

Appendices

Table of contents

Appendix A: CONSORT Flow Diagram	I
Appendix B: Blood and urine samples collected.....	II
Appendix C: Questionnaire	III
Appendix D: Sample size calculation	IV
Appendix E: Full list of baseline demographics, medication and blood sample results.....	V
Appendix F: Logistic regression	VIII
References	IX

Appendix A: CONSORT Flow Diagram

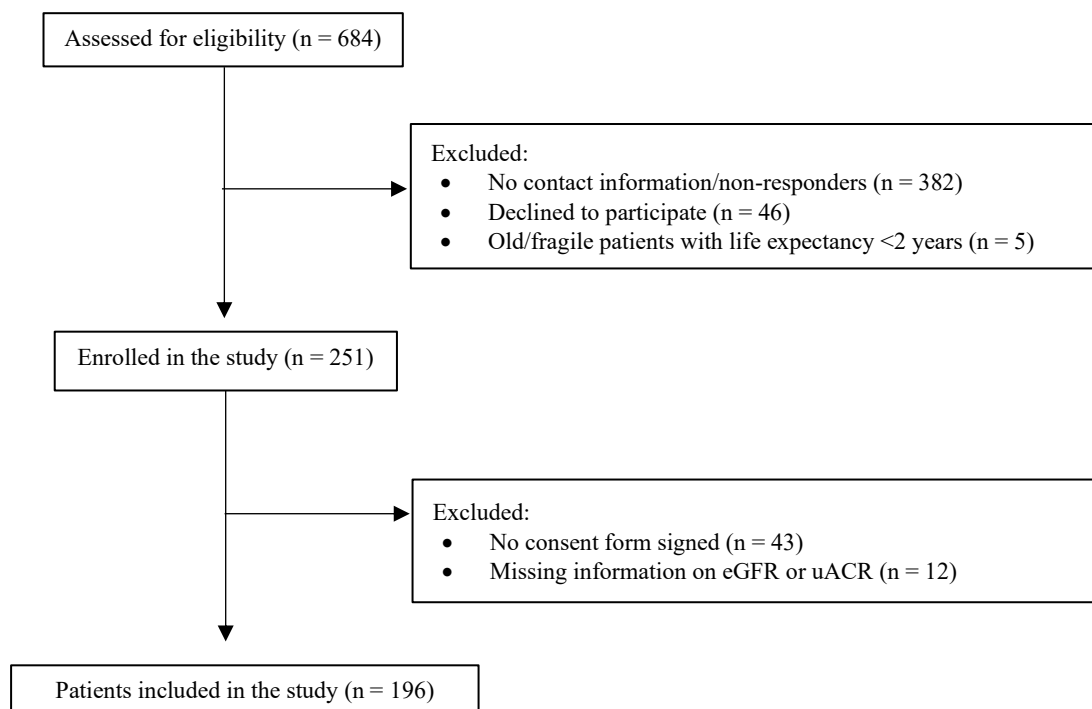


Figure A.1: CONSORT Flow Diagram showing inclusion and exclusion of patients in the study.

A total of 382 patients were excluded due to the absence of Digital Post and/or failure to respond to phone calls during the recruitment process.

eGFR: estimated glomerular filtration ratio; uACR: urine albumin/creatinine ratio.

Appendix B: Blood and urine samples collected

Table B.1: Blood and urine samples obtained from patients.

Electrolyte panel	Creatinine, eGFR, sodium, potassium, albumin
Calcium and phosphate metabolism	Phosphate, calcium, parathyroid hormone, D-vitamin
Anaemia	Haemoglobin, MCV, MCHC, reticulocytes, iron, ferritin, transferrin
Haematology	Leukocytes, thrombocytes
Liver function	ALAT, alkaline phosphate, LDH
Lipid panel	Total cholesterol, LDL, HDL, triglycerides
Endocrinology	HbA1c
Acid-base metabolism	Bicarbonate
Urine	Urine albumin/creatinine ratio

eGFR was analysed with the Chronic Kidney Disease-Epidemiology (CKD-EPI) equation estimated based on creatinine, age, and sex.

eGFR: estimated glomerular filtration ratio; MCV: Mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; ALAT: alanine transaminase; LDH: lactate dehydrogenase; LDL: low-density lipoprotein; HDL: high-density lipoprotein; HbA1c: haemoglobin A1c

Appendix C: Questionnaire

Table C.1: Patients characteristics. Survey of questions asked to patients included in the study.

Demographics:	Risk factors:
<ul style="list-style-type: none"> ▪ Age (years) ▪ Sex 	<ul style="list-style-type: none"> ▪ BMI ▪ Smoking status (active, former, never smoker) ▪ Family history of kidney disease
Former medical history	
<ul style="list-style-type: none"> ▪ Known heart disease <ul style="list-style-type: none"> ○ Heart failure (HFpEF, HFmrEF, HFrEF) ○ Arrhythmia (atrial fibrillation, atrial flutter, AVNRT, AVRT, VT, SSS) ○ Valve disorder (AS, AR, MR, MS, TR, BAV, AVR, MVR) ○ Ischaemic heart disease (ACS, CCS) ▪ Known kidney disease <ul style="list-style-type: none"> ○ CKD ○ AKI ○ Glomerulonephritis ○ Kidney cysts ○ Kidney stones ○ Single-functioning kidney ○ Kidney cancer ▪ Diabetes mellitus (type I/type II) ▪ Hypertension ▪ Hypercholesterolaemia ▪ Autoimmune disease 	
Anthropometrics	Other information
<ul style="list-style-type: none"> ▪ Blood pressure ▪ Ejection fraction ▪ Symptoms of kidney disease (fatigue, nausea, vomiting, oedema, dry/itching skin, metallic taste). 	<ul style="list-style-type: none"> ▪ Regular screening/control of kidney function (once a year, including eGFR and uACR) ▪ New refer or follow-up visit in the Cardiology Clinic
Medical treatment	
<ul style="list-style-type: none"> ▪ Antidiabetics <ul style="list-style-type: none"> ○ SGLT2i ○ GLP-1 ○ DPP4i ○ Insulin ○ Metformin ○ Finerenon ▪ Antihypertensives <ul style="list-style-type: none"> ○ Beta blockers ○ ACEi/ARB ○ CCA ○ MRA ○ Thiazides ○ Loop-diuretics 	<ul style="list-style-type: none"> ▪ Treatment of kidney disease <ul style="list-style-type: none"> ○ Sodium bicarbonate ○ Calcium-carbonate ○ Phosphate binders ○ Calcimimetica ○ Erythropoietin ○ Antiemetics ○ Iron supplements ○ Vitamin D supplements ▪ Antihyperlipidemic drugs

Prevalence and treatment of chronic kidney disease in a cardiology outpatient clinic

APPENDICES

BMI: body mass index; HFpEF: heart failure with preserved ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFrEF: heart failure with reduced ejection fraction; AVNRT: atrioventricular nodal reentry tachycardia; AVRT: atrioventricular reentry tachycardia; VT: ventricular tachycardia; SSS: sick sinus syndrome; AS: aortic stenosis; AR: aortic regurgitation; MR: mitral regurgitation; MS: mitral stenosis; TR: tricuspid regurgitation; BAV: bicuspid aortic valve; AVR: aortic valve repair/replacement; MVR: mitral valve repair/replacement; ACS: acute coronary syndrome; CCS: chronic coronary syndrome; CKD: chronic kidney disease; AKI: acute kidney injury; eGFR: estimated glomerular filtration ratio; uACR: urine albumin/creatinine ratio; SGLT2i: sodium glucose cotransport-2 inhibitor; GLP-1: glucagon-like peptide-1; DPP4i: dipeptidyl peptidase-4 inhibitor; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CCA: calcium channel blocker; MRA: mineralocorticoid receptor antagonist.

Appendix D: Sample size calculation

Sample size calculation for a qualitative variable (proportion) with a 5% type 1 error (Z), expected prevalence of CKD of at least 15% (p), and absolute error/precision of 5% (d) [1]:

Eq. (D.1): Sample size estimation

$$size = \frac{Z^2 \cdot p(1 - p)}{d^2} = \frac{1.96^2 \cdot 0.15(1 - 0.15)}{0.05^2} = 196 \text{ patients}$$

Appendix E: Full list of baseline demographics, medication and blood sample results

Table E.1: Full list of demographic variables, including missing values.

	No CKD	CKD	Missing	Test
	97 (49.5%)	99 (50.5%)		
Age (years)	67.0 [62.0 74.0]	77.0 [70.0 81.0]	0 (0%)	<0.001***
Sex				
<i>Male</i>	62 (63.9%)	61 (61.6%)	0 (0%)	0.739
<i>Female</i>	35 (36.1%)	38 (38.4%)	0 (0%)	
Smoking status				
<i>Never smoker</i>	40 (41.7%)	34 (34.3%)	1 (0.51%)	0.563
<i>Former smoker</i>	44 (45.8%)	52 (52.5%)		
<i>Active smoker</i>	12 (12.5%)	13 (13.1%)		
Family history of kidney disease	6 (9.2%)	10 (15.4%)	66 (33.7%)	0.286
Follow-up visit in the clinic	54 (56.2%)	80 (80.8%)	0 (0%)	<0.001***
Diabetes	13 (13.4%)	29 (29.3%)	0 (0%)	0.007**
Hypertension	50 (51.5%)	68 (68.7%)	0 (0%)	0.014*
Cardiovascular disorder ^a	67 (69.1%)	92 (92.9%)	0 (0%)	<0.001***
Ischemic heart disease				
<i>No ischemia</i>	73 (75.3%)	57 (57.6%)	0 (0%)	0.015*
<i>ACS</i>	7 (7.2%)	19 (19.2%)		
<i>CCS</i>	17 (17.5%)	23 (23.2%)		
Heart failure				
<i>No heart failure</i>	79 (83.2%)	63 (64.9%)	5 (2.0%)	0.018*
<i>HFpEF</i>	1 (1.1%)	3 (3.1%)		
<i>HFmrEF</i>	3 (3.2%)	2 (2.1%)		
<i>HFrEF</i>	12 (12.6%)	29 (29.9%)		
Atrial fibrillation/flutter	30 (30.9%)	51 (51.5%)	0 (0%)	0.003**
Heart valve disease ^b	27 (27.8%)	45 (45.5%)	0 (0%)	0.011*
BMI (kg/m ²)	26.6 [24.2 30.8]	27.2 [24.0 30.7]	20 (10.2%)	0.982
BP systolic (mmHg) ^c	127.5 [117.0 138.0]	132.0 [121.0 144.0]	24 (12.2%)	0.053

^a A diagnosis of heart failure, ischemic heart disease, arrhythmia, or valve disease.

^b A diagnosis of aortic stenosis, aortic regurgitation, mitral stenosis, mitral regurgitation, tricuspid regurgitation, bicuspid aortic valve, aortic or mitral valve replacement/repair.

^c Statins or other lipid-lowering drugs.

CKD: chronic kidney disease; ACS: acute coronary syndrome; CCS: chronic coronary syndrome; HFpEF: heart failure with preserved ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFrEF: heart failure with reduced ejection fraction; BP: blood pressure

Prevalence and treatment of chronic kidney disease in a cardiology outpatient clinic
APPENDICES

Table E.2: Blood and urine sample results collected from patients. Full list of test results, including missing values.

	No CKD 97 (49.5%)	CKD 99 (50.5%)	Missing	Test
Erythrocytes (10 ¹² /L)	4.8 [4.5 5.1]	4.4 [4.0 4.8]	49 (25%)	<0.001***
MCV (fL)	91.0 [88.5 94.0]	93.0 [89.0 96.0]	34 (17.4%)	0.038
Ferritin (µg/L)	140.0 [79.0 260.0]	150.0 [67.0 260.0]	44 (22.5%)	0.650
Haemoglobin (mmol/L)	8.9 [8.3 9.5]	8.5 [7.6 9.1]	0 (0%)	<0.001***
MCHC (mmol/L)	20.8 [20.4 21.3]	20.9 [20.3 21.2]	44 (20.0%)	0.586
Iron (µmol/L)	17.5 [15.0 21.0]	14.0 [10.0 16.0]	54 (27.6%)	<0.001***
Leukocytes (10 ⁹ /L)	6.8 [5.9 8.2]	7.2 [6.2 8.5]	6 (3.1%)	0.300
Reticulocytes (10 ⁹ /L)	71.0 [62.0 91.0]	72.0 [58.0 96.0]	46 (23.5%)	0.886
Transferrin (µmol/L)	31.0 [28.0 34.0]	31.0 [28.0 35.0]	50 (25.5%)	0.766
Thrombocytes (10 ⁹ /L)	251.0 [209.0 288.0]	234.0 [196.0 296.0]	1 (0.5%)	0.460
Albumin (g/L)	44.0 [41.0 46.0]	43.0 [40.0 46.0]	12 (6.1%)	0.369
Calcium (mmol/L)	2.4 [2.3 2.4]	2.4 [2.3 2.4]	28 (14.3%)	0.737
Calcium ion (mmol/L)	1.2 [1.2 1.3]	1.2 [1.2 1.2]	142 (72.5%)	0.502
Phosphate (mmol/L)	1.0 [0.9 1.1]	1.1 [0.9 1.2]	54 (27.6%)	0.028*
Potassium (mmol/L)	4.0 [3.8 4.2]	4.1 [3.8 4.3]	0 (0%)	0.497
Creatinine (µmol/L)	77.0 [66.0 87.0]	103.0 [84.0 132.0]	0 (0%)	<0.001***
eGFR (mL/min/1.73 m ²)	84.0 [76.0 90.0]	52.0 [45.0 59.0]	0 (0%)	<0.001***
Sodium (mmol/L)	141.0 [139.0 142.0]	140.0 [138.0 141.0]	0 (0%)	0.068
Bicarbonate (mmol/L)	23.8 [23.0 24.4]	23.2 [21.7 25.1]	54 (27.6%)	0.083
ALAT (U/L)	24.0 [18.0 31.5]	21.0 [17.0 31.0]	1 (0.5%)	0.474
ALP (U/L)	75.5 [64.0 93.0]	87.5 [71.0 106.0]	6 (3.1%)	0.003**
LDH (U/L)	193.0 [175.0 218.0]	216.0 [184.0 239.0]	14 (7.1%)	0.002**
HbA1c (mmol/mol)	38.0 [36.0 42.0]	41.0 [38.0 46.0]	0 (0%)	<0.001***
Cholesterol (mmol/L)	4.8 [3.9 5.5]	4.2 [3.7 5.1]	1 (0.5%)	0.020*
HDL (mmol/L)	1.4 [1.1 1.7]	1.4 [1.2 1.7]	1 (0.5%)	0.679
LDL (mmol/L)	2.6 [1.8 3.3]	2.0 [1.5 3.0]	1 (0.5%)	0.002**
Triglycerides (mmol/L)	1.3 [1.0 1.7]	1.4 [1.0 2.1]	1 (0.5%)	0.081
25-hydroxy-vitamin D (nmol/L)	58.0 [43.0 80.0]	68.0 [47.0 91.0]	43 (21.9%)	0.208
Parathyroidea hormone (pmol/L)	4.6 [3.7 6.4]	6.2 [4.8 8.7]	59 (30.1%)	<0.001***
uACR (mg/g)	9.0 [5.0 14.0]	31.0 [9.0 83.0]	0 (0%)	<0.001***

Continuous variables in median (IQR), and p-values from the Kruskal-Wallis test. Categorical variables in frequency (percentage %), p-values from Person's chi-squared test.

*p<0.05; **p<0.01; ***p<0.001.

CKD: chronic kidney disease; MCV: Mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; eGFR: estimated glomerular filtration ratio; ALAT: alanine transaminase; ALP: alkaline phosphatase; LDH: lactate dehydrogenase; HbA1c: haemoglobin A1c; HDL: high-density lipoprotein; LDL: low-density lipoprotein; uACR: urine albumin/creatinine ratio.

Prevalence and treatment of chronic kidney disease in a cardiology outpatient clinic
APPENDICES

Table E.3: Full list of medication prescribed to patients included in the study, including missing values.

	No CKD 97 (49.5%)	CKD 99 (50.5%)	Missing	Test
Metformin	11 (11.3%)	12 (12.1%)	0 (0%)	0.865
SGLT2i	10 (10.3%)	34 (34.3%)	0 (0%)	<0.001***
GLP-1	6 (6.2%)	12 (12.1%)	1 (0.5%)	0.157
Insulin	1 (1.0%)	8 (8.1%)	0 (0%)	0.018*
DPP4i	0 (0.0%)	0 (0.0%)	1 (0.5%)	.
Finerenon	0 (0.0%)	2 (2.0%)	0 (0%)	0.159
Beta blockers	38 (39.2%)	54 (54.5%)	0 (0%)	0.031*
ACEi/ARB	46 (47.4%)	73 (73.7%)	0 (0%)	<0.001***
MRA	14 (14.4%)	20 (20.2%)	0 (0%)	0.286
CCA	23 (23.7%)	40 (40.4%)	0 (0%)	0.012*
Thiazide	10 (10.3%)	22 (22.2%)	0 (0%)	0.024*
Loop diuretics	17 (17.5%)	45 (45.5%)	0 (0%)	<0.001***
Statins	48 (49.5%)	71 (71.7%)	0 (0%)	0.001**
Sodium bicarbonate	0 (0.0%)	1 (1.0%)	0 (0%)	0.321
Calcium carbonate	0 (0.0%)	0 (0.0%)	0 (0%)	.
Calcimimetika	0 (0.0%)	0 (0.0%)	0 (0%)	.
Cation exchange	0 (0.0%)	0 (0.0%)	0 (0%)	.
EPO	0 (0.0%)	1 (1.0%)	0 (0%)	0.321
Metoclopramide	28 (41.2%)	25 (36.2%)	0 (0%)	0.552
Iron supplements	0 (0.0%)	1 (1.0%)	59 (30.1%)	0.321
D vitamin supplements	38 (55.9%)	42 (60.0%)	58 (29.6%)	0.624
Phosphate binders	0 (0.0%)	0 (0.0%)	0 (0%)	.

Continuous variables in median (IQR), and p-values from the Kruskal-Wallis test.

Categorical variables in frequency (percentage %), p-values from Person's chi-squared test.

*p<0.05; **p<0.01; ***p<0.001.

SGLT2i: sodium glucose cotransport-2 inhibitor; GLP-1: glucagon-like peptide-1; DPP4i: dipeptidyl peptidase-4 inhibitor; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; MRA: mineralocorticoid receptor antagonist; CCA: calcium channel blocker.

Appendix F: Logistic regression

Table F.1: Logistic regression determining the association between risk factors, demographic variables, and impaired kidney function.

CKD	Odds ratio	P-value	[95% conf. interval]	
Age (years)	1.124195	<0.001***	1.068656	1.18262
Sex (female)	1.624828	0.263	0.6951053	3.798081
Cardiovascular disease	2.384623	0.169	0.6913974	8.224539
Ischemic heart disease	0.8638394	0.749	0.3522614	2.118366
Heart failure				
<i>HFpEF</i>	1.824694	0.629	0.1588245	20.96344
<i>HFmrEF</i>	0.964025	0.972	0.1262145	7.363212
<i>HFrEF</i>	5.00332	0.003**	1.742664	14.36491
BMI (kg/m ²)	1.031961	0.479	0.9457905	1.125983
Smoking (active)	1.399928	0.554	0.4592541	4.26735
Diabetes	2.42551	0.091	0.8674423	6.78212
Hypertension	2.803901	0.013*	1.245542	6.311998
Hypercholesterolemia	2.119484	0.221	0.6361683	7.061357

*p<0.05; **p<0.01; ***p<0.001.

HFpEF: heart failure with preserved ejection fraction; HFmrEF: heart failure with mildly reduced ejection fraction; HFrEF: heart failure with reduced ejection fraction; BMI: body mass index.

A Pearson goodness of fit test found a better fit when excluding concurrent occurring risk factors (i.e. smoking, obesity, hypercholesterolemia, T2DM, and HT present at the same time), however both models found a reasonable fit. A likelihood-ratio test found a p-value >0.05 indicating that the concurrent risk factors do not improve the fit of the model.

Table F.2: Logistic regression determining the association between risk factors, demographic variables, and impaired kidney function with inclusion of concurrently occurring risk factors.

CKD	Odds ratio	P-values	[95% conf. interval]	
Age (years)	1.130233	<0.001***	1.072766	1.190779
Sex (female)	1.915441	0.152	0.7866266	4.66411
Cardiovascular diagnosis	2.337703	0.200	0.6385495	8.55823
Ischemic heart disease	0.9634644	0.937	0.3811716	2.435291
Heart failure				
<i>HFpEF</i>	2.254028	0.533	0.1746777	29.08582
<i>HFmrEF</i>	0.8849727	0.918	0.0852496	9.186871
<i>HFrEF</i>	5.545554	0.003**	1.797617	17.10775
BMI (kg/m ²)	1.024495	0.650	0.9229417	1.137222
Smoking (active)	0.829826	0.798	0.199414	3.453173
Diabetes	1.215246	0.766	0.337289	4.37851
Hypertension	2.642746	0.070	0.922604	7.569994
Hypercholesterolemia	2.317264	0.212	0.6189354	8.67572
One risk factor ^a	0.4145364	0.472	0.0376654	4.562285
Two risk factors ^a	0.1608224	0.053	0.0253171	1.021596
Three risk factors ^a	0.3295563	0.127	0.0792105	1.371123

^a One, two, or three of the following: active smoking, diabetes, hypertension, hypercholesterolemia, or BMI >25 kg/m².

HFpEF: Heart Failure with preserved Ejection Fraction; HFmrEF: Heart Failure with mildly reduced Ejection Fraction; HFrEF: Heart Failure with reduced Ejection Fraction; BMI: body mass index.

References

1. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian J Psychol Med* 2013;35:121–6.