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### Original article

# Living alone and risk of cardiovascular events following discharge after acute myocardial infarction in Japan



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## $A\ R\ T\ I\ C\ L\ E\quad I\ N\ F\ O$

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#### ABSTRACT

*Background:* Little is known about the long-term risk of cardiovascular events after discharge among acute myocardial infarction (AMI) survivors living alone in Japan.

Methods and results: A large-scale prospective, observational study in the Osaka region involved consecutive patients with AMI from January 2002 through December 2010. We evaluated the association between living alone and longitudinal risk of cardiovascular events following discharge after AMI. A Cox proportional-hazards model was used to assess the association between living alone and the primary composite endpoint consisting of major adverse cardiovascular events and total deaths. During the study period, 5845 patients (4415 male patients, 1430 female patients) were registered. Living alone was found to be independently associated with a higher risk of composite endpoint consisting of major adverse cardiovascular events and total deaths [adjusted hazard ratio (HR) 1.32; 95% confidence interval (CI): 1.11–1.58]. Multivariate-adjusted HRs of composite endpoint were 1.34 (95% CI: 1.08–1.68) among male patients and 1.31 (95% CI: 0.95–1.81) in the female patients. AMI survivors living alone tend to have a higher adjusted HR of composite endpoint than those not living alone irrespective of age and gender groups.

Conclusions: From this large AMI registry in Osaka, AMI survivors living alone after discharge had a higher risk of cardiovascular events and total deaths than those not living alone.

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#### Introduction

Acute myocardial infarction (AMI) is an important public health problem in the industrialized world [1,2], and approximately 42,000 patients die of AMI in Japan every year [3]. As secondary prevention for cardiovascular events after AMI onset, the effectiveness of dietary therapy, physical rehabilitation, and drug intervention has been shown [4,5], but the impact of sociopsychological factors on cardiovascular events after AMI has not been well investigated in Japan.

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In previous studies, living alone was reported to be an independent predictor of cardiovascular events after discharge among AMI survivors [6–10]. Although the number of elderly living alone in Japan is increasing with the rapid aging of society [11], little is known about the risk of cardiovascular events and total deaths after discharge among AMI survivors living alone in Japan.

The Osaka Acute Coronary Insufficiency Study (OACIS) is a large-scale, prospective, multicenter observation in the Osaka region of Japan and has been collecting demographic, procedural, and outcome data among patients with AMI. Using this database, we investigated the association between living alone and longitudinal risk of cardiovascular events and total deaths following discharge after AMI.

#### Methods

Study patients

The OACIS is a prospective, multicenter observational study that enrolls consecutive patients with AMI in collaborating hospitals from the Osaka region of Japan. It is conducted to assess clinical variables at admission, therapeutic procedures, and subsequent clinical events in patients with AMI, and is registered to the University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) in Japan (ID: UMIN000004575). Details of OACIS are reported elsewhere [12–15].

This study enrolled consecutive patients admitted directly or transferred to the 25 collaborating hospitals between January 2002 and December 2010 within 1 week of the onset of AMI. AMI was diagnosed if 2 of the following 3 criteria were met: (1) clinical history of central chest pressure, pain, or tightness lasting ≥30 min; (2) ST segment elevation >0.1 mV in at least one standard or 2 precordial leads; and (3) a rise in serum creatine phosphokinase (CPK) concentration to more than twice the normal laboratory value. Participants provided written informed consent for data collection, blood sampling, and long-term follow-up, which was approved by the respective hospitals' ethics review committee, before discharge from the hospital. Patients who died in the hospital, were unable to communicate verbally with attending physicians, had a major psychological disease, or refused entry into this study were excluded. Follow-up clinical data were obtained at 3, 6, and 12 months after the onset of AMI and annually thereafter for 5 years.

Data were prospectively collected using a specific reporting form, and the following variables were extracted from the OACIS registry database: age, gender, living arrangement, employment status, body mass index (BMI), ST-elevation myocardial infarction (STEMI), coronary risk factors [diabetes, hypertension, dyslipidemia, smoking, drinking, and previous myocardial infarction (MI)], Killip class, re-perfusion therapy, laboratory data at admission [estimated glomerular filtration rate (eGFR) and CPK], and medications at discharge [angiotensin-converting enzyme inhibitor (ACEI) and/or angiotensin receptor blocker (ARB), betablocker, statin, and anti-platelet]. AMI patients were asked at admission whether they lived with their family or others, and those who did not live with their family or others were classified into the living alone group. All data acquired in the respective hospitals were transmitted to the data collection center at the Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine, Suita, Japan for processing and analysis. The study protocol complied with the Helsinki declaration and was approved by the Institutional Review Board of Osaka University Hospital. The corresponding author had full access and validated all data in the study.

#### Statistical analysis

Patient characteristics were compared between AMI survivors with discharge who were living alone and those not living alone.

Categorical data are expressed in percentages and differences were analyzed by chi-square statistics. Continuous data are presented as the median (25–75 percentiles) and differences were analyzed by t-test. The primary outcome of this study was the composite endpoint consisting of major adverse cardiovascular events (MACEs; heart failure, recurrent myocardial infarction, unstable angina, and stroke) and total deaths. The secondary endpoint was each MACE and total deaths. In addition, the primary and secondary endpoints were assessed by gender (male, female) and age (<65 years, >65 years) groups. The Kaplan-Meier method was used to estimate cumulative event rates, and estimated differences were compared by the log-rank test. A Cox proportional-hazards model was used to assess the association between living arrangements (living alone, not living alone) and the primary and secondary endpoints; hazards ratios (HRs) and their 95% confidence intervals (CIs) were also calculated. Potential confounding factors based on biological plausibility and previous studies [12–15] were included in the multivariable analysis. These variables included age (10-year increment of age), gender [only for all patients (male, female)], employment status (yes, no, unknown), BMI (<25 kg/m<sup>2</sup>,  $\geq$  25 kg/m<sup>2</sup>), STEMI (yes, no), each coronary risk factor (yes, no), Killip class ( $<2, \ge 2$ ), re-perfusion therapy (yes, no), laboratory data at admission [eGFR ( $<60 \text{ mL/min}/1.73 \text{ m}^2$ ,  $\ge 60 \text{ mL/min}/1.73 \text{ m}^2$ ) and CPK ( $<3000 \, IU/L$ ,  $\geq 3000 \, IU/L$ )], and each medication at discharge (yes, no). All statistical analyses were performed using PASW statistical package ver18.0J (SPSS, Inc., Chicago, IL, USA) and R software ver.2.13.1 (http://cran.r-project.org/). All tests were 2-tailed, and *p*-values of <0.05 were considered statistically significant.

#### Results

Between 2002 and 2010, a total of 6657 AMI patients were confirmed (Fig. 1). Of them, 494 died at the hospital and 6163 were discharged. Excluding 318 patients without information on living arrangements, 5845 patients (4415 male patients, 1430 female patients) were eligible for our analyses, and the median follow-up period was 735 days after discharge. The proportion of patients living alone was 16.2% (717/4415) in male patients and 25.0% (358/1430) in female patients, and did not vary in both sexes during the study period. In this study, the follow-up rate after discharge was 91.2% (5329/5845) among all patients and 89.9% (3010/3348) among elderly patients aged  $\geq$ 65 years.

Table 1 shows the baseline characteristics of eligible patients living alone and those not living alone. Median age was higher in the living alone group than in the not living alone group. AMI survivors living alone were more likely to be unemployed and have Killip of

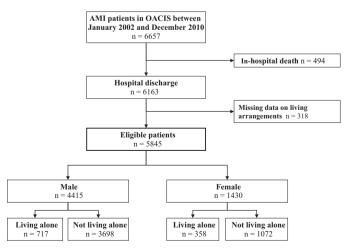


Fig. 1. Patient flow. AMI, acute myocardial infarction; OACIS, Osaka Acute Coronary Insufficiency Study.

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