The Danish multicentre randomized study of fibrinolytic therapy vs. primary angioplasty in acute myocardial infarction (the DANAMI-2 trial): outcome after 3 years follow-up

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Background
The DANAMI-2 trial showed that in patients with ST-elevation myocardial infarction (STEMI), a strategy of inter-hospital transfer for primary angioplasty was superior to on-site fibrinolysis at 30 days follow-up. This paper reports on the pre-specified long-term composite endpoint at 3 years follow-up in DANAMI-2.

Methods and results
We randomized 1572 patients with STEMI to primary angioplasty or intravenous alteplase; 1129 patients were enrolled at 24 referral hospitals and 443 patients at 5 angioplasty centres. Ninety-six percent of inter-hospital transfers for angioplasty were completed within 2 h. No patients were lost to follow-up. The composite endpoint (death, clinical re-infarction, or disabling stroke) was reduced by angioplasty when compared with fibrinolysis at 3 years (19.6 vs. 25.2%, \( P = 0.006 \)). For patients transferred to angioplasty compared with those receiving on-site fibrinolysis, the composite endpoint occurred in 20.1 vs. 26.7% (\( P = 0.007 \)), death in 13.6 vs. 16.4% (\( P = 0.18 \)), clinical re-infarction in 8.9 vs. 12.3% (\( P = 0.05 \)), and disabling stroke in 3.2 vs. 4.7% (\( P = 0.23 \)).

Conclusion
The benefit of transfer for primary angioplasty based on the composite endpoint was sustained after 3 years. For patients with characteristics as those in DANAMI-2, primary angioplasty should be the preferred treatment strategy when inter-hospital transfer can be completed within 2 h.

Keywords
Acute myocardial infarction • Primary angioplasty • Fibrinolysis • Long-term outcome
angioplasty has been shown previously.\textsuperscript{3,4,12,13} Long-term results obtained by a retrospective method have only been reported from one randomized trial (PRAGUE-2), in which inter-hospital transfer for angioplasty was compared to on-site treatment with streptokinase.\textsuperscript{14} The Danish multicentre randomized study of fibrinolytic therapy vs. primary angioplasty in acute myocardial infarction (DANAMI-2) is the largest trial that has compared on-site fibrinolysis with inter-hospital transfer for primary angioplasty.\textsuperscript{3} We used accelerated treatment with tissue plasminogen activator as fibrinolytic therapy. The patients in DANAMI-2 were prospectively followed until 3 years after randomization for assessment of the long-term composite endpoint, which was pre-specified in the study protocol.\textsuperscript{15} In the present paper, we report on the clinical outcome after 3 years of follow-up in DANAMI-2.

Methods

Study design

The DANAMI-2 study has been described in detail in two previous publications.\textsuperscript{3,15} In brief, we randomly assigned patients with STEMI to primary angioplasty or fibrinolytic therapy and followed them for 3 years. The patients were enrolled at 24 referral hospitals without angioplasty facilities and at 5 angioplasty centres with on-site surgical back-up. Primary angioplasty was performed on a 24 h basis, 7 days a week. No patients were excluded from randomization or did not undergo angioplasty due to lack of cath lab availability. The protocol called for randomization of 1100 patients at referral hospitals and 800 patients at angioplasty centres. Enrolment commenced in December 1997 and was terminated in accordance with the study protocol on 1 October 2001 when the third interim analysis showed a significant benefit of angioplasty in the referral hospital substudy. At that time, 1572 patients had been randomized including 1129 patients at referral hospitals and 443 patients at angioplasty centres.

Treatment

In both randomization groups, patients were treated with aspirin, beta-blocker, and unfractionated heparin. Patients randomized to fibrinolysis received accelerated treatment with tissue plasminogen activator (alteplase).\textsuperscript{15} In patients randomized to primary angioplasty, stenting of the culprit lesion was attempted in all patients, unless the vessel had a diameter of less than 2.0 mm. Only the culprit artery was treated at the index-angioplasty.\textsuperscript{15} Ticlopidine (500 mg) or clopidogrel (75 mg) was given daily for 1 month after stent implantation. Platelet glycoprotein IIb/IIIa-receptor blockers were administered at the discretion of the physician. A bicycle exercise test was performed prior to discharge in both randomization groups to assess the need for ischaemia driven mechanical revascularization.

Follow-up

The patients were followed as per protocol at 30 days, 1, 2, and 3 years after the index-infarct. Follow-up was performed at the hospital where the patient was randomized. None of the 1572 patients were lost to follow-up. Six patients who emigrated were followed up by telephone interview or during visits to Denmark. Furthermore, every month a crosscheck was performed between the study database and the National Person Identification Register to identify deaths among randomized patients. When such deaths were identified, a predesigned questionnaire was sent to the local investigator who was requested to obtain the relevant information about the patient’s state of health before death and the circumstances of the death from general practitioners, nurses, local hospitals, ambulance services, and from autopsy data. Information about the occurrence of new myocardial infarctions or strokes since the previous follow-up was also recorded. In all cases of coronary treatment during follow-up [new fibrinolytic treatment, new angioplasty, or coronary artery by-pass grafting (CABG)], the hospital files were obtained. All endpoints were continuously reviewed by an endpoint committee blinded to randomization.\textsuperscript{15,16}

Endpoints

The primary endpoint of DANAMI-2 was a composite of total mortality, clinical re-infarction, and disabling stroke at 30 days of follow-up.\textsuperscript{3} In the present paper, we report on the composite endpoint after 3 years of follow-up. We also present long-term results on cardiac death, non-cardiac death, procedure-related re-infarction, total re-infarction rate, non-disabling stroke, and total stroke rate. Prospective long-term follow-up on these outcomes were pre-specified in the study protocol.\textsuperscript{15} Re-infarction was classified into 18 pre-specified categories on the basis of symptoms, ECG changes, and increases in creatine kinase MB or troponin T above the reference limit.\textsuperscript{15} Clinical re-infarction (nine categories) was diagnosed when re-infarction was not related to an interventional procedure. In patients without normalization of coronary markers, an increase of at least 50% from the last non-normalized measurement was required. Periprocedural re-infarction (nine categories) was diagnosed when re-infarction occurred in relation to CABG or angioplasty during follow-up. Furthermore, we recorded long-term data on angina pectoris [according to the Canadian Cardiovascular Society Angina Grading System (CCS class 1–4)], heart failure [according to the New York Heart Association Classification (NYHA class 2–4)], mechanical revascularization (angioplasty or CABG), number of re-admissions (for cardiac and non-cardiac disease), and number of days of re-admission (for cardiac and non-cardiac disease).

Criteria for eligibility

The criteria for inclusion were an age of 18 years or more, the presence of symptoms for at least 30 min, but less than 12 h, and cumulative ST-segment elevation > 4 mm in at least two contiguous leads. The criteria for exclusion were a contraindication to fibrinolysis, left bundle-branch block, acute myocardial infarction and fibrinolytic treatment within the previous 30 days, pulseless femoral arteries, previous coronary-bypass surgery, chronic renal failure, diabetes treated with metformin, non-schaemic heart disease, and non-cardiac disease associated with a life expectancy of less than 12 months. Patients who were judged to be at high risk during transportation because of cardiogenic shock or severe heart failure (a sustained systolic blood pressure < 65 mmHg), persistent life-threatening arrhythmias, or a need for mechanical ventilation were excluded from randomization. The study complied with the Declaration of Helsinki and was approved by the National Ethics Committee of Denmark. All patients provided written informed consent.

Statistical design and analysis

The trial was designed as two simultaneously conducted substudies, one involving patients randomized at referral hospitals and the other involving patients randomized at angioplasty centres.\textsuperscript{15} Each substudy was designed with an overall two-sided alpha of 5% and a power (1-beta) of 80%. Results were analysed according to the intention-to-treat principle. For the comparison of categorical variables, Pearson’s $\chi^2$ test was used. Values for continuous variables
are reported as medians and interquartile ranges (IQRs). Groups were compared using the Mann–Whitney rank-sum test. Kaplan–Meier estimates were used to describe event rates at 3 years, and Kaplan–Meier curves were used to illustrate the cumulative event rates. The curves were compared using the log-rank test.

Results

Baseline characteristics and medication

Baseline characteristics did not differ between patients randomized to angioplasty vs. fibrinolysis. This was found both in the total study population (Table 1) and in the referral hospital and angioplasty centre sub-studies.1 Medication at the end of follow-up was similar in the two treatment groups (Table 2).

Time from onset of symptoms to treatment

Detailed results on times from onset of symptoms to admission, randomization, transfer, and treatment have been described previously.5 In brief, median time from onset of symptoms to randomization was 135 min (IQR 85–230 min) for the total study population and there was no difference between randomization groups (Table 1). Median time from admission to start of fibrinolysis was 50 min (IQR 40–70 min). Median time from randomization to start of fibrinolysis was 20 min (IQR 15–30 min). Median distance for transfer from referral hospitals to angioplasty centres was 50 km with a range of 3–150 km. Median transfer time from randomization at referral hospitals to arrival at the catheterization laboratory was 67 min (IQR 50–85 min). Transfer time was below 2 h in 96% of transferred patients. Median total interval from onset of symptoms to start of treatment was 224 min (IQR 171–317 min) for patients transferred to angioplasty compared to 169 min (IQR 110–270 min) for patients randomized at referral hospitals to receive fibrinolysis. Thus, inter-hospital transfer for angioplasty was associated with a median treatment delay of 55 min.

Study treatment

Ninety-nine percent of patients randomized to fibrinolysis received the assigned treatment, and 98% of patients randomized to angioplasty underwent immediate coronary angiography. Balloon inflation was performed in 87% of patients randomized to angioplasty, and bare metal stents were implanted in 93% of patients undergoing angioplasty.3

Composite endpoint

The superiority of primary angioplasty over fibrinolysis based on the composite endpoint was maintained after 3 years (Table 3 and Figure 1). For the total study population, the absolute reduction of the composite endpoint rate was 5.7% at 30 days5 and 5.6% after 3 years. Among transferred patients, the absolute reduction of 5.7% after 30 days increased to 6.6% after 3 years. The number needed to treat to avoid one combined endpoint within 3 years was 18 for all hospitals and 15 for referral hospitals. In the incomplete sub-study on patients enrolled at angioplasty centres, the absolute 5.6% reduction of the composite endpoint rate after 30 days (P = 0.05) had weakened to 3.0% after 3 years (Table 3). For the total study population, the lower rate of the composite endpoint after angioplasty was consistent across a number of pre-specified subgroups (Figure 2). One subgroup in which primary angioplasty was not associated with a lower rate of the composite endpoint was diabetics (n = 113). This was due to a higher re-infarction rate after angioplasty in diabetics as previously reported.17

Table 1 Baseline characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fibrinolysis (n = 782)</th>
<th>Angioplasty (n = 790)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>63 (54–73)</td>
<td>63 (54–72)</td>
<td>0.32</td>
</tr>
<tr>
<td>Range</td>
<td>28–96</td>
<td>23–94</td>
<td></td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>73.4</td>
<td>73.5</td>
<td>0.95</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>20.5</td>
<td>20.1</td>
<td>0.82</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>7.1</td>
<td>7.4</td>
<td>0.80</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>58.6</td>
<td>58.1</td>
<td>0.85</td>
</tr>
<tr>
<td>Previous myocardial infarction (%)</td>
<td>11.8</td>
<td>11.0</td>
<td>0.61</td>
</tr>
<tr>
<td>Previous angioplasty (%)</td>
<td>2.6</td>
<td>4.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Previous stroke (%)</td>
<td>4.1</td>
<td>2.7</td>
<td>0.12</td>
</tr>
<tr>
<td>Anterior index myocardial infarction (%)</td>
<td>52.6</td>
<td>53.2</td>
<td>0.81</td>
</tr>
<tr>
<td>Heart rate (b.p.m.), median (IQR)</td>
<td>72 (61–84)</td>
<td>75 (61–87)</td>
<td>0.44</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg), median (IQR)</td>
<td>135 (115–150)</td>
<td>136 (120–152)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Table 2 Use of medication at the end of follow-up

<table>
<thead>
<tr>
<th>Medication (%</th>
<th>Fibrinolysis (n = 722)</th>
<th>Angioplasty (n = 740)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>92.4</td>
<td>92.7</td>
<td>0.82</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>68.6</td>
<td>70.0</td>
<td>0.55</td>
</tr>
<tr>
<td>ACE-inhibitors</td>
<td>43.8</td>
<td>42.4</td>
<td>0.61</td>
</tr>
<tr>
<td>Calcium antagonist</td>
<td>15.8</td>
<td>12.2</td>
<td>0.05</td>
</tr>
<tr>
<td>Nitrates</td>
<td>13.3</td>
<td>11.6</td>
<td>0.33</td>
</tr>
<tr>
<td>Diuretics</td>
<td>34.2</td>
<td>32.3</td>
<td>0.44</td>
</tr>
<tr>
<td>Lipid-lowering drug</td>
<td>73.4</td>
<td>72.8</td>
<td>0.81</td>
</tr>
<tr>
<td>Coumarines</td>
<td>5.1</td>
<td>5.3</td>
<td>0.90</td>
</tr>
<tr>
<td>Digitalis</td>
<td>6.2</td>
<td>4.9</td>
<td>0.25</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td>0.0</td>
<td>0.7</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 3 Baseline characteristics of the patients

IQR, interquartile range.
Secondary endpoints

After 3 years, the benefit of primary angioplasty on the composite endpoint was achieved by lower rates of all three secondary endpoints, but statistical significance was only reached for clinical re-infarction (Table 3). Total mortality and the rate of cardiac death did not differ between randomization groups (Table 3 and Figure 3). The rate of non-cardiac death was 4.9% in both groups (Figure 3). Among the 149 patients suffering clinical re-infarction during 3 years follow-up, mortality was substantially higher than in the remaining 1423 patients without clinical re-infarction (26.3 vs. 13.1%, \( P < 0.001 \)). Procedure-related re-infarction did not differ during long-term follow-up after primary angioplasty vs. fibrinolysis (2.7 vs. 4.1%, \( P = 0.12 \), Figure 3). When procedure-related re-infarctions and clinical re-infarctions were combined, primary angioplasty was associated with a significant reduction in total re-infarction rate (Figure 3). Only one death was observed within 30 days after a procedure-related re-infarction. There was no difference in disabling stroke (Table 3) or non-disabling stroke (Figure 3) between randomization groups. Total stroke rate was 3.7% for primary angioplasty vs. 5.5% for fibrinolysis (Figure 3).

Mechanical revascularization, angina pectoris, heart failure, and readmissions during follow-up

In both randomization groups, ischaemia driven mechanical revascularization during follow-up was mainly performed within the first 0.5 year (Figure 4). During the last 2.5 years, there were few coronary interventions and the event curves remained parallel for the two groups. Mechanical revascularization during follow-up was more frequent after fibrinolysis than primary angioplasty: angioplasty was performed in 34% after fibrinolysis as compared with 16% after primary angioplasty (\( P < 0.001 \)) and CABG in 12 vs. 9% (\( P = 0.07 \)). More patients in the fibrinolysis group than in the angioplasty group reported that they had angina pectoris at discharge (10 vs. 5%, \( P < 0.001 \)) and at 30 days follow-up (25 vs. 18%, \( P = 0.003 \)). In patients alive at 3 years follow-up, the difference was no longer significant (18 vs. 16%, \( P = 0.42 \)). Results on heart failure did not differ significantly between randomization groups. Fibrinolysis was associated with a higher mean number of re-admissions for cardiac disease compared with angioplasty (1.26 vs. 0.83 re-admissions pr. patient, \( P < 0.001 \)), whereas there was no difference on re-admissions for non-cardiac disease (0.51 vs. 0.50, \( P = 0.66 \)). Correspondingly, the mean number of days of readmissions for cardiac disease was significantly higher in the fibrinolysis group (6.2 vs. 4.5 days pr. patient, \( P < 0.001 \)), whereas there was no difference in the mean number of days of readmissions for non-cardiac disease (4.4 vs. 4.2, \( P = 0.65 \)).

Discussion

DANAMI-2 is the largest randomized trial that has compared fibrinolysis and primary angioplasty. The superiority of primary angioplasty on the composite endpoint of death, clinical re-infarction, and disabling stroke was maintained after 3 years, both for transferred patients and for the total study population. Furthermore, primary angioplasty significantly reduced the rates of clinical re-infarction, coronary revascularization, and readmission for cardiac disease. Based on our long-term findings, primary angioplasty should be the preferred reperfusion strategy when inter-hospital transfer can be completed within 2 h.

Composite endpoint

In the total DANAMI-2 population and in transferred patients, the absolute 6% reduction of the composite endpoint achieved with primary angioplasty at 30 days was maintained and still highly significant after 3 years. This finding is in accordance with long-term results from the PRAGUE-2 trial.\(^{14}\) A sustained benefit of primary angioplasty during long-term follow-up was also reported from the smaller but pioneering Zwolle and PAMI trials, in which all patients, however, were admitted directly to angioplasty centres.\(^{9,10}\) Thus, the short-term superiority of primary angioplasty over fibrinolysis was maintained during long-term follow-up both in studies performed at angioplasty centres and in large-scale trials where patients had inter-hospital transfer for primary angioplasty. In DANAMI-2, the lower rate of the composite endpoint after primary angioplasty was consistent across a number of pre-specified subgroups. This included

<table>
<thead>
<tr>
<th>Outcome, n (%)</th>
<th>Referral hospitals</th>
<th>P</th>
<th>Angioplasty centres</th>
<th>P</th>
<th>All hospitals</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Fibrinolysis (n = 562)</td>
<td>92 (16.4)</td>
<td>77 (13.6)</td>
<td>0.18</td>
<td>25 (11.4)</td>
<td>31 (13.9)</td>
</tr>
<tr>
<td></td>
<td>Angioplasty (n = 567)</td>
<td>77 (13.6)</td>
<td>77 (13.6)</td>
<td>0.18</td>
<td>31 (13.9)</td>
<td>31 (13.9)</td>
</tr>
<tr>
<td>Clinical re-infarction</td>
<td>Fibrinolysis (n = 220)</td>
<td>63 (12.3)</td>
<td>46 (8.9)</td>
<td>0.05</td>
<td>26 (12.4)</td>
<td>14 (6.9)</td>
</tr>
<tr>
<td></td>
<td>Angioplasty (n = 223)</td>
<td>46 (8.9)</td>
<td>46 (8.9)</td>
<td>0.05</td>
<td>14 (6.9)</td>
<td>14 (6.9)</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>Fibrinolysis (n = 220)</td>
<td>24 (4.7)</td>
<td>17 (3.2)</td>
<td>0.23</td>
<td>6 (2.8)</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td></td>
<td>Angioplasty (n = 223)</td>
<td>17 (3.2)</td>
<td>17 (3.2)</td>
<td>0.23</td>
<td>5 (2.5)</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>Composite endpoint</td>
<td>Fibrinolysis (n = 782)</td>
<td>150 (26.7)</td>
<td>114 (20.1)</td>
<td>0.007</td>
<td>47 (21.4)</td>
<td>41 (18.4)</td>
</tr>
<tr>
<td></td>
<td>Angioplasty (n = 790)</td>
<td>114 (20.1)</td>
<td>114 (20.1)</td>
<td>0.007</td>
<td>41 (18.4)</td>
<td>41 (18.4)</td>
</tr>
</tbody>
</table>

*Death reflects all cause mortality. Clinical re-infarction does not include procedure-related re-infarctions. Disabling stroke includes strokes with a permanent handicap of a moderate to severe degree.\(^{15}\) The composite endpoint includes death, clinical re-infarction, and disabling stroke.*

*Percentages are Kaplan–Meier estimates at 3 years.*

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**Table 3 Clinical outcome at 3 years**

Death was not significantly different between randomization groups (angioplasty vs. fibrinolysis, 9.5% vs. 5.5%, \( P = 0.46 \)). When procedure-related re-infarctions and clinical re-infarctions were combined, primary angioplasty was associated with a significant reduction in total re-infarction rate (angioplasty vs. fibrinolysis, 2.7 vs. 4.1%, \( P = 0.12 \), Figure 3). When procedure-related re-infarctions and clinical re-infarctions were combined, primary angioplasty was associated with a significant reduction in total re-infarction rate (angioplasty vs. fibrinolysis, 2.7 vs. 4.1%, \( P = 0.12 \), Figure 3).
patients in whom the symptom duration was short (<2 h), intermediate (2 to <4 h), or relatively long (≥4 h). The better long-term outcome with primary angioplasty was achieved despite a median treatment delay of 1 h. Our findings are in accordance with a recent meta-analysis that showed a consistently better short-term outcome with primary angioplasty when compared with fibrinolysis regardless of symptom duration and treatment delay.1

**Secondary endpoints**

There was no difference in total mortality or cardiac death for primary angioplasty when compared with fibrinolysis. Non-cardiac mortality was the same in the two groups indicating that they had been properly matched at randomization. Among the 1129 patients enrolled at referral hospitals, inter-hospital transfer for primary angioplasty carried an absolute 3% lower mortality than on-site fibrinolysis. The result did not reach significance as DANAMI-2 was not designed as a mortality study and was terminated in accordance with the study protocol when the third interim analysis showed a significant benefit of angioplasty on the primary composite endpoint.3,15 However, our result on mortality was similar to findings in two meta-analyses, in which an absolute 2–3% reduction of short-term mortality after primary angioplasty as compared with fibrinolysis was found to be highly significant.1,2 In the Zwolle trial performed at a single angioplasty centre, long-term mortality was significantly lower in the primary angioplasty group after a mean follow-up of 5 years.9

The superiority of primary angioplasty over fibrinolysis based on the composite endpoint was achieved by lower rates of all three secondary endpoints but statistical significance was only reached for clinical re-infarction. Re-infarction within 30 days after STEMI has previously been associated with a significant increase in mortality.18,19 We monitored clinical re-infarction during 3 years after STEMI and found twice as many deaths in patients with clinical re-infarction as in patients without clinical re-infarction. Thus, preventing so-called non-fatal re-infarctions might carry a long-term survival benefit. However, so far no published study has had the statistical power and necessary long-term follow-up to support this hypothesis. The rate of procedure-related re-infarction also tended to be higher after fibrinolysis than primary angioplasty. This reflected a higher rate of mechanical revascularization during follow-up in the fibrinolysis group.

There was no difference in the rate of disabling stroke or in the rate of non-disabling stroke for the two reperfusion modalities. Our data on total stroke rates are in accordance with a meta-analysis showing a lower stroke rate for primary angioplasty when compared with fibrinolysis.2

Angina pectoris was more frequently reported in the fibrinolysis group at discharge and at 30 days, whereas the difference when compared with the angioplasty group was no longer significant among patients alive after 3 years. This corresponded to a higher rate of ischaemia driven mechanical revascularization in the fibrinolysis group during the first 0.5 year of follow-up. In accordance with our results on angina pectoris and heart failure, medication at the end of follow-up was similar in the two groups (Table 2). Due to the higher rates of re-infarction and ischaemia driven revascularizations, more patients assigned to fibrinolysis had re-admissions for cardiac disease during long-term follow-up. The number of days of re-admission for cardiac disease was also higher after fibrinolysis. Thus, primary angioplasty was associated with an improved long-term clinical outcome on several pre-specified parameters in DANAMI-2.

**Figure 1** The composite endpoint (total mortality, clinical re-infarction, or disabling stroke) in the two groups
Limitations

(i) One major limitation of this trial was that the substudy on patients randomized at angioplasty centres only recruited half of the stipulated patients. The premature termination of the angioplasty centre substudy was mandated by the study protocol when the third interim analysis in the referral hospital substudy showed a highly significant difference with respect to the primary composite endpoint.3,15

(ii) The secondary endpoints angina pectoris and heart failure were classified by the primary investigators who were not blinded to the study treatment. Results on angina pectoris, however, corresponded with the higher rates of revascularization and re-admission for cardiac disease in the fibrinolysis group.

(iii) At the time of planning DANAMI-2, the benefit of long-term treatment with clopidogrel both in relation to angioplasty20 and fibrinolysis21 and the benefit of using platelet glycoprotein IIb/IIIa-receptor blockers in primary angioplasty22 and enoxaparin in fibrinolysis23 had not been shown. Thus, an improved long-term outcome might be achieved with both reperfusion strategies nowadays.

(iv) Patients with failed fibrinolysis received repeated fibrinolysis ($n = 26$) or underwent rescue angioplasty ($n = 15$) within the first 12 h.3 The performance of more rescue angioplasties might have reduced the re-infarction rate as reported by others.24 However, clinical re-infarction only occurred in one patient receiving repeated fibrinolysis and in one patient undergoing rescue angioplasty in DANAMI-2.

Conclusion

Inter-hospital transfer for primary angioplasty improves the long-term composite outcome of death, clinical re-infarction, or disabling stroke when compared with on-site fibrinolysis. For patients with clinical characteristics as those in DANAMI-2, primary angioplasty should be recommended when inter-hospital transfer can be completed within 2 h.
The DANAMI-2 trial was supported by grants from the Danish Heart Foundation, the Danish Medical Research Council, AstraZeneca, Bristol-Myers Squibb, Cordis, Pfizer, Pharmacia–Upjohn, Boehringer Ingelheim, and Guerbet, all Denmark.

Conflict of interest: none declared.

References


