Transferring patients for primary angioplasty in eastern Melbourne (the SHIPEM registry): are we meeting the guidelines?

Michael J Moore, Louise Roberts, Hounge-Bang Liew, Esther M Briganti and Gishe New

Primary percutaneous coronary intervention (PCI) is the preferred strategy for reperfusion in patients with ST-elevation myocardial infarction (STEMI). The use of PCI for STEMI has been widely embraced in Australia. Over 23 randomised controlled trials have provided Level 1, class A evidence that PCI is superior to fibrinolysis for management of STEMI, and time to reperfusion is directly related to mortality. Current American and European guidelines recommend a “door-to-balloon” time (see below) of ≤90 minutes for patients with STEMI. For patients presenting to a non-PCI-capable unit, the European guidelines also recommend PCI if it can be performed within 120 minutes of first medical contact.

Unlike American and European guidelines, the Cardiac Society of Australia and New Zealand/National Heart Foundation of Australia (CSANZ/NHFA) guidelines recommend PCI over fibrinolysis, based on evidence from two multicentre randomised trials. The CSANZ/NHFA guidelines recommend PCI over fibrinolysis, if (i) the time from symptom onset to presentation is ≤60 minutes and PCI is available in ≤60 minutes; or (ii) the time from symptom onset to presentation is >60 minutes and PCI is available in ≤90 minutes. For patients with STEMI presenting to a non-PCI-capable hospital, the guidelines recommend a first-door-to-balloon time of ≤120 minutes (including transfer time), if the time from symptom onset to presentation is between 3 and 12 hours. The DANAMI-2 (Danish Multicenter Randomized Study of Fibrinolysis versus Primary Angioplasty in Acute Myocardial Infarction-2) trial showed that 30-day clinical outcomes were superior for patients transferred to a PCI site from a peripheral hospital compared with patients who received onsite fibrinolysis, despite the time delay to reperfusion (median door-to-balloon time, 118 minutes). The feasibility and outcomes for such transfer programs have not been formally tested in Australia. We report our 6-year experience of onsite PCI and transfer for PCI. Our aim was to determine whether the current CSANZ/NHFA targets, predicated by symptom-to-first-door time, are not being met and have not improved over time, which suggests that strategies to improve symptom-to-first-door, first-door-to-balloon and transfer times need to be addressed.

METHODS

Setting

The Eastern Health network in Melbourne, Victoria, serves a population of about

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>BHH</td>
<td>Box Hill Hospital</td>
</tr>
<tr>
<td>CAGB</td>
<td>Coronary artery bypass graft</td>
</tr>
<tr>
<td>CSANZ</td>
<td>Cardiac Society of Australia and New Zealand</td>
</tr>
<tr>
<td>DANAMI-2</td>
<td>Danish Multicenter Randomized Study of Fibrinolysis versus Primary Angioplasty in Acute Myocardial Infarction-2</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>MACE</td>
<td>Major adverse cardiac event</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>NHFA</td>
<td>National Heart Foundation of Australia</td>
</tr>
<tr>
<td>PCI</td>
<td>Percutaneous coronary intervention</td>
</tr>
<tr>
<td>SHIPEM</td>
<td>Shipping Infarcts for Primary Angioplasty in Eastern Melbourne</td>
</tr>
<tr>
<td>STEMI</td>
<td>ST-elevation myocardial infarction</td>
</tr>
<tr>
<td>TVR</td>
<td>Target vessel revascularisation</td>
</tr>
</tbody>
</table>

Objective: To compare clinical outcomes between patients with ST-elevation myocardial infarction (STEMI) presenting to a hospital with facilities for primary percutaneous coronary intervention (PCI) and patients transferred from a non-PCI-capable unit, and to determine the success rate of meeting clinical guidelines for management of STEMI.

Design, setting and participants: Prospective study of patients with STEMI who underwent PCI at Box Hill Hospital (BHH), Melbourne, between 1 July 2002 and 30 June 2008. We compared two patient groups: “BHH patients”, who were admitted directly to BHH (a hospital with PCI capability), and “SHIPEM (Shipping Infarcts for Primary Angioplasty in Eastern Melbourne Registry) patients”, who were transferred from other hospitals without PCI capability.

Main outcome measures: Clinical outcomes; symptom-to-first-door time (time between symptom onset and arrival at first hospital); first-door-to-balloon time (time between arrival at the first hospital and inflation of the angioplasty balloon); compliance with Cardiac Society of Australia and New Zealand/National Heart Foundation of Australia (CSANZ/NHFA) guidelines for management of patients with STEMI.

Results: There were 598 patients in the BHH group and 189 in the SHIPEM group. The median first-door-to-balloon time was 89 minutes (interquartile range [IQR], 69–107 minutes) for BHH patients and 128 minutes (IQR, 104–157 minutes) for SHIPEM patients. These figures did not vary significantly over the 6 years of the registry. In the BHH group, 180 patients (30.1%) had a symptom-to-first-door time of ≤60 minutes, with 32 (17.8%) receiving PCI in ≤60 minutes. The corresponding figure for the SHIPEM group was 48 patients (25.4%), with 1 (2.1%) receiving PCI within 60 minutes. In the BHH group, 304 patients (50.8%) had a symptom-to-first-door time of 61–180 minutes, with 166 (54.6%) receiving PCI in ≤90 minutes. In the SHIPEM group, 50 patients (26.5%) had a symptom-to-first-door time of >180 minutes, with 21 (42.0%) receiving PCI in ≤120 minutes.

Conclusion: Our study demonstrates that transfer for PCI is feasible and safe in selected patients, with outcomes comparable to those of patients presenting to a PCI-capable unit. However, the CSANZ/NHFA targets, predicated by symptom-to-first-door time, are not being met and have not improved over time, which suggests that strategies to improve symptom-to-first-door, first-door-to-balloon and transfer times need to be addressed.
880 000 people. It includes three acute hospitals, one of which is Box Hill Hospital (BHH). In July 2002, PCI was introduced as the reperfusion therapy of choice at BHH on a 24-hour basis. A formal referral service was established within our network. However, transfer was not mandated for all patients with STEMI, as there remained clinical equipoise as to the superiority of transferring patients for PCI versus administering onsite fibrinolysis treatment. We also accepted referrals for PCI from rural hospitals and other metropolitan Melbourne hospitals within a reasonable distance of BHH. The two main suburban referring hospitals were Maroondah and Angliss hospitals (15 km and 27 km from BHH, respectively).

Definitions

The following definitions were used:
- **Symptom-to-first-door time**: The time from symptom onset to arrival at the first hospital (Box 1).
- **First-door-to-balloon time**: The time from arrival at the first hospital to inflation of the angioplasty balloon.
- **Symptom-to-balloon time**: The time from symptom onset to inflation of angioplasty balloon.
- **Procedural success**: Less than 30% residual stenosis, with no procedural complications (death, recurrent myocardial infarction [MI] or emergency coronary artery bypass graft [CABG] surgery).  
- **Major adverse cardiac event (MACE)**: The composite of mortality, recurrent MI and target vessel revascularisation (TVR).
- **Recurrent myocardial infarction**: The recurrence of chest pain for ≥30 minutes, with new ST elevation, or a rise in creatine phosphokinase (to three or more times the upper limit of normal or to at least 50% higher than the pre-PCI level).
- **Target vessel revascularisation**: PCI or CABG involving the target vessel.
- **Procedural complications**: Other procedural complications included haemorrhage (defined according to TIMI [thrombolysis in myocardial infarction] criteria),10 stroke, CABG, cardiogenic shock and groin complications.

Patients re-presenting with another STEMI (involving the index lesion or a different lesion or vessel) ≤30 days or ≤12 months after the initial PCI were excluded from the analysis. Likewise, patients re-presenting with another STEMI ≥12 months after the initial PCI were excluded from the analysis.

**Transfer protocol**

The decision to transfer patients with STEMI was at the discretion of the referring hospital. Clinical details and electrocardiogram (ECG) results were communicated by telephone and facsimile to the on-call cardiologist at BHH. Although priority was requested for transfers, availability of ambulances and waiting times varied. On arrival at BHH, patients were transferred directly to the catheterisation laboratory, by-passing the emergency department. Outside office hours, the on-call team was activated during transfer.

**Procedural protocol**

Following coronary angiography, PCI was performed. If the patient was unsuitable for PCI, they were referred for CABG or treated medically. All patients received a loading dose of aspirin and clopidogrel before or during PCI. Use of glycoprotein IIb/IIIa inhibitors or a thrombus aspiration device was at the discretion of the interventional cardiologist. Drug-eluting stents were used in patients at high risk of restenosis according to Victorian Department of Human Services criteria.11 Duration of clopidogrel treatment was at the discretion of the cardiologist.

**Ethics approval**

Ethics approval for our study was obtained from the Eastern Health Research and Ethics Committee. Informed consent was obtained from all patients.

**Data collection and analysis**

Data were prospectively collected for all consecutive patients between 1 July 2002

---

**Table 1 Components of time to PCI treatment**

<table>
<thead>
<tr>
<th>BHH group (nontransferred PCI patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom-to-first-door time</td>
</tr>
</tbody>
</table>

**B. SHIPEM group (transferred PCI patients)**

| Symptom-to-first-door time | First-door transfer time | Transfer time | BHH door-to-cathlab time | Cathlab-to-balloon time |

**Definitions**

- **Symptom-to-first-door time**
- **First-door transfer time**
- **Transfer time**
- **BHH door-to-cathlab time**
- **Cathlab-to-balloon time**

**Notes**

- PCI = percutaneous coronary intervention. BHH = Box Hill Hospital. SHIPEM = Shipping Infarcts for Primary Angioplasty in Eastern Melbourne. *Cathlab = catheterisation laboratory.
and 30 June 2008 and entered into a database (Cardiobase, version 6, Magnus Medical Software, Greensborough, Vic, Australia). Rescue PCI (following failed fibrinolysis) (n = 33) and facilitated PCI (planned, immediate PCI following pharmacotherapy) (n = 7) cases were excluded from this analysis. Demographics, clinical presentation, symptom-to-door and door-to-balloon times, procedural details and clinical outcomes were recorded. Follow-up at 30 days and 12 months was performed by telephone and review of patient records.

### Statistical analysis

All analyses were conducted using Stata software, version 9 (StataCorp, College Station, Tex, USA). We compared the clinical outcomes of patients presenting to BHH, a PCI-capable unit (the “BHH patients”), with those of patients transferred from non-PCI-capable units (the “SHIPEM [Shipping Infarcts for Primary Angioplasty in Eastern Melbourne] patients”). Variables were reported as mean (SD), median (interquartile range) or as number (percentage). Differences between groups were tested by two-tailed unpaired t-test or Kruskal–Wallis rank test for continuous data, and χ² test for categorical data.

The primary endpoints were mortality, recurrent MI, TVR and MACE at 30 days and at 12 months. Associations between groups and the primary endpoints, adjusted for age and cardiovascular risk factors, were determined by odds ratios (95% confidence intervals) using logistic regression. Cardiovascular risk factors included in the adjusted model were age, sex, diabetes, hypertension, hypercholesterolaemia and current smoking. All P-values were two-sided, and a P-value of ≤ 0.05 was considered statistically significant.

### RESULTS

#### Patient population and treatment

Of the 838 patients with STEMI who proceeded to emergency coronary angiography, 13 (1.6%) were patients re-presenting with a second STEMI during the study period. They included one with acute stent thrombosis, two with subacute stent thrombosis, four with late stent thrombosis, two with very late stent thrombosis, two with STEMI involving a different lesion from the index artery and two with STEMI involving the non-index artery. These 13 events were therefore excluded from being counted as index procedures, but were counted as MACEs.

Of the remaining 825 patients, 620 (75.2%) presented to BHH and 205 (24.8%) were transferred from a non-PCI-capable unit.

Of the 620 BHH patients, 598 (96.5%) proceeded to PCI. Eight patients not suitable for PCI (1.3%) were referred for CABG, and 14 (2.3%) were managed medically. Of the 205 SHIPEM patients, 189 (92.2%) proceeded to PCI, seven (3.4%) patients were referred for CABG and nine (4.4%) were managed medically. Of the 598 BHH patients who proceeded to PCI, 542 (90.6%) were successfully followed up at 12 months and 176 of the 189 SHIPEM patients who proceeded to PCI (93.1%) had a 12-month follow-up. Outcomes were known for all these patients except one from BHH who was lost to follow-up after the 30-day contact.

### Patient demographics and clinical status

The BHH patients were significantly older than the SHIPEM patients and had a higher prevalence of hypercholesterolaemia (Box 2). There was no difference in procedural details between the groups (Box 3), and no patients required “bail-out” CABG for a procedural complication.

### Time from symptoms to treatment

Fewer than a third of patients in either group presented within 60 minutes of symptom onset: 180 of 598 BHH patients (30.1%), and 48 of 189 SHIPEM patients (25.4%) (P = 0.214). The majority of patients presented within 3 hours: 484 of 598 (80.9%) BHH patients and 139 of 189 SHIPEM patients (73.5%) (P = 0.029). Patients in the SHIPEM group had significantly longer median symptom-to-first-door, first-door-to-balloon and symptom-to-balloon times than the BHH patients (Box 4). Median first-door-to-balloon times did not change significantly over the 6-year study period (data not shown). The median transfer time for the SHIPEM group was 36 minutes (interquartile range 23–48 minutes).

A small minority of patients in the shortest symptom-to-door time category (≤ 60 minutes) received PCI within the 60-minute time interval recommended by the CSANZ/NHFA guidelines. Thirty-two of 180 BHH patients (17.8%) and one of 48 SHIPEM patients (2.1%) received PCI within 60 minutes. Of patients with a symptom-to-door time of 61–180 minutes, 166 of 304 BHH patients (54.6%), and 12 of 91 SHIPEM patients (13.2%) received PCI within 90 minutes. Of the patients with a symptom-to-door time of > 180 minutes, 57 of 114 BHH patients (50.0%) received PCI within 90 minutes, and 21 of 50 SHIPEM patients (42.0%) received PCI within 120 minutes.

In the BHH group, 52.1% of patients achieved a door-to-balloon time of ≤ 90 minutes. Only 13.9% of the SHIPEM group achieved a first-door-to-balloon time of 90 minutes.
Clinical outcomes

There was no significant difference in 30-day mortality, recurrent MI, TVR or MACE between the BHH and SHIPEM groups. There were also no differences in bleeding, stroke or groin complications. There was no significant difference in 12-month mortality, MI, TVR or MACE for BHH and SHIPEM patients. Six patients died of non-cardiac causes within 12 months in the BHH group and none in the SHIPEM group (Box 5).

Effect of transfer on clinical outcomes

No significant difference was found in 30-day and 12-month outcomes (death, recurrent MI, TVR and MACE) between BHH and SHIPEM patients, when adjusted for age and cardiovascular risk factors (Box 6).

DISCUSSION

Our 6-year registry with 12-month follow-up of PCI in both onsite and transferred patients demonstrates that transfer for PCI is safe and feasible for selected patients, and produces outcomes comparable with those of patients who receive onsite PCI, despite longer door-to-balloon times. These SHIPEM study results may reflect a selection bias towards better outcomes, which may offset the negative effect of longer door-to-balloon times. Our findings are comparable with those of other large randomised controlled trials.1

Timely access to PCI for patients presenting to hospitals without PCI facilities remains a challenge in real hospital settings. The DANAMI-2 study demonstrated that, in a coordinated trial with a 30-day combined end point of death, re-infarction and stroke for patients transferred for PCI, with a median door-to-balloon time of 118 minutes, PCI was superior to onsite fibrinolysis.8 Our SHIPEM patient treatment times were comparable to those in the DANAMI-2 trial, with a median first-door-to-balloon time of 128 minutes, despite not having the same dedicated transfer process. A meta-analysis of five randomised controlled trials also reported that transfer for PCI achieved a 42% reduction in death, re-infarction and stroke when compared with onsite fibrinolysis.12

Major trials have shown a correlation between door-to-balloon times and 30-day outcomes following PCI.1 The American and European guidelines specify a maximum door-to-balloon time of 90 minutes for onsite PCI,3,4 but the CSANZ/NHFA guidelines stratify their recommendations on symptom-to-door times.5 Our results demonstrate that the proportion of patients presenting early is low, and that in a real hospital situation, the CSANZ/NHFA guidelines may not be attainable. The guidelines also only include recommendations for door-to-balloon times for transferred patients with symptom-to-door times of 3–12 hours.5

The American College of Cardiology Door-to-Balloon Alliance suggests that centres aim for ≥75% of patients achieving a door-to-balloon time of ≤90 minutes, but does not address the issue of transfer.13 In the BHH group in our study, 52.1% of patients achieved a door-to-balloon time of ≤90 minutes. This compares with US registry data demonstrating that 40% of non-transferred and 5% of transferred STEMI patients achieve a door-to-balloon time of ≤90 minutes.14-16 The median transfer time for SHIPEM patients was 36 minutes, and the DANAMI-2 trial demonstrated that PCI was the preferred reperfusion strategy, provided transfer times were ≤120 minutes.8
5 Clinical outcomes at 30-day and 12-month follow-up

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>BHH</th>
<th>SHIPEM*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td>n = 598</td>
<td>n = 189</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>30 (5.0%)</td>
<td>11 (5.8%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>9 (1.5%)</td>
<td>2 (1.1%)</td>
<td>0.65</td>
</tr>
<tr>
<td>TVR</td>
<td>6 (1.0%)</td>
<td>2 (1.1%)</td>
<td>0.95</td>
</tr>
<tr>
<td>MACE</td>
<td>39 (6.5%)</td>
<td>13 (6.9%)</td>
<td>0.73</td>
</tr>
<tr>
<td>MACE excluding shock</td>
<td>27 (4.5%)</td>
<td>7 (3.7%)</td>
<td>0.63</td>
</tr>
<tr>
<td>12 months</td>
<td>n = 542</td>
<td>n = 176</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>37 (6.8%)</td>
<td>14 (8.0%)</td>
<td>0.61</td>
</tr>
<tr>
<td>MI</td>
<td>11 (2.0%)</td>
<td>2 (1.1%)</td>
<td>0.44</td>
</tr>
<tr>
<td>TVR</td>
<td>10 (1.8%)</td>
<td>3 (1.7%)</td>
<td>0.90</td>
</tr>
<tr>
<td>MACE</td>
<td>48 (8.9%)</td>
<td>17 (9.7%)</td>
<td>0.75</td>
</tr>
</tbody>
</table>

BHH = Box Hill Hospital. SHIPEM = Shipping Infarcts for Primary Angioplasty in Eastern Melbourne. MI = myocardial infarction. TVR = target vessel revascularisation. MACE = major adverse cardiac event.

* Patients transferred to BHH.

6 Effect of transfer on 30-day and 12-month outcomes*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age-adjusted</td>
</tr>
<tr>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1.26 (0.61–2.57)</td>
</tr>
<tr>
<td>Recurrent MI</td>
<td>0.72 (0.15–3.43)</td>
</tr>
<tr>
<td>TVR</td>
<td>1.09 (0.22–5.49)</td>
</tr>
<tr>
<td>MACE</td>
<td>1.19 (0.62–2.30)</td>
</tr>
<tr>
<td>MACE excluding shock</td>
<td>0.83 (0.36–1.95)</td>
</tr>
<tr>
<td>12 months</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1.31 (0.69–2.51)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.62 (0.14–3.16)</td>
</tr>
<tr>
<td>TVR</td>
<td>0.65 (0.08–5.64)</td>
</tr>
<tr>
<td>MACE</td>
<td>1.12 (0.61–2.04)</td>
</tr>
</tbody>
</table>

CV = cardiovascular. MI = myocardial infarction. TVR = target vessel revascularisation. MACE = major adverse cardiac event.

* SHIPEM (Shipping Infarcts for Primary Angioplasty in Eastern Melbourne) group compared with Box Hill Hospital group. † CV risk factors included: age (per year); sex (male, female); diabetes (yes, no); hypertension (yes, no); hypercholesterolaemia (yes, no); and current smoking (yes, no).

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACUTE CORONARY SYNDROMES — RESEARCH

ACKNOWLEDGEMENTS

We would like to thank Yew Mun Cheong, Dhars Fernando, Chris Good, Georgios Pimios, Michael Rowe, Wayne Childs, Sue Ling Ching, Jennifer Coller, Bon-Chun Chou, Pallav Garg, Chris Lim, Kang-Teng Lim, Edward Mah, Swati Mukherjee, Vicki Pandeli, James Sapontis, Matthew Swale and Andrew Teh for their involvement in procedures and data collection.

COMPETING INTERESTS

Esther Briganti has received speaker fees from Novo Nordisk and Merck Sharp & Dohme, and an educational grant from Novo Nordisk. These are not related to issues covered in this article.
REFERENCES


(Received 29 Jul 2009, accepted 20 Jan 2010)