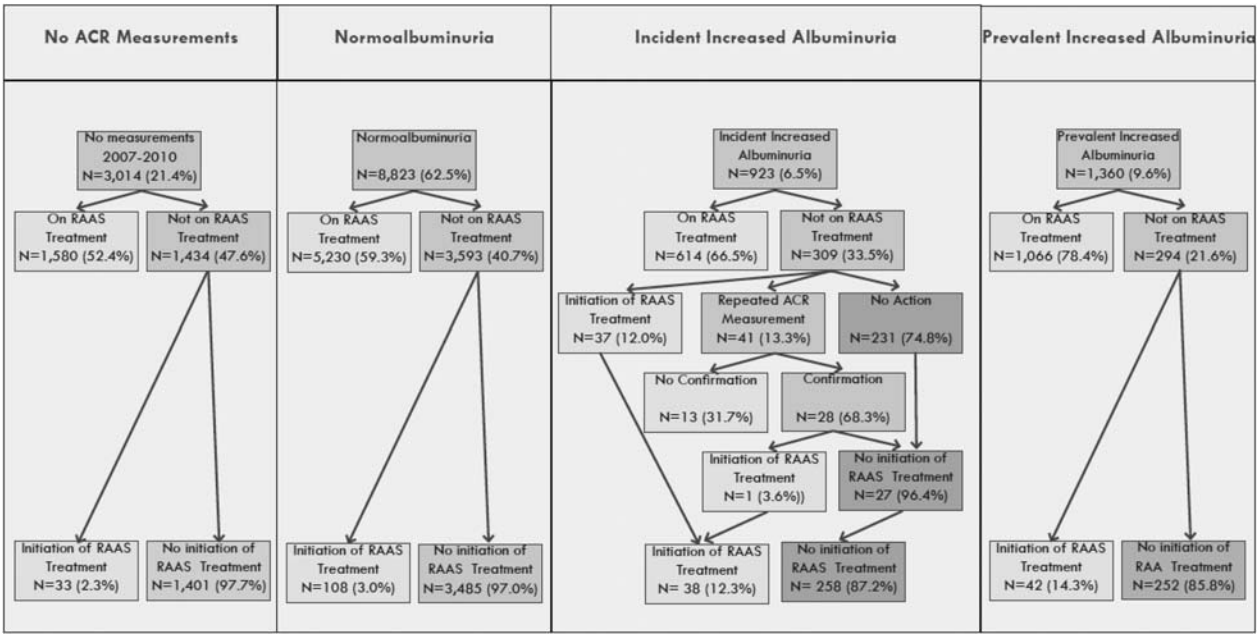

Fig. 2. Flowchart of RAAS treatment and RAAS-treatment initiation. Left two panels: RAAS-treatment status and RAAS-treatment initiation in patients without any ACR measurements and patients with normoalbuminuria. Right two panels: RAAS-treatment status and guideline implementation in patients with incident increased albuminuria and patients with prevalent increased albuminuria, respectively. Dark gray colour indicates failure to adhere to guidelines. RAAS, renin–angiotensin–aldosterone system.

(intraclass correlation coefficient 0.02). Repeating these analyses on the provider level instead of the practice level yielded only minor changes, with ACR measurement, blood pressure and the number of antihypertensives already used by the patient being the most relevant determinants (Supplementary table S1). Gender and practice experience of the provider did not explain any differences in ACR measurement or RAAS-treatment initiation. The variation explained at the provider level was equal to or smaller than that explained at the practice level (intraclass correlation coefficients between 0.02 and 0.18).

Discussion

In this study evaluating albuminuria screening and treatment in T2DM patients in Dutch primary care, we observed that an ACR measurement was documented for less than 60% of these patients in 2009, even in patients below 75 years of age. ACR measurement was more common in patients with previous ACR measurements, in patients receiving more medication, and in those receiving additional care by a diabetes support facility. Patients with increased albuminuria were frequently treated with RAAS blockers (78.4% in prevalent albuminuria and 66.5% in incident albuminuria). In patients with increased albuminuria not yet received RAAS treatment, actions as recommended in the prevailing primary care guideline for T2DM were applied in only a small proportion of patients (<15%).

Albuminuria screening was lower than anticipated based on the published screening rates of other renal/cardiovascular risk factors [10–12]. Although the proportion of patients being screened increased when the interval was extended above 12 months, as proposed in a recent study [24], this was a marginal increase leaving more than a third of patients not being screened in 2009. Also, limiting the population to those who had a longer life expectancy did not substantially increase the albuminuria screening rate. One possible reason for the low screening rates could be that patients did not frequently visit their GPs or even avoided care, although this is not plausible as 3 monthly visits are common for patients with T2DM in the Netherlands. In addition, >90% of the included patients had their HbA1c measured at least once yearly in the study period, and the number of care avoiders in this cohort is estimated to be ≤5% on the basis of other available visit data and measurements [11]. It is, therefore, unlikely that care avoidance contributed to the low albuminuria screening rate. Another possibility is that GPs start RAAS treatment without testing for microalbuminuria, since these agents are proven to prevent both cardiovascular and renal complications. Our results, however, show that this was not the case since the initiation of RAAS treatment was 2-fold higher in patients with versus without prior ACR measurement. Another reason may be logistical issues regarding albuminuria screening (i.e. urine collection instructions, requirement of specific urine cups or inadequate patient recall system when patients do not bring a urine sample). This may explain why additional care from a diabetes support facility was an important determinant of ACR measurement, as they may be more attentive to laboratory procedures and patient instructions and follow-up [25].

Of the patients who had prevalent or incident micro/macroalbuminuria, a substantial proportion already

received RAAS treatment. It is unclear to what extent RAAS treatment was prescribed to these patients because of increased albuminuria or because of (previous) uncontrolled blood pressure. Given the fact that RAAS treatment was also common in patients without any ACR measurements and in patients with normoalbuminuria, it is tempting to assume that in many patients, the main indication for RAAS treatment was uncontrolled blood pressure rather than increased albuminuria. The finding that blood pressure and number of antihypertensive drugs used (other than RAAS) were determinants of RAAS-treatment initiation in patients with unknown albuminuria or normoalbuminuria supports this idea. Furthermore, RAAS treatment was also more likely to be initiated in patients with increased albuminuria when they already used more antihypertensive drugs and with incident cardiovascular events, suggesting that RAAS-treatment initiation in these patients is driven by other cardiovascular diseases. This suggests that increased albuminuria in itself is insufficiently recognized as an indication for RAAS-treatment prescription. Nevertheless, across all groups, the proportion of patients who started RAAS treatment was highest in patients with prevalent increased albuminuria followed by patients with incident increased albuminuria, although the proportion of patients who received RAAS treatment upon detection of increased albuminuria was disappointingly low (∼13%).

It is widely recognized that there can be many barriers for the implementation of guidelines in clinical practice [26]. Cognitive and attitudinal barriers have been described which may explain why practitioners do not comply with the guideline recommendations [26]. A questionnaire among European GPs showed some internal barriers with respect to albuminuria guideline implementation. According to this questionnaire, a repeat ACR test in T2DM patients with incident microalbuminuria was deemed necessary by only 45–77% GPs (depending on the country). Even more worrisome was the notion that only 23–50% of GPs would prescribe RAAS treatment for a T2DM patient with confirmed microalbuminuria. These findings, together with our data, show that awareness and implementation of guidelines regarding albuminuria screening and treatment in primary care need to be improved [27]. It is, however, important to note that there may be sensible arguments not to comply with guideline recommendations. Non-compliance to a guideline is not necessarily 'wrong'. Rather, the guidelines offer recommendations and should not be followed blindly without taking the individual patient into account. We observed considerable variation at GP practice level regarding guidelines implementation for albuminuria screening and RAAS-treatment initiation. The factors that may explain variation among GPs include differences in beliefs about the necessity of certain actions, in prioritization of actions, in patient interaction and in organization of care [28, 29].

It is also important to consider the guideline itself when evaluating barriers for guideline implementation. The Dutch primary care guideline differs in some aspects from the standards of medical care by the American Diabetes Association (ADA) [7]. The main discrepancy between the Dutch primary care guideline and the ADA guideline is that RAAS treatment is only recommended in patients with increased albuminuria, whereas the ADA guideline recommends RAAS treatment in all patients with T2DM irrespective of their albuminuria status. This may to some extent limit extrapolation of our results. Although there are several arguments to favour the recommendations of the ADA guideline over the Dutch primary care guideline, Dutch primary care physicians are expected to follow the national primary care guideline, which is considered the standard for GPs in the Netherlands. These guidelines are broadly adopted and accepted by the Dutch GPs [30].

As in many other European countries, the Dutch GP plays a central role in providing diabetes care including screening for and treatment of albuminuria. A study from the UK reported on the quality of diabetes care and presented data on albuminuria screening and treatment thereof [9]. In this population, 75% of patients with T2DM were screened for increased albuminuria in a 15-month period in 2006 which was also lower when compared with other risk factors. Of patients with a diagnosis of micro/macroalbuminuria 86.4% was treated with an ACEi or ARB but no information was presented on subsequent RAAS treatment initiation. Both the proportion of patients screened and the proportion of patients treated with RAAS treatment were modestly higher in the UK-setting than we observed in the Dutch setting. The higher proportion of screened patients in the UK study can partly be explained by the longer study period (15 as opposed to 12 months) and the measurement in 'high quality data' general practices. Also, the higher rates of screening and treatment in the UK may be positively influenced by the implementation of the quality and outcomes framework in 2004 [9]. In our study, we observed improvement in albuminuria screening in 2008–2009 compared with 2007, a trend which was also shown in another Dutch cohort [31]. As the current guideline dates from 2006, this improvement illustrates that new guideline recommendations may take time and extra effort before they are fully implemented in practice [32, 33].

A limitation of this study is that we looked at the most recent ACR measurement and the subsequent actions, whereas some patients may have a history of previous events or outcomes which may influence these actions. To take this into account, we included a wide range of potential patient-related determinants when assessing guideline adherence. Another limitation is that we only looked at new prescriptions of RAAS treatment and not at changes in RAAS treatment such as dose adjustment. This may underestimate the proportion of patients in whom action is undertaken regarding RAAS treatment on the basis of the ACR measurement. For assessing guideline adherence in our study, however, these patients were considered to be adequately managed. An important strength of this study is that the data reflect a large longitudinally followed group of T2DM patients treated in primary care. All collected data were registered during regular care and this process was unaffected by this study. Data collection and registration have been validated in prior studies underscoring the robustness of the results [20]. Moreover,

the GIANTT patient cohort is similar to other Dutch outpatient cohorts of type 2 diabetic patients regarding general characteristics, such as age and gender, and also regarding hypertension and albuminuria-related parameters [31]. Participating GPs are not self-selected but have consented to providing anonymized data as part of a contract to get reimbursed for their diabetes care. Such contracts are common for most GPs in the Netherlands, increasing the generalizability of the results.

In conclusion, in the primary care setting, the adherence to guidelines with respect to albuminuria screening and treatment was modest and should be further improved in order to accomplish optimal risk management in patients with T2DM. It is well recognized that albuminuria is one of the strongest cardio-renal risk markers, and early screening and appropriate treatment have the potential to substantially reduce the risk of cardio-renal complications. Nevertheless, in comparison to the management of other risk factors in T2DM, albuminuria receives little attention. Better support systems for regular ACR measurement and more attention for albuminuria as a risk factor beyond blood pressure may improve albuminuria screening and treatment in primary care.

Supplementary data

Supplementary data are available online at http://ndt.oxfordjournals.org.

Authors' contributions

P.D., H.J.L.H., D.D.Z and M.E.H. developed and formulated the research questions. P.D. and J.V. contributed to the acquisition of data. M.E.H. and J.V. conducted the analysis, and H.J.L.H., P.D. and D.D.Z. contributed to the analysis and interpretation of data. M.E.H. wrote the manuscript, contributed to discussions, and reviewed and edited the manuscript and D.D.Z., H.J.L.H., J.V. and P.D. contributed to discussions, and reviewed and edited the manuscript.

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