The RATPAC (Randomised Assessment of Treatment using Panel Assay of Cardiac markers) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department

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Executive summary

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Executive summary

Background

Patients with acute chest pain require rapid and accurate diagnostic assessment for acute myocardial infarction (AMI). Standard care currently involves hospital admission for measurement of troponin at least 12 hours after worst symptoms. As most patients do not ultimately have AMI this is inconvenient for patients and wastes health-care resources.

Point-of-care biomarker assessment with the combination of creatine kinase MB (mass) [CK-MB (mass)], myoglobin and troponin measured at presentation and 90 minutes later could potentially reduce the need for hospital admission and improve patient care. This combination has been shown to have high sensitivity for AMI, allowing earlier identification than laboratory testing and expedited decision-making. However, existing studies do not reliably tell us whether the panel would alter patient care, improve outcomes or reduce health service costs.

Objectives

We aimed to measure the effect of using a point-of-care cardiac marker panel upon successful discharge home after emergency department (ED) assessment, length of hospital stay, use of coronary care, cardiac tests and treatments, subsequent hospital attendance and/or admission, and major adverse events, and then estimate the cost-effectiveness of the point-of-care panel in terms of mean costs and quality-adjusted life-years (QALYs) accrued compared with standard care.

Methods

We undertook a multicentre pragmatic randomised controlled trial and economic evaluation of a point-of-care cardiac marker panel in the management of patients with acute chest pain in six EDs. We recruited people presenting to hospital with chest pain due to suspected but not proven AMI, and no other potentially serious alternative pathology or comorbidity. Participants were randomly allocated to receive either (1) diagnostic assessment using the point-of-care biochemical marker panel or (2) conventional diagnostic assessment without the panel. All tests and treatments other than the panel were provided at the discretion of the clinician. Data were collected from hospital records and a questionnaire mailed to participants at 1 and 3 months, measuring health and social care resource use, health utility [European Quality of Life-5 Dimensions (EQ-5D)] and satisfaction with care.

The primary outcome was the proportion of patients successfully discharged home after ED assessment, defined as patients who had (1) either left the hospital or were awaiting transport home with a discharge decision having been made at 4 hours after initial presentation and (2) suffered no adverse event (as defined below) during the following 3 months.

Secondary outcomes were (1) length of initial hospital stay and total inpatient days over 3 months; (2) health utility measured using the EQ-5D self-complete questionnaire at 1 and 3 months after attendance; (3) satisfaction with care measured at 1 month after attendance using an 11-question self-complete Likert-scale questionnaire; (4) the proportion of patients admitted to the coronary care unit, receiving cardiac medications or cardiac interventions

(such as angiography, percutaneous intervention or bypass grafting); (5) re-attendance at, and/or re-admission to, hospital and outpatient attendances over the following 3 months; (6) major adverse events (death, non-fatal AMI, life-threatening arrhythmia, emergency revascularisation or hospitalisation for myocardial ischaemia); and (7) the proportion of admitted patients ultimately diagnosed as having AMI by the universal definition.

We planned to recruit 1565 to each arm of the trial to give 80% power to detect a 5% absolute difference in the proportion of patients successfully discharged (55% vs 50%) and a 2% absolute difference in the major adverse event rate (2% vs 4%) at the two-sided significance level of 5%. We estimated that this could be achieved by six hospitals recruiting 550 patients each over 12 months, assuming that 70% of those eligible were recruited. Actual patient recruitment was slower than anticipated and varied between 300 and 400 patients per centre per year of recruitment, with 35% of eligible patients recruited instead of the 70% anticipated. After 1800 patients had been recruited, a futility analysis undertaken by the Data Monitoring Committee at the request of the funders suggested that there were grounds for termination on the basis of futility, with the trial having >99% conditional power to detect a 5% difference in the proportion successfully discharged and <10% power to detect a 2% difference in major adverse events. Recruitment was terminated with 2263 patients recruited.

An economic analysis was undertaken from a health and social care perspective using trial data to estimate the mean cost per patient of chest pain-related care and the mean number of QALYs accrued by patients in each arm of the trial up to 3 months after recruitment. A microcosting study of 30–40 participants at each site was used to obtain precise estimates of the costs of initial diagnostic assessment. The trial analysis was augmented with a decision-analytic model to explore the potential effect of differences in major adverse event rates upon long-term costs and outcomes.

Results

We recruited 2263 participants, of whom 2243 had usable data [mean age 54.5 years, 1307/2243 (58%) male and 269/2243 (12%) with known coronary heart disease (CHD]. In the point-of-care group 358/1125 (32%) were successfully discharged compared with 146/1118 (13%) in the standard-care group [odds ratio (OR) adjusted for age, gender and history of CHD 3.81; 95% confidence interval (CI) 3.01 to 4.82, $p < 0.001$]. The effect on the primary outcome varied between hospitals with point-of-care panel assessment increasing successful discharges at four hospitals, having no effect at one and decreasing successful discharges at one. The ORs for successful discharge at individual hospitals varied from 0.12 (95% CI 0.01 to 1.03, $p = 0.054$) to 11.07 (95% CI 6.23 to 19.26, $p < 0.001$).

Mean length of the initial hospital stay was 29.6 hours in the point-of-care group versus 31.8 hours in the standard-care group (mean difference = 2.1 hours, 95% CI –3.7 to 8.0 hours, $p = 0.462$), while median length of initial hospital stay was 8.8 hours versus 14.2 hours ($p < 0.001$). More patients in the point-of-care group had no inpatient days recorded during follow-up (54% vs 40%, $p < 0.001$), but mean inpatient days did not differ between the two groups (1.8 vs 1.7, $p = 0.815$). More patients in the point-of-care group were managed on coronary care [50/1125 (4%) vs 31/1118 (3%), $p = 0.041$].

There were no significant differences between the groups in the proportions receiving glyceryl trinitrate, heparin, glycoprotein inhibitors, antacids or beta-blockers. More patients in the point-of-care group received clopidogrel (21% vs 16%, $p = 0.002$), while more patients in the standard-care group received aspirin (60% vs 55%, $p = 0.031$). There were no significant differences in the use of non-biomarker cardiac investigations, cardiac interventions, re-attendances or subsequent

admissions, although there were non-significant trends towards increased use of cardiac interventions with point-of-care that influenced cost analysis. Patients in the point-of-care group were slightly more likely to have a chest pain-related outpatient review (21% vs 18%, $p = 0.05$).

There were no significant differences in mean EQ-5D scores at 1 or 3 months (point-of-care 0.742 vs standard care 0.759 at 1 month, $p = 0.614$, and 0.752 vs 0.759 at 3 months, $p = 0.638$). Most patients were satisfied with most aspects of their care, with only a small proportion rating their care as poor. Point-of-care panel assessment was favoured in two of the 10 dimensions (urgency of assessment and personal interest in care) and in the question rating overall care.

There were 36 patients (3%) with major adverse events in the point-of-care group and 26 (2%) in the standard-care group (adjusted OR 1.31, 95% CI 0.78 to 2.20, $p = 0.313$). The proportion of patients ultimately diagnosed as having AMI was 82/1125 (7.3%) in the point-of-care group and 76/1118 (6.8%) in the standard-care group ($p = 0.650$).

Mean costs per patient were £1217 with point-of-care versus £1006 with standard care ($p = 0.056$), while mean QALYs were 0.158 versus 0.161 ($p = 0.250$). The probability of standard care being dominant (i.e. cheaper and more effective) was 0.888, whereas the probability of the point-of-care panel being dominant was 0.004.

Conclusions

Point-of-care panel assessment increases the proportion of patients successfully discharged home, leading to reduced median length of initial hospital stay, but no change in mean hospital stay or total inpatient days. Point-of-care panel assessment is associated with increased use of coronary care and may be associated with increased use of other interventions. Cost-effectiveness is mainly driven by differences in mean cost, with point estimates suggesting that point-of-care panel assessment is £211 per patient more expensive than standard care. It is unlikely to be considered cost-effective in the NHS, with a 0.888 probability that standard care is dominant.

Further research is required to identify factors that influence the effectiveness and cost-effectiveness of point-of-care panel assessment, explore alternative ways of managing patients with low-risk chest pain and evaluate new cardiac biomarkers.

Trial registration

This study is registered as ISRCTN37823923.

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Publication

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The research reported in this issue of the journal was commissioned by the HTA programme as project number 06/302/19. The contractual start date was in April 2007. The draft report began editorial review in January 2010 and was accepted for publication in October 2010. As the funder, by devising a commissioning brief, the HTA programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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