



Original article

The prognostic impact of worsening renal function in Japanese patients undergoing percutaneous coronary intervention with acute coronary syndrome



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ABSTRACT

Background: The prognostic impact of worsening renal function (WRF) in acute coronary syndrome (ACS) patients is not fully understood in Japanese clinical practice, and clinical implication of persistent versus transient WRF in ACS patients is also unclear.

Methods: With a single hospital-based cohort in the Shinken database 2004–2012 ($n = 19,994$), we followed 604 ACS patients who underwent percutaneous coronary intervention (PCI). WRF was defined as an increase in creatinine during hospitalization of ≥ 0.3 mg/dl above admission value. Persistent WRF was defined as an increase in creatinine during hospitalization of ≥ 0.3 mg/dl above admission value and maintained until discharge, whereas transient WRF was defined as that WRF resolved at hospital discharge.

Results: WRF occurred in 78 patients (13%), persistent WRF 35 patients (6%) and transient WRF 43 patients (7%). WRF patients were older and had a higher prevalence of chronic kidney disease, history of myocardial infarction (MI), and ST elevation MI. WRF was associated with elevated inflammatory markers and reduced left ventricular (LV) ejection fraction in acute, chronic phase. Incidence of all-cause death and major adverse cardiac events (MACE: all-cause death, MI, and target lesion revascularization) was significantly higher in patients with WRF. Moreover, in the WRF group, incidences of all-cause death and MACE were higher in patients with persistent WRF than those with transient WRF. A multivariate analysis showed that as well as older age, female gender, and intubation, WRF was an independent determinant of the all-cause death in ACS patients who underwent PCI.

Conclusions: In conclusion, WRF might have a prognostic impact among Japanese ACS patients who underwent PCI in association with enhanced inflammatory response and LV remodeling. Persistent WRF might portend increased events, while transient WRF might have association with favorable outcomes compared with persistent WRF.

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Introduction

The association between cardiovascular disease and chronic kidney disease (CKD) has been extensively explored all over the world [1–3] including Japan [4,5]. Similarly it was reported that worsening renal function (WRF) in acute coronary syndrome (ACS)

also has a prognostic impact and WRF is an independent predictor of all-cause death from baseline renal function [6,7]. However, the prognostic impact of WRF in Japanese ACS patients is not fully understood, and the clinical implication of improvement in renal function by the time of discharge in ACS patients is also unclear. Therefore, our primary aim was to explore the prognostic impact of WRF that developed during hospitalization in Japanese ACS patients who underwent percutaneous coronary intervention (PCI), and secondary aim was to explore the clinical implications of transient versus persistent WRF.

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Methods

Study population

We established a single hospital cohort, called the Shinken database [8–10], which has been including all new patients visiting the Cardiovascular Institute Hospital, Tokyo, Japan, since June 2004. It has excluded patients with known active cancers and travelers. Until March 2013, 19,994 patients had been enrolled, for whom background characteristics, risk factors, diagnosis of cardiovascular diseases, blood laboratory data, physiological test results, medications, and outcomes were available in the cohort database. Patients were thoroughly investigated through routine clinical examinations. Among the Shinken database, all patients diagnosed with ACS [ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI), unstable angina (UA)] and who underwent successful PCI were identified. The diagnosis of ACS was decided by cardiologists in our hospital based on definitions of the joint committee of the American College of Cardiology (ACC)/American Heart Association (AHA) [11–13]. The population in the present study comprised 616 patients who were hospitalized for ACS and underwent successful PCI at the initial visit. We defined successful PCI as less than 50% stenosis and over thrombolysis in myocardial infarction grade 3 flow in final angiography without intervention-related complications [14]. Patients undergoing regular dialysis treatments were excluded (*n* = 12). Finally, a total of 604 patients were examined in the present study (Fig. 1). The median follow-up period was 1315 ± 903 days.

Renal function

Blood was sampled daily during the ACS hospitalization to monitor serum creatinine (Cr). Glomerular filtration rate (GFR) was estimated from gender, age, and Cr, using established equations for Japanese patients with CKD: $GFR = 194 \times Cr^{-1.094} \times age^{-0.287}$ (if male), $GFR = 194 \times Cr^{-1.094} \times age^{-0.287} \times 0.739$ (if female), CKD was defined as eGFR <60 ml/min/1.73 m² [15,16]. WRF development was defined as a peak increase in serum Cr by ≥0.3 mg/dl from the admission for ACS [7,17,18]. We defined persistent WRF as an increase in creatinine during hospitalization of ≥0.3 mg/dl above admission value and maintained until discharge, whereas transient WRF as that WRF resolved at hospital discharge [19,20].

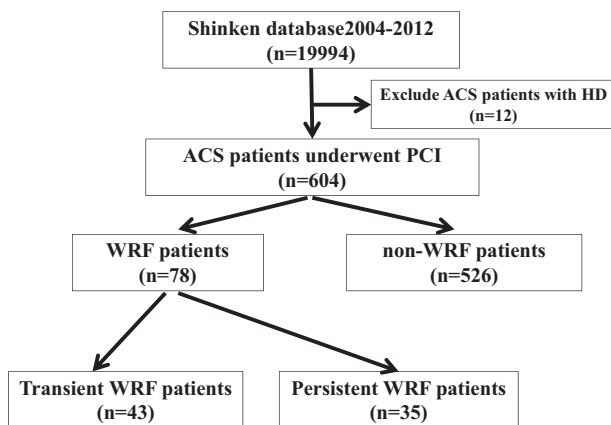


Fig. 1. Patient flow chart of the present study. ACS, acute coronary syndrome; HD, hemodialysis; PCI, percutaneous coronary intervention; WRF, worsening renal function.

Outcomes

The primary outcome was all-cause death. The secondary outcome was major adverse cardiac events (MACE), including all-cause death, myocardial infarction (MI), and target lesion revascularization (TLR). Major adverse cardiac and cerebrovascular events (MACCE) included MACE and stroke. These outcomes were ascertained with medical records or reports on follow-up questionnaires sent to the patients every year. Outcomes were compared with two groups, WRF group and non-WRF group. Similarly in sub-analysis, outcomes were compared with another two groups, persistent WRF group and transient WRF group.

Statistical analysis

All continuous data were expressed as means ± standard deviation and the mean differences between groups were analyzed using Student's *t*-test. Proportional differences were analyzed using the χ^2 test. Group differences in the temporal change in Cr during the treatment course were assessed using the repeated measures analysis of variance. Kaplan–Meier curves were used to assess the unadjusted all-cause death and MACE and the log-rank test was used to compare these curves. Cox proportional hazards modeling was used to obtain hazard ratios with adjustment for factors potentially associated with patient survival and the risk factors for the WRF development identified in this study. Sub-analysis was examined with similar statistic methods between two groups WRF sustained, or not. A *p*-value of <0.05 was considered statistically significant. All data were analyzed using SPSS version 19.0 for Windows (SPSS, Inc., Chicago, IL, USA).

Results

Baseline characteristics

Baseline characteristics of the study population are shown in Table 1. WRF was observed in 13% (*n* = 78) of the present population. The WRF group was significantly older (70 ± 12 years vs 63 ± 12 years, *p* < 0.001) and had higher prevalence of CKD (51% vs

Table 1
Baseline characteristics of the study population.

	Non-WRF (<i>n</i> = 526)	WRF (<i>n</i> = 78)	<i>p</i> -value
Age (years)	63 ± 12	70 ± 12	<0.001
BMI (kg/m ²)	25 ± 4	24 ± 4	0.498
Male gender, <i>n</i> (%)	460 (87)	64 (82)	0.189
Diabetes, <i>n</i> (%)	158 (30)	25 (32)	0.718
Hypertension, <i>n</i> (%)	312 (59)	51 (65)	0.307
Dyslipidemia, <i>n</i> (%)	317 (60)	44 (56)	0.517
CKD, <i>n</i> (%)	127 (24)	40 (51)	<0.001
Smoking, <i>n</i> (%)	236 (45)	28 (36)	0.136
Family history, <i>n</i> (%)	77 (15)	8 (10)	0.299
History of MI, <i>n</i> (%)	25 (5)	8 (10)	0.046
History of PCI, <i>n</i> (%)	30 (5)	5 (6)	0.803
History of CABG, <i>n</i> (%)	7 (1)	1 (1)	0.972
LMT disease, <i>n</i> (%)	14 (3)	4 (5)	0.232
Multi-vessel disease, <i>n</i> (%)	133 (25)	26 (33)	0.132
STEMI, <i>n</i> (%)	238 (45)	45 (58)	0.040
Killip more than 2, <i>n</i> (%)	76 (14)	35 (45)	<0.001
IABP, <i>n</i> (%)	38 (7)	24 (31)	<0.001
PCPS, <i>n</i> (%)	4 (1)	6 (8)	<0.001
Intubation, <i>n</i> (%)	13 (2)	10 (13)	<0.001

WRF, worsening renal function; BMI, body mass index; CKD, chronic kidney disease; MI, myocardial ischemia; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; LMT, left main trunk; STEMI, ST elevation myocardial ischemia; IABP, intra-aortic balloon pumping; PCPS, percutaneous cardiopulmonary support.

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