Prevalence of Chronic Kidney Disease among Patients Attending a Specialist Diabetes Clinic in Jamaica

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Short title: Chronic Kidney Disease at University Hospital of the West Indies, Jamaica

Synopsis: This study estimated the prevalence of chronic kidney disease (CKD) among patients of the University Hospital of the West Indies diabetes clinic in Jamaica and evaluated the proportion of patients at high risk for adverse outcomes. Approximately 86% of patients had CKD and 70% were at high risk for adverse outcomes.

ABSTRACT

Objective: To estimate the prevalence of chronic kidney disease (CKD) among patients attending the University Hospital of the West Indies (UHWI) Diabetes Clinic and to determine the proportion of patients at high risk for adverse outcomes.

Methods: We conducted a cross-sectional study among patients attending the UHWI Diabetes Clinic between 2009 and 2010. Trained nurses administered a questionnaire, reviewed dockets, and performed urinalyses. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Albuminuria was assessed using urine test strips for protein and microalbumin. Chronic kidney disease was defined as an eGFR < 60 ml/min/1.73m^2 or albuminuria ≥ 30 mg/g creatinine. Risk of adverse outcome (all-cause mortality, cardiovascular disease and kidney failure) was determined using the Kidney Disease: Improving Global Outcome (KDIGO) 2012 prognosis grid.

Results: Participants included 100 women and 32 men (mean age, 55.4 ± 12.9 years, mean duration of diabetes, 16.7 ± 11.7 years). Twenty-two per cent of participants had eGFR < 60 ml/min/1.73 m^2. Moderate albuminuria (30–300mg/g) was present in 20.5% of participants and severe albuminuria (> 300 mg/g) in 62.1%. Overall prevalence of CKD was 86.3% (95%CI 80.4%, 92.2%). Based on KDIGO risk categories, 50.8% were at high risk and 17.4% at very high risk of adverse outcomes.

Conclusion: Most patients at the UHWI Diabetes Clinic had CKD and were at high or very high risk of adverse outcomes. Further studies to determine the burden of CKD in other clinical settings and to identify the best strategies for preventing adverse outcomes in developing countries need to be conducted.

Keywords: Albuminuria, chronic kidney disease, diabetes mellitus, diabetic nephropathy, glomerular filtration rate, Jamaica

INTRODUCTION

Chronic kidney disease (CKD) includes a spectrum of pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate [GFR] (1–3). The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines defines CKD as abnormalities of kidney structure or function present for greater than three months with implications for health (4). Abnormal kidney function is defined as estimated GFR < 60 ml/min/1.73 m^2, while markers of kidney damage include any of the following: albuminuria, abnormal urinary sediments, renal tubular disorders, histological abnormality on renal biopsy, or structural abnormalities on renal imaging (4). The KDIGO Guidelines also recommends staging of CKD based on the underlying cause, estimated GFR and level of albuminuria (4).

Chronic kidney disease is now recognized as a global public health problem and is associated with a range of adverse outcomes including increased all-cause mortality, cardiovascular disease, progression to end-stage renal disease (ESRD), acute kidney injury, anaemia and cognitive decline (2, 3). Worldwide prevalence is estimated to be between 8% and 16%, with a prevalence of 11.5% in the United States of America [USA] (2, 3). In Jamaica, the prevalence of chronic renal failure (defined as serum creatinine > 150 μmol/L) was estimated at 327 per million in 1999 (5). The Caribbean Renal Registry was established in 2006 with a goal of documenting the epidemiology of renal disease in the Caribbean (6). In 2007, the registry included 968 patients with CKD in Jamaica, of which 576 were on renal replacement therapy (7).

Hypertension is the most common cause of CKD or ESRD in Jamaica, while diabetes mellitus is the second most common cause (6).

Chronic kidney disease prevalence among persons with diabetes mellitus in the USA is estimated at 20–40% (8). In Jamaica, a previous study at the University Hospital of the West Indies (UHWI) Diabetes Clinic found that 10% of patients had chronic renal failure defined as creatinine > 150 μmol/L and 14% had proteinuria of 2+ or greater on dipstick (9). The overall prevalence of CKD among patients with diabetes mellitus in Jamaica is unknown. This study therefore aims to estimate the prevalence of CKD among patients attending the UHWI Diabetes Clinic, and to determine the proportion of patients at high risk for adverse outcomes.

SUBJECTS AND METHODS

A cross-sectional study was conducted on patients attending the UHWI Diabetes Clinic, a specialist clinic staffed by endocrinologists, diabetes specialists and residents in the internal medicine training programme at UHWI. Measurements were performed between August 2009 and September 2010. The original study included 188 clinic participants and was designed primarily to estimate the prevalence of diabetic foot complications, but included data to assess other diabetes complications and co-morbidities. Details of the study design, recruitment and measurements have been previously published (10, 11). The study was approved by the University Hospital of the West Indies/University of the West Indies/Faculty of Medical Sciences Ethics Committee. Written informed consent was obtained from each participant prior to enrolment.

Measurements

Trained research nurses administered a structured questionnaire and performed blood pressure and anthropometric measurements. They also performed urinalyses and reviewed medical records in order to obtain the last creatinine measurement of the participants. Blood pressure (BP) was measured using a mercury sphygmomanometer and included three measurements which were taken at one-minute intervals from the right arm after the participant had been seated for five minutes. The mean of the second and third systolic and diastolic BP measurements were used in the analysis.

Body weight was measured using a portable digital scale, while height was measured using a portable stadiometer. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres and participants categorized as normal (BMI < 25 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2) or obese (BMI ≥ 30 kg/m^2).

Glycosylated haemoglobin ($HbA1_c$) was measured from a capillary blood sample using a point of care instrument (NycoCard® Reader II, AXIS-SHIELD, Rodelokka, Oslo, Norway). Participants were classified as having good control ($HbA1_c$ <7.0), inadequate control ($HbA1_c$ 7.0–8.9) or poor control ($HbA1_c \geq 9.0$).

Urine protein excretion was measured on a freshly voided urine specimen using standard urine test strips. A colorimetric principle was used to obtain a semi-quantitative estimate of urine protein excretion coded as negative or positive. Urine samples that were negative for protein were tested for microalbumin using a semi-quantitative test strip (Teco Diagnostics, Anaheim, CA, USA). Participants were then classified as 'No albuminuria' if negative on both urine dipstick and microalbumin tests. Those with positive test for microalbumin only were classified as moderate albuminuria, indicating a urine albumin to creatinine ratio of 30–300 mg/g

creatinine, while those with positive test on conventional urine test strips were classified as severe albuminuria indicating albumin to creatinine ratio of > 300 mg/g creatinine.

Estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation (12). The SI unit equations (creatinine in μmol/L) were obtained from formulae published on the National Kidney Disease Education Programme website as shown in the box. Chronic kidney disease was defined as having eGFR < 60 ml/min/1.73 m^2 or albuminuria ≥ 30 mg/g creatinine (*ie* positive test for protein or microalbumin). We then used the combination of eGFR and albumin excretion levels to classify persons in risk categories (low, moderate, high or very high) based on the KDIGO 2012 prognostic grids (13).

Statistical analyses

All analyses were performed using Stata 12.1 (Stata Corp, College Station, Texas). We obtained means and proportions for participant characteristics and CKD–related variables. We then obtained prevalence estimates for the reduced GFR, albuminuria and overall CKD. Differences in proportions for categorical variables were compared using χ^2 tests or Fisher's exact test as appropriate, while the *t*-test was used for difference in means. Analyses were limited to 132 of the 188 participants enrolled because some participants had missing data on serum creatinine or urine albumin excretion. For the variable for duration of diabetes, missing values were imputed based on the participant's age and gender.

Multivariable binary logistic regression was used to identify factors associated with CKD and reduced GFR in separate models. The initial models included variables which were associated with CKD or reduced GFR in bivariate analyses or were believed to be associated

based on previous studies. The final models were derived by assessing the impact of individual variables using the likelihood ratio test.

RESULTS

Characteristics of participants included in the analyses (100 women and 32 men) are shown in Table 1. The mean age was 55.4 years and mean duration of diabetes was 17.0 years with no significant differences for men compared to women. Women had higher mean BMI and higher mean $HbA1_c$ and were more likely to be obese but otherwise had similar characteristics when compared to men. Except for a higher mean BMI (30.1 kg/m^2 *vs* 28.0 kg/m^2), there were no significant differences in the characteristics of persons included in the analyses compared to those excluded.

Prevalence estimates for CKD, reduced GFR and albuminuria are shown in Table 2. Overall 86.3% (96% CI 80.4, 92.2%) had CKD. Twenty-two per cent had reduced GFR, 20.5% had moderate albuminuria and 62.1% had severe albuminuria. There were no significant gender differences in the prevalence of CKD, reduced GFR or albuminuria. Figure 1 shows the proportion of participants in each category of GFR and albuminuria using the KDIGO risk grid. When categorized by GFR, the majority of participants were in the lower risk categories, with 49% in G1 category (GFR $\geq$ 90) and only 3% in the G5 (GFR < 15) category. The reverse was true for albuminuria with 17% in the A1 category (urinary albumin < 30 mg/g) compared to 62% in the A3 category (urinary albumin > 300 mg/g creatinine). Using the combined GFR and

albuminuria categories, approximately 51% of participants were classified as being at high risk of adverse outcomes and 17% at very high risk (Fig. 2).

In order to identify factors associated with CKD, reduced GFR and albuminuria, we compared the characteristics of participants with and without the respective conditions (Table 3). Increased duration of diabetes was associated with CKD. Those with low GFR were older, had a longer duration of diabetes, lower diastolic BP, and were less likely to be at their blood pressure goal but had better glucose control. There were no significant differences in the characteristics of participants with and without albuminuria in the bivariate analyses.

Results for multivariable analyses are shown in Table 4. Separate logistic regression models were created for CKD and reduced GFR. Only duration of diabetes remained statistically significant among the factors associated with CKD with a 37% increase in the odds for every five years of diabetes. Participants with reduced GFR were more likely to be older (odds ratio (OR) 1.56 for each five-year increment, $p < 0.001$) and more likely to have good glycaemic control (OR 2.76, $p = 0.024$).

DISCUSSION

In this study, we have found that almost 90% of study participants had evidence of CKD with approximately 80% having albuminuria and 22% having GFR < 60 ml/min/1.73 m^2. Although the larger proportion of CKD was due to the presence of albuminuria, the majority of patients were classified at high or very high risk of adverse outcomes based on the KDIGO 2012 prognostic grid. Duration of diabetes was the major factor associated with CKD in multivariable models, but reduced GFR was associated with older age.

The prevalence of CKD reported in this study is higher than that seen in most other reports, but the characteristics of patients in those studies tend to be different from that of our patients and some studies used different definitions for CKD. For example, a study among diabetic patients in primary care practices in Spain reported a CKD prevalence of 27.9%, but while these patients were older than those in this study, the mean duration of diabetes was only nine years compared to 17 years in this study (14). One study among urban community-based participants in China reported a CKD prevalence of 29.6% (15), but another study among participants over 30 years old from 'downtown Shanghai' reported a CKD prevalence of 63.9% (16). Additionally, one study from the United Kingdom (UK) reported a prevalence of clinically significant CKD (stage 3–5 based on eGFR) of 31.3%, while another study among Canadian First Nation adults reported a prevalence of reduced GFR of 15.5% and found that 58.5% of participants with GFR > 60 ml/min/1.73m^2 had albuminuria (17, 18). Data from the United Kingdom Prospective Diabetes Study (UKPDS) suggest that after 15 years, approximately 28% of patients have microalbuminuria or worse nephropathy and project that this would increase to 38% by 25 years (19). Based on these studies, while the overall prevalence of CKD in this study is very high, it is probably not surprising given that the patients are from a tertiary care clinic and that the majority of participants have had long duration of diabetes. It should also be noted that the larger proportion of participants with CKD was due to albuminuria, and the prevalence of reduced GFR was less than that reported in the study among patients in UK general practices (18). The association between duration of diabetes and CKD has been reported in other studies (16, 17, 20) and is generally consistent with the pathophysiology of diabetes complications. The lack of an association with age was probably due to the small size of the study and the high overall prevalence of proteinuria. As expected, reduced GFR was associated with older age.

While the findings from this study may not be generalizable to all patients with diabetes in Jamaica, it has potentially far reaching implications. Given the limited access to renal replacement therapy in the Jamaican context, such a high prevalence of CKD is worrisome, as it is unlikely that all patients who go on to develop ESRD will be able to access renal replacement therapy. Additionally, the high risk of cardiovascular disease complications will place an added burden on the cardiovascular care services. It should be noted also that the study participants are still relatively young and therefore the expected complications are likely to have a great impact on their families in terms of loss of income and productivity and increased dependency ratios. Given these potentially grave implications, renal and endocrinology services will need to ensure the full implementation of preventive strategies in order to reduce the expected negative outcomes. With the projected increases in the prevalence of diabetes (21, 22) globally and in the Caribbean, the challenge of CKD in patients with diabetes is likely to become an evenly larger problem in the next decades.

Limitations of this study include the fact that only a single creatinine value and single urinary albumin test was used to assess CKD and that the study was conducted in a tertiary care clinic. Missing data from some of the original study participants resulted in a smaller sample and thus less power to test associations. The findings of the study, however, represent important additions to the literature on CKD in Jamaica and the Caribbean and can begin to inform practice and policy.

CONCLUSION

Most of the patients at the UHWI Diabetes Clinic have some level of chronic kidney disease with a majority of these patients being at a high or very high risk for adverse outcomes. This suggests that CKD is a major concern for persons with diabetes in Jamaica. It is important, however, that further studies evaluate the burden of CKD among a broader cross-section of persons with diabetes and in the general population and seek to identify the best strategies for preventing adverse outcomes in Jamaica and other developing countries.

ACKNOWLEDGEMENTS

This study was supported by a grant from the Caribbean Health Research Council. The authors thank the study participants, project staff, including nurses (C Bennett, B Walker and R Walters), administrative staff (N Campbell), and driver (J Campbell) for their contribution to the project. The authors also thank UWI Medical Alumnus Dr Earl O'Brien and the National Health Fund (Jamaica) for assistance with equipment for the project.

Author Contributions

TS Ferguson conceived paper, oversaw data collection, conducted data analysis, wrote manuscript and approved final version. MK Tulloch-Reid participated in study design, data analysis and interpretation, critically revised manuscript and approved final version. NO Younger participated in study design, data analysis, and interpretation of data and revision of manuscript and approved final version. RA Wright-Pascoe participated in study design, interpretation of data and revision of manuscript and approved final version. MS Boyne

participated in study design and interpretation of data; critically revised manuscript and approved final version. AK Soyibo participated in study design and interpretation of data, critically revised manuscript and approved final version. RJ Wilks provided oversight to study, participated in data interpretation and revision of manuscript, and approved final version. The authors declare that they have no conflicts of interest.

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Box: Equations for calculation of estimated glomerular filtration rate using serum creatinine in SI units (µmol/L) based on the Chronic Kidney Disease Epidemiology Collaboration Equation

Black female with serum creatinine ≤ 61.9 µmol/L

- $GFR = 166 \times (Scr/61.9)^{-0.329} \times (0.993)^{Age}$

Black female with serum creatinine > 61.9 µmol/L

- $GFR = 166 \times (Scr/61.9)^{-1.209} \times (0.993)^{Age}$

Black male with serum creatinine ≤ 79.6 µmol/L

- $GFR = 163 \times (Scr/79.6)^{-0.411} \times (0.993)^{Age}$

Black male with serum creatinine >79.6 µmol/L

- $GFR = 163 \times (Scr/79.6)^{-1.209} \times (0.993)^{Age}$

Scr = serum creatinine

Source: National Kidney Disease Education Program Website: http://nkdep.nih.gov/lab-evaluation/gfr/estimating.shtml [Cited 2013 Apr 24]

Table 1: Characteristics of participants in the study

Characteristic	Men n = 32	Women n = 100	All participants n = 132
	Mean ± standard deviation		
Age (years)	57.1 ± 12.2	54.9 ± 13.1	55.4 ± 12.9
Duration of diabetes mellitus (years)	19.2 ± 13.6	16.2 ± 10.1	17.0 ± 11.1
Body mass index (kg/m^2)**	27.3 ± 4.9	31.0 ± 6.4	30.1 ± 6.2
Systolic blood pressure (mmHg)	131.3 ± 20.4	129.4 ± 22.5	129.9 ± 21.9
Diastolic blood pressure (mmHg)	71.3 ± 13.7	70.9 ± 12.1	71.3 ± 12.4
Creatinine[1] (µmol/L)	113.2 ± 67.8	105.5 ± 99.8	107.3 ± 92.9
Estimated glomerular filtration rate (ml/min/1.73m^2)	87.2 ± 32.1	84.1 ± 34.2	84.8 ± 33.6
Haemoglobin A1$_c$* (%)	7.1 ± 1.6	8.0 ± 2.1	7.8 ± 2.0
Fasting glucose[2] (µmol/L)	9.1 ± 6.0	8.5 ± 4.9	8.6 ± 5.2
	Proportion (%) ± standard error		
Hypertension (blood pressure ≥ 130/80 mmHg)	75.0 ± 7.8	72.0 ± 4.5	72.7 ± 3.9
Obese (BMI ≥ 30kg/m^2)**	22.6 ± 7.9	50.0 ± 5.0	43.5 ± 4.3
Good control (HbA1c <7%)	50.0 ± 9.0	40.0 ±4.9	42.4 ± 4.3

*$p < 0.05$; **$p < 0.01$

[1]Last creatinine recorded in the docket. Median values for creatinine were 92 for men, 75.5 for women and 81 for the combined group, with $p = 0.005$ for difference in medians. Median time between last creatinine and date of interview was 1.2 years. [2]Last fasting glucose recorded in docket. Estimates from 128 participants

Table 2: Prevalence of chronic kidney disease, reduced glomerular filtration rate (GFR), moderate and severe albuminuria by gender and for all participants

Characteristic	Men n = 32 %(95%CI)	Women n = 100	All Participants n = 132
Chronic kidney disease	**78.1** (63.4, 92.8)	**89.0** (82.8, 95.2)	**86.3** (80.4, 92.2)
Reduced GFR (< 60 ml/min/1.73 m^2)	**18.8** (4.9, 32.6)	**23.0** (14.6, 31.4)	**22.0** (14.8, 29.1)
Moderate albuminuria (30–300 mg/g creatinine)	**12.5** (0.7, 24.2)	**23.0** (14.6, 31.4)	**20.5** (13.5, 27.4)
Severe albuminuria (> 300 mg/g creatinine)	**59.4** (41.9, 76.8)	**63.0** (53.4, 72.6)	**62.1** (53.7, 70.5)

Note: There were no statistically significant gender differences

Table 3: Comparison of characteristics by chronic kidney disease (CKD), glomerular filtration rate (GFR) and albuminuria categories

Characteristic	CKD n = 114	No CKD n = 18	GFR < 60 n = 29	GFR ≥ 60 n = 103	No Albuminuria n = 23	Albuminuria n = 109
Age (years)	55.8	53.7	63.9***	53.0	54.6	55.6
Duration of diabetes (years)	17.7*	11.9	23.8***	15.0	16.0	17.1
Body mass index (kg/m^2)	30.2	29.8	31.7	29.7	29.8	30.1
Systolic blood pressure	130.5	129.8	136.4	128.0	126.1	130.6
Diastolic blood pressure	71.2	71.4	66.7*	72.6	71.4	71.2
Creatinine (median)[1]	82.5*	71.5	150***	73.0	81	81
Estimated GFR	81.6**	105.5	35.7***	98.7	90.5	83.6
HbA_{1c}	7.9	7.3	7.3	7.9	7.0	7.9
Fasting glucose (mμol/L)[2]	8.5	9.2	9.6	8.3	8.1	8.7
Blood pressure at goal (<130/80)	50.0	55.6	34.5*	55.3	52.2	50.5
Obese (≥ 30kg/m^2)	43.9	41.2	55.2	40.2	45.5	43.1
Good control (HbA_{1c} < 7%)	41.1	50.0	65.5*	35.9	56.5	39.5

* $p < 0.05$; ** $p < 0.01$ *** $p < 0.001$

[1] Last creatinine recorded in docket

[2] Last fasting glucose recorded in docket. Estimates from 128 participants

Table 4: Factors associated with chronic kidney disease (CKD) and reduced glomerular filtration rate (GFR) in multivariable models

Characteristic	**CKD**		**Reduced GFR**	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Gender (male *vs* female)	**0.29** (0.13, 1.16)	0.089	**0.53** (0.18, 1.59)	0.260
Age (5-year increments)	**1.02** (0.82, 1.28)	0.836	**1.56** (1.22, 1.99)	< 0.001
Duration of DM (5-years increments)	**1.37** (1.00, 1.87)	0.049	**1.21 (0.98, 1.50)**	0.072
Good control (HbA1c < 7% *vs* ≥ 7%)	**0.67** (0.23, 1.97)	0.468	**2.76** (1.14, 6.67)	0.024
Overweight (BMI 25-29.9 *vs* <25)	**-**	**-**	**1.31** (0.32, 5.31)	0.714
Obese (BMI ≥ 30 *vs* < 25)	**-**	**-**	**2.54** (0.64, 10.02)	0.184

DM = diabetes mellitus; $HbA1_c$ = haemoglobin A1c; BMI = body mass index. Separate models were created for CKD and reduced GFR (GFR < 60 ml/min/1.73 m^2). Model for CKD included age, gender, duration of diabetes and $HbA1_c$. Model for reduced GFR included age, gender, duration of diabetes, $HbA1_c$ and BMI categories, with normal weight as reference BMI category.

		Albuminuria Categories			Total GFR Category
		A1 <30 mg/g	A2 30-300 mg/g	A3 (>300 mg/g)	
GFR Category ml/min/1.73 m^2	G1 (≥ 90)	9.9	10.6	28.8	49.2
	G2 (60-89)	3.8	6.8	18.2	28.8
	G3a (45-59)	0.8	1.5	6.8	9.1
	G3b (30-44)	2.3	0.8	1.5	4.6
	G4 (15-29)	0.8	0.0	4.6	5.3
	G5 (<15)	0.0	0.8	2.3	3.0
Total Albuminuria Category		17.4	20.4	62.1	100

Fig. 1: Prevalence of chronic kidney disease in specific glomerular filtration rate (GFR) and albuminuria risk categories with colour-coded risk categories

Colours indicate risk categories for adverse outcomes (death, cardiovascular disease or need for renal replacement therapy): green = low risk; yellow = moderately increased risk; orange = high risk; red = very high risk

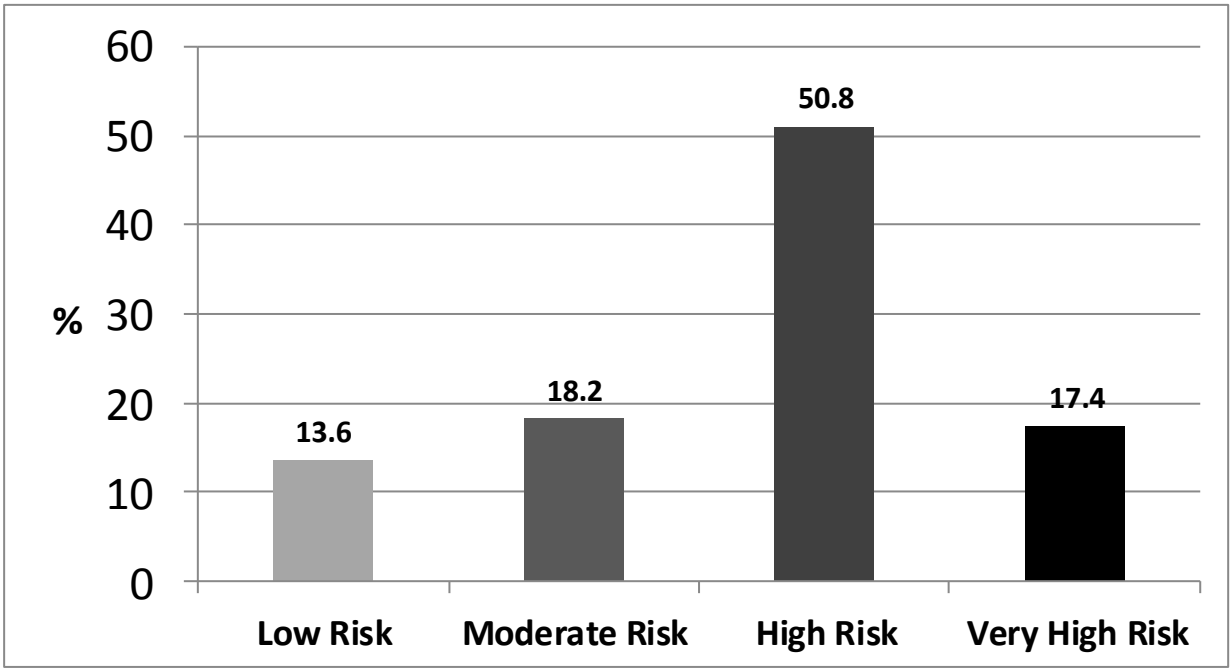

Fig. 2: Proportion of participants in the Kidney Disease: Improving Global Outcomes (KDIGO) prognostic risk groups.