

Reperfusion Strategy and Mortality in ST-Elevation Myocardial Infarction among Patients with and without Impaired Renal Function

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Abstract

Introduction: Several randomised controlled trials have demonstrated better outcomes with primary percutaneous coronary intervention (PCI) over fibrinolytic therapy in the treatment of patients with ST-segment elevation myocardial infarction (STEMI) and normal renal function. Whether this benefit extends to patients with impaired renal function is uncertain. **Materials and Methods:** We studied 1672 patients with STEMI within 12 hours of symptom onset who were admitted to 2 major public hospitals in Singapore from 2000 to 2002. All patients received either upfront fibrinolytic or PCI as determined by the attending cardiologist. Serum creatinine was measured on admission and the glomerular filtration rate (GFR) was determined using the Modification of Diet in Renal Disease equation. The impact of reperfusion strategy on 30-day mortality was then determined for patients with $\text{GFR} \geq 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ and $\text{GFR} < 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$. **Results:** The mean age was 56 ± 12 years (85% male) and mean GFR was $81 \pm 30 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$. Unadjusted 30-day mortality rates for fibrinolytic-treated vs primary PCI-treated patients were 29.4% vs 17.9%, $P < 0.05$, in the impaired renal function group and 5.4% vs 3.1%, $P < 0.05$, in the normal renal function group. After adjusting for covariates, primary PCI was associated with a significantly lower mortality in the normal renal function group [odds ratio (OR), 0.41; 95% confidence interval (CI), 0.19-0.89] but not in the impaired renal function group [OR, 0.70; 95% CI, 0.31-1.60]. **Conclusions:** Primary PCI was associated with improved 30-day survival among patients with normal renal function but not among those with impaired renal function. Randomised trials are needed to study the relative efficacy of both reperfusion strategies in patients with impaired renal function.

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Key words: Acute coronary syndrome, Fibrinolysis, Kidney disease, Primary angioplasty

Introduction

Randomised controlled trials have demonstrated better outcomes with primary percutaneous coronary intervention (PCI) over fibrinolytic therapy in the treatment of ST-segment elevation myocardial infarction (STEMI) patients with normal renal function.¹ Practice guidelines consider primary PCI as the preferred reperfusion strategy for patients presenting with STEMI, conditional upon timely performance of the PCI procedure.^{2,3}

However, among patients with impaired renal function presenting with STEMI, uncertainty remains as to which reperfusion strategy achieves superior outcomes. Although

there are no published randomised studies comparing primary PCI vs fibrinolytic therapy among STEMI patients with impaired renal function, several observational studies have analysed treatment outcomes associated with either reperfusion strategy in this population.^{4,5} These retrospective studies produced conflicting results – a multicentre retrospective study in Israeli showed a trend towards better survival with fibrinolysis compared with primary PCI,⁴ whereas a larger multinational study by the GRACE investigators showed no overall difference in adjusted outcomes with either primary PCI or fibrinolysis, but identified patients with moderate renal dysfunction as a subgroup in which clinical outcomes favoured primary PCI.⁵

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We sought to compare the differential effect of fibrinolysis vs primary PCI on 30-day mortality among STEMI patients with and without impaired renal function. We also sought to determine the prevalence of impaired renal function and patterns of care in a contemporary cohort of STEMI patients receiving reperfusion therapy at 2 large public hospitals in Singapore. We hypothesised that patients with renal dysfunction undergoing either primary PCI or fibrinolysis would encounter treatment equipoise, when considering the endpoint of all-cause mortality. Anticipation of this negative treatment effect is based on the higher expected risk of contrast-induced nephropathy with primary PCI vs the higher expected bleeding risk with fibrinolysis in this population.

Materials and Methods

We studied 1672 patients with STEMI who were admitted to 2 major public hospitals in Singapore, the National University Hospital and Tan Tock Seng Hospital, from 2000 to 2002. All data were collected by trained coordinators from the Singapore Cardiac Databank for inclusion in the Singapore Myocardial Infarction Registry, using a standardised case report form. The rationale and methods of this registry have been previously published.⁶ Briefly,

potential cases of acute MI are identified from discharge summaries (based on the International Classification of Diseases, 9th revision, codes 410 to 414), cardiac enzyme results, the Registry of Births and Deaths, and post-mortem reports. Patients are classified according to a local modification of the Glasgow MONICA algorithm under one of 9 diagnostic categories, as previously reported.⁶

For this analysis, we included cases of clinically diagnosed Q-wave or STEMI who received either fibrinolytic or primary PCI within 12 hours of symptom onset. We excluded patients with non-STEMI ($n = 3898$), patients presenting beyond 12 hours ($n = 263$) and patients who presented within 12 hours but did not receive reperfusion therapy ($n = 126$). The choice of reperfusion therapy was determined by the treating physician. Serum creatinine was measured on admission and the glomerular filtration rate (GFR) was determined using the Modification of Diet in Renal Disease equation,⁷ which has been validated in various Asian populations.⁸⁻¹² The impact of reperfusion strategy on 30-day mortality was then determined for patients with $\text{GFR} \geq 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ and $\text{GFR} < 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$. We selected a GFR cut-off point of $60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ because of multiple prior studies showing consensus on a threshold effect of sharply increased mortality below this level of renal function in acute coronary syndromes.¹³⁻¹⁷

All statistical analyses were carried out using the Statistical Package for Social Sciences version 11.5 (SPSS Inc, Chicago, IL, USA). Associations between categorical variables were assessed using Pearson's chi-square or Fisher's Exact tests. Adjusted 30-day mortality odds ratios (ORs) were generated with multiple logistic regression using the following covariates: age, sex, presence of diabetes mellitus, Killip class, systolic blood pressure, pulse rate, electrocardiographic localisation of infarction (anterior vs inferior), peak CKMB mass levels, admission serum creatinine and haemoglobin levels. Statistical significance was set at $P < 0.05$.

Results

The mean age was 56 ± 12 years, 85% were male and the mean GFR was $81 \pm 30 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$. Of the 1672 patients studied, 19.8% had impaired renal function. Compared to patients with normal renal function, patients with impaired renal function were older, more likely to be hypertensive and diabetic, less

Table 1. Baseline Differences

Variable	GFR <60 (n = 331)		GFR ≥60 (n = 1341)		P
	PCI (n = 117)	Fibrinolytic (n = 214)	PCI (n = 587)	Fibrinolytic (n = 754)	
Age (y)	62.5 ± 10.8	64.69 ± 10.3	53.0 ± 10.8	55.0 ± 11.2	<0.001
Gender (female) (%)	14.5	33.6	13.8	11.1	<0.001
GFR	46.1 ± 12.4	45.5 ± 12.6	90.8 ± 33.7	88.5 ± 20.7	<0.001
Hypertension (%)	61.7	61.5	42.8	46.2	<0.001
Diabetes mellitus (%)	26.5	38.3	24.7	28.4	0.002
Smoking (%)	40.2	34.1	54	57.7	<0.001
Hyperlipidaemia (%)	38.3	30.8	34.8	34.9	0.577
Prior myocardial infarction (%)	11.1	12.1	7.3	8.4	0.134
Heart failure (Killip ≥II) (%)	38.5	54.7	22.8	36.3	<0.001
Anterior myocardial infarction (%)	39.3	42.1	46	39	0.072
Peak creatine kinase (U/L)	4952 ± 5071	3719 ± 3685	3436 ± 2755	3278 ± 2298	<0.001
Systolic blood pressure (mm Hg)	125.3 ± 32.3	123.5 ± 27.9	126.4 ± 74.7	128.2 ± 23.8	0.102
Diastolic blood pressure (mm Hg)	75.5 ± 20.1	75.2 ± 18.0	74.68 ± 14.1	78.5 ± 16.4	<0.001
Heart rate (beats per min)	77.4 ± 19.1	80.0 ± 24.1	77.1 ± 16.7	79.95 ± 18.2	0.028
Haemoglobin (g/L)	14.3 ± 6.0	13.7 ± 2.0	14.5 ± 1.7	15.1 ± 7.5	0.008

GFR: glomerular filtration rate in $\text{mL min}^{-1} 1.73 \text{ m}^{-2}$; PCI: percutaneous coronary intervention

Table 2. Treatment Differences

Treatment	GFR <60		GFR ≥60		P
	PCI (n = 117)	Fibrinolytic (n = 214)	PCI (n = 587)	Fibrinolytic (n = 754)	
Angiography	100	42.1	100	68.7	<0.001
PCI	90.1	21.6	95.3	42.1	<0.001
Aspirin	89.7	91.6	95.2	94.2	0.059
Thienopyridine	88	22.9	92.3	25.5	<0.001
CABG	0.9	2.8	0.5	1.7	0.061
Beta-blockers	69.2	66.8	83.3	82.9	<0.001
Calcium channel blocker	6.8	6.1	2.7	4.2	0.067
ACE-inhibitors/ ARB	65.8	50.9	70	60.9	<0.001
GP 2b-3a inh	33.3	0	30.5	1.5	<0.001
Statin	68.4	69.2	83	83.2	<0.001
Diuretics	35.9	39.3	15.8	26.5	<0.001
Inotropes	28.2	32.7	12.1	13.8	<0.001

CABG: coronary artery bypass graft; GFR: glomerular filtration rate in mL min⁻¹ 1.73 m⁻²; GP 2b-3a inh: glycoprotein IIb-IIIa inhibitors; PCI: percutaneous coronary intervention

likely to be active smokers, and more likely to have had a prior MI (Table 1). They were also more likely to have acute heart failure at presentation and to have higher peak creatine kinase levels, despite showing a trend towards a lower incidence of anterior MI.

Among patients with impaired renal function, women were much more likely than men to receive fibrinolytic therapy instead of primary PCI as the initial reperfusion strategy, while in the normal renal function group, women were slightly more likely than men to receive primary PCI as the primary reperfusion strategy (Table 1). There was also a trend towards higher use of fibrinolytic therapy instead of primary PCI in patients with anterior MI among patients with impaired renal function, with the opposite trend seen among patients with normal renal function. Moreover, patients in the impaired renal function cohort who received upfront fibrinolytic therapy had lower haemoglobin levels compared with patients with impaired renal function who received upfront primary PCI, while patients with normal renal function who received fibrinolytic therapy had higher haemoglobin levels compared to patients with normal renal function who received primary PCI.

Compared to patients with normal renal function, patients with impaired renal function were more likely to receive diuretics and inotropes but less like to receive aspirin,

thienopyridines, beta-blockers, statins and angiotensin converting enzyme inhibitors or angiotensin receptor blockers (Table 2). Approximately 40% of patients with impaired renal function who received upfront fibrinolytic therapy underwent subsequent angiography compared to approximately 70% of patients with normal renal function who received upfront fibrinolytic therapy. While the rates of percutaneous revascularisation were high in both the normal and impaired renal function groups who underwent primary PCI, patients with impaired renal function who received upfront fibrinolytic therapy were two times less likely to undergo subsequent percutaneous revascularisation compared to patients with normal renal function who received upfront fibrinolytic therapy.

The unadjusted 30-day mortality rate was 9%, 4% and 25% for the overall study population, the cohort with normal renal function and the cohort with impaired renal function respectively. As shown in Figure 1, there was a stepwise increase in 30-day mortality with worsening GFR. Mortality was lowest at 3.1% in the group with GFR >90 mL min⁻¹ 1.73 m⁻², and highest at 40.0% in the group with GFR <15 mL min⁻¹ 1.73 m⁻²; the largest stepwise increase in mortality was observed as GFR decreased from 60-90 mL min⁻¹ 1.73 m⁻² to 30-60 mL min⁻¹ 1.73 m⁻², with patients in the latter GFR stratum experiencing 5 times the mortality of patients in the GFR 60-90 mL min⁻¹ 1.73 m⁻² group.

The unadjusted 30-day mortality rates for fibrinolytic-treated vs primary PCI-treated patients were 29.4% vs 17.9% in the impaired renal function group and 5.4% vs 3.1% in the normal renal function group (Fig. 2). The majority of deaths were due to cardiovascular causes (non-cardiovascular death rates 0.4% vs 0.8% in the impaired renal function group and 0.2% vs 0% in the normal renal function group). After adjusting for covariates, the OR comparing mortality rates among patients treated with primary PCI vs fibrinolytic therapy did not reach statistical significance for the impaired renal function group, but remained statistically

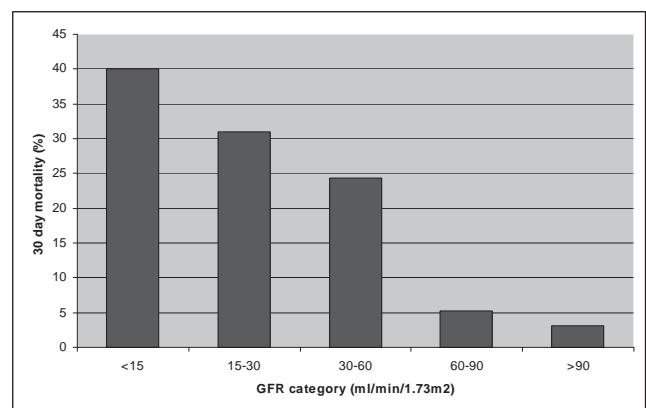


Fig. 1. Thirty-day mortality according to glomerular filtration rate category.

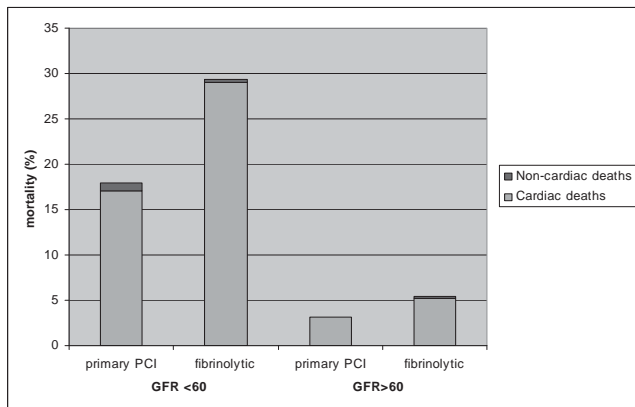


Fig. 2. Thirty-day mortality stratified by reperfusion strategy and GFR. GFR: glomerular filtration rate; PCI: percutaneous coronary intervention

Table 3. Adjusted 30-Day Outcomes

GFR group	% undergoing primary PCI	% undergoing fibrinolysis	Mortality	OR for 30-day mortality (95% CI)	P
GFR <60 (n = 331)	44	56	25	0.70 (0.31-1.60)	0.4
GFR >60 (n = 1341)	35	65	4	0.41 (0.19-0.89)	0.02
Total (n = 1672)	42	58	9	0.52 (0.30-0.88)	0.02

GFR: glomerular filtration rate; PCI: percutaneous coronary intervention; OR: odds ratio

significant for the normal renal function group (Table 3). Primary PCI was also associated with a smaller reduction in the point estimate for the impaired renal function group compared to the normal renal function group (0.7 vs 0.41, interaction $P < 0.05$).

Discussion

Although there are no published randomised studies comparing the relative efficacy of primary PCI vs fibrinolysis among patients with renal dysfunction and STEMI, a limited number of observational studies have investigated this treatment effect.^{4,5} In the present retrospective analysis of STEMI patients from 2 large public hospitals in Singapore, we showed that patients with an admission GFR $< 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ who were treated with primary PCI experienced a lower 30-day unadjusted mortality compared to patients treated with fibrinolysis. Adjusted mortality revealed a point estimate (adjusted OR, 0.7) favouring primary PCI over fibrinolysis; however, this did not achieve statistical significance ($P = 0.4$). In contrast, among patients with an admission GFR $\geq 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$, primary PCI was associated with a greater improvement in the point estimate (adjusted OR, 0.4), which achieved statistical significance

($P = 0.02$). These data suggest a differential treatment effect favouring primary PCI over fibrinolysis among patients with normal renal function but not among patients with impaired renal function.

Consistent with the results of other observational studies,^{4,16-20} our study showed a stepwise increase in mortality with worsening renal function (Fig. 2). In the GRACE multinational population of 12,532 patients with STEMI, moderate renal dysfunction (GFR $60\text{--}90 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$) was associated with a greater than 4-fold increase in inhospital mortality, while severe renal dysfunction (GFR $< 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$) was associated with a greater than 10-fold increase in mortality, compared to patients with normal renal function.⁵ In another study of 6834 East Asians with acute myocardial infarction, inhospital mortality was 1.3%, 3.8%, 7.4%, 10.9% and 16.9% for patients with normal renal function (GFR $> 90 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$), normal-mild renal dysfunction (GFR 75-89), mild GFR 60-74.9), moderate (GFR 45-59) and severe (GFR < 45) renal dysfunction, respectively.²⁰ In contrast to the GRACE study in which the greater increase in mortality occurred as GFR decreased from 30-60 to < 30 , the greatest increase in mortality in our study occurred as GFR decreased from 60-90 to < 60 .⁵ These geographically-different data suggest that mild-to-moderate renal dysfunction influence clinical outcomes to a much greater extent among patients in a local population, highlighting the need to be sensitive to milder degrees of renal dysfunction in daily practice.

Conflicting results have arisen from previous studies comparing primary PCI and fibrinolysis among patients STEMI and renal dysfunction. In a multicentre retrospective analysis of 132 patients with STEMI and serum creatinine $> 1.5 \text{ mg/dL}$, Dragu et al⁴ found that patients treated with fibrinolysis had a lower unadjusted 30-day mortality compared with patients treated with primary PCI (8% vs 40%), and an OR of 8.1 (95% CI, 1.9-56.5) favouring fibrinolysis, after adjusting for age as a covariate. Conversely, in a much larger multinational study of 3383 patients with STEMI and chronic kidney disease, defined as GFR $< 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$, Medi et al⁵ found that, after adjustment for admission GRACE risk scores, primary PCI was associated with a lower inhospital mortality compared to fibrinolysis [OR, 0.65; 95% CI, 0.45 to 0.93] among patients with moderate renal dysfunction but not among patients with severe renal dysfunction [OR, 0.72; 95% CI, 0.31 to 1.72]. In our study, the 331 patients with GFR $< 60 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ who underwent primary PCI experienced a lower unadjusted 30-day mortality compared with patients undergoing fibrinolysis (29.4% vs 17.9%), although the adjusted OR did not achieve statistical significance. Unlike the aforementioned studies, we performed a formal interaction analysis comparing the differential treatment effect of primary PCI vs fibrinolysis among patients with

(n = 331) and without renal dysfunction (n = 1341). The interaction *P* was significant at <0.05, suggesting an attenuated treatment benefit with primary PCI vs fibrinolysis when patients with renal dysfunction were compared to patients without renal dysfunction. Our results are therefore more consistent with the results of Medi et al,⁵ however, no further subgroup analyses were performed in our study because of the relatively small sample size of the renal dysfunction cohort.

Patients with renal dysfunction have poorer outcomes with PCI compared to patients with normal renal function, possibly explained by a greater burden of comorbidity, disparities in medical treatment and the nephrotoxic effects associated with vascular procedures and radiographic contrast.¹³⁻¹⁵ Although we adjusted for a comprehensive set of covariates in our analysis, including the presence of diabetes and haemoglobin levels, unmeasured biological confounders which may be associated with renal dysfunction state remain unaccounted for. In general, patients with renal dysfunction are less likely to receive aspirin, thienopyridines, beta-blockers, statins and angiotensin-converting enzymes compared to patients with normal renal function,^{18,19,21} a trend that was replicated in our study (Table 2). Patient with renal dysfunction also received more diuretics and inotropes in our study; these medications, which are associated with deleterious renal and neurohumoral effects, may have further contributed to the increased mortality among patients with renal dysfunction.

Our study had a number of limitations. Firstly, our analysis was a non-randomised treatment comparison in which we could not account for differences in treatment selection bias. Eliminating confounding remains a major limitation of an observational comparison of treatment effect like ours. A randomised trial is necessary, given the increasing prevalence of renal insufficiency among patients with STEMI. Secondly, the relatively small sample size of the cohort with renal dysfunction (n = 331) compared to the cohort without renal dysfunction (n = 1341) limited our ability to achieve statistical significance in multivariable analyses and subgroup analyses of the renal dysfunction cohort. Thirdly, because serial creatinine measurements were not collected, we could not study how contrast-induced nephropathy might have influenced the treatment effect. Fourthly, the angiographic success rate of primary PCI was not investigated in our study. We therefore could not ascertain if a higher angiographic failure rate contributed to the poorer outcomes with primary PCI compared to fibrinolytic therapy among patients with renal dysfunction. Fifthly, bleeding outcomes were not recorded in this population, so we were unable to investigate the influence of bleeding on differential mortality.

Conclusion

In this series of patients with STEMI treated with primary PCI or fibrinolytic therapy, patients with renal dysfunction experienced greater 30-day mortality compared to patients with normal renal function. Renal dysfunction was associated with a lower use of evidence-based medical therapies, but a greater use of diuretics and inotropes. Primary PCI was associated with a better adjusted 30-day survival among patients with normal renal function (GFR ≥ 60 mL min⁻¹ 1.73 m⁻²) but not among those with renal dysfunction. This differential effect suggests the need for randomised trials of primary PCI vs fibrinolytic therapy among patients with renal dysfunction who present with STEMI.

REFERENCES

1. Weaver WD, Simes RJ, Betriu A, Grines CL, Zijlstra F, Garcia E, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. *JAMA* 1997;278:2093-8.
2. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: developed in collaboration With the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction, Writing on Behalf of the 2004 Writing Committee. *Circulation* 2008;117:296-329.
3. King SB, 3rd, Smith SC, Jr, Hirshfeld JW, Jr, Jacobs AK, Morrison DA, Williams DO, et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: 2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee. *Circulation* 2008;117:261-95.
4. Dragu R, Behar S, Sandach A, Boyko V, Kapeliovich M, Rispler S, et al. Should primary percutaneous coronary intervention be the preferred method of reperfusion therapy for patients with renal failure and ST-elevation acute myocardial infarction? *Am J Cardiol* 2006;97:1142-55.
5. Medi C, Montalescot G, Budaj A, Fox KA, Lopez-Sendon J, FitzGerald G, et al. Reperfusion in patients with renal dysfunction after presentation with ST-segment elevation or left bundle branch block: GRACE (Global Registry of Acute Coronary Events). *JACC Cardiovasc Interv* 2009;2: 26-33.
6. Chan MY, Woo KS, Wong HB, Chia BL, Sutandar A, Tan HC. Antecedent risk factors and their control in young patients with a first myocardial infarction. *Singapore Med J* 2006;47:27-30.
7. Hallan S, Asberg A, Lindberg M, Johnsen H. Validation of the Modification of Diet in Renal Disease formula for estimating GFR with special emphasis on calibration of the serum creatinine assay. *Am J Kidney Dis* 2004;44:84-93.
8. Li H, Zhang X, Xu G, Wang X, Zhang C. Determination of reference intervals for creatinine and evaluation of creatinine-based estimating equation for Chinese patients with chronic kidney disease. *Clin Chim Acta* 2009;403:87-91.
9. Dong X, He M, Song X, Lu B, Yang Y, Zhang S, et al. Performance and

- comparison of the Cockcroft-Gault and simplified Modification of Diet in Renal Disease formulae in estimating glomerular filtration rate in a Chinese Type 2 diabetic population. *Diabet Med* 2007;24:1482-6.
10. Imai E, Horio M, Nitta K, Yamagata K, Iseki K, Hara S, et al. Estimation of glomerular filtration rate by the MDRD study equation modified for Japanese patients with chronic kidney disease. *Clin Exp Nephrol* 2007;11:41-50.
 11. Gerchman F, Tong J, Utzschneider KM, Hull RL, Zraika S, Udayasankar J, et al. Superiority of the Modification of Diet in Renal Disease equation over the Cockcroft-Gault equation in screening for impaired kidney function in Japanese Americans. *Diabetes Res Clin Pract* 2007;77:320-6.
 12. Ma YC, Zuo L, Zhang CL, Wang M, Wang RF, Wang HY. Comparison of ^{99m}Tc-DTPA renal dynamic imaging with modified MDRD equation for glomerular filtration rate estimation in Chinese patients in different stages of chronic kidney disease. *Nephrol Dial Transplant* 2007;22:417-23.
 13. Assali AR, Brosh D, Ben-Dor I, Solodky A, Fuchs S, Teplitsky I, et al. The impact of renal insufficiency on patients' outcomes in emergent angioplasty for acute myocardial infarction. *Catheter Cardiovasc Interv* 2007;69:395-400.
 14. Bartorelli AL. Primary angioplasty for acute myocardial infarction--the emerging prognostic role of renal insufficiency. *Catheter Cardiovasc Interv* 2007;69:401-2.
 15. Celik T, Iyisoy A, Yuksel CU, Kilic S, Yilmaz MI, Akgul EO, et al. Impact of admission glomerular filtration rate on the development of poor myocardial perfusion after primary percutaneous intervention in patients with acute myocardial infarction. *Coron Artery Dis* 2008;19:543-9.
 16. Keough-Ryan TM, Kiberd BA, Dipchand CS, Cox JL, Rose CL, Thompson KJ, et al. Outcomes of acute coronary syndrome in a large Canadian cohort: impact of chronic renal insufficiency, cardiac interventions, and anemia. *Am J Kidney Dis* 2005;46:845-55.
 17. Schiele F, Legalery P, Didier K, Meneveau N, Seronde MF, Caulfield F, et al. Impact of renal dysfunction on 1-year mortality after acute myocardial infarction. *Am Heart J* 2006;151:661-7.
 18. Wright RS, Reeder GS, Herzog CA, Albright RC, Williams BA, Dvorak DL, et al. Acute myocardial infarction and renal dysfunction: a high-risk combination. *Ann Intern Med* 2002;137:563-70.
 19. Yan AT, Yan RT, Tan M, Constance C, Lauzon C, Zaltzman J, et al. Treatment and one-year outcome of patients with renal dysfunction across the broad spectrum of acute coronary syndromes. *Can J Cardiol* 2006;22:115-20.
 20. Lee SH, Kim YJ, Kim W, Park JS, Shin DG, Hur SH, et al. Clinical outcomes and therapeutic strategy in patients with acute myocardial infarction according to renal function: data from the Korean Acute Myocardial Infarction Registry. *Circ J* 2008;72:1410-8.
 21. Tessone A, Gottlieb S, Barbash IM, Garty M, Porath A, Tenenbaum A, et al. Underuse of standard care and outcome of patients with acute myocardial infarction and chronic renal insufficiency. *Cardiology* 2007;108:193-9.
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