Long-Term Prognosis in an ST-Segment Elevation Myocardial Infarction Population Treated With Routine Primary Percutaneous Coronary Intervention
From Clinical Trial to Real-Life Experience

Sune Pedersen, MD; Soren Galatius, MD, DMSc; Rasmus Mogelvang, MD, PhD; Ulla Davidsen, MD; Anders Galloe, MD, PhD; Steen Z. Abildstrom, MD, PhD; Ulrik Abildgaard, MD, DMSc; Peter Riis Hansen, MD, PhD, DMSc; Jan Bech, MD, DMSc; Allan Iversen, MD; Erik Jorgensen, MD, DMSc; Henning Kelbaek, MD, DMSc; Kari Saunamaki, MD, DMSc; Jan Kyst Madsen, MD, DMSc; Jan Skov Jensen, MD, PhD, DMSc

Background—We sought to describe the long-term prognosis after routine primary percutaneous coronary intervention (pPCI) in a contemporary consecutive population of patients with presumed ST-segment elevation myocardial infarction, compare it with similar results from the landmark DANAMI-2 trial, and to identify a possible impact of time of presentation and referral pattern.

Methods and Results—Long-term prognosis in 1019 presumed ST-segment elevation myocardial infarction patients, treated according to modern routine pPCI during the year 2004, was analyzed and compared with similar data from the DANAMI-2 trial. Furthermore, we analyzed the impact of patient presentation to the angioplasty center during “off hours” (4 PM to 8 AM plus weekends and holidays) and the impact of being referred from noninvasive hospitals. At 3 years, 20.4% in the routinely treated population versus 19.6% in the DANAMI-2 trial reached the combined end point of death, reinfarction, or stroke (P=0.68), whereas the all-cause mortality was 13.0% and 13.7%, respectively (P=0.65). Patients admitted during off hours had the same risk of reaching the combined end point of death, reinfarction, or stroke compared with patients admitted during office hours (hazards ratio, 1.04; 95% CI, 0.8 to 1.5; P=0.81). Door-to-balloon times of less than 90 minutes were achieved in 60% among patients admitted directly to an invasive center but only in 40% among transferred patients (P<0.001). Despite this difference, no difference in unadjusted or adjusted long-term prognosis was found between the 2 groups.

Conclusions—This study shows that ST-segment elevation myocardial infarction patients treated with contemporary routine pPCI achieve a similar long-term prognosis as patients in the landmark randomized pPCI trial (DANAMI-2). Furthermore, the long-term prognosis was the same regardless of whether the pPCI was performed during off hours or office hours. Thus, pPCI including transportation of patients from noninvasive centers can be applied successfully in a real-life population. (Circ Cardiovasc Intervent. 2009;2:392-400.)

Key Words: myocardial infarction ▪ door-to-balloon ▪ long-term ▪ off-hours ▪ primary PCI

Primary percutaneous coronary intervention (pPCI) is the recommended treatment for ST-segment elevation myocardial infarction (STEMI).1-4 In Denmark, pPCI is performed at 5 tertiary high-volume invasive centers, with patients being either directly admitted to the local emergency department or transported from regional noninvasive hospitals. The short-term benefit of pPCI compared with fibrinolyses has been demonstrated in a number of trials, the largest of which was the Danish multicenter randomized study on thrombolytic therapy versus acute coronary angioplasty in acute myocardial infarction (DANAMI)-2 trial.1-8 However, only a limited number of long-term follow-up data have been published—and apart from the recently published long-term results from the DANAMI-2 and PRAGUE trials9,10—the available long-term data are derived from smaller clinical trials with study populations included more than 15 years ago.2,11,12 It is well recognized that results after routine treatment, only to a limited extent, may mirror those of clinical trials. So far, the long-term prognosis after routine pPCI in a large consecutive STEMI population, including patients transported from hospitals without PCI facilities, has never been described.

Received December 19, 2008; accepted June 19, 2009.
From the Department of Cardiology (S.P., S.G., R.M., U.D., A.G., U.A., P.R.H., J.B., A.I., J.K.M., J.S.J.), Gentofte University Hospital, Copenhagen, Cardiovascular Research Unit, Department of Internal Medicine, Copenhagen University Hospital Glostrup, Glostrup (S.Z.A.); and Department of Cardiology (E.J., H.K., K.S.), Rigshospitalet University Hospital, Copenhagen, Denmark.
Correspondence to Sune Pedersen, MD, Department of Cardiology P, Gentofte Hospital, Niels Andersens Vej 65, DK-2900, Copenhagen, Denmark. E-mail sunped01@geh.regionh.dk
© 2009 American Heart Association, Inc.
Circ Cardiovasc Intervent is available at http://circinterventions.ahajournals.org DOI: 10.1161/CIRCINTERVENTIONS.108.845636

392
Clinical Perspective on p 400

Patients with STEMI require immediate emergency care, and it is essential that hospitals involved in the treatment of these patients maintain a high quality of care around the clock. However, it has been reported that patients admitted to hospitals with acute myocardial infarction during “off hours” have poorer prognosis compared with patients treated during regular office hours.1,13-15 Whether the prognosis is dependent on the actual pPCI performed during off hours is a different question. A number of studies have investigated this issue, but with very diverging results.16-20

We present the long-term prognosis in a large STEMI population of consecutive patients treated with modern routine pPCI during the year 2004, from 2 high-volume invasive centers covering 43% of the Danish population; ie, 2.4 million inhabitants. The findings from this cohort were compared with long-term results from patients enrolled in the pPCI arm of the DANAMI-2 trial.9 Furthermore, we analyzed the prognostic impact of time of presentation to the invasive center during office hours versus off-hour and the impact of being transferred to the invasive centers from noninvasive hospital compared with directly admitted patients.

Methods

Study Population
Routine treatment with pPCI for STEMI, including interhospital transportation, was introduced and implemented in Denmark in 2002 following the presentation of the DANAMI-2 trial at the 2002 American College of Cardiology meeting.1 From January 2004 to December 2004, 1019 consecutive patients admitted to the angioplasty centers at Gentofte University Hospital or Rigshospitalet University Hospital (Denmark) with presumed STEMI were included in this study. The 2 invasive centers have a catchments area of 2.4 million persons, ie, 43% of the entire Danish population. This is primarily an urban population. Each center performed more than 1500 PCIAs per year (approximately 1/3 pPCI), with each individual PCI operator performing approximately 300 PCIs per year. Each center has on-site surgical capacity.

Baseline and procedural data were prospectively collected from all patients and entered in dedicated registries at the 2 institutions. Hypertension was defined as use of blood pressure–lowering drugs. Diabetes was defined as use of antidiabetic treatment, fasting plasma glucose concentration ≥7 mmol/L, or nonfasting plasma glucose concentration ≥11.1 mmol/L. “Symptom-to-balloon” time was defined as time from onset of symptoms reported by the patient to first pPCI balloon inflation, and “door-to-balloon” time was defined as time from arrival to the first hospital to first balloon inflation.

Comparison With the DANAMI-2 Population
The DANAMI-2 trial demonstrated that pPCI, including treatment of transported patients from noninvasive centers, was feasible and superior to on-site fibrinolyses.1 Event rates at 3 years of follow-up from the current routinely treated population of presumed STEMI were compared with similar event rates from the patients randomized to pPCI in the DANAMI-2 trial (angioplasty arm; n=790). As the DANAMI-2 trial had an “intention-to-treat” design and follow-up, we included all patients with presumed STEMI, examined with acute coronary angiography and potentially treated with pPCI.

Subanalysis
1. Impact of time of arrival to the angioplasty center:
   - Office hours: weekdays—8 AM to 3.59 PM versus
   - Off hours: weekdays—4 PM to 7.59 AM + weekends + holidays.

2. Impact of referral pattern:
   - Patient directly admitted to 1 of the 2 invasive centers versus
   - Patients admitted through the 25 noninvasive referring hospitals using physician-manned interhospital transportation (interhospital transfer).

A number of variables were by nature obtained only for patients actually treated with pPCI (use of drug-eluting stent [DES], glycoprotein IIb/IIIa inhibitors, coronary characteristics, and treatment delay), and because our aim was to evaluate pPCI treatment in different settings, we focused the subanalysis on pPCI-treated patients (n=847).

Follow-Up and Study End Points
Follow-up was 99.8% complete (2 patients were lost to follow-up because of emigration). All patients were followed up for exactly 3 years. In case of more than 1 PCI procedure within the study period, the first pPCI procedure was the index procedure and the following invasive procedures were registered as new revascularizations.

All Danish citizens are registered at birth with a unique personal identification number. Information regarding death or emigration is entered in the National Person Identification Registry. Follow-up data on reinfarction, stroke, and new revascularization were collected from the Danish National Board of Health’s National Patient Registry, using ICD-10 codes. In this registry, information on all hospital admissions with their corresponding diagnoses (ICD-10) is registered for every individual patient. If an event was registered in these registries, they were later validated by cross-checking with hospital source data. Reinfarction was defined as recurrent chest pain combined with significant increase in creatine kinase MB and troponin I levels. Stroke was defined as neurological symptoms consistent with stroke, combined with a possible computed tomography scan. Additional information about any new revascularization procedure (PCI/coronary artery bypass graft) was obtained from dedicated registries at the 2 institutions.

Study end points were all-cause mortality, reinfarction, stroke, and a composite of these 3 end points. Furthermore, rates of new revascularization were described. These end points were compared with the corresponding long-term event rates from the DANAMI-2 trial.9

Primary PCI in the Routine Setting
If pPCI was indicated, it was performed according to contemporary interventional guidelines, using pretreatment with 10 000 IU unfractionated heparin, 300 to 500 mg acetyl salicylic acid, and 300 to 600 mg clopidogrel. The transfemoral approach was used with 6- or 8-French sheath, conventional devices, and Iomeron contrast fluid (Bracco, United Kingdom). The infantar-related artery was stented by 1 or more DES or bare metal stent, either by direct stenting or by following balloon predilatation. POBA was used only in a limited number of cases. Glycoprotein IIb/IIIa inhibitors were used at the discretion of the operator. Subsequent medical treatment included anti-ischemic, lipid-lowering, and antithrombotic drugs and was given according to current guidelines.

Transfer Protocol
Ambulance crews were instructed to drive to the nearest emergency department, regardless of the invasive capability. Patients with a presumed STEMI admitted directly to an invasive center were evaluated at the emergency department, and in cases of ECG-suspected STEMI, the patient was transported to the catheterization laboratory for immediate pPCI. Patients initially admitted to a noninvasive center were evaluated by the local physician with the ambulance crew on stand-by. In case of ECG-suspected STEMI, the invasive center was alerted and the patient was immediately transferred (accompanied by a physician) to the catheterization laboratory at the invasive center, thereby bypassing the emergency departments.

During off hours, the catheterization laboratory staff was activated from their homes (~30 minutes away) by the hospital on-call resident cardiologist.
Table 1. Comparison of Baseline Variables Between Real-Life Patients With Presumed STEMI Versus the Angioplasty Arm in the DANAMI-2 Trial and Patients Actually Treated With pPCI During Office Hours or Off Hours in the Real-Life Population

<table>
<thead>
<tr>
<th>Infarct related artery</th>
<th>Real-Life Presumed STEMI (n=1019)</th>
<th>DANAMI 2 Angioplasty Arm (Intention to Treat) (n=790)</th>
<th>Real-Life (pPCI Performed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 (±12)</td>
<td>63</td>
<td>64 (±12)</td>
</tr>
<tr>
<td>Male sex</td>
<td>73</td>
<td>73</td>
<td>71</td>
</tr>
<tr>
<td>Hypertension</td>
<td>33</td>
<td>20</td>
<td>32</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>Current smoker</td>
<td>53</td>
<td>58</td>
<td>48</td>
</tr>
<tr>
<td>Prev MI</td>
<td>7</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Door-to-balloon time, min*</td>
<td>97 (65–135)</td>
<td>109</td>
<td>90 (60–140)</td>
</tr>
<tr>
<td>Symptom-to-balloon time, min*</td>
<td>214 (145–310)</td>
<td>216</td>
<td>210 (135–306)</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa*</td>
<td>28</td>
<td>N/A</td>
<td>30</td>
</tr>
<tr>
<td>Heart failure</td>
<td>8</td>
<td>N/A</td>
<td>7</td>
</tr>
<tr>
<td>Hereditary IHD</td>
<td>26</td>
<td>N/A</td>
<td>25</td>
</tr>
<tr>
<td>Nonstenotic vessels</td>
<td>9</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>1-vessel disease</td>
<td>55</td>
<td>54</td>
<td>57</td>
</tr>
<tr>
<td>2-vessel disease</td>
<td>21</td>
<td>25</td>
<td>26</td>
</tr>
<tr>
<td>3-vessel disease</td>
<td>15</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Type A lesion</td>
<td>4</td>
<td>N/A</td>
<td>4</td>
</tr>
<tr>
<td>Type B lesion</td>
<td>50</td>
<td>N/A</td>
<td>62</td>
</tr>
<tr>
<td>Type C lesion</td>
<td>29</td>
<td>N/A</td>
<td>34</td>
</tr>
</tbody>
</table>

| Statistics            |                                     |                                                    |                             |
|                       | Categorical baseline characteristics were compared by the χ² test, Gaussian-distributed continuous variables by the Student unpaired t test, and non–Gaussian-distributed variables by the Mann-Whitney test. Comparisons between the DANAMI-2 population and the current population were made using event rates up till exactly 3 years of follow-up by χ² test. Associations between prognostic variables and end points in the present population were examined by Kaplan–Meier plots and log-rank test and univariate/multivariable Cox proportional hazards regression models. All assumptions (linearity and proportional hazards) for the Cox analysis were fulfilled. Relevant variables (all baseline variables presented in Table 1) were initially entered in the multivariable analysis. A backward elimination model was used to identify variables with independent predictive value (removal level P>0.05). Only patients actually treated with pPCI (n=847) were entered in the Cox analysis. A P value ≤0.05 was considered statistically significant. SPSS for Windows version 15.0 was used. The study was approved by the local scientific ethical committee and the Danish Data Protection Agency and complies with the Declaration of Helsinki. All authors provided substantial contributions to conception of design and collection and analysis and interpretation of the data. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written. |

Data are presented as mean (±SD), %, or median (IQR). IHD indicates ischemic heart disease; LAD, left anterior descending artery; RCA, right coronary artery; Cx, circumflex; LM, left main; POBA, plain old balloon angioplasty; BMS, bare metal stent. *Analyzed only for patients actually treated with pPCI. †χ² test including the entire group.
**Long-Term Prognosis**

All patients were followed up for exactly 3 years. At 3 years, 20.4% of the current population versus 19.6% of the patients in the DANAMI-2 trial reached the combined end point of death, reinfarction, or stroke \( (P=0.68) \). When all-cause mortality, reinfarction, and stroke were analyzed separately, no statistically significant differences existed between the 2 study populations. However, only 18.0% in the real-life population had a new revascularization, compared with 25% in the DANAMI-2 trial \( (P=0.01) \) (Figure 1).

**Routine pPCI**

Patients with presumed STEMI, who did not receive pPCI \( (n=172) \), were diagnosed at discharge with acute heart failure of nonischemic origin \( (n=59) \), pericarditis \( (n=45) \), ischemic heart disease (treated medically \( n=48 \) or with acute CABG \( n=2) \), or another diagnosis \( (n=18) \). A total of 880 patients \( (86\%) \) were referred from hospitals without PCI facilities. Patients from referral hospitals were treated with pPCI in 83% of the cases compared with 86% of the cases admitted directly to invasive centers \( (P=0.3) \). Patients not treated with pPCI \( (n=172) \) had a trend toward an impaired prognosis compared with pPCI-treated patients, with an all-cause mortality of 17.4% versus 12.0% in the pPCI group \( (P=0.06) \).

A number of variables were by nature obtained only for patients actually treated with pPCI (use of DES, glycoprotein IIb/IIIa inhibitors, coronary characteristics, and treatment delay). Furthermore, because our aim was to evaluate pPCI treatment in different settings, we focused the subsequent analysis on pPCI-treated patients \( (n=847) \).

For patients with STEMI treated with pPCI, known left ventricular dysfunction, left anterior descending artery lesions, multivessel disease, and increased “door-to-balloon” time (per 1 hour increase) independently predicted impaired prognosis (Table 2). The use of DES did not significantly affect the prognosis.

---

**Figure 1.** Event rates at 3 years of follow-up. A, Real-life patients with presumed STEMI versus DANAMI-2 angioplasty arm. B, Real-life patients with STEMI: off hours versus office hours. C, Real-life patients with STEMI: interhospital transfer versus directly to invasive center. *Combined end point (death, reinfarction or stroke). A person can only enter the composite analysis with 1 end point.

**Table 2. Multivariable Cox Regression Analysis Including Patients Treated With pPCI (n=847)**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95% CI</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presentation during off hours</td>
<td>1.04</td>
<td>0.75–1.45</td>
<td>0.81</td>
</tr>
<tr>
<td>Admitted via invasive centers</td>
<td>0.98</td>
<td>0.61–1.58</td>
<td>0.93</td>
</tr>
<tr>
<td>Age (per 5-y increase)</td>
<td>1.07</td>
<td>0.99–1.15</td>
<td>0.08</td>
</tr>
<tr>
<td>Male</td>
<td>1.15</td>
<td>0.81–1.62</td>
<td>0.44</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.46</td>
<td>0.94–2.26</td>
<td>0.09</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.31</td>
<td>0.95–1.81</td>
<td>0.10</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2.18</td>
<td>1.40–3.40</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hereditary IHD</td>
<td>1.08</td>
<td>0.74–1.57</td>
<td>0.69</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.06</td>
<td>0.77–1.47</td>
<td>0.72</td>
</tr>
<tr>
<td>Previous MI</td>
<td>1.43</td>
<td>0.87–2.38</td>
<td>0.16</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitors</td>
<td>1.02</td>
<td>0.73–1.43</td>
<td>0.90</td>
</tr>
<tr>
<td>LAD vs other lesions</td>
<td>1.52</td>
<td>1.11–2.08</td>
<td>0.01</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>1.68</td>
<td>1.22–2.31</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Complex lesions</td>
<td>1.11</td>
<td>0.81–1.52</td>
<td>0.53</td>
</tr>
<tr>
<td>Use of DES</td>
<td>0.79</td>
<td>0.57–1.09</td>
<td>0.15</td>
</tr>
<tr>
<td>Door-to-balloon (per 1 h increase)</td>
<td>1.14</td>
<td>1.04–1.25</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Step 12</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (per 5-y increase)</td>
<td>1.09</td>
<td>1.02–1.17</td>
<td>0.01</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2.23</td>
<td>1.44–3.46</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LAD vs other lesions</td>
<td>1.47</td>
<td>1.09–2.00</td>
<td>0.01</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>1.78</td>
<td>1.31–2.42</td>
<td>0.01</td>
</tr>
<tr>
<td>Door-to-balloon (per 1 h increase)</td>
<td>1.13</td>
<td>1.03–1.23</td>
<td>0.01</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio; IHD, ischemic heart disease; LAD, left anterior descending artery.

*A backward elimination model was used, and the first and last steps are displayed (removal level \( P>0.05) \).
Time of Patient Presentation (Office Hours Versus Off Hours)

Sixty-eight percent were admitted during off hours, whereas 32% were admitted during office hours. Patients admitted during office hours had a higher mean age compared with patients admitted during off hours (64 versus 62 years, \( P=0.02 \)). Otherwise, no significant differences were found in baseline and procedural characteristics between the 2 groups, and in particular, the symptom-to-balloon time and door-to-balloon time were independent of time of arrival (Table 1). Patients treated during off hours did not seem to have poorer long-term outcomes compared with patients treated during office hours. For example, event rates at 3 years of follow-up were similar in the 2 groups (Figure 1). Kaplan–Meier curves depicting the composite end point in the 2 populations were almost super imposable (Figure 2). This noninferiority remained significant in the adjusted multivariable analysis (hazards ratio, 1.04; 95% CI, 0.75 to 1.45; \( P=0.81 \)) (Table 2).

Interhospital Transfer Versus Direct Admission to the Invasive Centers

Of 847 pPCI-treated patients, 738 (87%) were referred from hospitals without PCI facilities. No significant baseline differences were found between the 2 groups, apart from a lower mean age and higher incidence of diabetes and 3-vessel disease among referred patients. Furthermore, the median symptom-to-balloon time and door-to-balloon time was shorter for patients with STEMI directly admitted to an invasive center compared with patients referred from noninvasive hospitals (180 minutes versus 218 minutes; \( P<0.01 \), and 73 minutes versus 100 minutes; \( P<0.01 \)) (Table 1). Door-to-balloon times of less than 90 minutes were achieved in 60% of patients admitted directly to an invasive center, but only in 40% of transferred patients (\( P<0.001 \)) (Figure 3). Despite this difference, we did not find that “transferred” patients experienced poorer long-term outcome, apart from an increased risk of having a new revascularization procedure (Table 2 and Figures 1 and 2).

Discussion

This study demonstrates that a prognosis similar to that of the DANAMI-2 trial can be obtained when treating a real-life population of presumed patients with STEMI with routine pPCI. Furthermore, we demonstrate that patients treated with pPCI in high-volume centers have the same prognosis independent of the time of presentation to the pPCI centers.

The DANAMI-2 trial and a number of other trials have shown that transfer of patients with STEMI for pPCI is feasible and superior to on-site fibrinolyses in the controlled environment of the randomized trial and when time to treatment is short.1–8 This study describes a real-life population of patients with STEMI treated with routine pPCI at 2 high-volume invasive centers (85 pPCI/operator/yr). During just 1 year (2004), 1019 patients were admitted with presumed STEMI to the 2 centers, and 847 had the diagnosis STEMI confirmed and were treated with pPCI. The importance of high-volume centers and PCI operators with respect to the quality of pPCI treatment has previously been described in the study by Spaulding et al.21

Interestingly, the baseline and procedural variables, including the symptom-to-balloon time in our routinely treated population of patients with STEMI, were similar to the findings in the DANAMI-2 trial. This indicates that the inclusion and exclusion criteria of the DANAMI-2 trial reflected a real-life STEMI population, and this provides a reasonable background for comparison of outcomes in the 2 populations. Indeed, the long-term (3 years) prognosis in our population and in DANAMI-2 patients was similar, both with respect to the individual end points and the combined end point. Actually, the rate of new revascularization was significantly lower in the real-life population, which could be explained by the lack of DES use in the DANAMI-2 population. Furthermore, the current population was treated...
with a more aggressive pharmacological therapy, eg, glycoprotein IIb/IIIa inhibitors and angiotensin-converting enzyme inhibitors because of changes in treatment guidelines. Nevertheless, we believe that this result is of great importance because it demonstrates that routine pPCI (including interhospital transfer) can be applied in a real-life STEMI population with favorable results that resembles the long-term results from randomized trials, such as the DANAMI-2 trial. An important factor influencing the outcome among patients with STEMI is time to reperfusion.22,23 National guidelines in the United States and in Europe state that the benchmark door-to-balloon time should be less than 90 minutes.4,24 Most patients with STEMI, in Denmark and in other countries, including the United States, are primarily admitted to a noninvasive center. In the current study, the mean distance from a noninvasive to an invasive center was 28 miles (range, 2 to 59 miles), and more than 95% of the population had less than 1 hour of transportation time to the invasive center. Furthermore, our preinvasive organization (see Methods section) was quite effective during the time of the study, partly because the 2 invasive centers, as well as most of the referral hospitals, had been engaged in the DANAMI-2 trial, and partly because the Danish Society of Cardiology endorsed and strongly recommended the implementation of pPCI treatment. One could expect that the preprocedure organization at the noninvasive hospitals (eg, ambulance on stand-by) could inflict additional costs on the health system. However, in most patients, this was not the case when compared with a conventional setting, where the patient is transferred to an emergency room, medical history is delivered to the physician, and finally a new ambulance is requested for the transfer to the invasive center. Still, we recognize that these geographical and political conditions do not necessarily apply to other regions. It is therefore our objective, only to demonstrate that short door-to-balloon-time and good long-term outcome can be obtained, when pPCI is performed within an effective organizational structure. In the United States, regional substantial differences exist in the availability of hospitals with

Figure 3. Cumulative histograms showing door-to-balloon and symptom-to-balloon times for patients admitted directly to an invasive center versus patients referred from noninvasive center. Door-to-balloon times of less than 90 minutes were achieved in 60% among patients admitted directly to an invasive center but only in 40% among transferred patients ($P<0.001$).
invasive facilities. Nevertheless, it is estimated that approximately 80% of the adult population live within 60 minutes—and 95% live within 90 minutes from an invasive center.25 In a recent analysis from the US CathPCI registry, including 15 049 patients with STEMI undergoing pPCI in 2005–2006, the median door-to-balloon time was 152 minutes (IQR, 116 to 211).26 Obviously, there is more to door-to-balloon time than geography, and local barriers, such as underserved rural areas, lack of local written guidelines and formal training, noncardiologist on duty, and inefficiencies in the reimbursement system, play essential roles in the effort of reducing delay in pPCI treatment.

In our study, we found a median door-to-balloon time of 97 minutes for all pPCI-treated patients and 100 minutes for patients transferred from noninvasive centers. When the independent impact of door-to-balloon time was evaluated in the multivariable analysis, we found that increased door-to-balloon time significantly predicted impaired prognosis. Since the year 2005, patients with STEMI have been referred directly to our 2 invasive centers after immediate triage with use of tele-transmission of the ambulance ECG (ie, bypassing noninvasive hospitals), resulting in even shorter symptom-to-balloon times.27 In the United States, a number of regional systems have been successfully implemented to reduce the treatment delay. Henry et al28 implemented a standardized system of care for patients with STEMI, including local transport- and hospital-specific protocols. The population was divided into 2 groups: patients with <60 miles and patients with 60 to 210 miles to the invasive center. The median door-to-balloon times were 95 minutes (IQR, 82 to 116) and 120 minutes (IQR, 100 to 145), respectively. In a similar program, Ting et al29 implemented a protocol to reduce treatment delay for 1 invasive center and 28 regional referral hospitals in a range of 150 miles. For transported patients with STEMI, they found a median door-to-balloon time of 116 minutes (IQR, 102 to 137). Finally, in the RACE study, Jollis et al30 managed to reduce the median door-to-device time (in transported patients) from 165 minutes (IQR, 129 to 229) to 128 minutes (IQR, 102 to 195). These results indicate that the benchmark door-to-balloon time of less than 90 minutes is within reach, especially when one considers that none of these setups routinely used tele-transmission of the ambulance ECG to the invasive center (ie, bypassing noninvasive hospitals).

Time of Patient Presentation (Office Hours Versus Off-Hours)
In the process of implementing a relatively complex treatment algorithm in a real-world setting, it is likely that the quality of STEMI treatment is also associated with the "state of readiness" at the involved institutions. Consequently, the prognosis may be relatively impaired for patients arriving during off hours. Furthermore, studies have shown that the physiological circadian rhythm (eg, changes in platelet aggregation, endothelial function, and adrenergic activity) may also affect outcome after PCI.31 Several studies have shown that patients admitted with acute myocardial infarction during off hours have impaired prognosis.13–15 It has been suggested that the higher mortality for patients with STEMI admitted during weekends was associated with a lower rate of invasive cardiac procedures. In the current study, we focused on patients with STEMI already selected for acute coronary angiography and invasive treatment. We found that patients with STEMI treated with pPCI had similar baseline and angiographic characteristics regardless of their time of arrival. More importantly, our results suggest that patients admitted during off hours do not experience poorer long-term outcomes compared with patients admitted during office hours. We believe that this result represents a very positive message because it indicates that routine pPCI can be performed around the clock, with results similar to those obtained in the carefully controlled environment of a randomized clinical trial. A number of studies have evaluated the quality of pPCI during off hours, but these studies were heterogeneous (eg, with patients included over several years), and apart from the studies of Ortolani et al18 and Jneid et al,20 patients were primarily included during the previous decade and thus treated according to noncontemporary clinical guidelines. Furthermore, these studies had limited follow-up periods ranging from in-hospital to 1 year results. The studies with inclusion periods ranging from 1998 to 2002 found that pPCI performed during off hours were associated with an impaired outcome compared with pPCI performed during office hours.15–17,19 On the contrary, Ortolani et al18 and Jneid et al20 have found that outcome was independent of off hours pPCI treatment. As in this current study with 1019 patients from 2004, the inclusion periods in these studies were relatively updated (2003–2005 and 2000–2005, respectively). Thus, it seems that the modern pPCI organization has overcome some of the off-hours–related problems.

Interhospital Transfer Versus Directly Admitted to the Invasive Centers
As mentioned earlier, the preprocedure logistic in pPCI treatment differs for patients directly admitted to an invasive center compared with patients admitted from noninvasive hospitals. Not surprisingly, the treatment delay tends to be prolonged for transferred patients. This was also reflected in our data, which showed that only 40% of transferred patients achieved door-to-balloon times of less than 90 minutes compared with 60% in patients directly admitted to an invasive center. It seems, however, that the increased treatment delay was insufficient to drive a significant difference in outcome between the 2 groups, although there was a tendency toward improved outcome for directly admitted patients.

In agreement with previous studies, we found that in pPCI-treated patients known left ventricular dysfunction, left anterior descending artery lesions, or multivessel coronary disease had a significantly independent prognostic value.18,32,33

Study Limitations
A direct comparison of results from the DANAMI-2 population with results from our real-life population may have some potential limitations. The DANAMI-2 3-year follow-up study was published in May 2008, although the enrolment was between 1997 and 2001. To obtain 3 years of follow-up, we included patients with STEMI treated in 2004, and consequently, some changes have been made in treatment guide-
lines. For example, one third of the current population was treated with DES and a more aggressive pharmacological therapy—such as glycoprotein IIb/IIIa inhibitors and angiotensin-converting enzyme inhibitors—was generally applied.

Furthermore, unadjusted event rates at exactly 3 years of follow-up in the 2 populations were compared, using a $\chi^2$ test. However, significant differences in baseline variables were found only in diabetes and hypertension, and in both cases, the real-life population had the highest rates. This obviously favors the DANAMI-2 population in an unadjusted comparison.

In the comparison of off hours versus office hours and referred versus directly admitted patients, we performed multivariable Cox analysis. Despite this effort to reduce confounding, the risk of unknown bias exists in a nonrandomized trial, and in addition, the confidence interval may seem relatively wide, which obviously weakens our conclusion. Furthermore, our geographical and organizational conditions may not necessarily apply to other countries and regions, and our findings should not be extrapolated to settings without high-volume PCI centers. Finally, our population is reasonably uniform from ethnic, cultural, socioeconomic, and public health standpoints. This issue should be considered in regions (eg, most areas in the United States) with heterogeneous population.

**Conclusion**

The aim of this study was to describe routine pPCI in a large real-life STEMI population. We demonstrate, for the first time, that these patients had similar baseline variables and exhibited a similar good long-term prognosis similar to that in patients in the landmark DANAMI-2 trial. Furthermore, our results suggest that patients treated with routine pPCI during off hours do not experience poorer long-term outcomes compared with patients treated during “office hours.” This indicates that routine pPCI—performed within an effective organizational structure—can be applied successfully in a real-life population around the clock, even when most patients are transported to the angioplasty center from noninvasive centers.

**Sources of Funding**

This work was supported by the Danish Heart Foundation (07-10-R60-A1822-B574-s22414) and the Murermester Laurits Peter Christiansen and Wife Kirsten Sigrid Christiansen Foundation.

**Disclosures**

None.

**References**


Clinical Perspective

Primary percutaneous coronary intervention (pPCI) is the recommended treatment for ST-segment elevation myocardial infarction. The short-term benefit of pPCI compared with fibrinolysis has been demonstrated in a number of trials, the largest of which was the Danish multicenter randomized study on thrombolytic therapy versus acute coronary angioplasty in acute myocardial infarction (DANAMI)-2 trial. However, our knowledge of long-term prognosis—especially in real-life ST-segment elevation myocardial infarction-populations—is very limited. Furthermore, it is questionable whether patients treated during off hours experience similar outcomes compared with patients treated during office hours. This article demonstrates that ST-segment elevation myocardial infarction patients treated with pPCI have similar baseline variables and exhibited similar good long-term prognosis similar to that in ST-segment elevation myocardial infarction patients in the landmark DANAMI-2 trial. Furthermore, our results suggest that patients treated with routine pPCI during off hours do not experience poorer long-term outcomes compared with patients treated during office hours. This indicates that routine pPCI—performed within an effective organizational structure—can be applied successfully in a real-life population around the clock, even when most patients are transported to the angioplasty center from noninvasive centers.
Long-Term Prognosis in an ST-Segment Elevation Myocardial Infarction Population Treated With Routine Primary Percutaneous Coronary Intervention: From Clinical Trial to Real-Life Experience

Sune Pedersen, Soren Galatius, Rasmus Mogelvang, Ulla Davidsen, Anders Galloe, Steen Z. Abildstrom, Ulrik Abildgaard, Peter Riis Hansen, Jan Bech, Allan Iversen, Erik Jorgensen, Henning Kelbaek, Kari Saunamaki, Jan Kyst Madsen and Jan Skov Jensen

*Circ Cardiovasc Interv.* 2009;2:392-400; originally published online August 18, 2009; doi: 10.1161/CIRCINTERVENTIONS.108.845636

*Circulation: Cardiovascular Interventions* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Copyright © 2009 American Heart Association, Inc. All rights reserved.

Print ISSN: 1941-7640. Online ISSN: 1941-7632

The online version of this article, along with updated information and services, is located on the World Wide Web at:

http://circinterventions.ahajournals.org/content/2/5/392

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation: Cardiovascular Interventions* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation: Cardiovascular Interventions* is online at:
http://circinterventions.ahajournals.org/subscriptions/