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Economic Evaluation of Complete Revascularization for Patients with Multivessel Disease Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Objectives: To determine the cost-effectiveness of complete revascularization at index admission compared with infarct-related artery (IRA) treatment only, in patients with multivessel disease undergoing primary percutaneous coronary intervention (P-PCI) for ST-segment elevation myocardial infarction. **Methods:** An economic evaluation of a multicenter randomized trial was conducted, comparing complete revascularization at index admission to IRA-only P-PCI in patients with multivessel disease (12-month follow-up). Overall hospital costs (costs for P-PCI procedure(s), hospital length of stay, and any subsequent re-admissions) were estimated. Outcomes were major adverse cardiac events (MACEs, a composite of all-cause death, recurrent myocardial infarction, heart failure, and ischemia-driven revascularization) and quality-adjusted life-years (QALYs) derived from the three-level EuroQol five-dimensional questionnaire. Multiple imputation was undertaken. The mean incremental cost and effect, with associated 95% confidence intervals, the incremental cost-effectiveness ratio, and the cost-effectiveness acceptability curve were estimated. **Results:** On the basis of 296 patients, the mean incremental overall hospital cost for complete revascularization was estimated to be –£215.96 (–£1390.20 to £958.29), compared with IRA-only, with a per-patient mean reduction in MACEs of 0.170 (0.044 to 0.296) and a QALY gain of 0.011 (−0.019 to 0.041). According to the cost-effectiveness acceptability curve, the probability of complete revascularization being cost-effective was estimated to be 72.0% at a willingness-to-pay threshold value of £20,000 per QALY. **Conclusions:** Complete revascularization at index admission was estimated to be more effective (in terms of MACEs and QALYs) and cost-effective (overall costs were estimated to be lower and complete revascularization thereby dominated IRA-only). There was, however, some uncertainty associated with this decision.

Keywords: economic evaluation, myocardial infarction, percutaneous coronary intervention, revascularization.

Introduction

Cardiovascular disease is a leading cause of mortality in the United Kingdom, with more than 150,000 deaths each year and annual costs of more than £15 billion [1]. Primary percutaneous coronary intervention (P-PCI) is the standard treatment for patients presenting with ST-segment elevation myocardial infarction (STEMI), with more than 90,000 such procedures undertaken in the United Kingdom each year [2]. P-PCI involves inserting a catheter via the groin or arm. A small balloon is then inflated in the narrowed artery to move the obstructing fatty tissue/clot and to widen the artery. Usually, at least one stent is then permanently implanted to hold the artery open and improve blood flow to the heart [2]. Of patients presenting with STEMI, 40% to 65% are estimated to have bystander stenosis in non–infarct-related arteries (N-IRAs) (multivessel disease) [3]. Until recently, treatment of the IRA alone was the internationally recommended strategy [4–6]. There is, however, growing trial evidence [7–9] that the additional treatment of N-IRAs (complete revascularization) is associated with fewer adverse cardiac events, and the previous "do-not-do" guidance by the American College of Cardiology has now been withdrawn [10]. Although these results need to be confirmed in larger trials, the emerging clinical evidence presents the opportunity to examine the cost-effectiveness of complete versus infarct-only revascularization. Revascularization may be associated with increased initial procedure costs, but it is important to also assess whether these costs are offset by reduced future hospital admissions and fewer

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adverse events. Here, we report an economic evaluation [11,12], which was conducted alongside the Complete versus Lesion-only Primary PCI Trial (CvLPRIT) [8], to assess whether complete revascularization constitutes a cost-effective use of health care resources. We are not aware of any previous economic evaluations of complete revascularization in this patient group.

Methods

Participants

As previously described [8], the CvLPRIT was a multicenter randomized trial comparing complete revascularization with IRA-only P-PCI for patients with bystander multivessel coronary artery disease. Patients were eligible if, after angiography, at least one other artery had a significant (70%) stenosis in addition to the occluded IRA. Inclusion and exclusion criteria are listed in the Appendix Table in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2017.02.002. Patients were randomized to either the IRA-only strategy or to complete revascularization, undertaken either at the time of P-PCI or during that index admission. Randomization was via an automated 24-hour telephone randomization system and stratified by infarct location (anterior/nonanterior) and symptom onset (≤3 hours or >3 hours). Patients were followed up for 12 months postrandomization. The study was approved by the National Research Ethics Service (NRES) Committee East Midlands Derby (reference number: 11/H0405/4).

Costs

Costs were estimated from the perspective of the UK National Health Service (NHS). Specifically, index admission P-PCI procedure(s) costs (based on procedure time, consumables, and equipment [e.g., catheter, balloon, and stents] used for both IRA and any N-IRA interventions performed, for both the initial procedure and any staged procedure), hospital length of stay costs (including time in critical care/high dependency and/or intensive care), and the costs of any hospital re-admissions were estimated. All centers were asked to prospectively collect detailed information on the PCI procedure and admission on study-specific case record forms. Follow-up data (including hospital re-admissions) were subsequently collected via telephone (6-month postrandomization) and face-to-face appointment (12-month postrandomization). Unit costs (in Great Britain pound [£] for the 2012–2013 financial year) were assigned to all items of resource use. When national unit cost data [13–15] were not available, for example, for stents and other P-PCI devices, we conducted a survey of participating centers to estimate the average cost for each item. Index admission (P-PCI procedure(s) and hospital length of stay) and re-admission costs were combined to estimate overall hospital costs.

In a subsample of sites (three out of the seven centers), all patients were asked to complete an additional resource use questionnaire at the 12-month visit. They were asked to report (1) all postdischarge health professional visits in the previous 12 months, (2) whether they were in paid employment at the point of randomization, and (3) whether they had returned to work at the 12-month follow-up point. Only the first three enrolled sites were asked to complete the additional resource use questionnaire because of the associated burden for staff and patients. Other sites that came on board later to boost recruitment were not asked to complete the additional resource use questionnaire. Health professional visits (including general practitioner visits, outpatient attendances, and therapist contacts) were costed as mentioned earlier and added to overall hospital costs to estimate overall NHS and personal social services (PSS) costs.

Outcomes

The primary outcome measure was a major adverse cardiac event (MACE) occurring within 12 months of randomization (a composite of all-cause mortality, recurrent myocardial infarction, heart failure, and need for repeat revascularization [PCI or coronary artery bypass grafting]), as defined in Appendix 2 of the main trial article [8]. Hospitals recorded MACE data, informed by telephone contact with the patients at 6 months postrandomization and hospital visits at approximately 12 months. Clinicians blinded to the randomization group adjudicated all MACEs. All MACEs across the 12-month follow-up period were included in the cost-effectiveness analyses (the primary end point in the clinical article was time to first MACE [8]). In line with the National Institute for Health and Care Excellence methods guide [12], quality of life was measured using the three-level EuroQol five-dimensional questionnaire (EQ-5D) [16] at initial discharge (baseline) and at 12 months postintervention. Utility scores (a scale in which 0 is equal to death and 1 is full health) [11] were derived from the UK York A1 tariff [17] and converted into quality-adjusted life-years (QALYs) using the area under the curve approach, with linear interpolation between the baseline EQ-5D and the 12-month follow-up point [18]. For patients who died during follow-up, an EQ-5D score of 0 was assigned at their date of death [19].

Analyses

The problem of missing data is common in randomized trials and can lead to bias and lack of precision [20]. As recommended for within-trial analysis of cost-effectiveness [20], patterns of missing data were examined to infer the assumed missing data mechanism, and complete case analysis [21] did not constitute the base-case analysis. Health professional visit costs were requested for only three of the centers and these costs constituted only a small component of the total cost (see Results section). Pragmatically, it was therefore considered inappropriate to undertake either complete case analysis or imputation for this variable and no further analysis was thereby undertaken for health professional visit costs or overall NHS and PSS costs. To impute missing data, multiple imputation was undertaken [20], where the "mi impute" command (Stata 12.1 [StataCorp LP, College Station, TX] [22]) was used to create 20 data sets (a rule of thumb is that the number of data sets should equal the percentage of missing data [23]), which were then pooled using Rubin rules [24]. In addition to the costs (procedure time, consumables and equipment, hospital length of stay, and re-admissions) and outcomes (baseline and 12-month EQ-5D scores), the multiple imputation model included variables ($P < 0.10$) associated with missing data, costs, or outcomes (time since symptom onset at randomization [≤3 hours or >3 hours], infarct location [anterior/nonanterior], medical history of treated hypercholesterolemia, medical history of treated diabetes, age, death, center, sex, and treatment allocation). Baseline and 12-month EQ-5D scores were included, rather than individual dimension scores, because if EQ-5D data were missing, then it would generally be for the whole questionnaire. Nevertheless, disaggregated costs were used (and then combined to estimate overall hospital costs) because different resource items had different levels of missing data.

Cost and outcome data were analyzed simultaneously using bivariate regression, which is generally robust for skewed data and allows for any correlation between costs and effects [25]. We followed the intention-to-treat approach, in which patients were analyzed according to the group to which they were allocated (regardless of treatment received). All the regressions included