Comparison of In-Hospital Clinical Outcomes of Acute Myocardial Infarction Between Nonagenarians and Octogenarians A Propensity Score-Matched Analysis

Masaru Seguchi,1 MD, Kenichi Sakakura,1 MD, Kei Yamamoto,1 MD, Yousuke Taniguchi,1 MD, Hiroshi Wada,1 MD, Shin-ichi Momomura,1 MD and Hideo Fujita,1 MD

Summary

Acute myocardial infarction (AMI) in the very elderly is associated with high morbidity and mortality. Although there are earlier studies regarding AMI in octogenarians, clinical evidences of AMI in nonagenarians are sparse. The aim of the present study was to compare in-hospital outcomes of AMI between octogenarians and nonagenarians. We included consecutive 415 very elderly (≥80 years) with AMI and divided them into the nonagenarian group (n = 38) and the octogenarian group (n = 377). Clinical characteristics and in-hospital outcomes were compared between the two groups. Furthermore, we used propensity score matching to find the matched octogenarian group (n = 38). Percutaneous coronary interventions (PCI) to the culprit of AMI were similarly performed between the nonagenarian (86.8%) and octogenarian (87.0%) groups. The incidence of in-hospital death in the nonagenarian group (10.5%) was similar to that in the octogenarian group (12.5%) (P = 0.487). After using the propensity score matching, the incidence of in-hospital death was less in the nonagenarian group (10.5%) than in the matched octogenarian group (18.4%) without reaching statistical significance (P = 0.328). The length of hospitalization was significantly shorter in the nonagenarian group [7.0 (4.0-9.0)] than in the matched octogenarian group [10.0 (6.5-15.0)] (P = 0.01). In conclusion, the in-hospital mortality of nonagenarians with AMI was comparable to that of octogenarians with AMI. In-hospital outcomes in nonagenarians with AMI may be acceptable as long as acute medical management including PCI to the culprit of AMI is performed.

Key words: Coronary intervention, Elderly, Ischemic heart disease, Prognosis

Acute myocardial infarction (AMI) has been a major cause of death in the elderly in developed countries. With increased life expectancy, AMI in the very elderly (≥80 years) is more frequently observed in recent clinical studies than in old clinical studies. As compared to AMI in the elderly aged <80 years, AMI in the very elderly had higher morbidity and mortality and received less percutaneous coronary intervention (PCI) or coronary artery bypass surgery. However, after the development of revascularization procedures, the prevalence of primary PCI is rapidly growing in the very elderly, which suggests that the very elderly with AMI would receive guideline-recommended therapy including primary PCI and optimal medical therapy in the current primary PCI era.

On the other hand, the majority of the study population in earlier studies focusing on the very elderly with AMI was octogenarians. Clinical evidences regarding AMI in nonagenarians are sparse. It is unknown whether clinical outcomes after AMI in nonagenarians are comparable to those in octogenarians, while the number of nonagenarians has rapidly been growing in developed countries. In fact, the number of nonagenarians has increased ten-fold from 1985 to 2017 in Japan, while the total population has slightly increased in the same period, indicating that the more medical resources are necessary for nonagenarians. Therefore, it is important to investigate the clinical characteristics and outcomes of AMI in nonagenarians. The aim of the present study was to compare clinical characteristics and in-hospital outcomes of AMI between octogenarians and nonagenarians.

Methods

Study population: We reviewed consecutive AMI patients in our medical center from January 2009 to July 2018. The patients aged <80 years old or ≥100 years old were excluded. The study patients were divided into the octogenarian group (80-89 years old) and the nonagenarian group (90-99 years old) according to the age at the timing of admission. Clinical characteristics and in-hospital outcomes were compared between the two groups. The pri-
ary outcome for this study was in-hospital death, and the secondary outcome was the length of hospitalization. This study was approved by the institutional review board, and written informed consent was waived because of the retrospective study design.

**Definition:** The diagnosis of AMI required the following criteria: symptoms consistent with AMI, elevated cardiac enzymes including troponin T, troponin I, and/or creatinine kinase (at least two-fold increase from the normal upper limit), and ST-segment elevation or depression in electrocardiograms compatible with AMI. Diagnostic ST elevation was defined as new ST elevation at the J point in at least two contiguous leads of 2 mm (0.2 mV), and the AMI patients with ST elevation were diagnosed as ST elevation myocardial infarction (STEMI). The other AMI patients without ST elevation were defined as non-ST elevation myocardial infarction (NSTEMI). Hypertension was defined as a medical treatment for hypertension and/or a history of hypertension before admission. Dyslipidemia was defined as a medical treatment for dyslipidemia and/or a history of dyslipidemia. Diabetes mellitus was defined as a hemoglobin A1c level (as NGSP value) ≥ 6.5% or a medical treatment for diabetes mellitus or a history of diabetes mellitus. We used the laboratory data at admission. Since we could not measure some laboratory data such as HbA1c or low-density lipoprotein (LDL) cholesterol levels at off hours (night or holidays), we substituted the earliest HbA1c or LDL cholesterol levels since admission as the laboratory data at admission when HbA1c or LDL levels at admission were not available. Significant coronary artery stenosis was defined as at least a 75% reduction in the internal diameter. Contrast volume used for the initial coronary angiography or coronary intervention was recorded. Acute kidney injury was defined as the increase in serum creatinine ≥ 0.3 mg/dL within 48 hours from admission. The type of revascularization to the culprit of AMI was classified to PCI, coronary artery bypass graft surgery (CABG), or medical treatment (no revascularization). Initial and final TIMI flow grades were recorded. A stent diameter and a stent length were recorded. If multiple stents were used for the culprit of AMI, an average diameter of all deployed stents was recorded as the stent diameter, and a sum of all deployed stents’ length was recorded as the stent length. Left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography during the hospitalization. LVEF was calculated through either a modified Simpson method, a Teichholz method, or an eyeball estimation. Ejection fraction measured by a Teichholz method was adopted only when a modified Simpson method was not available. Eyeball estimation of ejection fraction was adopted only when both a modified Simpson method and a Teichholz method were not available. The Global Registry of Acute Coronary Events (GRACE) risk score was also calculated. Syntax score I was calculated except for the patients who did not undergo CAG and/or who had a history of CABG. In order to evaluate patients’ preadmission activities of daily living (ADL), we routinely interviewed the patients and/or their representatives about their preadmission ADL in our institution. A questionnaire regarding preadmission ADL consisted of six variables: having meals, using toilets, maintaining cleanliness, washing face, changing clothes, and moving around. Those six variables were evaluated whether independence or dependence at their admission.

**Primary PCI:** Although we did not perform PCI to the patients who were uncooperative with the cardiac catheterization procedure or the patients who could not understand the necessity of PCI because of cognitive dysfunction, we performed PCI to the culprit of AMI regardless of the patient’s age. In our catheter laboratory, primary PCI were performed using standard techniques via radial artery, femoral artery, or rarely brachial artery. First, we advanced a conventional guidewire across the lesion and used a small balloon or thrombus aspiration catheter. The choice of devices was left to the discretion of each interventional cardiologist. Activated coagulation time was maintained > 250 seconds during PCI.

**Statistical analysis:** Data were expressed as mean ± SD for continuous variables and percentage for categorical variables. Categorical variables were compared using the Pearson chi-squared test or the Fischer exact test. The Shapiro-Wilk test was performed to determine if the continuous variables were normally distributed. Normally distributed continuous variables were compared using an unpaired Student’s t test. Otherwise, continuous variables were compared using a Mann-Whitney U-test. Nonparametric variables were described as median (quartile 1 - quartile 3). Because the number of the octogenarian group was much greater than that of the nonagenarian group, we used propensity score matching to find matched octogenarians. Propensity scores were estimated by fitting a logistic regression model using the confounding factors which have significant difference in the univariate analysis between the groups. For matching, the match tolerance was set as a width of 0.25 multiplied by the SD of the propensity score distribution. A P value less than 0.05 was considered statistically significant. All analyses were performed using statistical software, SPSS 24.0/Windows (SPSS, Chicago, IL, USA).

**Results**

A total of 1,996 AMI patients were admitted to our hospital during the study period. Among them, 1,581 AMI patients that were < 80 years old were excluded. There were no AMI patients who were ≥ 100 years old during the study period. Finally, 415 patients were included as the final study population, and they were divided into the nonagenarian group (n = 38) and the octogenarian group (n = 377) (Figure).

The comparison of clinical characteristics is shown in Table I. Patient characteristics were comparable between the two groups except the proportion of STEMI, GRACE risk score, serum albumin, and hemoglobin levels at admission. Coronary angiography was less frequently performed in the nonagenarian group (92.1%) than in the octogenarian group (98.4%) (P = 0.04). Angiographic and procedural findings including culprit lesion, final TIMI flow grade, approach site, and type of stent were comparable between the two groups. Dependence of maintaining cleanliness, washing face, and moving around were more
frequently observed in the nonagenarian groups than the octogenarian group.

The comparison of clinical outcomes is shown in Table II. The incidence of in-hospital death in the nonagenarian group (10.5%) was similar to that in the octogenarian group (12.5%) \((P = 0.487)\). The length of hospital stay was significantly shorter in the nonagenarian group \([7.0 \ (4.0-9.0)\) days] than that in the octogenarian group \([11.0 \ (7.0-17.0)\) days] \((P < 0.001)\). Transfer to other hospitals was more frequently observed in the nonagenarian group (34.2%) as compared to the octogenarian group (17.5%) \((P = 0.01)\).

**Propensity score matching analysis:** In order to perform the propensity score matching, we selected gender and three confounding factors as covariates (STEMI or NSTEMI, hemoglobin levels at admission, and transfer to other hospitals) that had significant differences between the two groups in the univariate comparison. Case-control matching found 38 fuzzy matches with maximizing matching performance. Thus, the matched 38 octogenarians were selected for further analysis. The comparison of clinical characteristics between the nonagenarian group and the matched octogenarian group is shown in Table III. Clinical characteristics were comparable between the two groups except age, suggesting that the propensity score matching was appropriate. The comparison of clinical outcomes between the nonagenarian group and the matched octogenarian group is shown in Table IV. The incidence of in-hospital death was less in the nonagenarian group (10.5%) than in the matched octogenarian group (18.4%) without reaching statistical significance. The length of hospitalization was significantly shorter in the nonagenarian group \([7.0 \ (4.0-9.0)\) days] than in the matched octogenarian group \([10.0 \ (6.5-15.0)\) days] \((P = 0.01)\).

**Discussion**

We included 38 nonagenarians and 377 octogenarians to compare clinical characteristics and in-hospital outcomes of AMI between nonagenarians and octogenarians. Although the GRACE risk score was higher in the nonagenarian group, the incidence of in-hospital death was similar between the two groups. The length of hospital stay was significantly shorter in the nonagenarian group than that in the octogenarian group. We also compared clinical characteristics and outcomes between 38 nonagenarians and 38 matched octogenarians to minimize the selection bias. The incidence of in-hospital death was not different between the nonagenarian group and the matched octogenarian group. The length of hospitalization was significantly shorter in the nonagenarian group than in the matched octogenarian group. Our results suggest that clinical outcomes of AMI in the nonagenarian may be comparable to those in the octogenarian, if appropriate acute management including primary PCI is considered.

In earlier studies, Numasawa, et al. investigated the clinical outcomes of elderly patients who underwent PCI and concluded that older patients, especially nonagenarians, carried a greater risk of in-hospital death.\(^{10}\) Lee, et al. reported that the in-hospital mortality was higher in nonagenarians than in octogenarians,\(^{2}\) which is different from our results. The difference may be explained by the fact that only 57.2% of nonagenarians with AMI received PCI in their study.\(^{2}\) Sahin, et al. also reported the high mortality in nonagenarians with STEMI.\(^{25}\) However, only 57.5% of nonagenarians received primary PCI in their study.\(^{25}\) On the other hand, Kim, et al. reported that the primary PCI can be performed with a high success rate and an acceptable in-hospital mortality among the nonagenarians with STEMI,\(^{26}\) suggesting the importance of PCI to the culprit lesion of AMI even in nonagenarians. Therefore, the high mortality of nonagenarians with AMI in
## Table 1. The Comparison of Clinical Characteristics Between the Nonagenarian Group and the Octogenarian Group

| Patient characteristics                                      | Nonagenarian group \(n = 38\) | Octogenarian group \(n = 377\) | \(P\) value |
|---------------------------------------------------------------|---------------------------------|---------------------------------|-------------|
| Age (years)                                                   | 92.0 (91.0-93.0) \((n = 38)\)   | 83.0 (81.0-86.0) \((n = 377)\)  | \(< 0.001\) |
| Female, \(n\) (%)                                            | 16 (42.1)                       | 152 (40.3)                      | 0.831       |
| Height (cm)                                                   | 154.5 (149.6-159.3) \((n = 36)\) | 155.3 (150.0-161.0) \((n = 356)\) | 0.164       |
| Body weight (kg)                                              | 50.4 (43.3-56.9) \((n = 37)\)   | 53.0 (46.3-60.8) \((n = 357)\)  | 0.126       |
| BMI                                                           | 21.9 (19.6-24.5) \((n = 36)\)   | 22.1 (19.9-24.3) \((n = 353)\)  | 0.796       |
| STEMI, \(n\) (%)                                             | 31 (81.0)                       | 226 (59.9)                      | 0.009       |
| NSTE-MI, \(n\) (%)                                           | 7 (18.4)                        | 151 (40.1)                      |             |
| Hypertension, \(n\) (%)                                      | 31 (81.6)                       | 292 (77.5)                      | 0.560       |
| Diabetes mellitus, \(n\) (%)                                 | 14 (36.8)                       | 159 (42.2)                      | 0.525       |
| Dyslipidemia, \(n\) (%)                                      | 11 (28.9)                       | 160 (42.4)                      | 0.107       |
| Hemodialysis, \(n\) (%)                                      | 1 (2.6)                         | 22 (5.8)                        | 0.439       |
| History of previous PCI, \(n\) (%)                           | 8 (21.1)                        | 69 (18.3)                       | 0.580       |
| History of previous CABG, \(n\) (%)                          | 1 (2.6)                         | 19 (5.0)                        | 0.544       |
| Systolic blood pressure on admission (mmHg)                   | 128.0 (104.5-140.8) \((n = 38)\) | 131.0 (111.3-154.0) \((n = 374)\) | 0.182       |
| Diastolic blood pressure on admission (mmHg)                  | 67.5 (59.0-81.8) \((n = 38)\)   | 72.0 (60.0-86.0) \((n = 373)\)  | 0.268       |
| Heart rate on admission (beats/minute)                       | 73.0 (62.3-91.0) \((n = 38)\)   | 80.0 (66.0-96.0) \((n = 374)\)  | 0.253       |
| Killip 3 or 4, \(n\) (%)                                     | 10 (26.3)                       | 111 (29.4)                      | 0.686       |
| Cardiac arrest before admission, \(n\) (%)                   | 0 (0.0)                         | 14 (3.7)                        | 0.255       |
| GRACE risk score                                             | 174.5 (166.3-196.0) \((n = 38)\) | 158.0 (143.8-184.0) \((n = 372)\) | \(\leq 0.001\) |
| Serum albumin (g/dL)                                         | 3.5 (3.2-3.8) \((n = 37)\)     | 3.7 (3.3-4.0) \((n = 375)\)    | 0.010       |
| Serum creatinine (mg/dL)                                     | 1.0 (0.8-1.6) \((n = 38)\)     | 1.0 (0.7-1.4) \((n = 377)\)    | 0.224       |
| Hemoglobin (g/dL)                                            | 11.5 (10.3-12.7) \((n = 38)\)  | 12.2 (10.8-13.3) \((n = 377)\) | 0.021       |
| HbA1c NGSP (%)                                               | 6.1 (5.7-6.6) \((n = 35)\)     | 6.0 (5.7-6.6) \((n = 340)\)    | 0.815       |
| Preadmission ADL                                              |                                |                                 |             |
| Dependence of having meal                                    | 1 (2.6)                         | 13 (3.4)                        | 0.625       |
| Dependence of using toilet                                   | 6 (15.8)                        | 34 (9.0)                        | 0.147       |
| Dependence of maintaining cleanliness                        | 12 (31.6)                       | 52 (13.8)                       | 0.004       |
| Dependence of washing face                                   | 7 (18.4)                        | 29 (7.7)                        | 0.037       |
| Dependence of changing clothes                               | 7 (18.4)                        | 34 (9.0)                        | 0.069       |
| Dependence of moving around                                  | 11 (28.9)                       | 53 (14.1)                       | 0.016       |
| Lesion and procedural characteristics                       |                                |                                 |             |
| Coronary angiography, \(n\) (%)                             | 35 (92.1)                       | 371 (98.4)                      | 0.040       |
| Revascularization                                            |                                |                                 | 0.403       |
| PCI, \(n\) (%)                                               | 33 (86.8)                       | 328 (87.0)                      |             |
| CABG, \(n\) (%)                                              | 0 (0.0)                         | 14 (3.7)                        |             |
| Medical therapy without revascularization, \(n\) (%)         | 5 (13.2)                        | 33 (8.8)                        |             |
| PCI and CABG                                                  | 0 (0.0)                         | 2 (0.5)                         |             |
| Infarct related artery                                       |                                |                                 | 0.490       |
| Left main trunk, \(n\) (%)                                   | 0 (0.0)                         | 17 (4.5)                        |             |
| Left anterior descending artery/diagonal, \(n\) (%)          | 18 (47.3)                       | 160 (42.4)                      |             |
| Left circumflex artery/HL, \(n\) (%)                        | 1 (2.6)                         | 46 (12.2)                       |             |
| Right coronary artery, \(n\) (%)                            | 14 (36.8)                       | 110 (29.2)                      |             |
| Graft, \(n\) (%)                                             | 1 (2.6)                         | 10 (2.7)                        |             |
| Not determined, \(n\)                                        | 1 (2.6)                         | 28 (7.4)                        |             |
| Number of narrowed coronary arteries                         |                                |                                 | 0.479       |
| 1 vessel disease, \(n\) (%)                                 | 14 (36.8)                       | 146 (38.7)                      |             |
| 2 vessel disease, \(n\) (%)                                 | 15 (39.5)                       | 130 (34.5)                      |             |
| 3 vessel disease, \(n\) (%)                                 | 6 (15.8)                        | 95 (25.2)                       |             |
| Syntax score 1                                                | 12.0 (8.0-15.8) \((n = 34)\)   | 13.0 (8.0-21.0) \((n = 353)\)  | 0.352       |
| Approach site                                                 |                                |                                 | 0.272       |
| Trans-radial coronary intervention, \(n\) (%)                | 21 (55.2)                       | 169 (44.8)                      |             |
| Trans-femoral coronary intervention, \(n\) (%)               | 12 (31.6)                       | 149 (39.5)                      |             |
| Trans-brachial coronary intervention, \(n\) (%)              | 0 (0.0)                         | 12 (3.2)                        |             |
| Procedure                                                    |                                |                                 | 0.097       |
| Drug-eluting stent, \(n\) (%)                               | 22 (57.9)                       | 247 (65.5)                      |             |
| Bare metal stent, \(n\) (%)                                 | 7 (18.4)                        | 56 (14.9)                       |             |
| DES and BMS, \(n\) (%)                                      | 2 (5.3)                         | 21 (5.6)                        |             |
| Percutaneous old balloon angioplasty alone, \(n\) (%)        | 0 (0.0)                         | 1 (0.3)                         |             |
| Other, failure, \(n\)                                        | 2 (5.3)                         | 5 (1.3)                         |             |
earlier studies may be derived from the low rate of PCI to the culprit of AMI in nonagenarians.

We should discuss the reasons why the in-hospital mortality was comparable between the nonagenarian and the octogenarian groups. The main reason should be the fact that PCI to the culprit of AMI were similarly performed between the nonagenarian (86.8%) and the octogenarian (87.0%) groups. Because the lesion complexity such as calcification would be affected by aging,27) PCI to the lesion in nonagenarians would be more complex than that in octogenarians. However, the recent development of PCI techniques and devices allows us to perform PCI to more complex lesions. Moreover, as population aging is rapidly progressing in Japan, our interventional cardiologists might have many opportunities to perform PCI to the lesions including non-AMI culprits in nonagenarians. Furthermore, all Japanese patients are covered by excellent public health insurance and social welfare service. If a patient’s age is ≥ 75 years, a self-pay ratio of all medical cost including PCI devices is 10% in Japan. Unlike other countries, it is rare to abandon PCI for poor elderly patients in Japan. Therefore, we might not hesitate to perform PCI to the culprit of AMI in nonagenarians.

We should also discuss the reason why the length of hospitalization in the nonagenarian group [7.0 (4.0-9.0) days] was shorter than that of the octogenarian group [11.0 (7.0-17.0) days]. In our study, a transfer to other hospitals was more frequently observed in nonagenarians (34.2%) than octogenarians (17.5%). Such transfer to other hospitals could shorten the length of hospital stay in our hospital. However, after adjustment for the transfer to other hospitals by the propensity score matching, the

| Table I. The Comparison of Clinical Characteristics Between the Nonagenarian Group and the Octogenarian Group (continued) |
|---------------------------------------------------------------|
|                     | Nonagenarian group | Octogenarian group | P value |
| Thrombus aspiration, n (%) | 10 (26.3)          | 88 (23.3)          | 0.661   |
| Temporary pacemaker, n (%) | 5 (13.2)           | 45 (11.9)          | 0.491   |
| Rotablator, n (%) | 1 (2.6)            | 20 (5.3)           | 0.410   |
| Onset to balloon time |                        |                    | 0.730   |
| < 6 hours | 16 (42.1)          | 109 (28.9)         |         |
| 6-<12 hours | 5 (13.2)           | 56 (14.9)          |         |
| 12-<24 hours | 2 (5.3)            | 36 (9.5)           |         |
| ≥ 24 hours | 10 (26.3)          | 126 (33.4)         |         |
| Not determined | 5 (13.2)           | 50 (13.3)          |         |
| Contrast volume (mL) | 114.0 (87.0-147.5) | 112.0 (81.1-144.7) | 0.549   |
| Acute kidney injury, n (%) | 6 (15.8)           | 60 (15.9)          | 0.248   |
| Initial TIMI flow grade |                  |                    |         |
| 0 | 12 (31.6)          | 113 (30.0)         |         |
| 1 | 4 (10.5)           | 33 (8.8)           |         |
| 2 | 10 (26.3)          | 63 (16.7)          |         |
| 3 | 8 (21.1)           | 134 (35.5)         |         |
| Final TIMI flow grade |                  |                    | 0.173   |
| 0 | 0 (0.0)            | 9 (2.4)            |         |
| 1 | 4 (10.5)           | 6 (1.6)            |         |
| 2 | 2 (5.3)            | 18 (4.8)           |         |
| 3 | 28 (73.7)          | 290 (76.9)         |         |
| Stent length (mm) | 22.0 (18.0-33.0) | 29.2 (25.3-30.0) | 0.988   |
| Stent diameter (mm) | 2.8 (2.5-3.0) | 23.0 (18.0-30.0) | 0.290   |
| Intra-aortic balloon pumping support, n (%) | 0 (0.0) | 17 (4.5) | 0.189   |

STEMI indicates ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; ADL, activities of daily living; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; HL, high lateral branch; DES, drug-eluting stent, BMS, bare metal stent; and TIMI, thrombolysis in myocardial infarction.

| Table II. The Comparison of Clinical Outcomes Between the Nonagenarian Group and the Octogenarian Group |
|---------------------------------------------------------------|
|                     | Nonagenarian group | Octogenarian group | P value |
| In-hospital death, n (%) | 4 (10.5)           | 47 (12.5)          | 0.487   |
| Transfer to other hospitals, n (%) | 13 (34.2)       | 66 (17.5)          | 0.012   |
| Length of hospital stay (days) | 7.0 (4.0-9.0) | 11.0 (7.0-17.0) | <0.001  |
| Length of CCU stay (days) | 3.0 (2.0-4.0) | 3.0 (2.0-6.0) | 0.109   |
| LVEF (%) | 48.0 (40.5-54.4) | 50.7 (40.0-61.8) | 0.152   |
| Peak CKP (U/L) | 631.5 (261.8-2340.5) | 742.0 (228.0-2024.0) | 0.912   |
| Peak CK-MB (U/L) | 57.5 (20.0-274.8) | 60.5 (16.8-198.8) | 0.912   |

CCU indicates coronary care unit; LVEF, left ventricular ejection fraction; CPK, creatine kinase; and CK-MB, creatine kinase MB.
### Table III. The Comparison of Clinical Characteristics Between the Nonagenarian Group and the Matched Octogenarian Group

|                      | Nonagenarian group | MATCHED OCTOGENARIAN GROUP | P value |
|----------------------|--------------------|-----------------------------|---------|
|                      | n = 38             | n = 38                      |         |
| **Patient characteristics** |                    |                             |         |
| Age (years)          | 92.0 (91.0-93.0)   | 88.0 (87.8-89.0)            | < 0.001 |
| Female, n (%)        | 16 (42.1)          | 18 (47.4)                   | 0.645   |
| Height (cm)          | 154.5 (148.9-159.8) | 150.1 (143.5-158.5)         | 0.442   |
| Body weight (kg)     | 30.4 (43.3-57.0)   | 47.3 (42.3-53.9)            | 0.225   |
| BMI                  | 22.0 (19.4-24.9)   | 21.2 (19.2-23.2)            | 0.265   |
| STEMI, n (%)         | 31 (81.6)          | 31 (81.6)                   | 1.000   |
| NSTEMI, n (%)        | 7 (18.4)           | 11 (28.9)                   | 0.280   |
| Hypertension, n (%)  | 31 (81.6)          | 31 (81.6)                   | 1.000   |
| Diabetes mellitus, n (%) | 14 (36.8)      | 14 (36.8)                   | 1.000   |
| Dyslipidemia, n (%)  | 11 (28.9)          | 14 (36.8)                   | 0.464   |
| Hemodialysis, n (%)  | 1 (2.6)            | 1 (2.6)                     | 0.740   |
| Previous PCI, n (%)  | 8 (21.1)           | 5 (13.2)                    | 0.306   |
| Previous CABG, n (%) | 1 (2.6)            | 3 (7.9)                     | 0.328   |
| Systolic blood pressure on admission (mmHg) | 128.0 (103.8-141.8) | 131.5 (113.5-155.8) | 0.436   |
| Diastolic blood pressure on admission (mmHg) | 67.5 (58.8-82.3) | 70.0 (61.3-80.5) | 0.779   |
| Heart rate on admission (/minute) | 73.0 (61.5-91.5) | 83.5 (74.5-90.0) | 0.182   |
| Killip 3 or 4, n (%) | 28 (73.6)          | 25 (68.5)                   | 0.454   |
| Cardiac arrest before admission, n (%) | 0 (0.0)          | 0 (0.0)                     | -       |
| **GRACE risk score** |                    |                             |         |
| Serum albumin (g/dL) | 3.5 (3.2-3.8)      | 3.5 (3.2-3.9)               | 0.577   |
| Serum creatinine (mg/dL) | 1.02 (0.83-1.59) | 0.9 (0.7-1.2) | 0.137   |
| Hemoglobin (g/dL)    | 11.5 (10.3-12.8)   | 11.3 (10.0-12.5)            | 0.626   |
| HbA1c NGSP (%)       | 6.1 (5.7-6.6)      | 5.8 (5.7-6.6)               | 0.584   |
| **Pre-admission ADL** |                    |                             |         |
| Dependence of having meal & toilet | 1 (2.6) | 1 (2.6) | 0.328   |
| Dependence of having meal | 6 (15.8) | 8 (21.1) | 0.515   |
| Dependence of maintaining cleanliness | 12 (31.6) | 11 (28.9) | 0.863   |
| Dependence of washing face | 7 (18.4) | 7 (18.4) | 0.955   |
| Dependence of changing clothes | 7 (18.4) | 9 (23.7) | 0.488   |
| Dependence of moving around | 11 (28.9) | 10 (26.3) | 0.854   |
| **Lesion and procedural characteristics** |                    |                             |         |
| Coronary angiography, n (%) | 38 (100.0) | 38 (100.0) | 0.120   |
| Revascularization     | 0.500             |                             |         |
| PCI, n (%)            | 33 (86.8)          | 34 (89.5)                   | 0.120   |
| CABG, n (%)           | 0 (0.0)            | 0 (0.0)                     | 0.000   |
| Medical therapy without revascularization, n (%) | 5 (13.2) | 4 (10.5) | 0.170   |
| **Infarct related artery** |                    |                             |         |
| Left main trunk, n (%) | 0 (0.0)          | 2 (5.3)                     | 0.535   |
| Left anterior descending artery/diagonal, n (%) | 18 (47.4) | 15 (39.5) | 0.806   |
| Left circumflex artery/HL, n (%) | 1 (2.6)      | 6 (15.8)                    | 0.626   |
| Right coronary artery, n (%) | 14 (36.8)  | 12 (31.6)                   | 0.474   |
| Graft, n (%)          | 1 (2.6)            | 1 (2.6)                     | 0.137   |
| Not determined, n (%) | 1 (2.6)            | 2 (5.3)                     | 0.535   |
| **Number of narrowed coronary arteries** |                    |                             |         |
| 1 vessel disease, n (%) | 14 (36.8)      | 14 (36.8)                   | 0.474   |
| 2 vessel disease, n (%) | 15 (39.5)      | 13 (34.2)                   | 0.474   |
| 3 vessel disease, n (%) | 6 (15.8)       | 11 (28.9)                   | 0.474   |
| Syntax score 1        | 12.0 (8.0-16.3)   | 13.0 (8.0-20.0)             | 0.478   |
| **Approach site**     |                    |                             | 0.381   |
| Trans-radial coronary intervention, n (%) | 21 (55.3) | 26 (68.4) | 0.381   |
| Trans-femoral coronary intervention, n (%) | 12 (31.6) | 6 (15.8) | 0.381   |
| Trans-brachial coronary intervention, n (%) | 0 (0.0)      | 2 (5.3)                     | 0.381   |
| **Procedures**        |                    |                             | 0.189   |
| Drug-eluting stent, n (%) | 22 (57.9)     | 25 (65.8)                   | 0.189   |
| Bare metal stent, n (%) | 6 (15.8)       | 7 (18.4)                    | 0.189   |
| Percutaneous old balloon angioplasty alone, n (%) | 13 (34.2) | 12 (31.6) | 0.189   |
| Other failure (%)     | 2 (5.3)           | 0 (0.0)                     | 0.189   |
| Aspiration (%)        | 10 (26.3)         | 6 (15.8)                    | 0.201   |
| Temporary pacemaker (%) | 5 (13.2)      | 6 (15.8)                    | 0.824   |
| Rotablator (%)        | 1 (2.6)           | 1 (2.6)                     | 0.739   |

*Int Heart J, Advance Publication*
length of hospital stay was still shorter in the nonagenarian group [7.0 (4.0-9.0) days] than in the matched octogenarian group [10.0 (6.5-15.0) days]. Although the clinical parameters such as peak CK/CK-MB or LVEF was similar between the two groups, the severity of AMI might be less in the nonagenarian group than in the octogenarian group. Furthermore, our clinical team might have a drive that we should reduce the length of hospital stay in nonagenarians to prevent cognitive decline or muscle weakness due to long hospitalization.

Clinical implications of the present study should be noted. If the current standard managements for AMI are performed, the in-hospital mortality in nonagenarians with AMI may be similar to that in octogenarians with AMI, maintaining the appropriate length of hospital stay. If a non-PCI-capable hospital receives nonagenarians with AMI, an early transfer to a PCI-capable hospital should be considered. If a PCI-capable hospital receives nonagenarians with AMI, the current standard managements including primary PCI should be considered for better clinical outcomes in nonagenarians.

**Study limitations:** Since this study was a single-center, retrospective, observational study, there is a risk of selection bias. Although we included consecutive AMI patients in our hospital, a non-PCI-capable hospital might not ask us to transfer frail patients who have multiple comorbidities. We could not perform CAG for all patients, partly because of patients’ cognitive dysfunction. However, we could not evaluate cognitive function in the present study. Because the study period was long (January 2009-July 2018), our strategy for AMI such as indication of primary PCI might not be consistent for the study period. We might underestimate the mortality, especially in nonagenarians, because we could not gather information regarding in-hospital death after transfer to other hospitals. Finally, the number of nonagenarian was smaller than that of octogenarian. Future studies including more nonagenarians are warranted to minimize the selection bias.

Table III. The Comparison of Clinical Characteristics Between the Nonagenarian Group and the Matched Octogenarian Group (continued)

| Onset to balloon time | Nonagenarian group | Matched octogenarian group | P value |
|----------------------|--------------------|-----------------------------|---------|
| < 6 hours            | 16 (42.1)          | 13 (34.2)                   | 0.242   |
| 6- < 12 hours        | 5 (13.2)           | 6 (15.8)                    |         |
| 12- < 24 hours       | 2 (5.3)            | 2 (5.3)                     |         |
| ≥ 24 hours           | 10 (26.3)          | 13 (34.2)                   |         |
| Not determined       | 5 (13.2)           | 4 (10.5)                    |         |
| Contrast volume (mL) | 114.0 (84.0-150.0) (n = 35) | 93.4 (65.1-140.1) (n = 38) | 0.108   |
| Acute kidney injury, n (%) | 6 (15.8)          | 8 (21.1)                    | 0.554   |
| Initial TIMI flow grade |                  |                             | 0.435   |
| 0                    | 12 (31.6)          | 12 (31.6)                   |         |
| 1                    | 4 (10.5)           | 4 (10.5)                    |         |
| 2                    | 10 (26.3)          | 10 (26.3)                   |         |
| 3                    | 8 (21.1)           | 8 (21.1)                    |         |
| Final TIMI flow grade |                  |                             | 0.348   |
| 0                    | 0 (0.0)            | 1 (2.6)                     |         |
| 1                    | 4 (10.5)           | 2 (5.3)                     |         |
| 2                    | 2 (5.3)            | 0 (0.0)                     |         |
| 3                    | 28 (73.7)          | 32 (84.2)                   |         |
| Stent length (mm)    | 2.8 (2.5-3.0) (n = 29) | 2.9 (2.5-3.0) (n = 32)       | 0.599   |
| Stent diameter (mm)  | 22.0 (18.0-35.5) (n = 29) | 19.0 (18.0-26.0) (n = 32)       | 0.132   |
| Intra-aortic balloon pumping support, n (%) | 3 (7.9)          | 4 (10.5)                    | 0.500   |
| Percutaneous cardio pulmonary support, n (%) | 0 (0.0)          | 2 (5.3)                     | 0.247   |

STEMI indicates ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; ADL, activities of daily living; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; HL, high lateral branch; DES, drug-eluting stent, BMS, bare metal stent; and TIMI, thrombolysis in myocardial infarction.

Table IV. The Comparison of Clinical Outcomes Between the Nonagenarian Group and the Matched Octogenarian Group

| In-hospital death, n (%) | Nonagenarian group | Matched octogenarian group | P value |
|-------------------------|--------------------|-----------------------------|---------|
| n = 38                  | 4 (10.5)           | 7 (18.4)                    | 0.328   |
| Transfer to other hospitals, n (%) | 13 (34.2)          | 15 (39.5)                   | 0.634   |
| Length of hospital stay (days) | 7.0 (4.0-9.0) (n = 38) | 10.0 (6.5-15.0) (n = 38)      | 0.010   |
| Length of CCU stay (days)  | 3.0 (2.0-4.25) (n = 38) | 3.0 (2.0-4.0) (n = 38)       | 0.979   |
| LVEF (%)                | 48.0 (40.0-57.5) (n = 34) | 47.3 (38.5-58.9) (n = 36)     | 0.789   |
| Peak CPK (U/L)          | 631.5 (260.5-2410.3) (n = 38) | 1196.0 (153.3-2083.8) (n = 38) | 0.901   |
| Peak CK-MB (U/L)        | 57.5 (18.8-296.5) (n = 38) | 96.5 (12.8-248.8) (n = 38)   | 0.767   |

CCU indicates coronary care unit; LVEF, left ventricular ejection fraction; CPK, creatine kinase; and CK-MB, creatine kinase MB.
Conclusions

The in-hospital mortality of nonagenarians with AMI was comparable to that of octogenarians with AMI. The length of hospital stay was significantly shorter in nonagenarians with AMI than in octogenarians with AMI. In-hospital clinical outcomes in nonagenarians with AMI may be acceptable as long as acute medical management including PCI to the culprit of AMI is performed.

Acknowledgments

We are grateful for the support of the entire staff of the catheterization laboratory of Saitama Medical Center, Jichi Medical University.

Disclosure

Conflicts of interest: Dr. Sakakura has received speaking honoraria from Abbott Vascular, Boston Scientific, Medtronic Cardiovascular, Terumo, OrbusNeich, Japan Lifeline, and NIPRO. He has served as a proctor for Rotablator for Boston Scientific and has served as a consultant for Abbott Vascular and Boston Scientific. Prof. Fujita served as a consultant for Mehergen Group Holdings, Inc.

References

1. Rosengren A, Wallentin L, Simoons M, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the EuroHeart acute coronary syndrome survey. Eur Heart J 2006; 27: 789-95.
2. Lee KH, Ahn Y, Kim SS, et al. Characteristics, in-hospital and long-term clinical outcomes of nonagenarian compared with octogenarian acute myocardial infarction patients. J Korean Med Sci 2014; 29: 527-35.
3. Lin X, Zhang S, Huo Z. Serum circulating miR-150 is a predictor of post-acute myocardial infarction heart failure. Int Heart J 2019; 60: 280-6.
4. Rumana N, Kita Y, Turin TC, et al. Trend of increase in the incidence of acute myocardial infarction in a Japanese population: Takashima AMI Registry, 1990-2001. Am J Epidemiol 2008; 167: 1358-64.
5. Alonso Salinas GL, Sanmartin M, Pascual Izco M, et al. Frailty is an independent prognostic marker in elderly patients with myocardial infarction. Clin Cardiol 2017; 40: 925-31.
6. Avezum A, Makdisse M, Spencer F, et al. Impact of age on management and outcome of acute coronary syndrome: Observations from the Global Registry of Acute Coronary Events (GRACE). Am Heart J 2005; 149: 67-73.
7. Velders MA, James SK, Libungan B, et al. Prognosis of elderly patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention in 2001 to 2011: A report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) registry. Am Heart J 2014; 167: 666-73.
8. Page M, Doucet M, Eisenberg MJ, Behloul H, Pilote L. Temporal trends in recanalization and outcomes after acute myocardial infarction among the very elderly. Can Med Assoc J 2010; 182: 1415-20.
9. Khera S, Kolte D, Palaniswamy C, et al. ST-elevation myocardial infarction in the elderly - Temporal Trends in incidence, utilization of percutaneous coronary intervention and outcomes in the United States. Int J Cardiol 2013; 168: 3683-90.
10. Numasawa Y, Inohara T, Ishii H, et al. Comparison of outcomes after percutaneous coronary intervention in elderly patients, including 10 628 nonagenarians: Insights from a Japanese Nationwide Registry (J-PCI Registry). J Am Heart Assoc 2019; 8: e011183.
11. Christensen K, Dobhlammer G, Rau R, Vaupel JW. Ageing populations: The challenges ahead. Lancet 2009; 374: 1196-208.
12. Ministry of Internal Affairs and Communications Statistics Bureau. Population Estimates, long-term time-series data of Japan’s estimated population. Available at: https://www.e-stat.go.jp/stat-search/files?page=1&layout=data&tablecode=t000000090001&cycle=0&class1=000000090004&class2=20 00000090005&class3=200000090006&stat_id=000000090263&second2=1. Accessed May 26, 2019.
13. Ministry of Internal Affairs and Communications Statistics Bureau. Population Estimates, long-term time-series data of Japan’s estimated population. Available at: https://www.e-stat.go.jp/stat-search/files?page=1&layout=data&tablecode=t000000090001&cycle=0&class1=000000090004&class2=20000010511800&stat_id=000013168603&second2=1. Accessed May 26, 2019.
14. Watanabe Y, Sakakura K, Taniguchi Y, et al. Determinants of slow flow in percutaneous coronary intervention to the culprit lesion of non-ST Elevation Myocardial infarction. Int Heart J 2018; 59: 1237-45.
15. Tsukui T, Sakakura K, Taniguchi Y, et al. Determinants of short and long door-to-balloon time in current primary percutaneous coronary interventions. Heart Vessels 2018; 33: 498-506.
16. Yamamoto K, Sakakura K, Akashi N, et al. Clinical outcomes of left main crossover stenting for ostial left anterior descending artery acute myocardial infarction. Heart Vessels 2018; 33: 33-40.
17. Kellum JA, Laneire N. Diagnosis, evaluation, and management of acute kidney injury: A KDIGO summary (part 1). Crit Care 2013; 17: 204.
18. Helal AM, Shaheen SM, Elhammady WA, Ahmed MI, Abdel-Hakim AS, Allam LE. Primary PCI versus pharmacoinvasive strategy for ST elevation myocardial infarction. Int J Cardiol Heart Vasc 2018; 21: 87-93.
19. Granger CB, Goldberg RJ, Dabbous O, et al. Predictors of hospital mortality in the global registry of acute coronary events. Arch Intern Med 2003; 163: 2345-53.
20. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009; 360: 961-72.
21. Otani A, Sakakura K, Yamamoto K, et al. Comparison of midterm clinical outcomes after acute myocardial infarction in diabetic men between living alone and living together. Heart Vessels 2019; 34: 1288-96.
22. Lindenauner PK, Pekow P, Wang K, Mamidi DK, Gutierrez B, Benjamin EM. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. N Engl J Med 2005; 353: 349-61.
23. Kosiborod M, Lam CSP, Kohsaka S, et al. Cardiovascular events associated with SGLT-2 inhibitors versus other glucose-lowering drugs. J Am Coll Cardiol 2018; 71: 2628-39.
24. Stuart EA. Matching methods for causal inference: A review and a look forward. Statist Sci 2010; 25: 1-21.
25. Sahin M, Ocal L, Kalkan AK, et al. In-Hospital and long term results of primary angioplasty and medical therapy in nonagenarian patients with acute myocardial infarction. J Cardiovasc Thorac Res 2017; 9: 147-51.
26. Kim JY, Jeong MH, Choi YW, et al. Temporal trends and in-hospital outcomes of primary percutaneous coronary intervention in nonagenarians with ST-segment elevation myocardial infarction. Korean J Intern Med 2015; 30: 821-8.
27. Newman AB, Naydeck BL, Sutton-Tyrrell K, Feldman A, Edmundowicz D, Kuller LH. Coronary artery calcification in older adults to age 99: Prevalence and risk factors. Circulation 2001; 104: 2679-84.