

**Original Paper**

# Determinants of Mortality in Patients with Chronic Kidney Disease Undergoing Percutaneous Coronary Intervention

Alexandros Papachristidis<sup>a</sup> Wei Yao Lim<sup>b</sup> Christos Voukalis<sup>a</sup>  
Salma Ayis<sup>c</sup> Christopher Laing<sup>b</sup> Roby D. Rakhit<sup>a</sup>

<sup>a</sup>Department of Cardiology and <sup>b</sup>Renal Department, Royal Free Hospital, and <sup>c</sup>Department of Primary Care and Public Health Sciences, King's College London, London, UK

**Key Words**

Cardiovascular disease · Chronic renal failure · Glomerular filtration rate · Kidney disease · Mortality · Percutaneous coronary intervention · Renal impairment

**Abstract**

**Background:** Renal impairment is a known predictor of mortality in both the general population and in patients with cardiac disease. The aim of this study was to evaluate factors that determine mortality in patients with chronic kidney disease (CKD) who have undergone percutaneous coronary intervention (PCI). **Methods:** In this study we included 293 consecutive patients with CKD who underwent PCI between 1st January 2007 and 30th September 2012. The primary outcome that we studied was all-cause mortality in a follow-up period of 12–69 months (mean 38.8 ± 21.7). **Results:** Age ( $p < 0.001$ ), PCI indication ( $p = 0.035$ ), CKD stage ( $p < 0.001$ ) and left ventricular ejection fraction ( $p < 0.001$ ) were significantly related to mortality. CKD stage 5 [hazard ratio (HR) = 6.39, 95% CI: 1.51–27.12] and severely impaired left ventricular function (HR = 4.04, 95% CI: 2.15–7.59) were the strongest predictors of mortality. Other factors tested (gender, hypertension, diabetes, hyperlipidaemia, established peripheral vascular disease/stroke, coronary arteries intervened, number of vessels treated, number of stents implanted and length of lesion treated) did not show any correlation with mortality. **Conclusions:** The mortality of patients with CKD undergoing PCI increases with age, worsening CKD stage and deteriorating left ventricular systolic function, and it is also higher in patients with acute coronary syndromes compared to those with stable coronary artery disease.

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## Introduction

Cardiovascular disease is a leading cause of death in patients with severe chronic kidney disease (CKD). Compared to the general population, cardiovascular mortality is much higher among patients with CKD [1]. Previous studies have demonstrated that moderate CKD and end-stage renal disease in patients undergoing percutaneous coronary intervention (PCI) are associated with higher rates of in-hospital mortality as well as with other complications such as non-fatal stroke, non-fatal myocardial infarction and prolonged hospitalization [2]. In the emergency setting, data from the HORIZON-AMI trial showed that patients with end-stage renal disease presenting with an acute ST-segment elevation myocardial infarction (STEMI) had an increased mortality and morbidity [3]. Also, in the setting of non-ST-segment elevation acute coronary syndrome, CKD is associated with adverse prognosis [4–6].

Therefore, we aimed to investigate the outcome of a contemporary cohort of patients with documented CKD in the real-world setting who receive treatment according to current guidance and clinical practice, and we sought to identify any factors that could contribute to this poor outcome.

## Methods

Data were collected from a registry of all patients who underwent PCI between 1st January 2007 and 30th September 2012 at the Royal Free Hospital, London, UK. A total of 293 patients with CKD were identified. In 9 patients PCI failed due to the inability to cross the culprit lesion with a guide wire; therefore these patients were excluded from the analysis. A general informed consent was obtained from all patients for use of anonymized data for research purposes.

The Kidney Disease Outcome Quality Initiative (KDOQI) classification was used to determine the severity of CKD. This classification uses the estimated glomerular filtration rate (eGFR) derived from the Modification of Diet in Renal Disease (MDRD) equation:  $GFR = 186 \times (\text{baseline creatinine})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$  [7]. We subdivided the patients with a moderate decrease in eGFR (30–59 ml/min/1.73 m<sup>2</sup>) into 2 categories, and we formed the following groups:

- 1 CKD stage 2: eGFR 60–89 ml/min/1.73 m<sup>2</sup> and evidence of kidney damage
- 2 CKD stage 3A: eGFR 45–59 ml/min/1.73 m<sup>2</sup>
- 3 CKD stage 3B: eGFR 30–44 ml/min/1.73 m<sup>2</sup>
- 4 CKD stage 4: eGFR 15–29 ml/min/1.73 m<sup>2</sup>
- 5 CKD stage 5: eGFR <15 ml/min/1.73 m<sup>2</sup> (end-stage renal disease, dialysis dependent)
- 6 Separate group including patients with renal transplantation

The patients were allocated to one of the above groups based on the pre-procedural value of creatinine. Patients with peri-procedural acute kidney injury as defined by an absolute increase in the serum creatinine concentration of  $\geq 0.3$  mg/dl (26.4  $\mu$ mol/l) from baseline or a percentage increase in the serum creatinine concentration of  $\geq 50\%$  were excluded from our series. Acute kidney injury is a well-known factor for poor outcome, but the number of patients (14 patients) in our cohort was too small to allow for comparisons.

All demographic data (age and sex), cardiovascular risk factors (hypertension, diabetes, hypercholesterolaemia, established peripheral vascular disease and previous stroke) and angiographic/procedural details were entered prospectively during the procedure into our hospital PCI database (Infoflex database). The left ventricular (LV) ejection fraction (EF) was obtained retrospectively. Myocardial infarction was defined according to the universal definition of myocardial infarction [8] by the presence of 2 of the following 3 criteria: chest pain, electrocardiographic changes and increased cardiac enzyme levels (at least twice the upper reference limit). For patients having more than 1 intervention, only the first one was included in the analysis. The primary outcome that was studied was all-cause mortality in a follow-up period of 12–69 months (mean  $38.8 \pm 21.7$ ). Mortality data were obtained from the Office of National Statistics.

All data were analysed with IBM SPSS version 20.0.0 (IBM Corporation Software Group, Somers, N.Y., USA) and STATA version 12.0 (Stata Corp, College Station, Tex., USA). Continuous data were analysed using analysis of variance or the Kruskal-Wallis test as appropriate and presented as mean values  $\pm$  SD. Categorical

data were analysed using the  $\chi^2$  and Fisher's exact test. All tests of significance were two tailed. A p value  $\leq 0.05$  was the criterion used to determine significance.

Each of the above 14 variables – age, sex, hypertension, diabetes, hyperlipidaemia, established peripheral vascular disease/stroke, LVEF, CKD stage, indication for PCI (elective or urgent), coronary arteries intervened, number of vessels treated, number of stents implanted, type of intervention [percutaneous transluminal coronary angioplasty (PTCA), bare-metal stent (BMS), 1st-generation drug-eluting stent (DES) and 2nd-generation DES] and length of lesion treated – was examined for its association with mortality using a univariable Cox regression analysis. Variables that were associated with mortality ( $p \leq 0.2$ ) in the univariable analysis were included in the multivariable Cox regression model. The proportionality-of-hazards assumption was assessed using the Schoenfeld test, and the assumption was met for all variables included.

## Results

In table 1 we present the baseline characteristics of 284 patients who underwent PCI, grouped by eGFR. We also include the group of renal transplant patients. In all, 236 patients were male (83.1%) and 48 female (16.9%). Overall, 84.5% of the patients were hypertensive, 47.5% had diabetes, 77.8% had hypercholesterolaemia and 14.8% had established peripheral vascular disease or previous stroke. Most of them (56.3%) had urgent PCI for acute coronary syndrome (including STEMI and non-STEMI) and the remaining 43.7% had elective PCI for stable coronary artery disease. The left anterior descending artery was involved in 51% of the patients, followed by the right coronary artery in 29% and the left circumflex in 25% of the patients. In the majority of patients, a single vessel was targeted (83.5%). Most of the patients (46.1%) had 1 stent implanted, 2 stents were used in 32.4% of the patients, while 6.3% had PTCA only. The remaining 15.2% of the patients required more than 2 stents. DES were used in 66.9% of the patients (21.8% of the patients had 1st-generation DES and 45.1% had 2nd-generation DES). The mean length of treated segments was  $20.5 \pm 8.8$  mm.

Comparing baseline characteristics between patients of different CKD stages, there was no significant difference apart from age, diabetes and EF. Transplant patients were significantly younger (mean age  $57.05 \pm 11.67$  years,  $p < 0.001$ ) than patients with CKD stage 2 ( $73.56 \pm 10.58$  years), stage 3A ( $72.74 \pm 10.16$  years), stage 3B ( $75.12 \pm 10.19$  years), stage 4 ( $75.53 \pm 9.59$  years) and stage 5 ( $66.75 \pm 12.10$  years). Diabetes was less prevalent in transplant patients (15.8%,  $p = 0.018$ ) compared to patients with CKD stages 2, 3A, 3B, 4 and 5 (62.5, 40.3, 50.0, 43.3 and 57.3%, respectively). A significant difference was noted in EF between groups ( $p = 0.003$ ). Transplant patients overall had better LV function. Moderate and severe LV impairment was observed only in 5.6% of those patients compared to patients in the other groups (50% in CKD stage 2, 33.4% in CKD stage 3A, 46.6% in CKD stage 3B, 48.1% in CKD stage 4 and 37.2% in CKD stage 5). Other known cardiovascular risk factors (hypertension, hypercholesterolaemia, known peripheral vascular disease and previous stroke) did not show significant differences between patient groups.

Patients in CKD 3A stage and transplant patients more commonly had PCI for stable coronary artery disease (58.1 and 52.6%, respectively). On the other hand, patients in CKD stages 2, 3B, 4 and 5 had PCI predominantly for acute coronary syndrome. However, those differences were not statistically significant. The number of vessels treated, number of stents used, type of stent implanted (i.e. BMS or DES) and length of treated segment were similar between patients with different CKD stages and transplant patients.

In the follow-up period of 12–69 months (mean  $38.8 \pm 21.7$ ), 93 patients died. Using a univariate analysis, 14 variables were explored in relation to mortality. Age ( $p = 0.001$ ), EF ( $p < 0.001$ ), CKD stage ( $p = 0.001$ ) and indication for PCI ( $p = 0.003$ ) were significantly associated with mortality. The type of stent ( $p = 0.052$ ) showed a relation to mortality that was very close to the level of significance (table 2). The 'type of stent' variable included 3 groups:

**Table 1.** Baseline characteristics

	CKD stage 2 (n = 16)	CKD stage 3A (n = 62)	CKD stage 3B (n = 82)	CKD stage 4 (n = 30)	CKD stage 5 (n = 75)	Transplant (n = 19)	p value
Age, years	73.56±10.58	72.74±10.16	75.12±10.19	75.53±9.59	66.75±12.02	57.05±11.67	<0.001
Sex (male)	13 (81.2%)	54 (87.1%)	70 (85.4%)	25 (83.3%)	57 (76.0%)	17 (89.5%)	0.509
Hypertension	14 (87.5%)	51 (82.3%)	67 (81.7%)	26 (86.7%)	67 (89.3%)	15 (78.9%)	0.721
Diabetes	10 (62.5%)	25 (40.3%)	41 (50.0%)	13 (43.3%)	43 (57.3%)	3 (15.8%)	<0.018
Increased cholesterol	14 (87.5%)	48 (77.4%)	68 (82.9%)	24 (80.0%)	55 (73.3%)	12 (63.2%)	0.365
PVD/stroke	4 (25.0%)	8 (10.8%)	13 (15.9%)	5 (16.7%)	10 (13.3%)	2 (10.5%)	0.837
LVEF							<0.003
>55%	5 (35.7%)	28 (54.9%)	19 (32.8%)	11 (40.7%)	34 (48.6%)	12 (66.7%)	
45–54%	2 (14.3%)	6 (11.86%)	12 (20.7%)	3 (11.1%)	10 (14.3%)	5 (27.8%)	
35–44%	4 (28.6%)	11 (21.6%)	7 (12.1%)	9 (33.3%)	20 (28.6%)	0 (0.0%)	
<35%	3 (21.4%)	6 (11.8%)	20 (34.5%)	4 (14.8%)	6 (8.6%)	1 (5.6%)	
PCI indication							0.086
Elective	7 (43.8%)	36 (58.1%)	35 (46.4%)	10 (33.3%)	26 (36.3%)	10 (52.6%)	
Urgent	9 (56.2%)	26 (41.9%)	47 (57.3%)	20 (66.7%)	49 (65.3%)	9 (47.4%)	
Target vessel							
Left main	2 (12.5%)	1 (1.6%)	2 (2.4%)	1 (3.3%)	2 (2.7%)	0 (0.0%)	0.355
LAD	7 (37.5%)	28 (45.2%)	43 (52.4%)	11 (36.7%)	44 (58.7%)	12 (63.2%)	0.252
LCx	5 (31.2%)	17 (27.4%)	18 (22.0%)	8 (26.7%)	20 (26.7%)	2 (10.5%)	0.666
RCA	6 (37.5%)	17 (27.4%)	28 (34.1%)	8 (26.7%)	16 (21.3%)	8 (42.1%)	0.362
Vein graft	1 (6.2%)	7 (11.3%)	5 (6.1%)	6 (20.0%)	6 (8.0%)	0 (0.0%)	0.201
Number of vessels							
1	12 (75.0%)	54 (87.1%)	69 (84.1%)	24 (80%)	62 (82.7%)	16 (84.2%)	
2	3 (18.8%)	8 (12.9%)	12 (14.6%)	6 (20%)	11 (14.7%)	3 (15.8%)	
3	1 (6.2%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	2 (2.7%)	0 (0%)	
Number of stents							0.560
0–2	14 (87.5%)	54 (87.1%)	61 (74.4%)	26 (86.7%)	69 (92%)	17 (89.5%)	
3–5	2 (12.5%)	8 (12.9%)	21 (25.6%)	4 (13.3%)	6 (8.0%)	2 (10.5%)	
Type of intervention							0.410
PTCA	1 (6.2%)	1 (6.2%)	5 (6.1%)	2 (6.7%)	7 (9.3%)	2 (10.5%)	
BMS	3 (18.8%)	16 (25.8%)	23 (28.0%)	10 (33.3%)	19 (25.3%)	5 (26.3%)	
1st-generation DES	3 (18.8%)	14 (22.6%)	13 (15.9%)	3 (10.0%)	23 (30.7%)	6 (31.6%)	
2nd-generation DES	9 (56.2%)	31 (50.0%)	41 (50.0%)	15 (50.0%)	26 (34.7%)	6 (31.6%)	
Length, mm	23.19±19.78	20.03±7.15	20.99±7.81	20.67±5.96	19.49±8.82	20.67±6.13	0.528

Values are expressed as means ± SD or n (%). Italics denote significance. PVD = Peripheral vascular disease; LAD = left anterior descending artery; LCx = left circumflex artery; RCA = right coronary artery.

BMS and 1st- and 2nd-generation DES. The PTCA group was a small group of patients consisting of 18 patients only. Thus, it was excluded from analysis, and mortality was investigated between patients who had stent(s) implanted. A direct comparison of the 1st- and 2nd-generation DES groups with the BMS group revealed a hazard ratio (HR) of 0.58 (95% CI: 0.33–1.00,  $p = 0.048$ ) and 0.59 (95% CI: 0.36–0.95,  $p = 0.031$ ) for the 1st- and the 2nd-generation DES group, respectively (table 2). The presence of diabetes also showed a correlation with mortality at a nearly significant level ( $p = 0.094$ ). The remaining variables were not significantly related to mortality.

Age, EF, CKD stage, PCI indication, diabetes and type of stent had a  $p$  value <0.20 and were therefore used in a multivariable Cox regression model. Age, EF, CKD and PCI indication were shown to be independently related to mortality (table 2). For both EF and eGFR there is an obvious trend for an increasing risk of death with deteriorating LV systolic function and worsening renal impairment. However, for EF, only severe LV systolic impairment (EF <35%) was

**Table 2.** Estimated HR for mortality among patients undergoing PCI

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p value	HR (95% CI)	p value
Age	1.03 (1.01–1.06)	<i>&lt;0.001</i>	1.05 (1.02–1.07)	<i>&lt;0.001</i>
EF		<i>&lt;0.001</i>		<i>&lt;0.001</i>
>55%	1.0 (reference)		1.0 (reference)	
45–54%	1.17 (0.58–2.35)	0.655	1.36 (0.67–2.75)	0.399
35–44%	2.17 (1.21–3.77)	<i>&lt;0.009</i>	1.49 (0.81–2.72)	0.200
<35%	3.34 (1.88–5.93)	<i>&lt;0.001</i>	4.04 (2.15–7.59)	<i>&lt;0.001</i>
CKD stage		<i>&lt;0.001</i>		<i>&lt;0.001</i>
2	1.0 (reference)		1.0 (reference)	
3A	1.21 (0.27–5.47)	0.809	1.30 (0.28–6.12)	0.738
3B	2.84 (0.67–11.92)	0.155	1.85 (0.42–8.07)	0.415
4	2.80 (0.61–12.81)	0.183	2.14 (0.46–9.97)	0.333
5	4.64 (1.12–19.23)	<i>&lt;0.034</i>	6.39 (1.51–27.12)	<i>&lt;0.012</i>
Transplant	1.20 (0.22–6.65)	0.834	1.74 (0.31–9.97)	0.538
Urgent PCI	1.93 (1.25–2.98)	<i>&lt;0.003</i>	1.74 (1.04–2.92)	<i>&lt;0.035</i>
Diabetes	1.42 (0.94–2.14)	<i>&lt;0.094</i>	1.35 (0.85–2.17)	0.207
Type of stent		<i>&lt;0.052</i>		0.169
BMS	1.0 (reference)		1.0 (reference)	
1st-generation DES	0.58 (0.33–1.00)	<i>&lt;0.048</i>	0.69 (0.36–1.30)	0.245
2nd-generation DES	0.59 (0.36–0.95)	<i>&lt;0.031</i>	0.59 (0.34–1.03)	<i>&lt;0.061</i>

Italics denote significance.

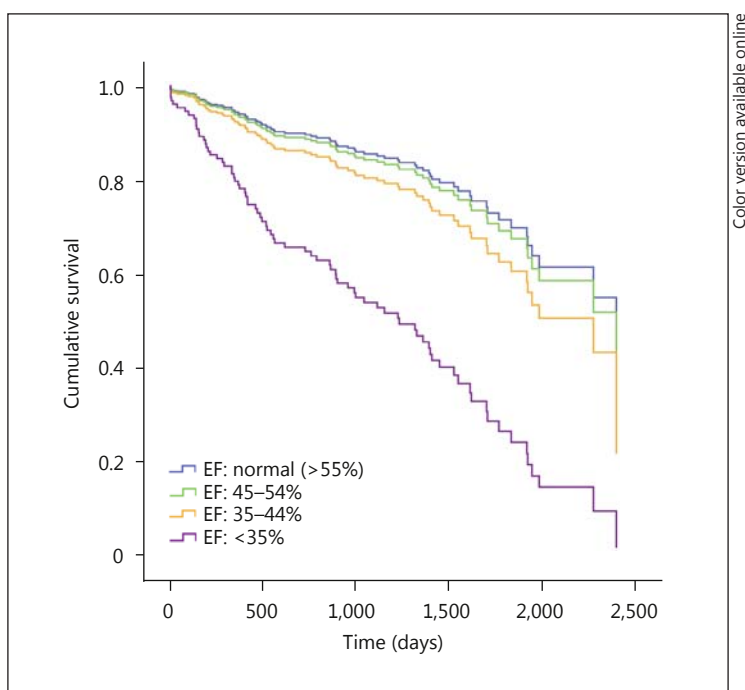
shown to be significantly related to mortality ( $p < 0.001$ , HR = 4.04, 95% CI: 2.16–7.59). Similarly, for renal impairment, only stage 5 of CKD (dialysis-dependent patients) was significantly related to mortality ( $p = 0.012$ , HR = 6.39, 95% CI: 1.51–27.12) and appeared to be the most robust predictor of mortality, carrying a 6-fold increase in risk of death compared to mild renal impairment (CKD stage 2). An interesting finding is that transplant patients had a mortality outcome similar to CKD stage 3B patients (table 2; fig. 2). Diabetes was not found to be significantly related to mortality in the multivariable model ( $p = 0.207$ ). A comparison between BMS and 2nd-generation DES showed that the latter carries a more favourable outcome (HR = 0.59, 95% CI: 0.34–1.03) at a nearly significant level ( $p = 0.061$ ).

Cox regression survival curves demonstrating all-cause mortality were calculated for EF, CKD stage, PCI indication and type of stent (fig. 1–4). Age was categorized in groups of 20-year units, and Kaplan-Meier curves were used to describe survival probabilities by age group (fig. 5).

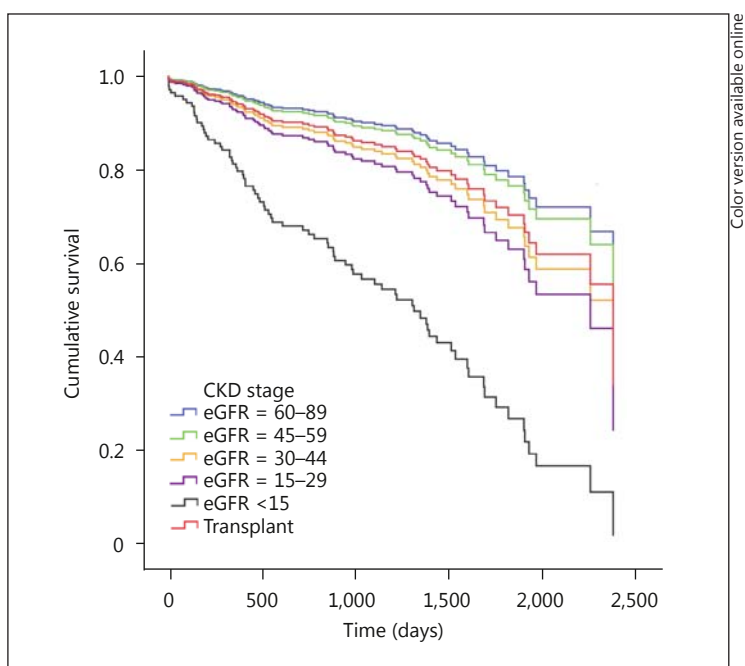
## Discussion

The principal finding of our study is that increasing age, deteriorating LV systolic impairment, worsening renal function and urgent indication for PCI (i.e. acute coronary syndrome) all are associated independently with an increased risk of death following PCI. Also there is a trend towards better outcome with more contemporary stents which is approaching a statistically significant level.

Previous studies have shown that renal impairment is a significant prognostic factor for mortality in patients with coronary artery disease [2, 3, 6, 9, 10]. In our study CKD stage 5 (eGFR  $< 15$  ml/min/1.73 m<sup>2</sup>) had the strongest association with mortality. EF is also signifi-



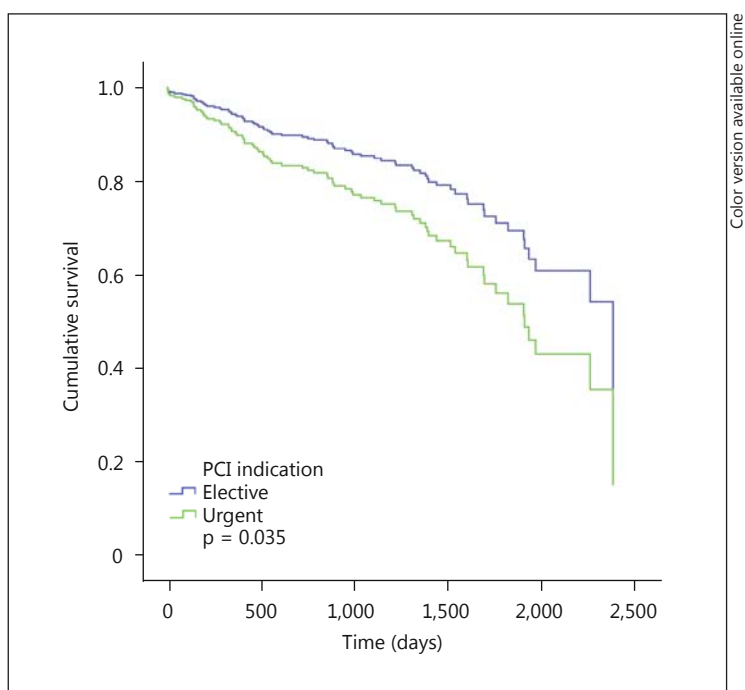
**Fig. 1.** Survival rate according to LVEF.



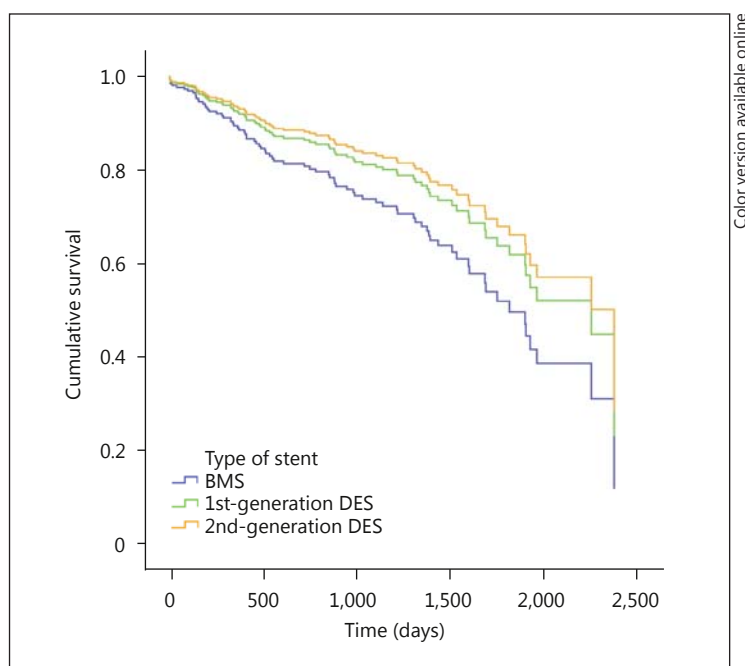
**Fig. 2.** Survival rate according to eGFR (ml/min/1.73 m<sup>2</sup>; CKD stage).

cantly associated with death. Severe LV dysfunction (EF <35%) is a more robust predictor of mortality (HR = 4.04, 95% CI: 2.16–7.59) than moderate and mild LV systolic dysfunction. Increasing age is also positively related to mortality, and that has been demonstrated in previous studies as well [2, 3, 6, 9, 10]. Our study showed that an urgent indication for PCI carries a 1.7-fold increased risk of mortality (HR = 1.74, 95% CI: 1.04–2.92). This is consistent with the findings of Parikh et al. [2], who demonstrated a strong correlation; however, they investigated in-hospital mortality only.



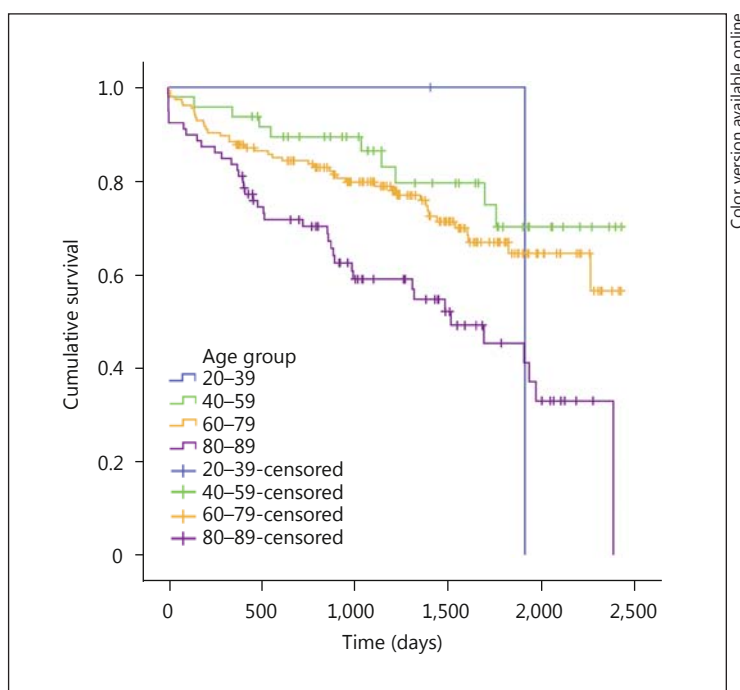


**Fig. 3.** Survival rate according to PCI indication.



**Fig. 4.** Survival rate of patients with different types of stents.

Another important finding in our study is that mortality is higher in patients who had BMS than in those with 1st- and 2nd-generation DES (fig. 4), showing a trend for increasing survival when more contemporary stents are used. The difference in mortality between the 3 groups is very close to statistical significance ( $p = 0.052$ ) in unadjusted univariate analysis, and patients with 2nd-generation DES had lower HR than those with BMS (HR = 0.59, 95% CI: 0.36–0.95,  $p = 0.031$ ). In the multivariate model, the lower HR for the patients treated with 2nd-generation DES compared to those with BMS remained with a  $p$  value very close to statis-



**Fig. 5.** Survival rate according to age group (20-year groups).

tical significance ( $p = 0.06$ ; table 2). Patients who received 1st-generation DES had also lower HR compared to those with BMS (HR = 0.69, 95% CI: 0.36–1.30), though it was not statistically significant ( $p = 0.25$ ). Previously published data by Das et al. [9] based on dialysis patients suggest more favourable outcomes with DES in terms of target vessel revascularization at 9 months compared to BMS ( $p = 0.030$ ). However, there was no difference in mortality. More recently, Barthelemy et al. [10] demonstrated that the use of DES versus BMS in patients with chronic renal failure was independently associated with the absence of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke and target lesion revascularization). They also showed that patients who received DES had lower event rates of cardiovascular death ( $p = 0.002$ ) in an unadjusted model.

In our population the patients who received BMS were older than those who received 2nd-generation DES (mean age  $75.0 \pm 12.1$  vs.  $70.4 \pm 11.5$  years,  $p = 0.007$ ). However, only 20.6% of the diabetic patients received BMS, as opposed to 55.6% who received 2nd-generation DES ( $p = 0.018$ ). The use of BMS and 2nd-generation DES was similar between the several groups of LVEF, CKD stage and PCI indication variables. Overall, this effect is depicted in our results. The 2nd-generation DES is a significant predictor of mortality in univariate analysis, but just below the level of significance when age and comorbidities are taken into account. It seems that adjustment for age makes the type of stent marginally non-significant. However, even after adjustment it remains very close to significance, which suggests that it could potentially have an independent effect on outcome that may show up in a larger sample population.

Other well-known cardiovascular risk factors such as diabetes, hyperlipidaemia, hypertension and established peripheral vascular disease/stroke did not show a significant association with mortality, suggesting that in our specific population of patients with CKD undergoing PCI, these factors may not play a pivotal role in outcome. These findings are partially consistent with those of Best et al. [11], who demonstrated that hypertension and hypercholesterolaemia are not significantly related to mortality in a similar cohort of patients. However,



their results suggest that diabetes, peripheral vascular disease and stroke are significant predictors of mortality. The prevalence range of diabetes amongst groups of patients was similar in the study by Best et al. [11] (20.4–50.0%) and our study (15.8–57.5%). Bevc et al. [12] also investigated mortality in CKD patients undergoing PCI, and they additionally included a group of patients with normal renal function. Their multivariate analysis showed that hypercholesterolaemia was significantly related to mortality but not hypertension and diabetes. Furthermore, Goldenberg et al. [6] studied a population with non-ST-segment elevation acute coronary syndrome and renal impairment and correlated renal function to outcome. In their study, hypertension and diabetes were not significantly correlated to mortality. In conclusion, classic cardiovascular risk factors interchangeably seem to be unrelated to mortality in previously published studies performed on a specific population of patients with renal impairment undergoing PCI. The sample size of our study population may also play a role in our findings.

In addition, our study shows that several angiographic variables such as the location of coronary artery intervention (i.e. target vessel), number of treated vessels, number of stents implanted and length of treated segment were not associated with mortality. Similarly, troponin levels did not show a significant association with mortality, but they were not available for the total population of patients. We recorded troponin levels only for 143 out of 284 patients. That may account for the non-significant results.

The above findings could possibly suggest that factors known to be associated with outcome after coronary artery intervention are not that significant in patients with CKD. It seems that renal impairment is a robust determinant of mortality that may obscure other ‘classic’ prognostic factors. It is well known that CKD is strongly associated with coronary artery disease and has a major impact on outcomes [13–15]. Manjunath et al. [16] demonstrated that the level of GFR is an independent risk factor for atherosclerotic cardiovascular disease and is related to outcomes. In post-myocardial infarction patients, an increase in creatinine above the upper reference limit is associated with an increase in overall mortality [17, 18]. In our study we demonstrate that GFR is a strong predictor of mortality in patients undergoing PCI for both stable and acute coronary syndromes and the risk of mortality is increasing as renal impairment deteriorates. It is believed that coexisting conditions and comorbidities such as diabetes mellitus, hypertension, hypercholesterolaemia and impaired LV function may contribute to adverse outcomes of patients with renal impairment. In our study CKD remained the major prognostic factor even after adjusting for the above variables, indicating a separate role of CKD. These outcomes can partially be explained by the chronic inflammation, elevated homocysteine levels, aggressive atherosclerosis, endothelial dysfunction and altered cytokine levels observed in this population [19–23]. There is also evidence that erythropoietin deficiency and anaemia are related to adverse ventricular remodelling and cardiac failure [24]. Chertow et al. [25] suggested that advanced atherosclerosis is related to abnormal vascular calcification driven by an elevated calcium-phosphorus product, and lowering of the calcium-phosphorus product may reduce or stabilize the coronary calcification process. Furthermore, medications with a proven outcome benefit such as beta-blockers, dual anti-platelet therapy and angiotensin-converting enzyme inhibitors are underused in this population [26, 27].

Our study is a retrospective observational study with the relevant limitations and bias. It also carries the bias inherent in a study performed in a single centre with a relatively small sample size. The small size may account for a type II statistical error, particularly regarding post-transplant patients. We did not take into consideration the pharmacological treatment given and the achievement of therapeutic targets. That may be a potential confounder, as it is known from previous studies [26–28] that guideline-recommended medications are underutilized in this population. We investigated only all-cause mortality and not cardiac mortality.

Other risk factors related to prognosis, including family history of coronary artery disease, smoking, socio-economic status and aetiology of renal impairment, were not included in our data and were not investigated as potential confounders.

## Conclusions

In our study we investigated mortality in a population of patients with established renal impairment of different stages undergoing PCI. Stage of CKD is independently associated with mortality even after adjustment for other risk factors. CKD stage 5 is the most robust predictor of death, carrying a 6.4-fold increase in risk of death. A significant association with mortality was also demonstrated for increasing age, deteriorating LV systolic function and urgent indication for PCI. These results suggest the prompt identification of patients at high risk and ensuring adequate evaluation, treatment and long-term management in terms of both renal impairment and coronary artery disease. Aggressive risk factor modification is warranted.

## Disclosure Statement

S. Ayis was partly funded/supported by the National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

## References

- 1 Wijns W, Kolh P, Danchin N, et al: Guidelines on myocardial revascularization. *Eur Heart J* 2010;31:2501–2555.
- 2 Parikh PB, Jeremias A, Naidu SS, et al: Impact of severity of renal dysfunction on determinants of in-hospital mortality among patients undergoing percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2012; 80:352–357.
- 3 Saltzman AJ, Stone GW, Claessen BE, et al: Long-term impact of chronic kidney disease in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention: the HORIZONS-AMI (Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction) trial. *JACC Cardiovasc Interv* 2011;4:1011–1019.
- 4 Hamm CW, Bassand J-P, Agewall S, et al: ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: the task force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2011;32:2999–3054.
- 5 Hasdai D: A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin. The Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). *Eur Heart J* 2002;23:1190–1201.
- 6 Goldenberg I, Subirana I, Boyko V, Vila J, Elosua R, Permanyer-Miralda G, Ferreira-González I, Benderly M, Guetta V, Behar S, Marrugat J: Relation between renal function and outcomes in patients with non-ST-segment elevation acute coronary syndrome: real-world data from the European Public Health Outcome Research and Indicators Collection Project. *Arch Intern Med* 2010;170:888–895.
- 7 Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D: A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;130:461–470.
- 8 Thygesen K, Alpert JS, Jaffe AS, et al: Third universal definition of myocardial infarction. *Eur Heart J* 2012;33: 2551–2567.
- 9 Das P, Moliterno DJ, Charnigo R, et al: Impact of drug-eluting stents on outcomes of patients with end-stage renal disease undergoing percutaneous coronary revascularization. *J Invasive Cardiol* 2006;18:405–408.
- 10 Barthelemy O, Helft G, Silvain J, et al: One-year clinical outcomes in patients with chronic renal failure treated by percutaneous coronary intervention with drug-eluting stent. *Arch Cardiovasc Dis* 2011;104:604–610.
- 11 Best PJM, Lennon R, Ting HH, et al: The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. *J Am Coll Cardiol* 2002;39:1113–1119.

- 12 Bevc S, Penko M, Kanic V, Hojs R: Mortality of patients with renal dysfunction after percutaneous coronary intervention. *Angiology* 2010;61:24–30.
- 13 Montalescot G, Sechtem U, Achenbach S, et al: 2013 ESC guidelines on the management of stable coronary artery disease: the task force on the management of stable coronary artery disease of the European Society of Cardiology. *Eur Heart J* 2013;34:2949–3003.
- 14 Di Angelantonio E, Danesh J, Eiriksdóttir G, Guðnason V: Renal function and risk of coronary heart disease in general populations: new prospective study and systematic review. *PLoS Med* 2007;4:e270.
- 15 Mann JF, Gerstein HC, Pogue J, Bosch J, Yusuf S: Renal insufficiency as a predictor of cardiovascular outcomes and impact of ramipril: the HOPE randomized trial. *Ann Intern Med* 2001;134:629–636.
- 16 Manjunath G, Tighiouart H, Ibrahim H, et al: Level of kidney function as a risk factor for atherosclerotic cardiovascular outcomes in the community. *J Am Coll Cardiol* 2003;41:47–55.
- 17 Furberg CD, Byington RP: What do subgroup analyses reveal about differential response to beta-blocker therapy? The Beta-Blocker Heart Attack Trial experience. *Circulation* 1983;67(pt 2):I98–I101.
- 18 Beattie JN, Soman SS, Sandberg KR, et al: Determinants of mortality after myocardial infarction in patients with advanced renal dysfunction. *Am J Kidney Dis* 2001;37:1191–1200.
- 19 Boushey CJ, Beresford SA, Omenn GS, Motulsky AG: A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: probable benefits of increasing folic acid intakes. *JAMA* 1995;274:1049–1057.
- 20 Thambyrajah J, Landray MJ, McGlynn FJ, Jones HJ, Wheeler DC, Townsend JN: Abnormalities of endothelial function in patients with predialysis renal failure. *Heart* 2000;83:205–209.
- 21 Sechi LA, Zingaro L, Catena C, Perin A, De Marchi S, Bartoli E: Lipoprotein(a) and apoprotein(a) isoforms and proteinuria in patients with moderate renal failure. *Kidney Int* 1999;56:1049–1057.
- 22 Kronenberg F, Kuen E, Ritz E, et al: Lipoprotein(a) serum concentrations and apolipoprotein(a) phenotypes in mild and moderate renal failure. *J Am Soc Nephrol* 2000;11:105–115.
- 23 Stenvinkel P, Heimbürger O, Paulter F, et al: Strong association between malnutrition, inflammation and atherosclerosis in chronic renal failure. *Kidney Int* 1999;55:1899–1911.
- 24 Silverberg DS, Wexler D, Sheps D, et al: The effect of correction of mild anemia in severe, resistant congestive heart failure using subcutaneous erythropoietin and intravenous iron: a randomized controlled study. *J Am Coll Cardiol* 2001;37:1775–1780.
- 25 Chertow GM, Burke SK, Raggi P; Treat to Goal Working Group: Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. *Kidney Int* 2002;62:245–252.
- 26 Rubenstein MH, Sheynberg BV, Harrell LC, Schunkert H, Bazari H, Palacios IF: Effectiveness of and adverse events after percutaneous coronary intervention in patients with mild versus severe renal failure. *Am J Cardiol* 2001;87:856–860.
- 27 Wright RS, Reeder GS, Herzog CA, Albright RC, Williams BA, Dvorak DL, Miller WL, Murphy JG, Kopecky SL, Jaffe AS: Acute myocardial infarction and renal dysfunction: a high-risk combination. *Ann Intern Med* 2002;137:563–570.
- 28 Latif F, Kleiman NS, Cohen DJ, et al: In-hospital and 1-year outcomes among percutaneous coronary intervention patients with chronic kidney disease in the era of drug-eluting stents: a report from the EVENT (Evaluation of Drug Eluting Stents and Ischemic Events) registry. *JACC Cardiovasc Interv* 2009;2:37–45.