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Clinical impact of complete revascularization in elderly patients with multi-vessel coronary artery disease undergoing percutaneous coronary intervention: A sub-analysis of the SHINANO registry☆

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ABSTRACT

Background: Prior reports have revealed that complete revascularization (CR) by percutaneous coronary intervention (PCI) decreased ischemic events. However, little is known about the efficacy of CR using PCI in elderly patients with multi-vessel coronary artery disease (CAD). We evaluated the 1-year effectiveness of CR-PCI in elderly patients (≥75 years old) with multi-vessel CAD.

Methods: The SHINANO Registry, a prospective, observational, multi-center, all-comer cohort study, has enrolled 1923 patients. From this registry, we recruited 322 elderly patients with multi-vessel CAD. The primary endpoint was major adverse cardiovascular events ([MACE]: all-cause mortality, myocardial infarction, and stroke).

Results: Of the 322 elderly patients with multi-vessel CAD, 165 (51.2%) received CR and 157 (48.8%) received incomplete revascularization (ICR). MACE occurred in 44 (13.7%) patients. The incidence of MACE by survival analysis was significantly lower in the CR group than in the ICR group (7.4% vs. 21.1%, $p < 0.001$). On multivariable Cox proportional hazards analysis of age, sex, and acute coronary syndrome (ACS), ACS and CR were independent predictors of MACE (hazard ratio [HR], 2.49; 95% confidence interval [CI], 1.29–4.80; $p = 0.007$, HR, 0.40; 95% CI, 0.20–0.77; $p = 0.007$, respectively). In propensity score matching of age, sex, previous heart failure, previous intracranial bleeding, ACS, and body mass index, the MACE rate was significantly lower in the CR group than in the ICR group (7.2% vs. 18.4%, $p = 0.015$).

Conclusions: Even in elderly patients over 75 years old with multi-vessel CAD, CR-PCI appears to suppress mid-term ischemic events.

Abbreviations: CR, complete revascularization; ICR, incomplete revascularization; PCI, percutaneous coronary intervention; CAD, coronary artery disease; STEMI, ST-segment elevated myocardial infarction; NSTEMI, non-ST-segment elevated myocardial infarction; UA, unstable angina; MACE, major adverse cardiovascular events; MI, myocardial infarction; IHD, ischemic heart disease; HF, heart failure; QOL, quality of life; ACS, acute coronary syndrome; CABG, coronary artery bypass surgery; BP, blood pressure; BMI, body mass index; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fracture; PAD, peripheral artery disease; SYNTAX, synergy between PCI with TAXUS™ and cardiac surgery; CTO, chronic total occlusion; IABP, intra-aortic balloon pumping; HR, hazard ratio; CI, confidence interval; ADL, activities of daily living; DES, drug eluting stent.

☆ All authors take full responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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1. Introduction

In most developed countries, the proportion of elderly people is rising. The proportion of patients aged 80 years or older was 4.7% in Europe and 3.8% in Northern America and Australia in 2015. In Japan, 7.8% of the whole population is 80 years old or over. In 2030, the proportion of patients aged 80 years or older is expected to reach 6.3% in Europe and 5.6% in Northern America and Australia, which is close to the current state in Japan [1]. In 2013, 7503 billion yen was spent in Japan on medical expenses related to ischemic heart disease, of which 43.8% was spent on patients aged 75 years or older [2].

Elderly patients generally have more comorbidities than younger patients, for example, chronic heart failure, chronic kidney disease, dementia, or weakness. The impact of complete revascularization (CR) for the elderly with these co-morbidities has been unknown.

A prior meta-analysis revealed that CR by percutaneous coronary intervention (PCI) decreased ischemic events for patients with a mean age of 63 ± 7 years [3]. Our group has previously reported that elderly age was not a strong predictor of procedural failure and in-hospital ischemic events [4]. The Shinshu Prospective Multi-Center Analysis for Elderly Patients with Coronary Artery Disease Undergoing Percutaneous Coronary Intervention (SHINANO) Registry was initiated to evaluate the clinical outcome, treatment, and clinical and lesion characteristics in elderly patients undergoing PCI [5]. This study is a sub-analysis of the SHINANO registry, and its aim was to evaluate the one-year efficacy of CR-PCI for elderly patients with multi-vessel coronary artery disease (CAD).

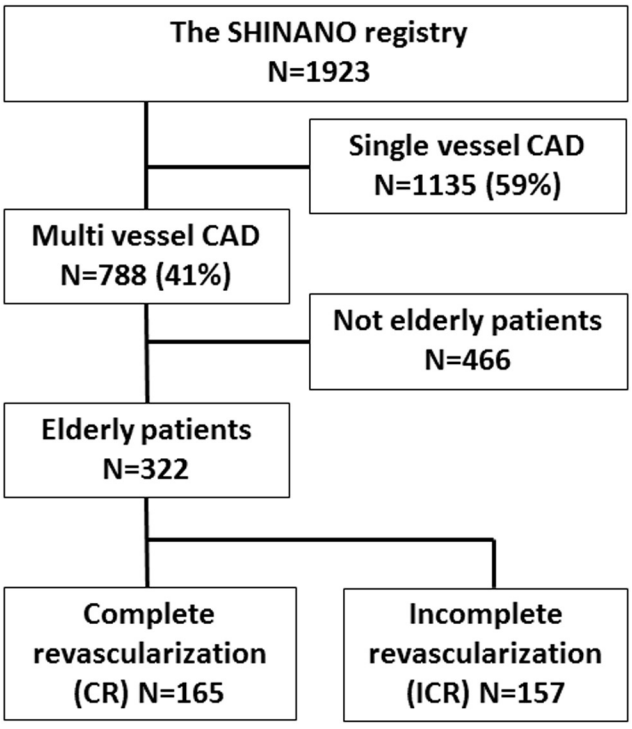

Fig. 1. Patient selection flow chart. CAD, coronary artery disease.

2. Methods

2.1. Study participants and design

The SHINANO registry was approved by the Medical Ethics Committee of Shinshu University School of Medicine. Patients who gave written informed consent were enrolled. The study was registered with the University Hospital Medical Information Network-Clinical Trials Registry (UMIN-CTR), as accepted by the International Committee of Medical Journal Editors (No. UMIN000010070).

The SHINANO Registry is a prospective, multicenter, observational registry designed to provide up to 12 months of clinical follow-up. This study had no exclusion criteria and was an all-comer registry. A total of 1923 consecutive patients with 2250 PCIs (2105 admissions) for any CAD (stable angina, ST-segment elevation myocardial infarction [STEMI], non-STEMI [NSTEMI], and unstable angina [UA]) were enrolled from 16 institutions in Nagano Prefecture between August 2012 and July 2013. In this sub-analysis, 788 patients had multi-vessel disease. Among them, 322 were elderly; 165 patients received CR and 157 patients did not (Fig. 1).

2.2. Endpoints

The primary endpoint was major adverse cardiovascular events (MACE), namely all-cause mortality, myocardial infarction (MI), and stroke at one year. The secondary endpoints were all-cause death, cardiac death, MI, stroke, major bleeding, stent thrombosis, hospitalization for ischemic heart disease (IHD), hospitalization for heart failure (HF), and exacerbation of renal function, which showed quality of life (QOL) for the elderly.

2.3. Definitions

Elderly age was defined as age greater than or equal to 75 years old.

Definitions were based on those of the original paper on the SHINANO registry [4]. Acute coronary syndrome (ACS) was a composite of STEMI, NSTEMI, and UA. ACS positive meant that initial PCI was performed for ACS patients during the enrolment period. STEMI was diagnosed in patients with chest symptoms, ST segment elevation 1 mV in two or more limb leads, or two contiguous precordial leads or left bundle branch block, and elevated biochemical markers of myocardial necrosis (troponin T levels 0.0.1 ng/mL or creatine phosphokinase two-fold above the normal range).

NSTEMI was diagnosed in patients with chest symptoms, ST-segment depression 0.05 mV, T-wave inversion ≥0.3 mV, or transient ST-segment elevation <0.05 mV, and elevated biochemical markers of myocardial necrosis (and no electrocardiogram abnormalities for STEMI). UA was diagnosed in patients with persistent resting or nocturnal chest pain together with additional findings. Angiographic success was defined as achievement of a minimum stenosis diameter reduction to <20% with grade 3 Thrombolysis In Myocardial Infarction flow. CR meant that all stenotic main vessels were revascularized and all side branches were >2 mm in diameter.

CAD was defined as >50% stenosis in a coronary vessel on angiography, history of coronary artery bypass graft surgery (CABG), PCI, or MI. Stroke was defined as ischemic stroke that persisted for ≥24 h and was diagnosed by a neurologist. HF was based on a previous diagnosis of HF, history of hospitalization for HF, or current treatment for HF. Diabetes was defined as a hemoglobin A1c level ≥6.5%, casual plasma glucose ≥200 mg/dL (in accordance with the National Glycohemoglobin Standardization Program) or treatment with oral hypoglycemic agents or insulin injection.

Hypertension was defined as systolic blood pressure (BP) ≥140 mmHg, diastolic BP ≥90 mmHg, or ongoing therapy for hypertension. Dyslipidemia was defined as a serum total cholesterol concentration ≥220 mg/dL, a low-density lipoprotein cholesterol concentration ≥140 mg/dL, or current treatment with lipid-lowering therapy. Body mass index (BMI) was defined as weight in kilograms divided by the square of the patient's height in meters. Estimated glomerular filtration rate (eGFR) was calculated with the following formula: male; eGFR (mL/min/1.73 m^2) = 194 × creatinine $(Cr)^{-1.094}$ × $age^{-0.287}$, female; eGFR = 194 × $Cr^{-1.094}$ × $age^{-0.287}$ × 0.739 [6]. Patients with a 30% decrease in eGFR at one year follow-up were defined as having "exacerbated renal function".

Left ventricular ejection fraction (LVEF) was measured by echocardiography, and an LVEF ≤40% indicated LV dysfunction.

Multi-vessel disease was defined as the presence of a ≥75% lesion in at least two major coronary arteries, as seen on angiography. Documented peripheral artery disease (PAD) met one or both of the following criteria: current intermittent claudication with an ankle-brachial index ≤0.9 or a history of intermittent claudication with a previous and related intervention, such as peripheral arterial bypass graft, stenting, angioplasty, atherectomy, or other vascular interventions, including amputation. The synergy between PCI with TAXUS™ and cardiac surgery (SYNTAX) score was calculated at the primary intervention to determine the complexity of the CAD [7].

2.4. Statistical analysis

Continuous variables were reported as mean ± standard deviation and compared using t-test. Continuous without a normal distribution were expressed as median (25th and 75th percentile) and compared using Mann-Whitney U test. Categorical variables were reported as frequencies and percentages. Patient characteristics of the two groups were compared using chi-squared tests. Kaplan-Meier curves were created for survival analysis. Univariate analysis was performed to extract items associated with MACE, and multivariate Cox proportional hazard models were performed to adjust for baseline risk factors on initial PCI. Propensity score matching, adjusted for the factors that were significantly related to MACE, was performed to reduce the treatment selection bias. $P < 0.05$ was considered statistically significant in all analyses. Analyses were performed using IBM SPSS Statistics version 22.0 (IBM Co. SPSS Inc., Chicago, IL).

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