Association of renal function screening frequency with renal function decline in patients with type 2 diabetes: a real-world study in primary health care

Henry Sundqvist1,2, Eveliina Heikkala1,2,3, Jari Jokelainen2, Giuseppina Russo4, Ilona Mikkola1† and Maria Hagnäs1,2*†

Abstract

Aims: To examine the association of the screening frequency of estimated glomerular filtration rate (eGFR) with the substantial reduction in eGFR (≥25%) among type 2 diabetes (T2D) patients with normal (eGFR≥60 ml/min/1.73 m²) and impaired kidney function (eGFR<60 ml/min/1.73 m²).

Methods: A longitudinal study involving 5104 T2D patients with follow-up period of 6.8 years (1.9 SD) were treated at the Rovaniemi Health Center, Rovaniemi, Finland during 2011–2019. The association between the screening frequency of eGFR (yearly vs. non-yearly) and the substantial reduction in eGFR was studied with logistical models and adjusted with biochemical variables and preventive medications.

Results: Among the T2D patients with normal kidney function, non-yearly eGFR screening was significantly associated with substantial eGFR reduction in both unadjusted (odds ratio [OR] 3.29, 95% confidence interval [CI] 2.54–4.33) and adjusted models (OR 2.06, 95% CI 1.21–3.73) compared with yearly screening frequency. In the group of patients with impaired kidney function in the unadjusted model, non-yearly eGFR screening was significantly associated with substantial eGFR reduction (OR 2.38, 95% CI 1.30–4.73), but became non-significant after adjustments (OR 1.89, 95% CI 0.61–7.21).

Conclusions: This study underscores the role of regular eGFR screening in the prevention of kidney function decline.

Keywords: Kidney Function, Primary Health Care, Screening Frequency, Type 2 Diabetes

Introduction

Type 2 diabetes (T2D) is an alarming global pandemic that is affecting a steadily increasing number of people. In 2019, it was estimated that 463 million (9.3%) of the world's adult population have diabetes, and the number is estimated to increase to 578 million (10.2%) by 2030 [1]. In high-income countries, diabetes is twice as common compared with low-income countries. For instance, in 2021, the age-adjusted prevalence of diabetes was estimated to be 10.7% in the United States [1].

It is well established that T2D is a major risk factor for a wide range of vascular diseases, including ischemic heart disease and stroke, as well as chronic kidney disease (CKD) [2, 3]. Furthermore, CKD alone largely accounts for the increased all-cause mortality in patients with T2D [4]. During the last three decades,
disability-adjusted life years (DALYs) attributable to diabetes and CKD have increased, whereas DALYs attributable to myocardial infarctions and strokes have declined [5].

The prevalence of CKD in patients with T2D is estimated to vary between 27.9 and 58.6% [5–10]. Traditionally, CKD in patients with T2D is characterized by the manifestation of albuminuria, followed by a decline in kidney function marked by a reduction in the glomerular filtration rate (GFR), finally leading to end-stage kidney disease (ESKD) [11]. However, recent studies state that CKD, especially in patients with T2D, is mostly characterized by renal impairment without measurable albuminuria [11, 12]. Many underlying causes of this non-albumic renal impairment have been hypothesized, for instance, the increased use of estimated GFR (eGFR), increased prescription of renoprotective medication, and earlier identification of CKD [11, 12].

In patients with T2D, regular screening and monitoring of CKD are widely recommended [2, 13, 14]. However, the screening and monitoring of CKD among patients with T2D have been shown to be inadequate [12, 15]. Recommendations are geared toward the regular monitoring of CKD, although evidence of the optimal screening frequency is scarce [2, 13, 14]. The current guidelines concerning monitoring frequency are based on expert opinion and indirectly derived from observational and renoprotective medication research [2, 13, 14]. As such, more in-depth knowledge of the relevance of optimal screening frequency is required.

The effective prevention of complications, especially CKD, is highly important in patients with T2D [13]. Intensive blood pressure (BP) and glucose control are still regarded as the cornerstones of CKD prevention, together with prognostic and renoprotective medication, such as glucagon-like peptide-1 receptor agonists (GLP-1 RAs), sodium-glucose co-transporter-2 inhibitors (SGLT2i), and renin-angiotensin-aldosterone system (RAAS) blocking therapy [13, 16]. Despite adequate interventions, CKD is considered to be a progressive disease, and therapy aims to slow the decline of kidney function [17, 18]. Therefore, the early identification of CKD through regular screening and adequate treatment is important.

The associations between cardiovascular risk factor control (glycosylated hemoglobin A1 (HbA1c), systolic blood pressure (sBP)) and prevention of renal function decline are well established [2, 11, 13, 14, 16]. However, the screening frequency of eGFR as a possible individual predictive factor of renal function decline among T2D patients has not been previously investigated. Therefore, the aim of this longitudinal study was to examine the association of the screening frequency of eGFR with a substantial reduction (≥ 25%) in eGFR among T2D patients with normal and impaired kidney function.

Methods

Study population

This study was a part of the Rovaniemi Primary Care T2D Study, which is a registry-based real-world study in a primary health care setting. Rovaniemi is a city and municipality located in northern Finland with a total population of 62,000 people living in both urban and rural areas. The study population consisted of 5104 patients who had received a T2D diagnosis between November 1, 2011 and February 19, 2019 at the Rovaniemi Health Center, Rovaniemi, Finland. The T2D diagnosis was based on the International Classification of Disease (ICD-10) codes for T2D (E11.1–E11.9) or the equivalent T2D code (T90) from the International Classification of Primary Care (ICPC). Patients with at least two evaluations of eGFR with a minimum interval of six months were included in the study. The data were retrieved from patient records. In the analyses, the baseline was considered as the first measurement of eGFR and the follow-up as the last measurement of eGFR within each patient. The study period was defined as the time between the baseline and follow-up, varying individually.

Data collection

Reduction of eGFR

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation formulation, which is based on age, sex, race, and serum creatinine level (μmol/l), was used to calculate the eGFR (ml/min/1.73 m²). A substantial reduction in eGFR was defined as a reduction of ≥25% between the baseline and the follow-up in accordance with the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines in CKD evaluation and management [2]. The “no substantial reduction” category included all others except those with substantial eGFR reduction.

Screening frequency of eGFR

The mean value of eGFR screening frequency between 2011 and 2019 was calculated and then dichotomized as yearly (365 days or under) vs. non-yearly (over 365 days), in line with the current national screening frequency recommendations [13, 19]. The first category was used as a reference.

Covariates

We assessed the sex, age, achievement of treatment goals of bioclinical variables (HbA1c, LDL, and sBP), and prescription of antihyperglycemic and cardiovascular medications (Anatomical Therapeutic Chemical, ATC codes): statins (C10AA), any long-acting insulin
(A10AE, A10AC), GLP-1 RAs (A10B), SGLT2i (A10BK), and angiotensin-converting enzyme inhibitors (ACEi) (C09A) or angiotensin II receptor blockers (ARB) (C09C) as potential covariates [2, 11, 13, 14, 16]. The preferred source of BP data was the patients’ own home measurements. If home measurements were not available, the measurements performed by a healthcare professional during the consultation visit were used [20, 21].

Age was measured at the follow-up. Achievement of the treatment targets for HbA1c, LDL, and sBP was defined according to the national guidelines as follows: HbA1c <53 mmol/mol, LDL <2.5 mmol/l, and sBP <135 mmHg [22]. This was estimated at the baseline and follow-up. The patients were divided into two groups in terms of all three variables: 1) had achieved the treatment target at both time points, and 2) had not achieved the treatment target at both time points.

Data on prescribed or renewed prescriptions of statins, any long-acting insulin, GLP-1 RAs, SGLT2i, and ACEi/ARB were collected from the national electronic prescription registry using ATC codes. Medication data (new prescriptions or prescription renewals) were further processed by calculating the midpoint of the study period for each patient. Baseline medication was defined as before whereas follow-up medication was defined as after the midpoint. If the prescription was valid at the midpoint, then it was assumed to be the same at the baseline and follow-up. Follow-up medication data were used in the logistic models.

Descriptive variables
Body mass index (BMI) was calculated by dividing the patient weight in kilograms by the square of their height in meters (kg/m²) and considered a continuous variable. In addition to the previously mentioned bioclinical variables and medications, the following measurements were gathered from the patient records: hemoglobin (Hb; g/l), diastolic BP (mmHg), and medications (ATC codes), such as calcium blockers (C08CA), beta blockers (C07AB), diuretics (C03), metformin (A10BA), glitazones (A10BH), glitazone (A10BG), sulphonylureas (A10BB), fibrates (C10AB), multiple daily insulin injections (A10AE or A10AC and A10AB), and ezetimibe (C10AX).

Study protocol and data collection
The data were recorded as part of each patient’s routine control visits at the health care center or during other visits and collected and handled anonymously using patient IDs for scientific purposes. Being a registry-based study, no written consent from the patients was required, in accordance with current Finnish legislation. The Ethics Committee of Lapland Central Hospital, Rovaniemi, Finland approved the study protocol in May 2018.

Table 1 Baseline and follow-up characteristics of the type 2 diabetes study population. Data are presented as mean (SD), except for sex, eGFR reduction, and medication (given as percentages of the population)

|                         | Baseline | Follow-up | P-value |
|-------------------------|----------|-----------|---------|
| n                       | 5104     | 5104      |         |
| Male                    | 2755 (54.0) | 2755 (54.0) |         |
| Female                  | 2349 (46.0) | 2349 (46.0) |         |
| Age, years              | 70.0 (12.7) |           |         |
| Study period, years     | 6.8 (1.9)  |           |         |
| Mean eGFR screening frequency, days | 344.5 (195.7) | 294.7 (118.8) | <0.001 |
| LDL-cholesterol, mmol/l | 2.9 (1.1)  | 2.5 (1.0)  | <0.001  |
| HbA1c, mmol/mol          | 51.0 (15.0) | 49.1 (13.2) | <0.001  |
| eGFR, ml/min/1.72 m²     | 81.9 (19.2) | 76.5 (22.2) | <0.001  |
| Plasma creatinine, µmol/l | 79.5 (34.1) | 85.5 (52.1) | <0.001  |
| Hemoglobin, g/l          | 141.4 (14.5) | 137.3 (18.5) | <0.001  |
| BMI, kg/m²               | 30.3 (6.0)  | 29.8 (5.8)  | <0.001  |
| Systolic BP, mmHg        | 148.3 (23.0) | 135.9 (18.4) | <0.001  |
| Diastolic BP, mmHg       | 83.0 (12.4)  | 77.9 (11.2)  | <0.001  |
| eGFR reduction <25%, n (%) | 4046 (87.4) | 582 (12.6)  | <0.001  |
| eGFR reduction ≥25%, n (%) | 3029 (59.3) | 4093 (80.2) | <0.001  |
| Any hypertensive medication | 3029 (59.3) | 4093 (80.2) | <0.001  |
| ACEi/ARB                | 2045 (41.9) | 1974 (40.4) | <0.001  |
| Ca blockers             | 1350 (27.7) | 2289 (44.8) | <0.001  |
| Beta blockers           | 1867 (36.6) | 1688 (33.1) | <0.001  |
| Metformin               | 2417 (47.4) | 3283 (64.3) | <0.001  |
| SGLT2i                  | 24 (0.5)   | 704 (13.8) | <0.001  |
| GLP-1 RAs               | 11 (0.2)   | 154 (3.0)  | <0.001  |
| Glicliflozin            | 917 (18.0)  | 1321 (25.9) | <0.001  |
| Glitazone               | 11 (0.2)   | 18 (0.4)   | 0.265   |
| Sulphonylureas          | 169 (3.3)  | 131 (2.6)  | 0.030   |
| Any long acting insulin | 811 (15.9)  | 1178 (23.1) | <0.001  |
| Multiple daily injections insulin therapy | 366 (7.2) | 709 (13.9) | <0.001  |
| Statin                  | 2741 (53.7) | 3479 (68.2) | <0.001  |
| Ezetimibe               | 243 (4.8)  | 370 (7.2)  | <0.001  |
| Fibrates                | 23 (0.5)   | 23 (0.5)   | 1.000   |

Note: The P-values present the differences between the groups tested with t-test or χ²-test. ACEi, Angiotensin-Converting Enzyme; ARB, Angiotensin Receptor Blockers; BMI, Body Mass Index; DPP-4, Dipeptidyl-Peptidase-4; eGFR, estimated Glomerular Filtration Rate; GLP-1 RAs, Glucagon-Like Peptide-1 Receptor Agonists; HbA1c, Glycosylated Hemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; BP, Blood Pressure; SGLT2i, Sodium-Glucose co-Transporter-2 Inhibitors

Statistical methods
Clinical outcome measures were presented as mean and standard deviation (SD) and categorical variables as proportions. Continuous variables were tested with the independent samples t-test, while the Pearson χ² test was
used to evaluate the difference between categorical values. A multiple-multivariable binomial logistic regression analysis with odds ratios (ORs) and 95% confidence intervals (CIs) was performed to study the potential associations between substantial eGFR reduction and the screening frequency of eGFR. The logistic models were stratified by the baseline kidney function as normal (eGFR ≥ 60 ml/min/1.73 m²) and impaired (eGFR < 60 ml/min/1.73 m²) kidney function, as the screening frequency recommendations differ between patients with and without impaired kidney function [2]. All statistical analyses were performed using the R software version 4.1.1. R Core Team (2020). A p-value < 0.05 was considered statistically significant.

Results
The T2D study population consisted of 5104 patients with a mean age of 70.0 years (SD 12.7). The characteristics of the study population are presented in Table 1. During the average of the 6.8-year follow-up period (SD 1.9), beneficial changes were noted in LDL, HbA1c, Glucose, and eGFR. The most common medication used was metformin, followed by GLP-1 RAs and SGLT2i. The baseline characteristics of the type 2 diabetes study population categorized as having normal or impaired kidney function are presented in Table 2. The groups were compared using t-test or χ²-test. The statistical analysis showed significant differences between the groups in terms of age, sex, and eGFR screening frequency, with patients with impaired kidney function having a higher mean eGFR screening frequency compared to those with normal kidney function. The results also indicated that patients with impaired kidney function were more likely to have a substantial reduction in eGFR, any hypertensive medication, ACEi/ARB, Ca blockers, beta blockers, diuretics, any diabetes medication, metformin, and SGLT2i.

Table 2  Baseline characteristics of the type 2 diabetes study population categorized as having normal or impaired kidney function. Data are presented as mean (SD), except for eGFR reduction, and medication (given as percentages of the population)

|                                | Normal kidney function group (eGFR ≥ 60 ml/min/1.73 m²) | Impaired kidney function group (eGFR < 60 ml/min/1.73 m²) | P-value |
|--------------------------------|----------------------------------------------------------|----------------------------------------------------------|---------|
| n (%)                          | 4336 (87.4)                                              | 625 (12.6)                                               | <0.001  |
| Male                           | 2416 (55.7)                                              | 261 (41.8)                                               |         |
| Female                         | 1920 (44.3)                                              | 364 (58.2)                                               | <0.001  |
| Mean age, years (SD)           | 68.9 (12.1)                                              | 81.3 (8.9)                                               | <0.001  |
| Study period years (SD)        | 6.9 (1.8)                                                | 6.3 (2.2)                                                | <0.001  |
| Mean eGFR screening frequency, days (SD) | 300.1 (118.7)                                            | 252.9 (111.7)                                            | <0.001  |
| LDL-cholesterol, mmol/l        | 2.5 (1.0)                                                | 2.4 (1.0)                                                | 0.012   |
| HbA1c, mmol/mol                | 48.7 (13.0)                                              | 52.4 (14.1)                                              | <0.001  |
| eGFR, ml/min/1.73 m²           | 81.1 (18.8)                                              | 45.3 (17.9)                                              | <0.001  |
| Plasma creatinine, μmol/l      | 77.7 (29.7)                                              | 139.5 (109.8)                                            | <0.001  |
| Hemoglobin, g/l                | 138.8 (17.9)                                             | 127.1 (19.6)                                             | <0.001  |
| BMI, kg/m²                     | 29.9 (5.8)                                               | 28.7 (5.1)                                               | 0.004   |
| Systolic BP, mmHg              | 136.0 (18.1)                                             | 135.2 (19.9)                                             | 0.469   |
| Diastolic BP, mmHg             | 78.4 (11.2)                                              | 75.4 (11.4)                                              | <0.001  |
| Substantial reduction in eGFR (≥25%) | 436 (10.8)                                               | 146 (25.0)                                               | <0.001  |
| Any hypertensive medication    | 364 (84.0)                                               | 585 (93.6)                                               | <0.001  |
| ACEi/ARB                       | 1714 (39.5)                                              | 325 (52.0)                                               | <0.001  |
| Ca blockers                    | 1115 (25.7)                                              | 233 (37.3)                                               | <0.001  |
| Beta blockers                  | 1890 (43.6)                                              | 389 (62.2)                                               | <0.001  |
| Diuretics                      | 1287 (29.7)                                              | 395 (63.2)                                               | <0.001  |
| Any diabetes medication        | 3566 (82.2)                                              | 490 (78.4)                                               | 0.023   |
| Metformin                      | 2975 (68.6)                                              | 278 (44.5)                                               | <0.001  |
| SGLT2i                         | 681 (15.7)                                               | 18 (2.9)                                                 | <0.001  |
| GLP-1 RAs                      | 137 (3.2)                                                | 15 (2.4)                                                  | 0.365   |
| Gliptin                        | 1035 (23.9)                                              | 279 (44.6)                                               | <0.001  |
| Glitazone                      | 15 (0.3)                                                 | 3 (0.5)                                                  | 0.869   |
| Sulphonylureas                 | 110 (2.5)                                                | 20 (3.2)                                                  | 0.403   |
| Any long-acting insulin        | 947 (21.8)                                               | 224 (35.8)                                               | <0.001  |
| Multiple daily injections of insulin therapy | 537 (12.4)                                               | 170 (27.2)                                               | <0.001  |
| Statin                         | 3060 (70.6)                                              | 405 (64.8)                                               | 0.004   |
| Ezetimibe                      | 330 (7.6)                                                | 38 (6.1)                                                  | 0.199   |
| Fibrates                       | 21 (0.5)                                                 | 2 (0.3)                                                  | 0.802   |

Note: The p-values present the differences between the groups tested with t-test or χ²-test. ACEi, Angiotensin-Converting Enzyme; ARB, Angiotensin Receptor Blockers; BMI, Body Mass Index; DPP-4, Dipeptidyl-Peptidase-4; eGFR, estimated Glomerular Filtration Rate; GLP-1 RAs, Glucagon-Like Peptide-1 Receptor Agonists; HbA1c, Glycosylated Hemoglobin; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein; BP, Blood Pressure; SGLT2i, Sodium-Glucose co-Transporter-2 Inhibitors.
BMI, and BP. The average systolic BP value decreased by 12.4 mmHg \((p < 0.001)\) in the total population. A significant reduction in eGFR \((\geq 25\%)\) was observed in 12.6\% \((n = 582)\) of the population. The total number of prescribed antihyperglycemic and cardiovascular medications increased during the study period, as well as the usage of GLP-1 RAs and SGLT2i.

At baseline, 87.4\% \((n = 4336)\) of the population had normal kidney function (Table 2). The patients with impaired kidney function were older \(81.3 [SD 8.9] \text{ vs. } 68.9 [SD 12.1] \text{ years}\) and more frequently screened for eGFR \((252.9 [SD 111.7] \text{ vs. } 300.1 [SD 118.7] \text{ days})\) compared with the patients with normal kidney function \((p < 0.001 \text{ for both})\). A substantial reduction in eGFR was observed among 25.0\% \((n = 146)\) of the patients with impaired kidney function and 10.8\% \((n = 436)\) among those with normal kidney function \((p < 0.001)\).

The associations between screening frequency and substantial reduction of eGFR in the groups of patients with normal and impaired kidney function are presented in Table 3 and Table 4, respectively. In the normal kidney function group, non-yearly eGFR screening was significantly associated with substantial eGFR reduction in both unadjusted (OR 3.29, 95% CI 2.54–4.33) and adjusted models (OR 2.06, 95% CI 1.21–3.73) compared with yearly screening frequency. In addition, age and prescription of ACEi/ARB were associated with substantial eGFR reduction in both models. However, the association of the achievement of the treatment targets for HbA1c and LDL at baseline and follow-up and the prescription of any long-acting insulin or SGLT2i with this outcome attenuated and became non-significant in the adjusted model.

In the impaired kidney function group, only unadjusted non-yearly eGFR screening was significantly associated with substantial eGFR reduction (OR 2.38, 95% CI 1.30–4.73), whereas the adjusted association did not reach statistical significance in the impaired kidney function group (OR 1.89, 95% CI 0.61–7.21). Many of the other variables showed the same attenuating trend, with the achievement of the treatment targets for LDL and HbA1c, alongside SGLT2i and any long-acting insulin, as well as the prescription of GLP-1 RAs and SGLT2i, showed the same pattern.

### Table 3

| eGFR reduction | < 25% | \(\geq 25\%) | OR (unadjusted) | OR (adjusted) |
|----------------|------|-------------|----------------|--------------|
| eGFR screened yearly | Yes | 1380 (95.2) | 69 (4.8) | 3.29 (2.54–4.33, \(p < 0.001\)) | 2.06 (1.21–3.73, \(p = 0.011\)) |
| No | 2228 (85.9) | 367 (14.1) | – | – |
| Sex n (%) | | | | |
| Male | 2013 (89.4) | 238 (10.6) | – | – |
| Female | 1595 (89.0) | 198 (11.0) | 1.05 (0.86–1.28, \(p = 0.632\)) | 0.98 (0.68–1.40, \(p = 0.900\)) |
| Age, mean (SD) | 68.8 (11.7) | 764 (10.4) | 1.07 (1.06–1.08, \(p < 0.001\)) | 1.07 (1.05–1.10, \(p < 0.001\)) |
| LDL, n (%) | | | | |
| < 2.5 mmol/l | 1897 (88.0) | 259 (12.0) | – | – |
| \(\geq 2.5\) mmol/l | 1521 (92.1) | 131 (7.9) | 0.63 (0.50–0.79, \(p < 0.001\)) | 0.95 (0.65–1.40, \(p = 0.808\)) |
| HbA1c, n (%) | | | | |
| < 53 mmol/mol | 2605 (91.2) | 250 (8.8) | 1.86 (1.50–2.29, \(p < 0.001\)) | 1.48 (0.93–2.34, \(p = 0.100\)) |
| \(\geq 53\) mmol/mol | 904 (84.9) | 161 (15.1) | – | – |
| systolic BP, n (%) | | | | |
| < 135 mmHg | 548 (85.2) | 95 (14.8) | – | – |
| \(\geq 135\) mmHg | 518 (86.5) | 81 (13.5) | 0.90 (0.65–1.24, \(p = 0.527\)) | 0.72 (0.51–1.02, \(p = 0.069\)) |
| ACEi/ARB in use | Yes | 2049 (86.9) | 310 (13.1) | 1.87 (1.51–2.33, \(p < 0.001\)) | 1.74 (1.16–2.66, \(p = 0.009\)) |
| No | 1559 (92.5) | 126 (7.5) | – | – |
| SGLT2i in use | Yes | 602 (92.8) | 47 (7.2) | – | – |
| No | 3006 (88.5) | 389 (11.5) | 0.60 (0.44–0.82, \(p = 0.002\)) | 0.70 (0.38–1.24, \(p = 0.244\)) |
| GLP-1 RAs in use | Yes | 119 (91.5) | 11 (8.5) | – | – |
| No | 3489 (89.1) | 425 (10.9) | 0.76 (0.38–1.36, \(p = 0.387\)) | 0.92 (0.14–3.66, \(p = 0.912\)) |
| Any long-acting insulin in use | Yes | 756 (82.6) | 157 (17.2) | – | – |
| No | 2852 (91.1) | 279 (8.9) | 2.12 (1.72–2.62, \(p < 0.001\)) | 1.40 (0.87–2.23, \(p = 0.162\)) |
| Statin in use | Yes | 2619 (89.1) | 322 (10.9) | – | – |
| No | 989 (89.7) | 114 (10.3) | 1.07 (0.85–1.34, \(p = 0.576\)) | 1.02 (0.67–1.58, \(p = 0.937\)) |

ACEi, Angiotensin-Converting Enzyme; ARB, Angiotensin Receptor Blockers; eGFR, estimated Glomerular Filtration Rate; GLP-1 RAs, Glucagon-Like Peptide-1 Receptor Agonists; HbA1c, Glycosylated Hemoglobin; LDL, Low-Density Lipoprotein; BP, Blood Pressure; SGLT2i, Sodium-Glucose co-Transporter-2 Inhibitors
being significantly associated in the unadjusted model but not in the adjusted model. Female sex and ACEi/ARB prescription were significantly associated in the adjusted model (OR 0.41 CI 0.20–0.84 and OR 5.16 CI 1.94–16.72).

**Discussion**

**Main findings**

In this longitudinal study, we found that annual eGFR screening frequency was associated with significant renal function decline among 5104 primary care T2D patients with normal kidney function. This association was independent of the sex, age, bioclinical variables, and prescribed antihyperglycemic and cardiovascular medications. A similar trend in the association between annual eGFR screening and significant renal function decline was observed in the impaired kidney function group.

**Screening frequency and current guidelines**

To the best of our knowledge, earlier studies have not investigated the association of eGFR screening frequency with renal function decline among patients with T2D. Although international guidelines recommend the annual screening of CKD in patients with T2D and more frequent monitoring of kidney function if CKD is diagnosed, these guidelines are derived from expert opinion and indirectly from renoprotective medication research [2, 13, 14]. This study improves the existing knowledge on the role of annual eGFR screening in significant renal function decline in a real-life setting. Our finding supports the current guidelines regarding annual eGFR screening in T2D patients, which earlier studies have shown to be lacking in 7–22% of patients [9, 13, 15, 19, 23].

Yearly eGFR screening was associated with renal function decline in patients with normal kidney function. In the present study, we used a cut-off level of 25% as the substantial reduction in eGFR, in accordance with KDIGO guidelines [2]. This further underscores the meaning of our novel findings. In addition to well-established confounders of the present study, the observed results could be attributed to early medical treatment with proper patient education and better overall compliance to treatment [13]. A similar association was noted in patients with impaired kidney function. However, after adjusting for confounders, the association did not reach statistical significance. One might speculate that the attenuation in the impaired kidney function group was due to the small patient sample size.

---

**Table 4** Associations of the screening frequency of eGFR and potential covariates with significant eGFR reduction among patients with impaired kidney function (eGFR<60 ml/min/1.73 m²)

|                         | eGFR reduction | OR (unadjusted) | OR (adjusted) |
|-------------------------|----------------|----------------|--------------|
|                         | < 25%          | ≥ 25%          |               |
| eGFR screened yearly    | Yes            | 77 (86.5)      | 2.38 (1.30–4.73, p = 0.008) | 1.89 (0.61–7.21, p = 0.301) |
|                         | No             | 361 (72.9)     |               |
| Sex n (%)               |                |                |              |
| Male                    | 170 (71.1)     | 69 (28.9)      |
| Female                  | 268 (77.7)     | 77 (22.3)      |
| Age, mean (SD)          |                |                |              |
|                         | 81.5 (8.9)     | 82.5 (8.0)     |
| LDL, n (%)              | < 2.5 mmol/l   | 216 (73.2)     | 0.71 (0.45–1.10, p = 0.130) | 0.55 (0.24–1.18, p = 0.138) |
|                         | ≥ 2.5 mmol/l   | 146 (79.3)     |               |
| HbA1c, n (%)            | < 53 mmol/mol  | 264 (81.7)     | 2.45 (1.65–3.67, p < 0.001) | 0.82 (0.31–2.09, p = 0.679) |
|                         | ≥ 53 mmol/mol  | 135 (64.6)     |               |
| systolic BP, n (%)      | < 135 mmHg     | 85 (75.2)      | 0.94 (0.52–1.70, p = 0.835) | 0.72 (0.36–1.41, p = 0.334) |
|                         | ≥ 135 mmHg     | 97 (76.4)      |               |
| ACEi/ARB in use         | Yes            | 289 (73.2)     | 1.37 (0.91–2.08, p = 0.140) | 5.16 (1.94–16.72, p = 0.002) |
|                         | No             | 149 (78.8)     |               |
| GLP-1 RAs in use        | Yes            | 12 (85.7)      | 0.49 (0.08–1.84, p = 0.358) | 0.95 (0.04–8.34, p = 0.965) |
|                         | No             | 426 (74.7)     |               |
| Any long-acting insulin in use | Yes | 131 (61.5) | 3.00 (2.05–4.43, p < 0.001) | 2.01 (0.81–5.09, p = 0.133) |
|                         | No             | 307 (82.7)     |               |
| Statin in use           | Yes            | 295 (75.4)     | 0.93 (0.63–1.39, p = 0.722) | 0.59 (0.26–1.36, p = 0.210) |
|                         | No             | 143 (74.1)     |               |

ACEI, Angiotensin-Converting Enzyme; ARB, Angiotensin Receptor Blockers; eGFR, estimated Glomerular Filtration Rate; GLP-1 RAs, Glucagon-Like Peptide-1 Receptor Agonists; HbA1c, Glycosylated Hemoglobin; LDL, Low-Density Lipoprotein; BP, Blood Pressure
size. Additionally, the heterogeneity (eGFR ranging from mildly impaired kidney function to ESKD) in the corresponding group may result in variability concerning treatment, medication usage, and monitoring. Moreover, patients with eGFR<30 ml/min/1.73 m² are more likely to be monitored more closely and treated by a nephrologist than a primary care doctor [2, 13].

Strengths and weaknesses
The main strengths of our study are the real-life primary care setting that captures the majority of the T2D patients in the region, the large population size, and the longitudinal design. In Finnish health care, electronic patient registry data and electronic medicine prescriptions are extensively used as sources of comprehensive medical data. All of the patient samples were taken, processed, and analyzed by the same laboratory, avoiding possible discrepancies in the results. Concurrently, the study has several limitations that need to be considered while interpreting our results. Data on the patients treated and monitored by nephrologists (e.g., patients with severely decreased kidney function or ESKD) were not available. The majority of CKD patients with T2D are diagnosed and treated in primary care by general practitioners in European countries, with only patients with severely decreased eGFR and moderately to severely increased albuminuria requiring referral to a nephrologist. The findings of the current study are derived from a single center, and mainly of older patients and therefore should not be directly generalized to other patient groups. The changes in medication therapy on control visits, smoking status, physical activity, socio-economic status, and patient mortality were also not available for analysis, which can be considered a limitation of our study.

Conclusion
In conclusion, the novel findings of the present study highlight the role of regular eGFR screening in the prevention of kidney function decline. This confirms the importance of regular eGFR screening in clinicians’ daily practice. Further studies are needed to determine the association of the screening frequency of albuminuria with renal function decline in the prevention of renal impairment in T2D patients, especially in primary health care settings.

Acknowledgements
Not applicable.

Authors’ contributions
HS, EH, JJ, IM and MH contributed to the concept and design of the study. All authors contributed to the acquisition, analysis, or interpretation of data for the work. HS, EH, IM and MH drafted the manuscript. JJ performed the statistical analysis. JJ and GR critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of work, thus ensuring integrity and accuracy.

Funding
This study has received funding from the Sakari Alhopuro Foundation.

Availability of data and materials
The data that support the findings of this study are available from Rovaniemi City Health Services, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the corresponding author, Maria Hagnäs upon reasonable request and with permission of Rovaniemi City Health Services.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of the Lapland Central Hospital, Rovaniemi, Finland (Reg. no.05/2018). In addition, the Ethics Committee of the Lapland Hospital District confirmed the ethics approval to the current study as the study is performed in the Lapland District. Informed consent to participate from patients was deemed unnecessary in accordance with Finnish legislation (Personal Data Act 523/1999). All methods were carried out in accordance with relevant guidelines and regulations. The access to the raw data used in the present study was authorized by the administrative senior physician of the city of Rovaniemi, Lapland, Finland. Only pseudoanonymized data were used.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1 Rovaniemi Health Center, Koskikatu 25, 96200 Rovaniemi, Finland.
2 Center for Life Course Health Research, University of Oulu, PO Box 8000, FI-90014 Oulu, Finland.
3 Medical Research Center Oulu, University of Oulu and Oulu University Hospital, PO Box 5000, 90014 Oulu, Finland.
4 Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy.

Received: 19 June 2022. Accepted: 20 October 2022

Published online: 04 November 2022

References
1. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022;183. https://doi.org/10.1016/j.diabres.2021.109119.
2. KDIGO Guideline Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter. Off J Int Soc Nephrol. 2013;3(11):1–150. https://doi.org/10.1038/kisup.2012.73.
3. The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. The Lancet. 2010;375(8):647–57. https://doi.org/10.1016/S0140-6736(10)60484-9.
4. Afkarian M, Sachs MC, Kestenbaum B, et al. Kidney Disease and Increased Mortality Risk in Type 2 Diabetes. J Am Soc Nephrol. 2013;24(2):302–8. https://doi.org/10.1681/ASN.2012070718.
5. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1204–22. https://doi.org/10.1016/S0140-6736(20)30925-9.
6. Metsärinne K, Broijersen A, Kantola I, et al. High prevalence of chronic kidney disease in Finnish patients with type 2 diabetes treated in primary care. Pm Care Diabetes. 2015;9(1):31–8. https://doi.org/10.1016/j.pcd.2014.06.001.
7. Korco CE, Lee BH, Bowlin SJ. Antidiabetic medication use and prevalence of chronic kidney disease among patients with type 2 diabetes mellitus in the United States. Clin Ther. 2009;31(11):2608–17. https://doi.org/10.1016/j.clinthera.2009.10.020.
8. Cid Ruzafa J, Paczkowski R, Boye KS, et al. Estimated glomerular filtration rate progression in UK primary care patients with type 2 diabetes and diabetic kidney disease: a retrospective cohort study. Int J Clin Pract. 2015;69(8):871–82. https://doi.org/10.1111/i MCP.12640.

9. Hagnäs M, Sundqvist H, Jokelainen J, et al. The prevalence of chronic kidney disease and screening of renal function in type 2 diabetic patients in Finnish primary healthcare. Prim Care Diabetes. 2020;14(6):639–44. https://doi.org/10.1016/j.pcd.2020.05.005.

10. Rodríguez-Poncelas A, Garre-Olmo J, Franch-Nadal J, Diez-Espino J, Mundet-Tuduri X. Prevalence of chronic kidney disease in patients with type 2 diabetes in Spain: PERCEDIME2 study. BMC Nephrol. 2013;14(48):8. https://doi.org/10.1186/1471-2369-14-46.

11. Thomas MC, Cooper ME, Zimmet P. Changing epidemiology of type 2 diabetes mellitus and associated chronic kidney disease. Nat Rev Nephrol. 2016;12(2):73–81. https://doi.org/10.1038/nrneph.2015.173.

12. Klimontov VV, Korbut AI. Albuminuric and non-albuminuric patterns of chronic kidney disease in type 2 diabetes. Diabetes Metab Syndr Clin Res Rev. 2019;13(1):474–9. https://doi.org/10.1016/j.dsx.2018.11.014.

13. American Diabetes Association Professional Practice Committee. 11. Chronic Kidney Disease and Risk Management: Standards of Medical Care in Diabetes.—2022. Diabetes Care. 2021;45(Supplement_1):S175–84. https://doi.org/10.2337/dc22-S011.

14. Guideline KDOQI. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. Am J Kidney Dis. 2007;49(2):S12–S154. https://doi.org/10.1053/j.ajkd.2006.12.005.

15. Bakke Å, Cooper JG, Thue G, et al. Type 2 diabetes in general practice in Norway 2005–2014: moderate improvements in risk factor control but still major gaps in complication screening. BMJ Open Diabetes Res Care. 2017;5(1):e000459. https://doi.org/10.1136/bm jdoc-2017-000459.

16. Zoungas S, Arima H, Gerstein HC, Holman RR, Woodward M, Reaven PD. Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials. Lancet Diabetes Endocrinol. 2017;5(6):431–7. https://doi.org/10.1016/S2213-8587(17)30104-3.

17. Hansen LJ, Siensma V, Beck-Nielsen H, de Fine ON. Structured personal care of type 2 diabetes: a 19 year follow-up of the study Diabetes Care in General Practice (DCGP). Diabetologia. 2013;56(8):1243–53. https://doi.org/10.1007/s00125-013-2893-1.

18. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int. 2003;63(1):225–32. https://doi.org/10.1046/j.1523-1755.2003.00712.x.

19. Diabetic kidney disease. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Nephrology Society. Helsinki: The Finnish Medical Society Duodecim, 2020. Accessed 17 May 2022. Available online at: www.kaypahoito.fi

20. Parati G, Stergiou GS, Asmar R, et al. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring. J Hypertens. 2008;26(8):1505–26. https://doi.org/10.1097/HJH.0b013e328308da66.

21. Heikikala E, Mikkola I, Jokelainen J, Timonen M, Hagnäs M. Multimorbidity and achievement of treatment goals among patients with type 2 diabetes: a primary care, real-world study. BMC Health Serv Res. 2021;21(1):964. https://doi.org/10.1186/s12913-021-06989-x.

22. Type 2 diabetes. Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim, the Finnish Internal Medicine Society and the Medical Council of the Finnish Diabetes Association. Helsinki: The Finnish Medical Society Duodecim, 2020. Accessed 17 May 2022. Available online at: www.kaypahoito.fi

23. Mansi-Nankervis JA, Thurasingham S, Lau P, et al. Screening and diagnosis of chronic kidney disease in people with type 2 diabetes attending Australian general practice. Aust J Prim Health. 2018;24(3):280. https://doi.org/10.1071/Py17156.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:
- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

Learn more biomedcentral.com/submissions