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The Impact of Renal Insufficiency on Clinical Outcomes in Patients Undergoing Percutaneous Coronary Interventions

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OBJECTIVES We sought to determine the effect of varying degrees of renal insufficiency on death and cardiac events during and after a percutaneous coronary intervention (PCI).

BACKGROUND Patients with end-stage renal disease have a high mortality from coronary artery disease. Little is known about the impact of mild and moderate renal insufficiency on clinical outcomes after PCI.

METHODS Cardiac mortality and all-cause mortality were determined for 5,327 patients undergoing PCI from January 1, 1994, to August 31, 1999, at the Mayo Clinic, based on the estimated creatinine clearance or whether the patient was on dialysis.

RESULTS In-hospital mortality was significantly associated with renal insufficiency ($p = 0.001$). Even after successful PCI, one-year mortality was 1.5% when the creatinine clearance was ≥70 ml/min (n = 2,558), 3.6% when it was 50 to 69 ml/min (n = 1,458), 7.8% when it was 30 to 49 ml/min (n = 828) and 18.3% when it was <30 ml/min (n = 141). The 18.3% mortality rate for the group with <30 ml/min creatinine clearance was similar to the 19.9% mortality rate in patients on dialysis (n = 46). The mortality risk was largely independent of all other factors.

CONCLUSIONS Renal insufficiency is a strong predictor of death and subsequent cardiac events in a dose-dependent fashion during and after PCI. Patients with renal insufficiency have more baseline cardiovascular risk factors, but renal insufficiency is associated with an increased risk of death and other adverse cardiovascular events, independent of all other measured variables. (J Am Coll Cardiol 2002;39:1113–9) © 2002 by the American College of Cardiology Foundation

Chronic renal failure is associated with a high cardiovascular mortality. The mortality rate in the first year after initiation of dialysis is 24% (1). Over half of these deaths are attributable to cardiovascular diseases. Although much is known about the effects of end-stage renal failure on coronary artery disease (CAD), little is known about the impact of mild renal insufficiency on CAD. Nearly 11 million Americans have mild renal insufficiency—over 30 times the number of people in the dialysis population—and this number continues to grow (2). Thus, further understanding of the coronary risks and outcomes of patients with mild renal insufficiency is necessary.

The clinical outcome of patients with end-stage renal disease undergoing a percutaneous coronary intervention (PCI) is poor (3,4). Balloon angioplasty is a feasible type of PCI, but it is associated with a 60% to 81% incidence of restenosis (3–5). Despite this high incidence of restenosis, symptoms of restenosis are often absent, and severe silent ischemia may account for the high cardiac mortality in this population. The clinical outcome after PCI in patients with mild renal insufficiency is unknown.

We sought to determine the mortality, cardiac-specific mortality and risk of other adverse coronary events as functions of creatinine clearance in patients undergoing PCI. Furthermore, we analyzed the impact of renal insufficiency on mortality after adjusting for other cardiovascular risk factors.

METHODS

Mayo Clinic PCI Registry. All patients undergoing PCI at the Mayo Clinic in Rochester, Minnesota, since 1979 are prospectively followed, and data are entered in a registry based on a protocol approved by the Institutional Review Board. This registry includes baseline demographic, clinical and angiographic data. Follow-up data are collected by telephone, using a standardized questionnaire, at six months, one year and then annually after the procedure. All adverse events are confirmed by reviewing the medical records of the patients followed at our institution and by contacting the patients' physicians and reviewing the hospital records of patients followed elsewhere.

Current study. In the current study, all patients who underwent PCI between January 1, 1994, and August 31, 1999, at the Mayo Clinic were eligible for inclusion. For patients who underwent more than one revascularization procedure during the study period, only the first intervention was included for analysis. Patients were excluded if they had undergone renal transplantation (n = 5), had acute renal failure before the PCI procedure (as defined by a rise

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CAD = coronary artery disease
CI = confidence interval
MI = myocardial infarction
PCI = percutaneous coronary intervention
RR = risk ratio

in serum creatine of 1 mg/dl above the baseline value) (n = 21), did not have their creatinine level measured at the Mayo Clinic before the procedure (n = 638) or were undergoing PCI within 24 h after myocardial infarction (MI) or had pre-procedural shock (n = 1,208). All patients who denied research authorization were also excluded (n = 133). The specific type of revascularization procedure (i.e., balloon angioplasty, atherectomy, stenting) was chosen by the interventional cardiologist.

Assessment of renal function. Using the creatinine level obtained closest to the time of, but before, the angiogram, renal function was assessed by the estimated creatinine clearance, using the Cockroft-Gault formula: creatinine clearance (ml/min) = [([140 − age] × weight [kg])/72 × serum creatinine (mg/dl)] (× 0.85 for women) (6). This equation has a close correlation with measured creatinine clearances (correlation coefficient 0.83) and gives a more accurate assessment of renal function than serum creatinine alone. Patients on hemodialysis or peritoneal dialysis were analyzed separately. Patients were categorized either by level of creatinine clearance (≥70, 50 to 69, 30 to 49 and <30 ml/min) or on-dialysis status.

Angiographic analysis. The severity of coronary stenosis was determined by two observers using visual assessment or by hand-held calipers by means of orthogonal views.

Definitions. The number of diseased coronary arteries was defined by the number of major coronary arteries with luminal diameter stenosis ≥70%. Patients with ≥50% stenosis in the left main coronary artery were considered to have two-vessel disease if there was right dominance and three-vessel disease if there was left dominance.

Angiographic success was defined as PCI with ≥20% improvement in luminal diameter stenosis of at least one treatment site, with residual stenosis <50%. Procedural success was defined as angiographic success without death, Q-wave MI or coronary artery bypass graft surgery (CABG) during the initial hospitalization. Complete revascularization was achieved if there were no remaining stenoses ≥70%. Myocardial infarction was defined by the presence of two of three criteria: chest pain, electrocardiographic changes and increased cardiac enzyme levels at least twice the upper limit of the normal range. Myocardial infarctions were identified as being Q-wave or non–Q-wave, whenever possible. The frequency of MI included all patients with Q-wave or non–Q-wave MI and, in rare cases, MI that could not be classified as Q-wave or non–Q-wave. To determine the causes of death, autopsy and medical records were reviewed when available, and family members were interviewed when such records were not available. Cardiac death was considered to have occurred if death occurred suddenly and autopsy failed to reveal another cause or if death was associated with documented MI or other cardiac causes such as congestive heart failure and arrhythmia.

Statistical analysis. Data are presented as the mean value ± SD or as a percentage. All analyses were performed using SAS software (SAS, Inc., Cary, North Carolina). Comparisons between groups were made by one-way analysis of variance, the Pearson chi-square test or the log-rank test. All tests of significance were two-tailed. Using the Kaplan-Meier method, event-free survival curves were constructed. Estimated risk ratios of follow-up death were determined for creatinine clearance analyzed as a continuous variable. Using variables significantly associated with mortality on univariate analysis, a multivariable model was created. This model was then simplified using backward selection. To estimate the effect of creatinine clearance, this variable was added to the previously selected model. Creatinine clearance was treated as a numerical variable with the potential for quadratic (curved) effects. Creatinine values for dialysis patients were ignored and forced to the reference level. A separate variable for dialysis treatment was included to estimate its effect. P values ≤0.05 were considered significant.

RESULTS

Baseline characteristics. The baseline characteristics of the 5,327 patients who underwent PCI (study population), grouped by estimated creatinine clearance or the need for dialysis, are shown in Table 1. The majority of dialysis patients (89%) were on hemodialysis; 11% were on peritoneal dialysis. Patients with a lower creatinine clearance were more likely to be older, women, diabetic and hypertensive, with less height and weight. Such patients more commonly had previous strokes, peripheral vascular disease, previous CABG and a lower left ventricular ejection fraction. Dialysis patients more frequently had diabetes mellitus, hypertension and peripheral vascular disease.

The most common indication for PCI was unstable angina in all groups. However, patients with the lowest creatinine clearance more frequently presented with a recent MI (<7 days) or with congestive heart failure as the indication for their procedure. Furthermore, patients undergoing dialysis were more likely to have ischemia on a functional test without angina than patients with milder renal insufficiency.

Angiographic analysis. Patients with a lower creatinine clearance more frequently had multivessel disease, vein graft disease, more complex lesions (according to the modified American College of Cardiology/American Heart Association classification) and greater use of rotational atherectomy (Table 2). Glycoprotein IIb/IIIa inhibitors were given before or during the procedure in 24.4% of the interven-

Table 1. Baseline Patient Characteristics by Estimated Creatinine Clearance or Dialysis

Characteristic	Creatinine Clearance (ml/min) ≥70 (n = 2,687)	50–69 (n = 1,537)	30–49 (n = 899)	<30 (n = 154)	Dialysis (n = 50)	p Value*
Height (m)	1.74 ± 0.09	1.69 ± 0.09	1.65 ± 0.09	1.63 ± 0.10	1.69 ± 0.09	<0.001
Weight (k)	93.1 ± 17.1	78.5 ± 11.6	70.9 ± 12.5	67.5 ± 14.7	79.7 ± 18.3	<0.001
Age (years)	58.9 ± 9.9	70.1 ± 7.8	76.8 ± 7.4	77.9 ± 9.2	64.1 ± 11.4	<0.001
Male (%)	82.3	67.6	50.7	42.9	70.0	<0.001
Diabetes mellitus (%)	20.4	20.8	23.8	30.5	50.0	<0.001
Insulin treatment	5.6	6.6	7.5	12.1	26.8	<0.001
Treatment with oral agents	6.9	7.9	7.5	9.3	4.9	0.60
Hypertension (%)	54.7	62.2	68.7	80.5	94.0	<0.001
Hyperlipidemia (%)	62.7	63.0	58.0	59.3	55.8	0.11
Smoking history (%)						
Past	70.2	59.5	52.9	44.4	66.0	<0.001
Current	24.4	11.6	6.1	5.2	12.0	<0.001
Previous PCI (%)	22.8	22.8	22.0	16.9	28.0	0.41
Previous CABG (%)	18.1	26.2	29.7	27.3	24.0	<0.001
Previous myocardial infarction (%)	48.2	47.9	52.9	66.9	57.4	<0.001
Previous stroke or TIA (%)	6.0	12.8	17.8	25.7	22.0	<0.001
Mean LVEF (%)	60.6 ± 13.9	58.2 ± 16.3	54.2 ± 16.8	47.9 ± 17.3	56.7 ± 13.5	<0.001
Peripheral vascular disease (%)	7.5	13.5	19.0	23.0	57.4	<0.001
Indications for PCI (%)						
Unstable angina	72.6	72.9	72.6	75.3	64.0	0.65
Stable angina	12.9	13.3	12.1	7.8	10.0	0.33
Myocardial infarction within 7 days	19.3	16.2	19.5	26.6	10.0	0.003
Positive functional test without angina	7.0	7.7	8.5	6.5	22.0	0.002
Congestive heart failure	3.6	7.5	14.7	31.8	16.0	<0.001

*Difference between the creatinine clearance groups. Data are presented as the mean value ± SD or percentage of patients.
CABG = coronary artery bypass graft surgery; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

tions, with no difference in the frequency of use of these agents in the different creatinine clearance groups. A dissection occurred 20.6% of the time, and the frequency was similar in all groups (p = 0.60). The angiographic success rate was similar in the groups. However, patients with a lower creatinine clearance and those on dialysis had more frequent complications, including death, non–Q-wave MI or the need for CABG during the hospital period, and thus the procedural success rate was lower. Furthermore, those patients with a lower creatinine clearance were less likely to have been completely revascularized after the procedure.

The frequency of adverse events in the hospital and at one-year follow-up is shown in Table 3. Patients with a lower creatinine clearance had an increased risk of death or MI (both Q-wave and non–Q-wave) in the hospital and in the year following the procedure, both including and excluding the in-hospital events. Of note, the marked increase in the frequency of in-hospital death in the lower creatinine clearance groups and in dialysis patients was associated with only a small increase in both Q-wave and non–Q-wave MI. Furthermore, there was a marked increase in acute renal failure in the lower creatinine clearance groups. The Kaplan-Meier curves demonstrating mortality and cardiac mortality are shown in Figures 1 and 2. The mean follow-up time was 2.7 ± 1.6 years. These figures demonstrate that creatinine clearance was significantly associated with mortality and cardiac mortality in patients after successful PCI.

Using a univariate model, the risk ratios (RR) for death after successful PCI were significant (p < 0.001) for all of the following variables: creatinine clearance in 10-ml/min units (RR 0.75, 95% confidence interval [CI] 0.7 to 0.8), age in 10-year units (RR 1.61, 95% CI 1.5 to 1.8), weight in 10-kg units (RR 0.86, 95% CI 0.8 to 0.9), diabetes (RR 2.43, 95% CI 2.0 to 2.9), previous MI (RR 1.68, 95% CI 1.4 to 2.0), previous stroke or transient ischemic attack (RR 2.09, 95% CI 1.7 to 2.7), congestive heart failure on presentation (RR 5.19, 95% CI 4.2 to 6.4), peripheral vascular disease (RR 2.93, 95% CI 2.4 to 3.6), multivessel disease (RR 1.94, 95% CI 1.6 to 2.3), right coronary artery intervention (RR 0.65, 95% CI 0.5 to 0.8) and vein graft intervention (RR 2.44, 95% CI 1.9 to 3.0). In the multivariate model (Table 4), the RR of death during follow-up was highest for dialysis patients, followed by patients with moderate renal dysfunction (creatinine clearance <50 ml/min). Moderate or severe renal insufficiency was associated with a greater risk of death than even diabetes. The association between renal dysfunction and death was dose-dependant. The use of a stent was not a significant factor in the multivariate model (p = 0.10).

DISCUSSION

The principal finding of this study is that renal dysfunction significantly increases the risk of death and cardiac death during and after PCI in a dose-dependent manner. Even mild renal insufficiency (creatinine clearance 70 ml/min) has

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Table 2. Angiographic and Procedural Characteristics of the Study Population

Characteristic	Creatinine Clearance (ml/min)					p Value*
	≥70 (n = 2,687)	50–69 (n = 1,537)	30–49 (n = 899)	<30 (n = 154)	Dialysis (n = 50)	
No. of coronary vessels diseased (%)						<0.001
One	51.5	46.9	39.3	28.3	31.3	
Two	34.3	36.1	38.1	36.6	37.5	
Three	12.1	15.2	20.2	34.5	29.2	
Coronary vessels treated (%)						0.69
One	84.6	83.6	83.6	87.0	76.0	
Two	14.7	15.8	15.7	12.3	24.0	
Three	0.7	0.6	0.7	0.6	0.0	
Coronary vessels treated (%)						
LAD	42.9	40.3	42.7	37.7	28.0	0.09
LCx	28.7	29.1	25.7	29.8	26.0	0.41
RCA	35.4	33.7	31.4	26.6	50.0	0.006
LMCA	1.5	1.6	2.2	3.2	4.0	0.23
Vein graft	7.0	11.7	14.3	16.9	18.0	<0.001
IMA	0.7	0.3	0.8	0.0	2.0	0.25
Modified ACC/AHA lesion class (%)†						<0.001
A	2.5	2.2	1.8	1.1	1.5	
B1	18.7	16.2	13.0	13.1	10.9	
B2	38.3	37.3	33.2	33.7	31.4	
C	40.5	44.3	52.0	52.0	56.2	
Device used (%)						
Balloon angioplasty alone	26.6	26.1	28.9	31.2	24.0	0.38
Stent	68.6	68.0	65.3	64.3	68.0	0.39
Directional atherectomy	2.4	1.6	1.3	0.0	4.0	0.04
Rotational atherectomy	7.0	9.2	10.2	11.0	16.0	0.002
Laser	1.0	1.4	0.9	0.6	0.0	0.56
Angiographic success (%)†	96.0	95.4	95.4	97.8	95.0	0.16
Procedural success (%)	95.2	94.9	92.1	91.6	92.0	0.003
Complete revascularization (%)	55.0	51.4	45.1	28.6	40.0	<0.001

*Difference between the creatinine clearance groups. †Denominator is the number of lesions attempted.

ACC/AHA = American College of Cardiology/American Heart Association; IMA = internal mammary artery; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMCA = left main coronary artery; RCA = right coronary artery.

an important association with one-year mortality (relative risk 1.46) and is nearly as predictive as diabetes mellitus. Moderate renal failure (creatinine clearance 50 ml/min) has a higher association with death than any variable, except for congestive heart failure on presentation. Severe renal failure has the highest association with one-year mortality, in both patients not requiring dialysis (creatinine clearance 30 ml/min) and those on dialysis (relative risk 3.70 and 8.91, respectively). In this study, the use of a stent did not significantly alter the high mortality of patients with renal insufficiency.

Renal failure and cardiovascular risk factors. The association between renal failure and CAD is well established, but the precise mechanisms of this interaction are not clearly understood. Explanations of this interaction include the greater frequency of risk factors, such as diabetes mellitus and hypertension, in patients with renal insufficiency, as well as the effects of renal failure on lipids, oxidative stress, homocysteine and fibrinogen (7–10).

Diabetes mellitus and hypertension are the leading causes of end-stage renal disease (11). Previous studies have demonstrated that the increased prevalence of CAD in patients on dialysis or with chronic renal insufficiency is partly due to the increased presence of these well-established cardiac risk factors (7,12,13). In our study, patients with renal dysfunction had a greater number of diseased coronary vessels. Diabetes mellitus and hypertension were associated with progressive renal dysfunction and also with the extent and severity of CAD. However, when renal failure is treated with renal transplantation, the risk of future cardiovascular events decreases, despite the persistence of these high-risk characteristics (1). Thus, advanced renal dysfunction independently contributes to cardiovascular mortality and increased cardiac risk. In our study, even mild renal insufficiency doubled the risk of death at one year.

Despite the association of diabetes mellitus and hypertension with renal dysfunction, our study did not identify an association with hyperlipidemia (defined as total cholesterol >240 mg/dl). Although total cholesterol levels were not increased with renal dysfunction in our study population, lipid profiles tend to be more atherogenic in patients with renal insufficiency, even when patients are not hyperlipidemic (14,15). Renal dysfunction increases homocysteine and oxidative stress, which enhance the oxidation of low-density lipoprotein, making it even more atherogenic (16,17). Hyperhomocysteinemia also promotes atherosclerotic plaque

Table 3. Adverse Events During the Initial Hospitalization and at One Year

Event	Creatinine Clearance (ml/min) ≥70 (n = 2,687)	50–69 (n = 1,537)	30–49 (n = 899)	<30 (n = 154)	Dialysis (n = 50)	p Value*
In-hospital events (%)						
Death	0.5	0.7	2.3	7.1	6.0	<0.001
Q-wave MI	0.7	0.8	1.8	0.6	0.0	0.03
CABG	1.3	1.4	1.6	0.0	0.0	0.54
Death, Q-wave MI or CABG	2.4	2.7	5.1	7.8	6.0	<0.001
Non–Q-wave MI	4.7	6.1	7.3	4.5	2.0	0.02
Stroke or TIA	0.2	0.5	0.4	0.6	0.0	0.63
Acute renal failure	0.1	0.3	2.0	6.5	0.0	<0.001
Subsequent events at 1 year (%)						
Death	1.5	3.6	7.8	18.3	19.9	<0.001
Q-wave MI	0.2	0.3	0.1	0.0	2.4	0.04
Non–Q-wave MI	1.8	2.4	2.0	7.5	9.9	<0.001
Any MI	2.9	3.5	4.1	8.3	14.4	<0.001
Target vessel revascularization						
PTCA (same lesion)	10.1	10.9	8.7	7.5	12.9	0.41
CABG	5.7	5.5	4.6	3.1	2.5	0.51
Any of the above	16.6	19.2	20.0	29.6	35.3	<0.001
Cumulative events at 1 year (%)						
Death	2.1	4.2	10.0	25.3	24.4	<0.001
Q-wave MI	0.9	1.1	1.9	0.6	2.4	0.02
Non–Q-wave MI	6.3	8.3	9.0	11.9	11.6	0.004
Any MI	8.4	10.3	13.0	14.5	17.8	<0.001
Target vessel revascularization						
PTCA (same lesion)	11.6	12.1	9.9	7.1	12.5	0.24
CABG	7.1	6.6	6.2	3.1	2.4	0.29
Any of the above	23.2	26.2	30.4	38.1	38.5	<0.001

*Difference between the creatinine clearance groups.
CABG = coronary artery bypass graft surgery; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; TIA = transient ischemic attack.

formation by increasing free apolipoprotein(a) (9,18). Thus, regardless of the similar rates of hyperlipidemia between the groups in our study, the atherogenic risk of cholesterol is higher in patients with renal dysfunction.

Percutaneous coronary interventions in patients with chronic renal failure. Management of CAD in patients on dialysis or with mild renal insufficiency is more difficult than that in patients with normal renal function. Medical management in patients with renal dysfunction has been based on therapy shown to be beneficial in other patient populations. Currently, these medications include aspirin, beta-blockers, nitrates, hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) and angiotensin-converting enzyme inhibitors. However, because of the routine exclusion of this patient population from clinical trials, the efficacy of these agents in patients with renal dysfunction is not proven.

Treatment of CAD by PCI in patients with chronic renal failure is feasible but is associated with poor long-term results (3,5). Restenosis rates are as high as 60% to 81% when evaluated by repeat angiography. However, clinical restenosis is not increased in patients with chronic renal failure, compared with patients with normal renal function (19). Thus, the absence of symptoms of restenosis in patients with chronic renal failure may lead to severe silent ischemia and contribute to the high risk of subsequent cardiac events. Other studies have not evaluated the role of stenting in patients with renal insufficiency. In our study population, stenting did not significantly improve survival after a successful intervention. In the only randomized study of dialysis patients comparing an invasive revascularization approach (including both PCI and CABG) with medical therapy, the invasive approach had a clear survival benefit (20). However, the medical therapy consisted of a calcium channel blocker and aspirin, which does not reflect current practice. Moreover, this study only evaluated diabetic patients on dialysis, which further limits the applicability of this study. With regard to milder renal insufficiency, little is known about the clinical outcome of patients after PCI. Such patients have been excluded from randomized studies. Increased restenosis after PCI in patients with mild renal insufficiency may account for part of the increased mortality rate after PCI in this population.

Coronary artery bypass graft surgery in patients with chronic renal failure. Coronary artery bypass graft surgery is also associated with a poor outcome in patients with chronic renal failure, with in-hospital mortality rates as high as 20% (21,22). Even mild renal insufficiency is associated with a doubling of hospital mortality after CABG (23). Coronary artery disease is more diffuse in patients with renal dysfunction, which undoubtedly contributes to the higher complication rate and worse outcomes after interventions.

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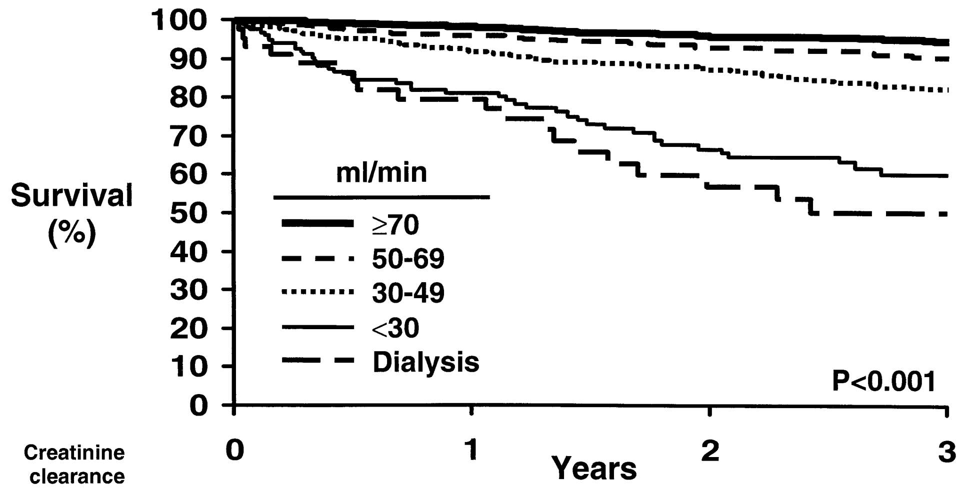
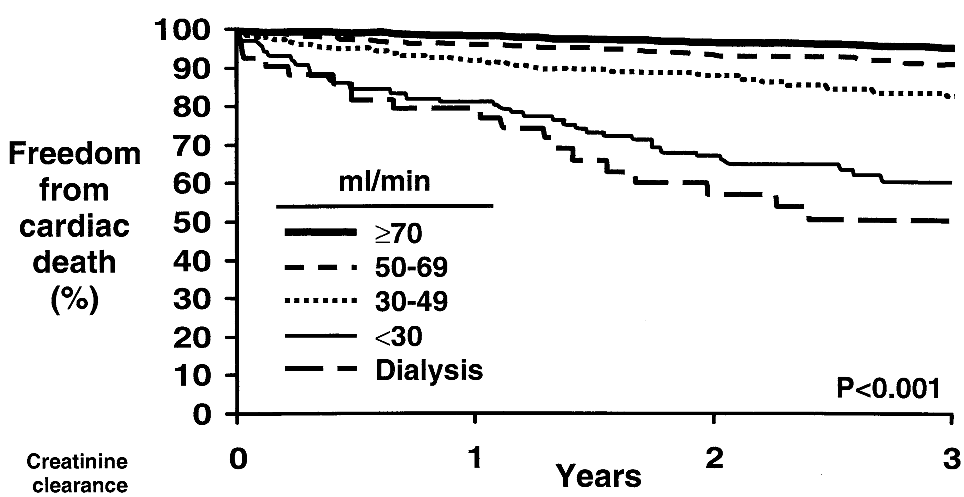


Creatinine clearance group (mL/min)	0	1	2	3
	Number at risk			
Dialysis	46	33	19	14
<30	141	97	64	38
30-49	828	671	470	313
50-69	1,458	1,207	903	641
≥70	2,558	2,159	1,681	1,234

Figure 1. All-cause mortality after successful percutaneous coronary intervention in patients, based on their estimated creatinine clearance.

Newer surgical techniques, such as the minimally invasive direct CABG, have been successful in high-risk patients with renal failure, but the long-term results, compared with other surgical and non-surgical techniques, have yet to be determined (24). When comparing PCI with CABG in patients on dialysis, retrospective studies suggest that CABG improves survival (25,26). Because these studies were retrospective, the bias toward treatment allocation limits the usefulness of these results. No studies have compared CABG or PCI with medical therapy in more mild forms of renal insufficiency. Thus, a better understanding of treatment options in patients with established CAD is necessary in patients with chronic renal failure and renal insufficiency.

Conclusions. Our study demonstrates that after PCI, renal dysfunction is independently associated with mortality and other adverse events during and after PCI, in a dose-dependent manner. This increased risk occurs even when



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50-69	1,458	1,207	903	641
≥70	2,558	2,159	1,681	1,234

Figure 2. Cardiac mortality after successful percutaneous coronary intervention in patients, based on their estimated creatinine clearance.

Table 4. Estimated Risk Ratios for Death in Patients With Successful Percutaneous Revascularization Procedures

Variable	Risk Ratio (95% CI)	p Value
Creatinine clearance, linear		<0.001
Creatinine clearance, quadratic		<0.001
90	1.00 (reference)	
70	1.46 (1.3–1.6)	
50	2.25 (1.8–2.9)	
30	3.70 (2.5–5.5)	
Dialysis	8.91 (5.3–15.0)	<0.001
Age (in 10-year units)	1.11 (1.0–1.3)	0.09
Weight (in 10-kg units)	1.07 (1.0–1.2)	0.08
Diabetes mellitus	1.66 (1.3–2.0)	<0.001
Previous myocardial infarction	1.23 (1.0–1.5)	0.04
Previous stroke or transient ischemic attack	1.29 (1.0–1.65)	0.05
Congestive heart failure on presentation	2.79 (2.2–3.5)	<0.001
Peripheral vascular disease	1.46 (1.2–1.8)	0.002
Multivessel disease	1.57 (1.3–1.9)	<0.001
Right coronary artery intervention	0.72 (0.6–0.9)	0.005
Vein graft intervention	1.39 (1.1–1.8)	0.01
Stents	0.85 (0.7–1.03)	0.10

renal insufficiency is mild, with a doubling of mortality at one year. More marked renal dysfunction exceeds the risk associated with diabetes mellitus and other cardiac risk factors. Further studies are needed to identify the most appropriate treatments of CAD in patients with renal insufficiency.

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REFERENCES

1. Wolfe RA, Port FK, Webb RL, et al. Excerpts from the United States Renal Data System, 1998 annual data report: V. Patient mortality and survival. Am J Kidney Dis 1998;32 Suppl 1:S69–80.
2. Jones CA, McQuillan GM, Kusek JW, et al. Serum creatinine levels in the U.S. population: third National Health and Nutrition Examination Survey. Am J Kidney Dis 1998;32:992–9.
3. Kahn JK, Rutherford BD, McConahay DR, Johnson WL, Giorgi LV, Hartzler GO. Short- and long-term outcome of percutaneous transluminal coronary angioplasty in chronic dialysis patients. Am Heart J 1990;119:484–9.
4. Koyanagi T, Nishida H, Kitamura M, et al. Comparison of clinical outcomes of coronary artery bypass grafting and percutaneous transluminal coronary angioplasty in renal dialysis patients. Ann Thorac Surg 1996;61:1793–6.
5. Schoebel FC, Gradaus F, Ivens K, et al. Restenosis after elective coronary balloon angioplasty in patients with end-stage renal disease: a case-control study using quantitative coronary angiography. Heart 1997;78:337–42.
6. Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31–41.
7. Cheung AK, Sarnak MJ, Yan G, et al. Atherosclerotic cardiovascular disease risks in chronic hemodialysis patients. Kidney Int 2000;58:353–62.
8. Kanani PM, Sinkey CA, Browning RL, Allaman M, Knapp HR, Haynes WG. Role of oxidant stress in endothelial dysfunction produced by experimental hyperhomocyst(e)inemia in humans. Circulation 1999;100:1161–8.
9. Herrmann W, Quast S, Ellgass A, et al. An increased serum level of free Apo(a) in renal patients is more striking than that of Lp(a) and is influenced by homocysteine. Nephron 2000;85:41–9.
10. Romanic AM, Arleth AJ, Willette RN, Ohlstein EH. Factor XIIIa cross-links lipoprotein(a) with fibrinogen and is present in human atherosclerotic lesions. Circ Res 1998;83:264–9.
11. Wolfe RA, Port FK, Webb RL, et al. Excerpts from the United States Renal Data System, 1998 annual data report: II. Incidence and prevalence of ESRD. Am J Kidney Dis 1998;32 Suppl 1:S40–53.
12. He J, Whelton PK. Elevated systolic blood pressure as a risk factor for cardiovascular and renal disease. J Hypertens 1999;17 Suppl S:7–13.
13. Keane WF, Collins AJ. Influence of co-morbidity on mortality and morbidity in patients treated with hemodialysis. Am J Kidney Dis 1994;24:1010–8.
14. Kiamk E, Solski J, Janicka L, Zagojska M. Lipid and lipoprotein ratios as risk factors of atherosclerosis in patients with chronic renal insufficiency. Int Urol Nephrol 1999;31:263–7.
15. Shoji T, Nishizawa Y, Kawagishi T, et al. Atherogenic lipoprotein changes in the absence of hyperlipidemia in patients with chronic renal failure treated by dialysis. Atherosclerosis 1997;131:229–36.
16. Schettler V, Wieland E, Methe H, Schuff-Werner P, Muller GA. Oxidative stress during dialysis: effect on free radical scavenging enzyme (FRSE) activities and glutathione (GSH) concentration in granulocytes. Nephrol Dial Transplant 1998;13:2588–93.
17. Gesquiere L, Loreau N, Minnich A, Davignon J, Blache D. Oxidative stress leads to cholesterol accumulation in vascular smooth muscle cells. Free Radic Biol Med 1999;27:134–45.
18. Dardik R, Varon D, Tamarin I, et al. Homocysteine and oxidized low density lipoprotein enhanced platelet adhesion to endothelial cells under flow conditions: distinct mechanisms of thrombogenic modulation. Thromb Haemost 2000;83:338–44.
19. Le Feuvre C, Dambrin G, Helft G, et al. Comparison of clinical outcome following coronary stenting or balloon angioplasty in dialysis versus non-dialysis patients. Am J Cardiol 2000;85:1365–8.
20. Manske CL, Wang Y, Rector T, Wilson RF, White CW. Coronary revascularisation in insulin-dependent diabetic patients with chronic renal failure. Lancet 1992;340:998–1002.
21. Labrousse L, de Vincentiis C, Madonna F, Deville C, Roques X, Baudet E. Early and long-term results of coronary artery bypass grafts in patients with dialysis-dependent renal failure. Eur J Cardiothorac Surg 1999;15:691–6.
22. Rostand SG, Kirk KA, Rutsky EA, Pacifico AD. Results of coronary artery bypass grafting in end-stage renal disease. Am J Kidney Dis 1988;12:266–70.
23. Anderson RJ, O'Brien M, MaWhinney S, et al. Renal failure predisposes patients to adverse outcome after coronary artery bypass surgery: VA Cooperative Study 5. Kidney Int 1999;55:1057–62.
24. Izzat MB, Yim AP, El-Zufari MH. Minimally invasive left anterior descending coronary artery revascularisation in high-risk patients with three-vessel disease. Ann Thorac Cardiovasc Surg 1998;4:205–8.
25. Simsir SA, Kohlman-Trigoboff D, Flood R, Lindsay J, Smith BM. A comparison of coronary artery bypass grafting and percutaneous transluminal coronary angioplasty in patients on hemodialysis. Cardiovasc Surg 1998;6:500–5.
26. Koyanagi T, Nishida H, Kitamura M, et al. Comparison of clinical outcomes of coronary artery bypass grafting and percutaneous transluminal coronary angioplasty in renal dialysis patients. Ann Thorac Surg 1996;61:1793–6.