Primary angioplasty is cost-minimizing compared with pre-hospital thrombolysis for patients within 60 min of a percutaneous coronary intervention center: the Comparison of Angioplasty and Pre-Hospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) cost-efficacy sub-study


Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The health interventions examined in the study were two strategies for the management of patients suffering from an acute myocardial infarction (AMI) with a travel distance to a percutaneous coronary intervention (PCI) centre within 60 minutes: primary coronary angioplasty (PCA) versus pre-hospital thrombolysis (PHT) with intravenous infusion of alteplase.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients suffering from an AMI and located within 60 minutes of a PCI centre. Patients were excluded if the duration of transfer to the PCI centre was expected to exceed 1 hour. Similarly, patients with cardiogenic shock, or any other contraindication to thrombolysis at presentation were also excluded.

Setting
The setting was hospital. The economic study was carried out in France.

Dates to which data relate
Effectiveness and resource use data were gathered from June 1997 to September 2000. The price year was 2000.

Source of effectiveness data
The effectiveness evidence came from a single study.

Link between effectiveness and cost data
It appears that the costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
Of the 840 patients included in the CAPTIM trial, a subgroup of 299 subjects was consecutively enrolled in the current ancillary study. There were 149 patients in the PCA group and 150 patients in the PHT group. The mean age was 59.4
+/- 12 years in the PCA group and 59.5 +/− 12 years in the PHT group. The proportion of men was 77.1% in the PCA group and 83.3% in the PHT group. For the current ancillary study, power calculations were not performed for clinical endpoints.

**Study design**
This was a prospective, randomised, clinical trial, carried out in three centres among all participating institutions. The length of follow-up was 30 days and was then extended to one year. All events were assessed up to 120 minutes after hospital admission, at discharge, and after one-year follow-up. Ten patients (6 in the PCA group and 4 in the PHT group) were lost to follow-up after initial hospitalisation since they moved to another area. It was not stated whether blinding was performed.

**Analysis of effectiveness**
The analysis of the clinical study was based on intention to treat. The primary outcome measure was a composite of death, non-fatal re-infarction, and non-fatal disabling stroke. Secondary outcome measures were frequency of major bleeding and a composite measure consisting of the primary clinical endpoint + major bleeding + revascularisations. In addition, the rates of immediate or subsequent mechanical revascularisation for patients receiving PCA or PHT were reported. At baseline, study groups were comparable with respect to demographic and clinical characteristics. In addition, the authors stated that patients included in the current ancillary study were comparable to the whole sample of patients included in the CAPTIM study (apart from a significantly higher percentage of patients with diabetes mellitus in the subgroup used for this analysis).

**Effectiveness results**
No statistically significant differences between the PCA and PHT groups were observed in the primary endpoint at 30 days (7.7% versus 12.3%) or after one year (14% versus 16.4%).

Major bleeding occurred in 5 PCA patients but did not occur in any PHT patient.

The secondary clinical end point after one year was significantly lower in the PCA group than in the PHT group (34% versus 61%; p<0.0001), showing better results for the PCA group.

The rate of immediate mechanical revascularisation was 88% for the PCA group and 35% for the PHT group (rescue angioplasty; difference: p<0.001), whereas the rate of subsequent revascularisation was significantly higher after PHT than after PCA, either during the initial hospitalisation period (42% versus 10%) or after one-year follow-up (49% versus 23%, p<0.001).

**Clinical conclusions**
The effectiveness analysis showed that the two treatments were equally effective with respect to the primary outcome measure both after 30 days and at one year. However, when major bleeding and revascularisations were taken into account, the frequency of adverse outcomes was significantly lower in PCA patients.

**Measure of benefits used in the economic analysis**
Health outcomes were left disaggregated and no summary measure of benefits was used in the economic analysis, thus a cost-minimisation analysis was carried out.

**Direct costs**
The perspective adopted in the study was not clear although the authors stated that a societal point of view was adopted. The following categories of direct medical costs were considered: hospitalisations (intensive coronary care unit (ICCU), medical ward, other intensive care unit (ICU), total in-hospital stay, cumulative re-hospitalisation, rehabilitation), revascularisations procedures (coronary angiographies, immediate or emergent PCI, stent, glycoprotein IIb/IIIa
inhibitors, thrombolysis, intra-aortic balloon pump, coronary artery bypass grafting (CABG), mobile care unit, other medications, and testing (exercise stress tests, nuclear cardiology studies, and echocardiography). Unit costs were presented separately from quantities of resources used for all items. Resource use was estimated from the CAPTIM trial using a micro-costing approach. The micro-costing evaluation was performed in two of the three hospitals and then extrapolated to the third institution, which had a similar accounting system. The authors stated that both fixed and variable items were included. Costs were estimated from the accounting system of one of the hospitals participating in the CAPTIM trial. Costs for drugs and devices were estimated using market prices. Details of the cost calculation were extensively reported. A 4% discount rate was applied. However, discounting was not relevant as the time horizon of the analysis was one year. The price year was 2000.

Statistical analysis of costs
Mean costs +/- standard deviation were presented as well as median values. Costs were compared using a Mann-Whitney nonparametric test. A power calculation was carried out for the ancillary analysis and suggested that a sample of 300 patients would be necessary to detect a 10% absolute reduction of the in-hospital total cost between the groups (alpha error of 0.05 and beta error of 0.15). Since only 289 patients were finally included, a post hoc analysis of the statistical power of the study showed that, with the same hypotheses for standard deviation, a difference of 10.25% for the in-hospital cost between the two groups was needed in order to be detected.

Indirect Costs
Indirect costs were not included.

Currency
US dollars ($). Costs were estimated in French francs and then converted into US dollars but the exchange rate was not reported.

Sensitivity analysis
A sensitivity analysis was performed to determine whether the cost estimates obtained in the current study could be transferred to other settings. Thus, UK and US unit costs were used as alternatives to French unit costs. The sources of data were reported. Subgroup analyses of costs were also performed.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results reported above.

Cost results
In-hospital total costs per patient were $8,287 +/- $5,160 in the PCA group and $9,170 +/- $4,323 in the PHT group, (p=0.0001).

One-year hospitalisation costs were $5,885 +/- $5,023 in the PCA group and $6,492 +/- $7,860 in the PHT group, (p=0.01).

One-year revascularisation costs were $2,552 +/- $1,449 in the PCA group and $2,774 +/- $1,118 in the PHT group, (p=0.04).

One-year mobile unit costs were $1,036 +/- $378 in the PCA group and $1,239 +/- $434 in the PHT group, (p=0.0003).

One-year testing costs were $1,984 +/- $961 in the PCA group and $2,105 +/- $950 in the PHT group, (p= not significant).

Thus, one-year total costs were $12,132 +/- $7,671 (median: $9,872; 25-75 percentile: $8,483 - $14,689) in the PCA
The subgroup analysis revealed that cost estimates were no different whether they were based on gender, age, or location of the AMI, with PCA being less expensive than PHT. However, costs were influenced by the presence of clinical risk factors at presentation (the Killip class, heart rate, systolic blood pressure, alone or combined). For example, PCA was less costly than PHT only for non-high-risk patients and there was no difference in cost between the two strategies for high-risk patients, these patients being significantly more expensive than non-high-risk patients whatever the treatment used. Similarly, PCA was less costly than PHT for patients free of a primary clinical end point, whereas no difference was seen in patients who experienced at least one event, and PCA was less costly than PHT whether or not an immediate or emergent PCI was performed.

Synthesis of costs and benefits
A synthesis of costs and benefits was not relevant and a cost-minimisation analysis was carried out as the primary clinical endpoint was comparable between groups. However, when the secondary outcome was considered, PCA was dominant because it was both more effective and less costly than PHT.

Authors’ conclusions
The authors concluded that PCA was as effective as and less costly than a combined strategy of PHT followed by rescue angioplasty in patients who had experienced an AMI and who were located less than 1 hour from a PCI centre.

CRD COMMENTARY - Selection of comparators
The selection of the comparators appears to have been appropriate as, in the authors’ setting, PCA and PHT were the two available treatment options for patients suffering an AMI and who were located within one hour from a PCI centre. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness data came from a sub-study of a previously published clinical trial, which was appropriate for the study question. Most details of the design and other aspects of the trial were published elsewhere, thus it is difficult to assess the robustness of the clinical evidence, although clinical trials usually have a high internal validity. In effect, no information on sample selection and randomisation was provided. However, the randomised design should have limited the impact of selection bias and confounding factors. Further strengths of the analysis were the use of intention to treat to analyse the clinical data, the appropriate length of follow-up, the baseline comparability of study groups, the representativeness of the study sample, and the use of power calculations (although these analyses were performed for the whole sample). Moreover, the evidence came from several institutions. These issues tend to increase the internal validity of the clinical estimates.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the commentary reported above under ‘validity of estimate of measure of effectiveness’.

Validity of estimate of costs
The perspective adopted in the study was not clear because only direct medical costs were taken into account despite the fact that the authors had stated that a societal perspective had been adopted. A breakdown of cost items was provided, and costs were estimated using a micro-costing approach. In addition, information on unit costs and quantities...
of resources used was extensively provided, which enhances the possibility of replicating the analysis of costs in other settings. A further strength of the analysis was the use of US and UK cost estimates which mean that the conclusions of the economic analysis can be transferred to other countries. Furthermore, extensive statistical analyses were carried out on cost estimates, not only to test the statistical significance of cost differences in the two treatment arms but also to enrol a number of patients sufficient to permit the identification of relevant cost differences. The source of data was reported for all items. The price year was reported, which simplifies reflation exercises in other time periods. These issues tend to strengthen the robustness of the economic analysis.

Other issues
The authors reported the results from other published clinical trials, which showed that better outcomes were in general achieved with PCA. The possible reasons for the different results of the current study (equivalence of the clinical outcome) were discussed. More consistent results were observed as regards resource use, since the majority of studies showed cost-savings associated with PCA. The issue of the generalisability of the study results to other settings was explicitly addressed in the sensitivity analysis, in which alternative cost estimates were taken into account, as reported above. The results of the main analysis and those of the sensitivity analysis were clearly reported. It was pointed out that the conclusions of the current study should not be extrapolated to other AMI patients, especially when the patient cannot be transported, within one hour, to a PCI centre.

Implications of the study
The study results suggest that patients presenting within 1 hour of the PCI centre should be referred directly to the catheterisation laboratory for PCA without performing PHT. The authors noted that some questions remain unresolved, such as whether immediate transfer to a PCI centre should be applied to all AMI patients after PHT, or should it be reserved only for high-risk patients with failed reperfusion or in haemodynamically unstable condition.

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