Prognostic factors in primary and elective percutaneous coronary intervention
Claessen, B.E.P.M.

Link to publication

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Chapter 9

Primary Percutaneous Coronary Intervention for ST Elevation Myocardial Infarction in Octogenarians; Trends and Outcomes

*Heart* 2010;96:854-859

ABSTRACT

Objective: The general population is gradually aging in the Western world. Therefore, the number of octogenarians undergoing primary Percutaneous Coronary Intervention (PCI) for ST-Elevation Myocardial Infarction (STEMI) is increasing. We aim to provide insight in temporal trends in the annual proportions of octogenarians among STEMI patients undergoing primary PCI and their clinical characteristics and outcomes over an eleven-year observational period.

Design: Single-centre observational study.

Patients: Between 1997 and 2007, we treated 4506 STEMI patients with primary PCI at our institution. Patients aged >80 years were identified.

Main outcome measures: We analyzed temporal trends in the annual proportion of octogenarian STEMI patients, and their baseline characteristics, 30-days and one-year mortality.

Results: A total of 379 octogenarians (8.4% of the total population) were treated with primary PCI between 1997 and 2007. Over time, the annual proportion of octogenarians gradually increased from 4/113 (3.5%) in 1997 to 51/579 (8.8%) in 2007 (p for trend <0.01). In the total cohort of 379 patients, 30-day mortality was 21% (81 patients), one-year mortality was 28% (107 patients). There was no improvement in survival among octogenarian STEMI patients over the eleven-year study period.

Conclusion: The annual proportion of octogenarian STEMI patients increased significantly over the eleven-year study period. Mortality among these high-risk patients was high and did not improve during the study period. Unfortunately, little is known about the optimal treatment of the elderly as they are underrepresented in many randomized clinical trials. Further studies into the optimal STEMI management strategy for the elderly are warranted.
INTRODUCTION

The general population is gradually aging in the Western world. The proportion of octogenarians in the general population is expected to be tripled by the year 2050. (1) Advanced age is associated with an increased incidence of myocardial infarction and the presence of severe cardiovascular co-morbidities. Even though octogenarians constitute an important high-risk subgroup of ST-Elevation myocardial infarction (STEMI) patients, they are underrepresented in randomized clinical trials investigating optimal reperfusion and adjunctive treatment strategies for STEMI. (2,3) Furthermore, only very few retrospective analyses have focused on octogenarians, all hampered by small patient numbers. (4-7) As a result, currently little is known about the clinical characteristics and outcome of octogenarians undergoing primary percutaneous coronary intervention (PCI).

In this paper, we provide insight into trends in the annual proportion of octogenarians in the STEMI population undergoing primary PCI and their clinical characteristics and outcomes over an observational period of eleven years.

METHODS

Between 1997 and 2007, a total of 4931 consecutive and unselected patients were admitted to our hospital with STEMI. Acute STEMI was diagnosed when patients had symptoms of an acute myocardial infarction lasting 30 minutes to 6 hours, accompanied by an electrocardiogram with ST-segment elevation >1 mm (0.1 mV) in ≥ 2 contiguous leads. Patients were immediately transported to the cardiac catheterization laboratory and underwent immediate coronary angiography with a view to perform primary PCI. PCI was performed by standard techniques, if the coronary anatomy was suitable. All procedural decisions, including device selection and adjunctive pharmacotherapy, such as glycoprotein IIb/IIIa inhibitors, were made at the discretion of the operator. All patients were treated with heparin (5000 IU) and aspirin (900 mg) prior to PCI. If a coronary stent was implanted, ticlopidine or clopidogrel was prescribed according to the guidelines.

Baseline data

All patients undergoing PCI at our institution were prospectively followed. Baseline clinical (i.e. gender, age, risk factors, and cardiac history), angiographic (i.e. multivessel disease), and procedural (i.e., stent implantation) information was entered by qualified cardiac catheterization laboratory personnel and interventional cardiologists in a dedicated electronic database.

Follow up

We obtained information on the vital status from the institutional follow-up database of PCI patients. Patients were surveyed one year after primary PCI using a mailed, self-administered questionnaire. Information on mortality was synchronized with the computerized records from the national population registry (Statistics Netherlands, Voorburg, the Netherlands) and was verified until January 1, 2008. We reviewed the outpatient files and contacted general practitioners by telephone in the case of conflicting or missing data.

Study cohort

Data for the 4931 patients were checked for consistency and completeness. For patients who underwent >1 primary PCI during the study period (n=147), only the first intervention was included in this analysis. Patients treated with rescue PCI for failed intravenous thrombolysis (n=145), patients without confirmed diagnosis of STEMI (n=76) and patients lost to follow-up (n=57) were excluded, resulting in a final cohort of 4506 STEMI patients. To provide insight into the differences in baseline, angiographic, and procedural characteristics, and 30-day and 1-year mortality, between younger and elderly STEMI patients we stratified patients into four age groups (≥80 years, 60-79 years, 40-59 years, <40 years).

Definitions

Multivessel disease was defined as at least 1 stenosis ≥70% in a non-infarct related epicardial artery. Shock was defined according to the criteria used in the “SHould we emergently revascularize
Chapter 9

Occluded Coronaries for cardiogenic shock?” (SHOCK) trial(8).

Primary outcome
The primary outcome for the present analysis was all-cause 30-day and one-year mortality.

Statistical Analysis
Statistical analysis was performed with SPSS statistical software, version 15.0 (SPSS, Inc., Chicago, Illinois). Discrete variables are summarized as percentages (frequency). Temporal trends in the proportion of octogenarians in the STEMI population, temporal trends in baseline characteristics and differences in baseline characteristics between the four age groups were tested for significance by the Chi² test. Statistical significance was defined as a p value <0.05.

Cumulative event-rates of all-cause death were estimated using the Kaplan-Meier method. A “landmark analysis” with a landmark set at 30 days was used to provide further insight into differences between early (<30 days) and long-term (one-year) mortality. The Log Rank statistic was used to test for significant differences in mortality between the four age groups.

Table 1 Baseline clinical, angiographic and procedural characteristics of 379 octogenarians treated with primary PCI between 1997 and 2007

<table>
<thead>
<tr>
<th>Baseline characteristics N,(%)</th>
<th>Patients</th>
<th>Patients</th>
<th>Patients</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;40 Years</td>
<td>40-59 Years</td>
<td>60-79 years</td>
<td>≥80 years</td>
</tr>
<tr>
<td>N=211</td>
<td>(4.7%)</td>
<td>(42%)</td>
<td>(45%)</td>
<td>(8.4%)</td>
</tr>
<tr>
<td>Male</td>
<td>165 (78)</td>
<td>1517 (80)</td>
<td>1368 (68)</td>
<td>171 (45)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34 (16)</td>
<td>504 (27)</td>
<td>720 (36)</td>
<td>132 (35)</td>
</tr>
<tr>
<td>Smoker</td>
<td>151 (72)</td>
<td>1119 (59)</td>
<td>653 (32)</td>
<td>47 (12)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12 (5.7)</td>
<td>161 (8.5)</td>
<td>300 (15)</td>
<td>66 (17)</td>
</tr>
<tr>
<td>Known hypercholesterolaemia at admission</td>
<td>37 (18)</td>
<td>449 (24)</td>
<td>449 (22)</td>
<td>43 (11)</td>
</tr>
<tr>
<td>Family history of CVD</td>
<td>118 (56)</td>
<td>929 (49)</td>
<td>663 (33)</td>
<td>72 (19)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>13 (6.2)</td>
<td>189 (10)</td>
<td>330 (16)</td>
<td>79 (21)</td>
</tr>
<tr>
<td>Shock</td>
<td>15 (7.1)</td>
<td>118 (6.2)</td>
<td>183 (9.1)</td>
<td>44 (12)</td>
</tr>
</tbody>
</table>

Angiographic characteristics

| LAD related MI                  | 106 (50) | 836 (44) | 843 (42) | 180 (48) |
| Pre-PCI TIMI flow grade         |          |          |          |          |
| TIMI 0                          | 135 (64) | 1265 (67) | 1319 (65) | 227 (60) |
| TIMI 1                          | 16 (7.7) | 152 (8.0) | 168 (8.3) | 44 (12)  |
| TIMI 2                          | 29 (14)  | 204 (11) | 229 (11) | 52 (14)  |
| TIMI 3                          | 31 (14)  | 275 (15) | 304 (15) | 56 (15)  |
| Post-PCI TIMI flow grade        |          |          |          |          |
| TIMI 0                          | 2 (0.9)  | 38 (2.0) | 67 (3.3) | 19 (5.0) |
| TIMI 1                          | 2 (0.9)  | 8 (0.4)  | 29 (1.4) | 10 (2.6) |
| TIMI 2                          | 12 (5.7) | 113 (6.0) | 188 (9.3) | 54 (14.2) |
| TIMI 3                          | 195 (92) | 1737 (92) | 1736 (86) | 296 (78) |
| Multivessel disease             | 30 (14)  | 498 (26) | 821 (41) | 202 (53) |

Procedural characteristics

| Glycoprotein IIb/IIIa Inhibitor | 62 (29) | 485 (26) | 535 (27) | 88 (23) |
| Thrombosuction performed        | 71 (34) | 616 (33) | 614 (30) | 96 (25) |
| Intra-aortic balloon counterpulsation | 14 (6.6) | 128 (6.8) | 201 (10) | 51 (14) |
| Stent placement                 | 142 (67) | 1433 (76) | 1499 (74) | 285 (75) |

CVD= Cardiovascular disease, MI= Myocardial infarction, LAD= Left anterior descending coronary artery, PCI= Percutaneous coronary intervention, TIMI= Thrombolysis In Myocardial Infarction
Logistic regression models were used to analyze the relation between age and one-year mortality. First, an unadjusted odds ratio (OR) and 95% confidence interval (CI) for one-year mortality was calculated for age as a continuous variable. Subsequently, adjusted ORs and 95%CIs were calculated using forward stepwise selection multivariate logistic regression analysis. Included covariates were: age, gender, hypertension, smoking, diabetes mellitus, hypercholesterolaemia, family history of cardiovascular disease (CVD), previous myocardial infarction, shock, LAD-related infarction, multivessel disease, and postprocedural Thrombolysis In Myocardial Infarction (TIMI) flow grade <3. A covariate was included in the model if it influenced the model with a p < 0.10 by the Wald test and was removed if its significance level exceeded p = 0.15. For both unadjusted and adjusted mortality models, the shape and strength of the relations between age and probability of death at one year were plotted graphically. If the relation was nonlinear, a model fitting approach involving cubic polynomials (splines) was used as previously employed by the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) trial investigators. (9-13)

RESULTS

Trends in Octogenarian STEMI patients

Between 1997 and 2007 we treated 379 patients aged ≥80 years (8.4%), 2020 patients aged 60-79 years (45%), 1896 patients aged 40-59 years (42%) and 211 patients aged <40 years (4.7%). Over time, the annual proportion of octogenarians gradually increased from 4/113 (3.5%) in 1997 to 51/579 (8.8%) in 2007 (p for trend < 0.01). Figure 1 shows the proportion of octogenarians in the annual total STEMI population for our eleven-year STEMI experience.

Clinical Characteristics

Baseline, angiographic and procedural characteristics are shown in table 1. The majority of octogenarian STEMI patients were female. Furthermore, octogenarians had a higher prevalence of diabetes, hypertension, and multivessel disease, and more often had a history of a previous infarction when compared to younger patients. When compared to younger patients, primary PCI in octogenarians was associated with a lower rate of attaining postprocedural TIMI flow grade

Figure 1 Eleven-year trend in the proportion of octogenarians undergoing primary PCI
3. Between 1997 and 2007 the rates of postprocedural TIMI flow grade 3 increased significantly from 75% in 1997 to 82% in 2007 (p for trend 0.02). We observed no other significant trends in the composition of baseline, clinical, and procedural characteristics during our eleven-year STEMI experience (data not shown).

Clinical Outcome

One-year follow-up was complete for all patients (n=4506). Table 2 shows mortality rates at 30 days, from 30 days to one year, and at one year. As expected, mortality was very high in octogenarians when compared to patients in the younger age groups. For octogenarians, the one-year mortality rate was 28.2%, compared to 12.8%, 6.3%, and 4.3% in patients aged 60-79, 40-59 and <40, respectively. Figure 2a shows cumulative one-year mortality stratified by age group. Figure 2b shows cumulative mortality until the landmark set at 30 days and mortality between 30 days and one-year follow-up. Both early (<30 days) and late (from 30 days to one year) mortality was significantly higher in the octogenarian groups when compared to the other three groups (log rank p-value <0.01). Interestingly, mortality was comparable in male and female octogenarians as illustrated by the Kaplan Meier curve in figure 3 (log rank p value 0.24). As shown in Figure 4, the probability of death at one-year follow-up increased with age (unadjusted OR 1.054 per year increase, 95% CI 1.045-1.06, p<0.01). After adjustment for other predictors of mortality, the relation between age and one-year mortality somewhat weakened as a result of the interaction with other risk factors. However, age remains a strong and independent predictor of one-year mortality with an OR of 1.032 per year increase in age. Table 3 shows unadjusted and adjusted ORs for all variables included in the model.

DISCUSSION

In this study conducted in a cohort of 4506 STEMI patients, covering 11 years of observations from a single center, we showed that the annual proportion of octogenarians among patients undergoing primary PCI for STEMI has gradually increased from 4/113 patients (3.5%) in 1997 to 51/579 patients (8.8%) in 2007 (p for trend <0.01). Furthermore, we showed that age is both an independent predictor of mortality and associated with a higher prevalence of cardiovascular risk factors. Therefore, one-year mortality among patients aged ≥80 years was high (28.2%). Noteworthy, one-year mortality was comparable in male and female octogenarians and remained unchanged during the study period of eleven years.

To our knowledge, this is the first paper investigating temporal trends regarding the proportion of octogenarians and their clinical characteristics and outcomes. The proportion of STEMI patients aged 80 years and older increased significantly during the study period of eleven years. The increasing number of octogenarians being referred for primary PCI for STEMI can be explained by the ageing of the general population (the fastest rate of growth in any segment of the population in the United States is occurring in octogenarians) and the fact that the incidence of STEMI in elderly patients is high.(3)

Previous papers concerning primary PCI in octogenarians studied only small series of patients ranging from 40-63 patients.(4-7) These small studies report one-year mortality rates varying from 10% to 43%. In the current study, the 30-day and one-year mortality rates for octogenarians were 21.4% and 28.2% respectively. Moreover, we performed a landmark survival analysis to provide further insight between early (<30 days) and late mortality (from 30 days to one year). The majority of deaths occurred within 30 days, however, the mortality rates continued to diverge significantly between 30 days and one year. Interestingly, we observed no difference in mortality between male and female octogenarians.

The high mortality rates can in part be explained by effects of advancing age itself, and in part by the higher incidence of cardiogenic shock complicating STEMI, the higher prevalence of multivessel coronary artery disease, previous myocardial infarction, and other co-morbidities such as hypertension and diabetes mellitus. This is demonstrated in table 3 and shown graphically in
**Table 2** 30-Day, 30-Day to One-Year, and Overall One-Year Mortality

<table>
<thead>
<tr>
<th>Age Group</th>
<th>30-Day Mortality (N=4506)</th>
<th>30-Day to One-Year Mortality* (N=4131)</th>
<th>Overall One-Year Mortality (N=4506)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>3.80%</td>
<td>0.50%</td>
<td>4.30%</td>
</tr>
<tr>
<td>40-59 years</td>
<td>5.10%</td>
<td>1.30%</td>
<td>6.30%</td>
</tr>
<tr>
<td>60-79 years</td>
<td>9.40%</td>
<td>3.80%</td>
<td>12.80%</td>
</tr>
<tr>
<td>≥80 years</td>
<td>21.40%</td>
<td>8.70%</td>
<td>28.20%</td>
</tr>
</tbody>
</table>

* For 30-day to one-year mortality, only patients who survived the first 30 days after myocardial infarction were included.

**Figure 2** Overall one-year mortality, 30-Day and 30-day to one-year mortality in 4506 STEMI patients

Log rank p-values for overall one year mortality: Octogenarians vs ages 60-79 p<0.01, octogenarians vs ages 40-59 p<0.01, octogenarians vs ages >40 P<0.01, ages 60-79 vs ages 40-59 P<0.01, ages 60-79 vs ages >40 P<0.01, ages 40-59 vs ages <40 p=0.6
Figure 3 Mortality in 379 octogenarian STEMI patients undergoing primary PCI stratified by sex

![Mortality Graph](image-url)

Figure 4 which shows that after adjusting for other known risk factors, the relation between age and one-year mortality somewhat weakens, although it remains significant (unadjusted OR 1.054 per year increment, adjusted OR 1.032 per year increment). Furthermore, octogenarians more often had a suboptimal angiographic result (postprocedural TIMI flow grade <3) after primary PCI. Although we observed a significant improvement in postprocedural TIMI flow grade 3 rates from 75% in 1997 to 82% in 2007, this is still lower than in younger patients. Finally, elderly patients with an acute myocardial infarction are less likely to present with ST-segment elevation and chest pain on presentation. Many present with dyspnea as the principal complaint. The lack of symptoms may delay presentation causing a delay in the administration of treatment.

Limitations

The retrospective nature of this study prohibits us from speculating how the prognosis of octogenarians treated with primary PCI for STEMI could be improved. Furthermore, although follow-up for one-year mortality was complete for all patients, we do not have detailed information on the causes of death. Therefore, the exact causes of the high case-fatality rates currently remain unknown. Moreover, a patient selection bias may have been introduced as this paper focuses on STEMI, and octogenarians are less likely to develop ST-elevation on the electrocardiogram in the setting of acute myocardial infarction. Data on time from symptom onset to treatment was unavailable; therefore we were not able to investigate differences in time from symptom onset to treatment between age groups. Detailed information on peri- and post-procedural medication was not available; therefore we were not able to assess differences in adherence to guideline-based post-STEMI therapies.
CONCLUSION

The annual proportion of STEMI patients aged 80 years and older has significantly increased during the eleven-year study period and it will keep increasing in the years to come. Octogenarians constitute a rapidly growing subgroup of patients with a high incidence of STEMI and a high case-fatality rate which did not improve during the study period. As octogenarians were either excluded from or underrepresented in major randomized clinical trials, the optimal treatment strategy remains unknown. This paper underscores the importance of future research into the optimal STEMI treatment for octogenarians.

Figure 3: Probability of death at one year after STEMI as a function of age
Reference List