Numerous randomized trials have successfully demonstrated the beneficial effects of early percutaneous coronary intervention (PCI) for patients with acute myocardial infarction (AMI). However, most patients with complications of renal insufficiency were excluded from randomized trials; therefore, the clinical effects of PCI for these patients have not been determined. In the past decade, patients with end-stage renal disease were associated with a decreased procedural success rate. The development of device technology has provided better procedural outcomes after PCI in such patients; however, little is known regarding the impact of varying degrees of renal insufficiency on the success rate of emergency PCI in patients with AMI.

As noted in a recent study, the success of PCI is a prime determinant of the clinical outcome of patients with AMI. However, renal insufficiency is associated with a worse clinical outcome in patients with coronary artery disease including AMI. It is also unclear whether successful PCI provides a better prognosis of AMI even in patients with renal insufficiency.

The aims of this study were: (1) to determine the association between renal insufficiency and the risk of unsuccessful primary PCI in AMI patients; and (2) to evaluate the correlation between unsuccessful primary PCI and the clinical outcomes at various levels of renal function.

**Methods**

**Study Population**

The subjects of the present study were selected from the Heart Institute of Japan Acute Myocardial Infarction Registry (HIJAMI) database. Full details of the HIJAMI registry have been described elsewhere. In brief, HIJAMI is a multicenter prospective cohort of consecutive patients with AMI who were admitted within 48 h after the onset of symptoms. Between January 1999 and July 2001, 3,021 consecutive patients from 17 participating hospitals in Japan were registered. As HIJAMI was meant for observational purposes, treatment strategies, such as drug therapies and early reperfusion treatment, were used at the discretion of the physician responsible at each hospital. Clinical and angiographic data, including the patients’ demographics, coronary risk factors, therapeutic modalities, complications, number of diseased vessels, infarct-related arteries, PCI strategies, laboratory data and in-hospital outcomes were prospectively collected using a standardized case report form. Serum creatinine concentrations and C-reactive protein were measured at each site immediately after admis-
Follow-up data were researched at each site by medical records or telephone contact with the patients. Of 3,021 consecutive patients from the HIJAMI, primary PCI was attempted in 1,755 patients (58.1%) within 24 h from the onset of symptoms. Thirty-four patients (1.9%) were excluded from analyses because of missing data for serum creatinine and/or C-reactive protein (6 because of early death, and 28 with no explanation provided). Fifteen patients (0.9%) undergoing regular dialysis were also excluded. Thus, the remaining 1,706 patients were included in the present study.

Definitions

Angiographic findings were assessed by visual interpretation and consensus readings among 2 or more cardiologists at each hospital site. Diseased vessel was defined as the presence of >50% diameter stenosis in the major coronary artery. Successful PCI was defined as achieving Thrombolysis In Myocardial Infarction flow grade 3 in the infarct-related artery.

Informed Consent

This study was approved by the local ethics committees of all participating hospitals, and informed consent was obtained from all enrolled patients.

Statistical Analysis

All analyses were performed using SAS software (version 8.2; SAS, Cary, NC, USA). Continuous variables are presented as the mean±standard deviation or the median with interquartiles, and categorical variables as frequency.

According to the chronic kidney disease practice guide (revised in May 2007) by the Japanese Society of Nephrology, renal functions were assessed using glomerular filtration rate (GFR) estimated by the modification of diet in renal disease equation modified by the Japanese coefficient:

\[
\text{Estimated GFR} = 0.741 \times 175 \times (\text{age})^{-0.203} \times (\text{serum creatinine [mg/dl]})^{-1.154}
\]

For women, the product of this equation was multiplied by a correction factor of 0.742.

For analyses, the patients were divided into 3 groups according to their estimated GFR on admission: ≥60, 30–60, and <30 ml·min⁻¹·1.73 m⁻². Comparisons of baseline clinical and angiographic characteristics among the 3 groups were made by means of 1-way analysis of variance for continuous variables, and by Pearson’s chi-square test for categorical variables. Comparison of Killip class, pre-hospital delay time, serum creatinine concentration, tertiles of serum C-reactive protein and the number of diseased vessels was made using the Kruskal–Wallis test.

Logistic regression models were used to identify the clinical and angiographic variables correlated with unsuccessful PCI. Univariate correlations with p-values of <0.1 were entered into multivariate models to determine the independent correlations to unsuccessful PCI. A comparison of in-hospital and post-discharge mortality between patients with successful compared with unsuccessful PCI was performed using univariate logistic regression models and Kaplan–Meier curves with log-rank test, respectively.

Multivariate Cox proportional hazards models were used to evaluate the correlations to death from any cause during the long-term follow up. All tests of significance were 2-tailed, and a p-value of <0.05 was considered statistically significant.

Results

Clinical Characteristics

Baseline clinical characteristics of the patients stratified by estimated GFRs are given in Table 1. Patients with a lower GFR were older, had a higher prevalence of hyper-
tension and previous myocardial infarction, had a higher Killip class, had a higher serum C-reactive protein concentration on admission and there was a higher proportion of females. Cigarette smoking was less frequent in patients with decreased GFR. The prevalence of diabetes mellitus did not differ among the 3 groups.

Angiographic and Procedural Characteristics

The GFRs correlated highly with the prevalence of multivessel disease and left main coronary stenosis. Regarding therapeutic strategy, the use of stent was similar in each group (Table 2).

Incidences and Correlates of Unsuccessful PCI

The overall incidence of unsuccessful PCI was 5.2%. Of 89 unsuccessful PCI, 70 provided an explanation. The failure of crossing the guide wire was the most common reason (40%) for an unfavorable result, followed by slow or no reflow on the final angiogram (27%).

The univariate and multivariate correlation of variables with unsuccessful PCI are listed in Table 3. The incidence of unsuccessful PCI was significantly higher in patients with a GFR of 30–60 ml·min⁻¹·1.73 m⁻² compared with those with a GFR of ≥60 ml·min⁻¹·1.73 m⁻². Univariate analysis also indicated that age ≥80 years, Killip class ≥2, a longer pre-hospital delay, the presence of left main stenosis and treatment of the right coronary artery had potential predictive value for unsuccessful PCI. In multivariate analysis, a GFR of 30–60 ml·min⁻¹·1.73 m⁻² or <30 ml·min⁻¹·1.73 m⁻², a longer pre-hospital delay and female gender were significantly associated with unsuccessful PCI.
delay and the presence of left main stenosis remained as independent correlates of unsuccessful PCI.

A Comparison of In-Hospital Clinical Outcomes of Patients According to Estimated GFR and PCI Results

The mean length of hospital stay was 23 days and in-hospital death was observed in 107 patients (6.3%) of the study population. The mortality rates of patient groups with a GFR \(\geq 60\) ml·min\(^{-1}\)·1.73 m\(^{-2}\), \(30-60\) ml·min\(^{-1}\)·1.73 m\(^{-2}\) or \(<30\) ml·min\(^{-1}\)·1.73 m\(^{-2}\) were 2.5%, 9.3% and 28.9%, respectively. The mortality rates of patients with successful compared with unsuccessful PCI are presented in Table 4. Patients with successful PCI had a significantly lower mortality rate compared with those with unsuccessful PCI in the GFR \(\geq 60\) ml·min\(^{-1}\)·1.73 m\(^{-2}\) group and the GFR of \(30-60\) ml·min\(^{-1}\)·1.73 m\(^{-2}\) group. In the GFR \(<30\) ml·min\(^{-1}\)·1.73 m\(^{-2}\) group, the difference in in-hospital mortality rates between patients with successful and unsuccessful PCI was not statistically significant.

A similar trend was observed regarding complications during hospitalisation (Table 4).

---

Table 4 In-Hospital Outcomes of Patients According to Estimated GFR and PCI Results

<table>
<thead>
<tr>
<th>Estimated GFR</th>
<th>PCI</th>
<th>Unsuccessful PCI</th>
<th>Successful PCI</th>
<th>p value</th>
<th>Unsuccessful PCI</th>
<th>Successful PCI</th>
<th>p value</th>
<th>Unsuccessful PCI</th>
<th>Successful PCI</th>
<th>p value</th>
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<tbody>
<tr>
<td>(\geq 60) ml·min(^{-1})·1.73 m(^{-2})</td>
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<td>Successful PCI</td>
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<tr>
<td>Unsuccessful PCI*</td>
<td>2.04</td>
<td>0.87–4.81</td>
<td>0.10</td>
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<td>(30-60) ml·min(^{-1})·1.73 m(^{-2})</td>
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<tr>
<td>Successful PCI*</td>
<td>1.51</td>
<td>1.11–2.06</td>
<td>0.008</td>
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<tr>
<td>Unsuccessful PCI*</td>
<td>2.07</td>
<td>1.19–3.62</td>
<td>0.01</td>
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<td>(&lt;30) ml·min(^{-1})·1.73 m(^{-2})</td>
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<tr>
<td>Successful PCI*</td>
<td>2.69</td>
<td>1.72–4.22</td>
<td>(&lt;0.001)</td>
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<tr>
<td>Unsuccessful PCI*</td>
<td>10.07</td>
<td>4.91–20.5</td>
<td>(&lt;0.001)</td>
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<tr>
<td>Age (per 10-year)</td>
<td>1.77</td>
<td>1.54–2.04</td>
<td>(&lt;0.001)</td>
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<tr>
<td>Female gender</td>
<td>0.70</td>
<td>0.52–0.93</td>
<td>0.02</td>
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<tr>
<td>Killip class (2)</td>
<td>3.92</td>
<td>2.99–5.15</td>
<td>(&lt;0.001)</td>
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<tr>
<td>Left main PCI</td>
<td>5.10</td>
<td>2.99–8.70</td>
<td>(&lt;0.001)</td>
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</table>

*The adjusted hazard ratios were calculated using patients who had a GFR of \(\geq 60\) ml·min\(^{-1}\)·1.73 m\(^{-2}\) and with successful PCI as the reference group.

Abbreviations as in Tables 1.3.
Long-Term Follow-up and Correlates of Mortality

The follow-up rate at 2 years was 98%, and the mean follow-up period of the study population was 29 months. The Kaplan–Meier survival curves according to the PCI results and estimated GFRs are shown in Fig 1. The survival rates at 24 months of patients with successful compared with unsuccessful PCI were 94% vs 82% in the GFR ≥60 ml·min⁻¹·1.73 m⁻² group (p=0.03), 84% vs 73% in the GFR 30–60 ml·min⁻¹·1.73 m⁻² group (p=0.004), and 63% vs 10% in the GFR <30 ml·min⁻¹·1.73 m⁻² group (p=0.002).

The adjusted hazard ratios for death from any cause are shown in Table 5. In patients with successful PCI, a decreased GFR was associated with an increased mortality in a stepwise fashion. In the GFR <30 ml·min⁻¹·1.73 m⁻² group, the risk of mortality was markedly high in patients with unsuccessful PCI. Compared to patients with successful PCI, patients with unsuccessful PCI had a nearly fourfold increase in mortality in this lowest GFR group. In the GFR ≥60 ml·min⁻¹·1.73 m⁻² or 30–60 ml·min⁻¹·1.73 m⁻² groups, differences in the hazard ratios between successful and unsuccessful PCI were modest.

Discussion

The present study demonstrated 2 principal findings: (1) both estimated GFR on admission of 30–60 ml·min⁻¹·1.73 m⁻² and <30 ml·min⁻¹·1.73 m⁻² are independently associated with unfavorable results of emergency PCI in patients with AMI; and (2) compared with patients undergoing successful PCI, unsuccessful PCI was associated with strikingly poor long-term survival in patients with GFR <30 ml·min⁻¹·1.73 m⁻².

Correlates of Unsuccessful PCI

Several previous studies have tried to predict the suboptimal PCI outcome from pre-procedural clinical and angiographic variables in patients with AMI who participated in randomized trials.19,20 These studies identified factors such as older age, symptom onset to emergency room presentation, increased heart rate and left ventricular ejection fraction as predictors for unsuccessful PCI. In the present study, based on ‘real-world’ registry data, a similar variable such as pre-hospital delay was found to be correlated to unsuccessful PCI. Also, the present study shows the novel finding that pre-procedural estimated GFR has a predictive value for unsuccessful PCI.

In the past decade, a lower success rate of conventional balloon angioplasty for patients with coronary artery disease on regular dialysis has been reported.4–6 After the introduction of intracoronary stents and rotational coronary atherectomy, the success rate of PCI has increased, and several studies have shown that the success rate of PCI in patients undergoing regular dialysis was as high as that of patients with normal renal function.7–9,21

In general, the success rate of PCI depends mainly on the lesion morphology of the target vessel, and it is well known that patients undergoing long-term dialysis often have complex lesion morphology. In the present study, a lower GFR was associated with a lower success rate of emergency PCI. A past report shows that patients with renal failure are more likely to have severe atherosclerosis than patients without renal failure, regardless of dialysis dependence.22 Reis and colleagues investigated 784 women with chest pain and found that mild renal insufficiency was associated with angiographic severity of coronary artery disease even in patients with a serum Cr level of <1.9 mg/dl.23 In fact, in the present study population, the prevalence of multivessel coronary stenoses in patients with GFR <60 ml·min⁻¹·1.73 m⁻² was greater than that of patients with GFR ≥60 ml·min⁻¹·1.73 m⁻². Thus, the GFR could be an indicator for severity of coronary atherosclerosis. Although the success rate of PCI has increased in those patients with coronary artery disease, differences in the severity of atherosclerosis may produce differences in the success rates of PCI under emergency conditions, such as AMI. This assumption might be supported by the fact that the most common cause of unsuccessful procedure was failure of crossing the guide wire.

Prognostic Importance of Successful PCI in Patients With Renal Insufficiency

Numerous randomized trials have shown the efficacy of early PCI for patients with AMI.1–3 However, as many of the patients with renal insufficiency were excluded in such trials, the beneficial effect of PCI in patients with renal insufficiency has not been determined. Therefore, cardiologists have made an empirical decision about the use of PCI in such patients. Also, the success of PCI is an important determinant of clinical outcome in patients with AMI who were selected for randomized trials.10 However, the prognostic importance of PCI success in patients with renal failure was not known.

The registry data of the present study have shown that not only severe, but also mild to moderate renal insufficiency are associated with a poor prognosis. This finding is in agreement with previous studies.2,24,25 Moreover, we have found that the long-term survival of patients after unsuccessful PCI were poorer than that of patients after successful PCI, especially in patients with GFR <30 ml·min⁻¹·1.73 m⁻². The patient group with a lower GFR were older, and it is known that aging strongly affects renal function and mortality. Also, the decreased GFR was associated with other comorbid conditions, such as a higher Killip class and left main coronary occlusion. However, even after adjustment for these conventional risk factors, the negative prognostic impact of unsuccessful PCI remained markedly strong in the GFR <30 ml·min⁻¹·1.73 m⁻² group.

Mechanisms by which renal insufficiency decreases long-term outcomes in patients with AMI are multifactorial. Factors associated with renal insufficiency such as anemia, elevation of pro-inflammatory cytokines, oxidative stress, endothelial dysfunction and conditions promoting coagulation, may contribute to the progression of arteriosclerosis and a worse prognosis. Underuse of ACE inhibitors, blockers and statin might also be related to a reduced survival rate in patients with renal insufficiency.12

In patients undergoing PCI, radio contrast toxicity may contribute to a worse clinical outcome in patients with AMI. Rihal et al have reported that an incidence of acute renal failure in patients with mild and severe renal insufficiency was 2.5% and >20%, respectively.26 Moreover, we have also reported an in-hospital death rate that was threefold greater in patients with acute renal failure compared with those patients without.27

Also, recent studies have suggested that the serum creatinine concentration is a prognostic indicator of AMI.11,16,29,30 Because serum creatinine reflects renal perfusion, a lower estimated GFR, as well as an elevated serum creatinine, sometimes indicates not only pre-existent renal impairment, but also acute hemodynamic instability.31 Thus, a higher mortality in patients with decreased GFR after PCI

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is thought to be largely because of the deterioration of renal function and/or acute circulatory failure. In patients after unsuccessful PCI, the deterioration of left ventricular function multiplies the impact of these risk factors. Therefore, the success of PCI has critical importance in patients with a decreased GFR.

**Clinical Implications**

Patients with a decreased GFR on admission were more likely to have an unfavorable PCI outcome than patients with a normal GFR. In order to deal with such high-risk patients, selection of the optimal arm for revascularization is needed. In some cases with multivessel coronary involvement and hemodynamic instability, complete revascularization by coronary artery bypass grafting may be superior to PCI.

In the use of catheter-based revascularization, to decrease the risk of contrast-induced nephropathy and subsequent mortality, minimizing the dose of contrast medium also should be important, as well as angiographic PCI success. Moreover, clinicians should consider adjunctive therapies, such as the aggressive use of temporary hemofiltration and administration of N-acetylcysteine.

With regard to medications after revascularization, the appropriate use of ACE inhibitors, ß-blockers and statins may improve the long-term outcome even for those patients with renal insufficiency.

Immediate risk stratification using estimated GFR and proper adjunctive medications have potential benefits for improving clinical outcomes of these high-risk patients with AMI.

**Study Limitations**

The present study was based on a multicenter registry database. The angiographic data were interpreted by 50 or more physicians from 17 hospitals. However, there was no way to determine interobserver differences among these variables.

The study subjects included in the study were only those patients who had received attempted emergency PCI. Of 3,021 patients of the entire HIJAMI cohort, 2,749 patients underwent successful primary percutaneous coronary intervention for acute myocardial infarction, and 2,749 patients had GFR ≤ 30 ml·min⁻¹·1.73 m⁻². The patients with decreased GFR were treated less often with PCI; therefore, there might be a selection bias and unidentified confounders that increased risk in those patients.

**Conclusions**

Decreased GFR on presentation was associated with the risk of unsuccessful primary PCI. Moreover, unsuccessful PCI was associated with strikingly poor long-term survival in patients with GFR <30 ml·min⁻¹·1.73 m⁻². Steady success is essential when using PCI in such a high-risk population.

**Acknowledgment**

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Appendix

HIJAMI Investigators and Committees

Executive Committee: Hiroshi Kanasuki (Chairman), Kazuo Haze, Takashi Honda, Tetsuya Sumiyoshi and Toshinobu Horie.


Participating Hospitals of HIJAMI Registry

Sendai Cardiovascular Center (Miyagi), Saitama Cardiovascular and Respiratory Center (Saitama), Saiseikai Kurihashi Hospital (Saitama), Shin-matsudo-Chuo General Hospital (Chiba), Tokyo Women’s Medical University (Tokyo), The Sakakibara Heart Institute (Tokyo), Fuchu Metropolitan Hospital (Tokyo), Kosei General Hospital (Tokyo), Nishiarai Hospital (Tokyo), NTT East Kanto Medical Center (Tokyo), Ebara Metropolitan Hospital (Tokyo), Shiseikai Second Hospital (Tokyo), Yokohama National Hospital (Kanagawa), Eastern Japan Cardiovascular Medical Center (Kanagawa), Seirei Hamamatsu General Hospital (Shizuoka), Osaka City General Hospital (Osaka) and Saiseikai Kumamoto Hospital (Kumamoto).