Age Differences in the Delivery of Cardiac Management to Women Versus Men With Acute Myocardial Infarction

An Evaluation of the TAMIS-II Data

Yoshihisa HIRAKAWA,¹ MD, Yuichiro MASUDA,¹ MD, Masafumi KUZUYA,¹ MD, Akihisa IGUCHI,¹ MD, Takaya KIMATA,¹ MD, and Kazumasa UEMURA,² MD

SUMMARY

It is of concern that women are more likely to undergo fewer diagnostic tests and receive less treatment for acute myocardial infarction (AMI) than men. Our retrospective Tokai Acute Myocardial Infarction Study (TAMIS) indicated that there were gender differences according to age groups; however, the exact nature of these gender differences remains unclear. Therefore, using data from TAMIS-II, we studied the influence of gender on the delivery of cardiac management according to 2 age groups (< 65, ≥ 65). TAMIS-II is a prospective study of all consecutive patients admitted to the 15 acute care hospitals in the Tokai region with the diagnosis of AMI from 2001 to 2003. A total of 169 younger women, 1246 younger men, 616 older women, and 1240 older men were included. Data on patient demographics, in-hospital course, comorbid conditions, electrocardiography (ECG), ultrasound-echocardiogram (UCG), treadmill test (TMT), coronary angiography (CAG), percutaneous coronary intervention (PCI), coronary artery bypass grafts (CABG), intra-aortic balloon pump (IABP), mechanical ventilation, and in-hospital or discharge medications (thrombolytics, vasopressors, aspirin, β-blockers, angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, nitrates) were collected. After controlling for these baseline variables, only lipid-lowering therapy tended to be more frequent in women than in men among the elderly (OR 1.55, 95%CI 1.00-2.38). The results from this Japanese chart review study, derived from detailed clinical data, indicated that the delivery pattern of cardiac management for female and male AMI patients during hospitalization and at discharge was very similar among the younger and older populations.

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Key words: Acute myocardial infarction (AMI), Gender, Patterns of practice, Percutaneous coronary intervention (PCI), Lipid-lowering therapy

From the ¹ Department of Geriatrics, Nagoya University Graduate School of Medicine, ² Center of Medical Education, Nagoya University School of Medicine, Aichi, Japan. Address for correspondence: Yoshihisa Hirakawa, MD, Department of Geriatrics, Nagoya University Graduate School of Medicine, 65 Tsuruma-cho, Showa-ku, Nagoya, Aichi 466-8550, Japan. Received for publication November 17, 2005. Revised and accepted January 6, 2006.
THE fact that women are less likely to undergo acute myocardial infarction (AMI) diagnostic tests and are less likely to receive treatments for AMI is an issue of concern.\textsuperscript{1-4} Some studies have demonstrated that women with AMI experience lower rates of revascularization and less success with other treatments than do men, while others suggest there is no significant difference between men and women after adjusting for differences in variables, including complications. Thus, the effect of gender on the in-hospital management of patients with AMI remains controversial.\textsuperscript{1, 4-12}

In addition, our previous retrospective study, TAMIS,\textsuperscript{13} demonstrated that the gender differences in AMI management are different between younger and older populations, which is consistent with the findings of another study.\textsuperscript{14}

The purpose of this multihospital prospective study was to confirm age-specific gender differences in the use of medications and the utilization of diagnostic and revascularization procedures in patients hospitalized for AMI, compared with the results reported by TAMIS.

**METHODS**

**Study population:** We used data from the Tokai Acute Myocardial Infarction Study II (TAMIS-II), a multicenter prospective observational study conducted in the Tokai region of Japan. Consecutive adult patients who were hospitalized for AMI at 15 acute care hospitals between January 2001 and December 2003 were included in the study. Their diagnoses were confirmed by an abstractor's subsequent chart review. A patient who was admitted more than once with a diagnosis of AMI was included in the analysis. With regards to the recruitment of participant hospitals, we first selected the major hospitals that had an interchange of personnel with Nagoya University Hospital, where we are based. Second, we sent a prospectus about our research to the selected hospitals. Fifteen hospitals then approved the study. Thirteen out of the 15 hospitals that participated in TAMIS were included in TAMIS-II. All 15 hospitals that participated in TAMIS-II were nonprofit general hospitals that could perform coronary angiography (CAG) and percutaneous coronary intervention (PCI). Not every hospital had a department of cardiovascular surgery or could perform coronary artery bypass grafting (CABG) during the study period. We were unable to identify those hospitals lacking such a department or ability, because we did not investigate it even by interviewing the hospital staff in charge after the study.

**Data collection:** We abstracted the baseline and procedural characteristics from detailed chart reviews, which included both physician notes and nursing notes by physicians or skilled nurses educated to obtain medical records, as soon as possible after the discharge or death of a study patient. However, we did not specify a
time limit on data collection due to the large number of study patients and the large amount of data. All of the skilled nurses were also abstractors in TAMIS. The questionnaire, which had the same format as that used in TAMIS, contained information on patient demographics, the in-hospital course (length of stay, ICU/CCU transfer), comorbid conditions, clinical presentation (body mass index, body temperature, systolic arterial pressure, heart rate, chest pain, pulmonary edema, shock, bleeding, ultrasound-echocardiogram (UCG), ejection fraction, treadmill test (TMT), MI location, and earlier admission activity of daily living (ADL)), and procedural characteristics (CAG, PCI, CABG, intra-aortic balloon pump (IABP), mechanical ventilation, time from onset to angiography, and in-hospital and discharge medication (thrombolytics, vasopressors, aspirin, \( \beta \)-blockers, angiotensin-converting enzyme (ACE) inhibitors, calcium antagonists, nitrates)). A history of various comorbid conditions was recorded as present if it was documented in the medical charts. If no information was documented, then the comorbid condition was recorded as absent.

**Statistical Analysis:** We compared the baseline and procedural characteristics and clinical outcomes between women and men according to 2 age groups (younger, < 65, older, \( \geq 65 \)). Statistical analysis was performed using the chi-square test for categorical variables and the unpaired \( t \) test for continuous variables. We also performed multiple logistic regression analysis to identify the independent association between gender and cardiac care according to age group, after adjusting for other baseline and procedural factors that differed significantly between women and men. Univariate predictors of cardiac care with a \( P \) value less than 0.05 could be entered in the model. We present the results as odds ratios and 95% confidence intervals. A \( P \) value less than 0.05 was considered statistically significant.

**RESULTS**

**Baseline characteristics:** A total of 169 younger women, 1246 younger men, 616 older women, and 1240 older men were included in the analysis. Among the group under age 65 (younger group), the women were significantly older than the men (Table I). Also, women were less likely to have lodgers in their home than were men. Systolic blood pressure among women was higher than among men. The women had a lower body mass index (BMI) score and were more likely to have a history of hypertension or heart failure, but they were less likely to have a history of smoking or peptic ulcer disease. Women were less likely to present with chest pain on admission and were more likely to have pulmonary edema on x-ray examination.
Among the group aged 66 and over (older group), the women were significantly older than the men. The initial heart rate was higher and the BMI score was lower in the women. They were more likely to have a history of hypertension or hypercholesterolemia, or to have dementia, but less likely to have a spouse, a history of myocardial infarction, a history of smoking, aortic aneurysm, or peptic ulcer disease. Women were less likely to present with chest pain on admission and less likely to be independent in their daily living.

**Procedural characteristics:** Among the young, women stayed in hospital almost as long as men (Table II). Gender was not associated with the likelihood of receiving UCG or TMT. They were as likely to receive CAG, PCI, or CABG as...
### Table II. Procedural Characteristics of the Patients

<table>
<thead>
<tr>
<th></th>
<th>Young group (&lt;65)</th>
<th>Old group (≥65)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women (n = 169)</td>
<td>Men (n = 1246)</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>17.54 ± 1.41</td>
<td>18.22 ± 0.51</td>
</tr>
<tr>
<td>Transfer to ICU/CCU</td>
<td>137</td>
<td>81.07</td>
</tr>
<tr>
<td>UCG</td>
<td>147</td>
<td>86.98</td>
</tr>
<tr>
<td>TMT</td>
<td>24</td>
<td>14.20</td>
</tr>
<tr>
<td>CAG</td>
<td>163</td>
<td>96.45</td>
</tr>
<tr>
<td>Time to CAG &lt; 6</td>
<td>44</td>
<td>26.04</td>
</tr>
<tr>
<td>6-12</td>
<td>18</td>
<td>10.65</td>
</tr>
<tr>
<td>&gt;12</td>
<td>18</td>
<td>10.65</td>
</tr>
<tr>
<td>PCI</td>
<td>147</td>
<td>86.98</td>
</tr>
<tr>
<td>CABG</td>
<td>4</td>
<td>2.37</td>
</tr>
<tr>
<td>Thrombolytic</td>
<td>19</td>
<td>11.24</td>
</tr>
<tr>
<td>Vasopressor</td>
<td>44</td>
<td>26.04</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>21</td>
<td>12.43</td>
</tr>
<tr>
<td>Discharge medication</td>
<td>105</td>
<td>62.13</td>
</tr>
<tr>
<td>Aspirin</td>
<td>136</td>
<td>80.47</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>7</td>
<td>4.14</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>72</td>
<td>42.60</td>
</tr>
<tr>
<td>Nitrates</td>
<td>79</td>
<td>46.75</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>25</td>
<td>14.79</td>
</tr>
<tr>
<td>Diuretics</td>
<td>14</td>
<td>8.28</td>
</tr>
<tr>
<td>Antihyperlipidemics</td>
<td>73</td>
<td>43.20</td>
</tr>
</tbody>
</table>

ICU/CCU indicates intensive care unit/coronary care unit; UCG ultrasound-electrocardiogram; TMT treadmill test; CAG, coronary angiography; EF, ejection fraction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; and IABP, intra-aortic balloon pump.

### Table III. Use of Medications, Diagnostic Tests, and Treatments for AMI Among Young Patients (below 65) Among Women Versus Men

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted OR</th>
<th>95%CI</th>
<th>Age adjusted OR</th>
<th>95%CI</th>
<th>Multivariable adjusted OR*</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>0.48</td>
<td>0.32-0.73</td>
<td>0.48</td>
<td>0.31-0.74</td>
<td>0.59</td>
<td>0.32-1.11</td>
</tr>
<tr>
<td>β-blocker</td>
<td>0.54</td>
<td>0.24-1.18</td>
<td>0.53</td>
<td>0.24-1.16</td>
<td>0.25</td>
<td>0.06-1.09</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>0.85</td>
<td>0.61-1.18</td>
<td>0.85</td>
<td>0.61-1.18</td>
<td>0.92</td>
<td>0.58-1.45</td>
</tr>
<tr>
<td>Lipid lowering therapy</td>
<td>1.36</td>
<td>0.99-1.89</td>
<td>1.38</td>
<td>1.00-1.93</td>
<td>1.35</td>
<td>0.84-2.17</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>0.88</td>
<td>0.64-1.22</td>
<td>0.86</td>
<td>0.62-1.19</td>
<td>0.94</td>
<td>0.59-1.49</td>
</tr>
<tr>
<td>Ca channel blocker</td>
<td>0.76</td>
<td>0.49-1.19</td>
<td>0.76</td>
<td>0.49-1.20</td>
<td>0.90</td>
<td>0.48-1.67</td>
</tr>
<tr>
<td>Diuretics</td>
<td>0.82</td>
<td>0.46-1.46</td>
<td>0.81</td>
<td>0.45-1.46</td>
<td>0.36</td>
<td>0.13-1.04</td>
</tr>
<tr>
<td>Vasopressor</td>
<td>1.06</td>
<td>0.73-1.53</td>
<td>0.99</td>
<td>0.68-1.44</td>
<td>0.85</td>
<td>0.46-1.56</td>
</tr>
<tr>
<td>Thrombolytics</td>
<td>0.63</td>
<td>0.38-1.03</td>
<td>0.67</td>
<td>0.40-1.10</td>
<td>1.07</td>
<td>0.48-2.39</td>
</tr>
<tr>
<td>IABP</td>
<td>1.04</td>
<td>0.68-1.60</td>
<td>1.03</td>
<td>0.67-1.59</td>
<td>0.62</td>
<td>0.29-1.31</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>1.34</td>
<td>0.82-2.19</td>
<td>1.24</td>
<td>0.75-2.04</td>
<td>1.12</td>
<td>0.49-2.52</td>
</tr>
<tr>
<td>CAG</td>
<td>0.40</td>
<td>0.16-1.02</td>
<td>0.41</td>
<td>0.16-1.07</td>
<td>1.93</td>
<td>0.21-17.54</td>
</tr>
<tr>
<td>PTCA</td>
<td>0.92</td>
<td>0.57-1.49</td>
<td>0.93</td>
<td>0.58-1.52</td>
<td>2.07</td>
<td>0.89-4.83</td>
</tr>
<tr>
<td>CABG</td>
<td>0.60</td>
<td>0.22-1.70</td>
<td>0.55</td>
<td>0.20-1.57</td>
<td>0.97</td>
<td>0.31-3.02</td>
</tr>
<tr>
<td>UCG</td>
<td>0.85</td>
<td>0.47-1.53</td>
<td>0.83</td>
<td>0.46-1.51</td>
<td>0.80</td>
<td>0.35-1.85</td>
</tr>
<tr>
<td>TMT</td>
<td>0.94</td>
<td>0.59-1.48</td>
<td>0.88</td>
<td>0.55-1.40</td>
<td>0.98</td>
<td>0.54-1.76</td>
</tr>
</tbody>
</table>

AMI indicates acute myocardial infarction; UCG ultrasound-electrocardiogram; TMT, treadmill test; CAG, coronary angiography; PTCA, percutaneous coronary intervention; CABG, coronary artery bypass graft; IABP, intra-aortic balloon pump; OR, odds ratio; and CI, confidence interval. *Controlling for age, systolic blood pressure, number of lodgers, heart failure, smoking, peptic ulcer, chest pain, and pulmonary edema.
Among the elderly, fewer women were transferred to the ICU or CCU than men. Gender was not associated with the likelihood of receiving UCG or TMT. Women were less likely to receive CAG or PCI, as likely to receive CABG, less likely to receive therapy with aspirin, an ACE inhibitor, or nitrates, and more likely to receive diuretics or antihyperlipidemics at discharge.

**Multivariable analyses:** Multiple regression analysis was carried out to more systematically examine the relations between gender and in-hospital management while controlling for differences in baseline variables, in which statistically significant differences were detected between women and men. Because we considered the presence of a lodger in the patient’s home to be strongly correlated to the presence of a spouse, the number of lodgers was not included in our regression models. The multivariable-adjusted results of in-hospital management are shown in Tables III and IV. Among the young group, after controlling for these baseline variables, the gender differences in aspirin use disappeared, and no gender differences were detected. Among the old group, women were more likely to receive
therapy with diuretics or antihyperlipidemics and less likely to receive therapy with aspirin, ACE inhibitors, nitroglycerin, CAG, or UCT before controlling for differences in previously described variables (Table IV). After controlling for the named variables, only lipid-lowering therapy tended to be more frequent in women than in men (OR 1.55, 95% CI 1.00-2.38).

**DISCUSSION**

The present study was conducted to investigate whether previously reported gender differences in the delivery of cardiac management in patients with acute myocardial infarction were also evident among Japanese patients. Because we expected on the basis of previous studies that differences in in-hospital management between women and men with AMI would be influenced by age, we examined the gender differences using 2 age groups.

In accordance with previous studies, the present findings indicate that women and men were different with respect to their baseline backgrounds, which could be a predictor of in-hospital management. Also, among procedural characteristics, a delay in seeking CAG was observed in our study. A lack of knowledge of AMI symptoms among female patients may be a possible explanation for the delay.

Our earlier study, TAMIS, suggested that there were age-specific gender differences in the use of lipid-lowering medication. To be more specific, the TAMIS results indicated that lipid-lowering medications were used more frequently among elderly women. Likewise in TAMIS-II, although cardiovascular medication use was similar between female and male patients, a difference in the use of lipid-lowering medications was noted specifically among patients who were 65 years old and over. Additionally, our findings suggested that older women were more likely to receive lipid-lowering therapy even after multivariable adjustment. Although it is still unclear whether there exists a difference in the administration of lipid-lowering therapy between women and men, our 2 large-scale studies, TAMIS and TAMIS-II, strongly support the presence of a gender difference.

It also appeared, according to TAMIS-II, that younger and older female patients were less likely to receive aspirin than were their male counterparts. However, consistent with a previous study, using multivariable regression analysis to adjust for the influence of other possible factors, gender was no longer statistically significant. The TAMIS results indicated that women were similarly treated with aspirin before adjustment for the influence of possible factors. Our results from TAMIS-II suggest that the gender difference is clinically relevant.

Consistent with TAMIS, the TAMIS-II data did not suggest that being female contributed to UCG or TMT use. The underuse of TMT among women
may not be problematic in Japan.

In TAMIS-II, inconsistent with TAMIS, there was no gender difference with respect to performing PCI. As TAMIS and other previous studies suggested, women had undergone less PCI than men in the younger but not in the older population. Robertson, et al\(^\text{18}\) suggested that less frequent use of coronary angioplasty in women has been attributed to higher complication rates, lower procedural success, and/or poorer clinical outcome reported for women compared to men. However, recently, technical innovations for coronary intervention have become prominent.\(^\text{7,19}\) For example, coronary artery stenting has become the mainstay of PCI for patients with AMI and has improved the outcome of acute myocardial infarction.\(^\text{20}\) It is possible that such technical innovations improved the lower rate of PCI among women. Another possible explanation for the increased PCI rate in women is that awareness by physicians of the results of clinical trials demonstrating that PCI is used less often for women than men with AMI altered their behavior toward PCI use in women after TAMIS, which took place from 1995 to 1997.

The present study has some limitations. First, the sample size was not as large as that used in previous studies. However, because there is no national database in non-Western countries that can be compared with Western countries, we believe the present study makes a contribution to the knowledge in this field.

Second, the patients in TAMIS-II were all treated by tertiary care cardiologists. It is possible that a gender bias may still exist in other institutions in which care is provided by physicians other than cardiology specialists.

Third, due to the lack of examiners, we should have secured personnel who are not physicians to regularly collect data. Although all the trained nurses were also abstractors in TAMIS and skilled in collecting the data, it is possible that the data collecting procedures varied among the hospitals depending on who was in charge of data collection at each hospital because not all trained nurses are familiar with medical data on circulatory illnesses.

Finally, although our intention was to construct a comprehensive questionnaire, we had a lot of missing laboratory data, such as the distributions of cholesterol levels, CK-MB, and ST elevation. Also, it is important to collect angiographic outcomes to confirm the gender differences in PCI use. The absence of such detailed data may limit our results.

**Conclusion:** We conducted a prospective observational study, TAMIS-II, to confirm the age differences in the delivery of cardiac management to women versus men with acute myocardial infarction in Japan, following our retrospective study (TAMIS). The findings suggested that there were no obvious gender differences in the in-hospital management of patients hospitalized with AMI among the younger and older populations.
REFERENCES