Longer-Term Follow-Up of Patients Recruited to the REACT (Rescue Angioplasty Versus Conservative Treatment or Repeat Thrombolysis) Trial

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Objectives
To evaluate the longer-term outcomes for rescue percutaneous coronary intervention (R-PCI).

Background
Thrombolysis remains an important, commonly used reperfusion therapy, yet failure to achieve complete reperfusion occurs relatively frequently. A number of recent trials have focused on the management of patients with thrombolytic failure, including the REACT (Rescue Angioplasty Versus Conservative Treatment or Repeat Thrombolysis) trial, which demonstrated a significant 6-month benefit favoring R-PCI. However, longer-term maintenance of benefit for R-PCI has not been demonstrated.

Methods
Rates of the primary composite end point (major adverse cardiac and cerebrovascular events) to 1 year and mortality to a median of 4.4 years in 427 patients included in the 3 randomized arms of the REACT trial (repeat lysis, conservative therapy, and R-PCI) were analyzed.

Results
One-year event-free survival for patients randomized to R-PCI was 81.5%, compared with 64.1% for repeat thrombolysis and 67.5% for conservative therapy (overall p = 0.004). Adjusted hazard ratio was 0.44 (95% confidence interval [CI]: 0.28 to 0.71; p = 0.0008) for R-PCI versus repeat thrombolysis and 0.51 (95% CI: 0.32 to 0.83; p = 0.007) for R-PCI versus conservative therapy. Adjusted hazard ratio for longer-term (median 4.4 years) overall mortality for R-PCI versus repeat thrombolysis was 0.41 (95% CI: 0.22 to 0.75; p = 0.004) and 0.43 (95% CI: 0.23 to 0.79; p = 0.006) for R-PCI versus conservative therapy. There was no difference in either analysis between repeat thrombolysis and conservative strategies.

Conclusions
Rescue PCI, previously shown to be superior in the short term to both repeat thrombolysis and conservative therapy, maintains benefit in terms of long-term mortality. This strategy for failed lysis should be mandated as part of thrombolytic-based ST-segment elevation myocardial infarction protocols. (J Am Coll Cardiol 2009;54:118–26) © 2009 by the American College of Cardiology Foundation

After acute coronary artery occlusion, the short-, medium-, and longer-term outcomes are improved if a patent infarct-related vessel (1,2) and better Thrombolysis In Myocardial Infarction (TIMI) flow grade can be achieved (3). Primary percutaneous coronary intervention (P-PCI) has increasingly become the preferred option for patients presenting with ST-segment elevation myocardial infarction (STEMI), because higher rates of TIMI flow grade 3 are achieved compared with thrombolysis (4,5). Although its apparent disadvantage compared with P-PCI has resulted in a reduction in the use of thrombolysis, it remains an important first-line treatment for at least one-third of those presenting with STEMI (6–8) due to geography, demographics, difficulties in initiating a P-PCI service and delivering P-PCI within recommended timelines, and lack of facilities and trained personnel at hospitals where many patients present, as well as difficulties in changing established practice.

Thrombolysis fails to achieve TIMI flow grade 3 in approximately 40% of patients (9,10), constituting “lytic failure” and recognized clinically as failure of ST-segment resolution. Until recently it was unclear how best to manage...
such patients. Given the advantages of P-PCI, it seemed intuitive to undertake so-called rescue percutaneous coronary intervention (R-PCI) to mechanically open the artery. However, patients who experience lytic failure are inherently different from those undergoing P-PCI, presenting later to percutaneous coronary intervention (PCI), potentially being clinically unstable due to prolonged occlusion times, and requiring PCI to be undertaken in the presence of systemic thrombolytic. Most importantly, although evidence exists supporting the advantages of P-PCI over lysis, until recently there was little evidence to support the use of R-PCI as an adjunct to thrombolysis, with no data to indicate longer-term benefits until now.

The REACT (Rescue Angioplasty Versus Conservative Treatment or Repeat Thrombolysis) trial randomized patients with failed thrombolysis to 1 of 3 groups: repeat thrombolysis, conservative therapy, or R-PCI. Primary end point outcomes to 6 months published in 2006 demonstrated a significant benefit for the R-PCI group (11). Long-term outcome in patients who have experienced lytic failure has been previously reported in only 1 other trial, MERLIN (Middlesbrough Early Revascularization to Limit Infarction) (12), which showed different early outcomes from those of the REACT trial. Furthermore, because events occurred in all 3 REACT treatment groups throughout the initial 6-month follow-up, any differences in outcome may have become attenuated over time. This study therefore reports the 1-year major adverse cardiac and cerebrovascular events (MACCE) and late (up to 5 years) mortality for the REACT trial patients.

Methods

Between December 1999 and March 2004, 427 patients were recruited from 35 sites across the United Kingdom, of which 19 had interventional facilities. Adults (age 21 to 85 years) presenting with acute STEMI within 6 h of onset of chest pain for whom any thrombolytic treatment had failed to achieve reperfusion (defined as <50% resolution of the maximal ST segment on 90-min electrocardiogram [ECG]) were considered for inclusion in the study. After written consent was obtained, patients were randomly assigned via a 24-h computer-generated random- allocation system to 1 of 3 groups: repeat (fibrin-specific) thrombolysis, conservative management (heparin for 24 h and routine care), or R-PCI, delivered as soon as feasible, with transfer if needed to an interventional center. Patients were excluded if the predicted ability to perform R-PCI was likely to be more than 12 h from symptom onset. Remaining exclusions were driven by safety, particularly considering bleeding risk for the repeat thrombolysis group. Baseline characteristics are shown in Table 1. Power calculations dictated 156 patients per group to demonstrate a 40% relative reduction in the primary end point (composite of death, recurrent acute myocardial infarction [re-AMI], severe [New York Heart Association functional class III or IV] heart failure, and cerebrovascular accident [CVA]), with 80% power at 6 months. Competition from other studies led to declining recruitment and, along with a finite funding period, necessitated termination of the trial with 427 patients recruited (repeat thrombolysis, n = 142; conservative treatment, n = 141; R-PCI, n = 144). Of the patients randomized to R-PCI, 16 crossed to alternative arms, 13 had patent arteries at angiography, and 115 proceeded to angioplasty, which was deemed successful in all but 9 cases. Median time from randomization to repeat thrombolysis administration was 190 min and to R-PCI was 274 min. The times from chest pain to initiation of these respective randomized strategies were 330 min (5.5 h) and 414 min (6.9 h). The composite end point outcomes at 6 months were published in 2006 (11).

Longer-term data collection. Patients were followed up to 1 year through clinic visit or telephone contact. All data were source-verified according to strictly controlled criteria. The incidence of the components of the primary composite outcome (death, re-AMI, severe heart failure, or confirmed CVA) was collected and event-free survival determined. Rates of ischemia-driven revascularization were collected as secondary end points. All events were adjudicated by a blinded independent end point committee. Although follow-up to 1 year was part of the original protocol, the observed trend in mortality difference at 6 months led us to consider long-term death rates as a point of further interest, and ethical committee approval was granted to determine late mortality. Mortality status (including mode of death [cardiac or noncardiac] and median time to death after randomization) was determined at each individual participating center through the National Health Tracing Service, which provides reliable, freely available mortality data from the United Kingdom Government Office of National Statistics via the patient–specific National Health Service identification number.

Statistical analyses. Analyses were performed on both an intention-to-treat basis and according to actual (initial) treatment received (18 patients did not receive their randomly assigned therapy). All 427 patients were included in the analyses, as censored observations at the time they were last assessed if necessary. Proportions of patients reaching an end point were compared using either the chi-square or
Fisher exact test as appropriate. Survival and event-free survival (time to first event) were plotted as Kaplan-Meier curves, and the log-rank test was used to compare them. For pairwise comparisons, hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Cox proportional hazards survival models investigated any potential influence of the covariates (age; sex; first thrombolytic treatment; infarction site; previous history of AMI, angina, percutaneous transluminal coronary angioplasty, and coronary artery bypass grafting [CABG]; diabetes; smoking history; hypertension) on treatment effects. These baseline covariates were selected for a final model by a forward-selection procedure. Median follow-up time has been calculated using the reversed Kaplan-Meier method. All statistical analyses were performed using SAS software version 9.1 (SAS Institute, Cary, North Carolina).

**Results**

As previously published (12), event-free survival at 6 months was significantly improved in patients randomized to R-PCI, even when adjusted for age and infarct site (R-PCI vs. repeat thrombolysis or conservative therapy: p = 0.001 and p = 0.004, respectively). All-cause mortality showed a nonsignificant trend in favor of R-PCI (repeat thrombolysis: 12.7%; conservative therapy: 12.8%; R-PCI: 6.2% [p = 0.12]) and significantly fewer revascularizations occurred (overall p = 0.05).

**1-year MACCE.** Complete clinical follow-up at 1 year was available for 388 of the 427 randomized patients (91%). The remaining patients were censored at the time of last follow-up. Information on all components of the primary end point between 6 months and 1 year were collected, and the overall event-free survival curve according to randomized treatment was plotted (Fig. 1). Between 6 and 12 months, there were 2 further deaths in each of the repeat thrombolysis and R-PCI groups and 3 in the conservative group. There were no further CVAs in any group, but severe heart failure requiring admission was recorded in 3 patients randomized to repeat thrombolysis, 2 allocated to conservative therapy, and 1 from the R-PCI group. The rate of event-free survival at 1 year in patients randomized to R-PCI was 81.5%, compared with 64.1% in the repeat thrombolysis and 67.5% in the conservative group (overall p = 0.004). Adjusting for age and infarct site, the HRs at 1 year were 0.44 (95% CI: 0.28 to 0.71; p = 0.0008) for R-PCI versus repeat thrombolysis and 0.51 (95% CI: 0.32 to 0.83; p = 0.007) for R-PCI versus conservative therapy. There was no difference between the repeat thrombolysis and conservative groups (HR: 0.87; 95% CI: 0.58 to 1.30; p = 0.48).

Results remain unchanged when the data are analyzed according to actual treatment received. Event-free survival

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**Table 1** Baseline Characteristics

<table>
<thead>
<tr>
<th>Variables, n (%)</th>
<th>Repeat Thrombolysis (n = 142)</th>
<th>Conservative Therapy (n = 141)</th>
<th>Rescue PCI (n = 144)</th>
<th>All Patients (n = 427)</th>
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<tr>
<td><strong>Age (yrs)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mean ± SD</td>
<td>61.3 ± 10.3</td>
<td>61.0 ± 10.7</td>
<td>61.1 ± 11.9</td>
<td>61.1 ± 11.0</td>
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<td>37–85</td>
<td>34–85</td>
<td>34–85</td>
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<tr>
<td>Male sex</td>
<td>114 (80.3)</td>
<td>111 (78.7)</td>
<td>113 (78.5)</td>
<td>338 (79.2)</td>
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<td><strong>Medical history</strong></td>
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<tr>
<td>Angina</td>
<td>32 (22.5)</td>
<td>29 (20.6)</td>
<td>32 (22.2)</td>
<td>93 (21.8)</td>
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<td>Acute myocardial infarction</td>
<td>23 (16.2)</td>
<td>17 (12.1)</td>
<td>14 (9.8)*</td>
<td>54 (12.7)*</td>
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<td>Percutaneous coronary intervention</td>
<td>6 (4.2)</td>
<td>4 (2.8)</td>
<td>6 (4.2)</td>
<td>16 (3.7)</td>
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<tr>
<td>Coronary artery bypass grafting</td>
<td>7 (4.9)</td>
<td>4 (2.8)</td>
<td>7 (4.9)</td>
<td>18 (4.2)</td>
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<td>Diabetes</td>
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<td>16 (11.3)</td>
<td>21 (14.6)</td>
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<td>Hypertension</td>
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<td>53 (37.6)</td>
<td>47 (32.6)</td>
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<td><strong>Smoking history</strong></td>
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<tr>
<td>Currently smoking</td>
<td>70 (49.6)*</td>
<td>65 (46.1)</td>
<td>68 (47.2)</td>
<td>203 (47.7)*</td>
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<tr>
<td>Formerly smoked</td>
<td>41 (29.1)*</td>
<td>42 (29.8)</td>
<td>40 (27.8)</td>
<td>123 (28.9)*</td>
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<tr>
<td>Never smoked</td>
<td>30 (21.3)*</td>
<td>34 (24.1)</td>
<td>36 (25.0)</td>
<td>100 (23.5)*</td>
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<tr>
<td><strong>Anterior infarct</strong></td>
<td>54 (38.0)</td>
<td>66 (46.8)</td>
<td>61 (42.7)*</td>
<td>181 (42.5)*</td>
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<td>Reteplase</td>
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<td>28 (19.9)</td>
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<td>Streptokinase</td>
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<td>88 (62.4)</td>
<td>84 (58.3)</td>
<td>254 (59.5)</td>
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<td>Tenecteplase</td>
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<td>5 (3.5)</td>
<td>3 (2.1)</td>
<td>10 (2.3)</td>
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<tr>
<td>Tissue plasminogen activator</td>
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<td>20 (14.2)</td>
<td>15 (10.4)</td>
<td>50 (11.7)</td>
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<td><strong>Time to first thrombolytic therapy (min)</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>135</td>
<td>150</td>
<td>140</td>
<td>140</td>
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<tr>
<td>Interquartile range</td>
<td>94–217</td>
<td>100–210</td>
<td>95–240</td>
<td>95–220</td>
</tr>
</tbody>
</table>

*Data were missing for 1 patient.
at 1 year in those patients who actually received R-PCI was 83.4%, compared with 67.3% of patients randomized to conservative therapy and 64.1% of patients who received repeat thrombolysis (p = 0.002).

1-year revascularization (PCI/CABG). With no mandated angiography in the REACT trial (except for the rescue procedure), all revascularization was clinically driven. Although the differences between groups in revascularization rates had been nonsignificant at 6 months, they reached significance at 12 months (Fig. 2). Repeat revascularization (PCI/CABG) was required in 41 patients cumulatively from the repeat thrombolysis group, 40 of those randomized to the conservative group, and 25 randomized to the R-PCI arm. Adjusted for first thrombolytic treatment and previous PCI, the HR was 0.53 (95% CI: 0.32 to 0.86; p = 0.011) for R-PCI versus repeat thrombolysis and 0.50 (95% CI: 0.30 to 0.83; p = 0.007) for R-PCI versus conservative therapy. There was no significant difference between repeat thrombolysis and conservative therapy (HR: 1.05; 95% CI: 0.68 to 1.62; p = 0.84).

Analysis by actual treatment received did not change the overall conclusion, with rate of freedom from revascularization (PCI/CABG) being 84.9% for R-PCI, compared with 66.8% for repeat thrombolysis and 66.6% for conservative therapy (overall p = 0.001).

Longer-term mortality. Live status, at median 4.4 years from randomization to data acquisition, was obtained for all but 11 patients who could not be traced due to National Health Service number retrieval difficulties. Of these, 3 patients had been randomized to repeat thrombolysis, 7 to conservative therapy, and 1 to R-PCI, and data were censored at time of last follow-up.

Of 77 total deaths, 11.2% (n = 16) (cardiovascular [CV], defined as cardiac or cerebrovascular death: n = 13) were reported in 143 patients randomized to R-PCI, compared with 22.3% (n = 31) (CV: n = 28) of 139 patients in the repeat thrombolysis group and 22.4% (n = 30) (CV: n = 23) of 134 patients in the conservative group (overall p = 0.026) (Fig. 3). Adjusted for age, previous history of angina, and diabetes, the HR for long-term mortality was 0.41 (95% CI: 0.22 to 0.75; p = 0.004) for R-PCI versus
repeat thrombolysis and $0.43$ (95% CI: 0.23 to 0.79; $p = 0.006$) for R-PCI versus conservative therapy. There was no mortality difference between repeated thrombolysis and conservative therapy (HR: $1.04$; 95% CI: 0.63 to 1.72; $p = 0.89$) (Fig. 4).

For CV deaths, the survival rates were as follows: 78.2% for repeat thrombolysis (95% CI: 69.7% to 84.6%), 81.7% for conservative therapy (95% CI: 73.0% to 87.8%), and 90.4% for R-PCI (95% CI: 83.9% to 94.3%) (log-rank $p = 0.0335$). HR was 0.43 (95% CI: 0.22 to 0.83;
p = 0.0116) for R-PCI versus repeat thrombolysis, 0.52 (95% CI: 0.27 to 1.04; p = 0.06280) for R-PCI versus conservative therapy, and 0.82 (95% CI: 0.47 to 1.42; p = 0.4746) for conservative therapy versus repeat thrombolysis. When cardiac death alone was considered (n = 26 for repeat thrombolysis, n = 20 for conservative therapy, and n = 13 for R-PCI), survival rates were as follows: 79.5% for repeat thrombolysis (95% CI: 71.0% to 85.7%), 85.1% for conservative therapy (95% CI: 77.7% to 90.1%), and 90.4% for R-PCI (95% CI: 83.9% to 94.3%) (log-rank p = 0.0669). The HR was 0.46 for R-PCI versus repeat thrombolysis (95% CI: 0.24 to 0.90; p = 0.0229), 0.60 for R-PCI versus conservative therapy (95% CI: 0.30 to 1.21; p = 0.1556), and 0.77 for conservative therapy versus repeat thrombolysis (95% CI: 0.43 to 1.37; p = 0.3692).

Again, the longer-term overall mortality differences remain unchanged when the data are analyzed according to actual treatment received. The survival rate in patients who actually received R-PCI was 81.2%, compared with 75.6% for repeat thrombolysis and 73.1% for conservative therapy (p = 0.018). Adjusted for age, previous history of angina, and diabetes, the HR was 0.39 (95% CI: 0.20 to 0.74; p = 0.004) for R-PCI versus repeat thrombolysis and 0.43 for R-PCI versus conservative therapy (95% CI: 0.22 to 0.82; p = 0.010).

Time to death. Time to death was analyzed for patients according to randomized group. Although patients in the R-PCI group tended to survive longer (R-PCI: 142.5 days [range 0 to 2,215 days]; repeat lysis: 14 days [range 0 to 1,470 days]; conservative therapy: 33.5 days [range 0 to 1,854 days]), this was not statistically significant (p = 0.10). Sensitivity analysis. As longer-term status was unavailable for 11 patients, a sensitivity analysis favoring non-R-PCI was performed, assuming death 1 day after the last known live date for the R-PCI patients and live status for the remaining patients. Conclusions were unchanged, with overall survival 80.0% for R-PCI versus 76.2% for repeat thrombolysis and 72.5% for conservative therapy (overall p = 0.04).

Discussion

Although thrombolysis continues to be commonly used as reperfusion therapy, the potential for “thrombolytic failure” will remain an important clinical issue. For trial purposes, “failed thrombolysis” has been previously been defined angiographically as failure to achieve TIMI flow grade 3 (13). However, in the real world, this definition is impractical, and by consensus, thrombolytic failure is defined as failure to resolve the maximal ST-segment deviation by either >50% or >70% when the ECG is repeated at either 60 or 90 min (14,15). For the REACT trial, we chose <50% ST-segment resolution at 90 min, as 60-min ECG may be premature for assessing reperfusion (especially in patients who are administered streptokinase, with its longer reperfusion times) and <50% was regarded as pragmatically easier and more consistently determined across multiple sites in the coronary care setting. Analgesic administration and patient pain threshold tend to confound the value of ongoing pain as an indicator of lytic failure.

The publication of the REACT results led to recommendation for R-PCI use being upgraded to Level of Evidence: IB (16). Historically, the studies had been small and underpowered and demonstrated no clear benefit of R-PCI (17–20), but this changed with the RESCUE I and II trials in the 1990s (21), with reductions in composite rates of death and severe heart failure, although no benefit was seen when each trial was considered separately. In 2005, the more substantial MERLIN trial (12) demonstrated significant benefit in event-free survival driven solely by a reduction in need for revascularization, again with no differences in the hard end points of death, re-AMI, or heart failure. The positive early result of REACT (10) was driven by hard clinical end points that comprised components of MACCE rather than survival alone, although the study had not been powered for mortality as a single outcome. Revascularization, the end point that drove the MERLIN trial, was not part of the REACT primary composite. Despite the realized expectation that outcome differences for the REACT trial would be seen early, 1-year outcome was prospectively set as a secondary study end point. With a trend toward reduced mortality at 6 months, additional longer-term analysis was also considered to be necessary. Furthermore, meta-analyses demonstrating improved outcomes for R-PCI are based only on short-term analyses (22–24), with long-term analysis remaining undetermined but of interest.

At 1 year, mortality was significantly less in the R-PCI group compared with that of repeat thrombolysis or conservative treatments. Even more compelling were the longer-term mortality data showing for the first time a significant mortality benefit for R-PCI out to a median of 4.4 years, with the median time to death extended in the R-PCI group. Although longer-term mortality benefit has been demonstrated in the primary angioplasty setting, it has not previously been shown in the setting of rescue angioplasty.

The apparent contradictory results when compared with the MERLIN data (25) do require consideration. Differences in mortality were seen between the 2 studies as early as 30 days (9.8% for the MERLIN trial vs. 4.9% for the REACT trial) and extend to the longer term for re-AMI, severe heart failure, and stroke rates, as well as death (Table 2) (26). R-PCI management differs in the 2 trials, particularly with respect to stent and glycoprotein IIb/IIIa inhibitor use, timing of trial-qualifying ECG, and rates of fibrin-specific thrombolytic therapy. Higher stenting rates may be especially important. Although in a meta-analysis stenting was not associated with a significant mortality reduction compared with balloon angioplasty in primary PCI, there was a significant relationship between patients’ risk profile, mortality benefits, and coronary stenting at 30 days (p = 0.022) and 1 year (p = 0.034) (27). Stenting compared with balloon angioplasty confers greater myocardial salvage as...
measured by single-photon emission computed tomography (28), which might be expected to translate to longer-term mortality benefit. Furthermore, paired scintigraphic studies performed 7 to 10 days apart at 1 year demonstrated the proportion of initial perfusion defect salvaged by rescue intervention to be significantly greater in the stent group than in the angioplasty group (p < 0.005) (29). Although the tendency toward lower mortality was not significant in this small study, nevertheless the authors concluded that benefit from rescue mechanical reperfusion in terms of myocardial salvage is augmented by coronary stenting, a view supported elsewhere (30). This explains in part the outcome differences between the MERLIN and REACT trials.

Published data would also support the use of glycoprotein IIb/IIIa inhibitor use in PCI for STEMI (31), another factor differentiating these studies, particularly as they were undertaken before pre-loading with 600 mg of clopidogrel was considered standard practice. Certainly the adjunctive clopidogrel use (32) associated with the higher stenting rate in the REACT trial in the R-PCI arm may also have conferred longer-term clinical benefits. Suggestions that mortality in the REACT trial is artificially low are unfounded, as it is broadly in keeping with the British Cardiovascular Intervention Society in-patient figure of 4.8%. However, the low 1-year stroke rate in the REACT trial compared with the apparent high level in the MERLIN trial may be explained by our selected low stroke-risk population, and the higher rate of antiplatelet therapy administered to this group as a result of high stenting rates may have influenced lower embolic stroke risk (33). It is difficult to make comparisons between heart failure rates, given that the definitions were so different between the 2 trials.

Apart from the rescue procedure, there was no mandated revascularization in the REACT trial. It is therefore of note that there was a significant difference at 1 year between need for revascularization in the R-PCI arm and the non-PCI groups. Post-STEMI angiography was not routine at the time of this study and remains so in the United Kingdom. We must assume that in those treated conservatively or with repeat thrombolysis, the residual untreated stenosis resulted in longer-term symptoms, highlighting the DANAMI-1 (DANish trial in Acute Myocardial Infarction) findings (34). Such revascularization need also supports the potential value of post-STEMI angiography in successful as well as failed thrombolysis (35).

The REACT trial has been criticized for including a highly selected population. The REACT trial was indeed different from other studies evaluating R-PCI in that it also studied repeat thrombolysis, necessitating for safety selection of patients with lower bleeding risk. However, this alone does not explain the mortality benefit, with no suggestion that the majority of MERLIN deaths were due to bleeding events. It has also been suggested that low center recruitment rates in comparison with the MERLIN trial may point to some element of selection bias and account for the differences in outcome, whereas the MERLIN trial was a single-center study, with all of the advantages and disadvantages (including potential difficulty extrapolating to a broad variety of sites) that this entails. It is important to note that centers were gradually rolled in to the REACT
trial, some recruiting for merely a few months, and although almost 75% of all patients were included from the top 10 centers (50% in the top 5), there was no correlation between death and total numbers recruited, indicating that low center recruitment had no effect on mortality.

Benefit was demonstrated in the REACT trial despite a prolonged pain-to-balloon time. The proportion of patients in the REACT trial with pre–R-PCI TIMI flow grade 0 to 1 (47%; TIMI flow grade 0 = 36%) versus TIMI flow grade 2 to 3 (53%; TIMI flow grade 3 = 23%) (unpublished data, A.H. Gershlick, March 2009) is in keeping with that of other studies (36,37). It has been suggested that even suboptimal antegrade TIMI flow (in the REACT trial, TIMI flow grade 1/2 = 43%) may enable some tissue preservation and mean that even late angioplasty is beneficial. Although P-PCI works due to early perfusion and late coronary artery patency, resulting in saved muscle and arrhythmia risk reduction, it may be that thrombolysis, despite having failed to restore full patency, has nevertheless allowed enough flow to attenuate myocardial cell death and enable additional (PCI) treatment to save further myocardial tissue (38) and gain at least partial benefit. Despite recent data suggesting an association between time delay to R-PCI and mortality (39), we are unable to confirm this with the REACT trial data, because subgroup analysis is confounded by small numbers per group.

Conclusions

The results of this long-term study clearly indicate that R-PCI is the treatment option of choice in patients with ECG criteria of failed thrombolysis, reducing mortality and composite clinical outcomes. Although recommendations for its use previously have relied on its effect on outcomes such as repeat revascularization and re-AMI, the longer-term REACT data demonstrate a significant effect on mortality reduction. R-PCI should therefore be a mandated part of any STEMI management protocols, and the current Class IIb American Heart Association/American College of Cardiology recommendations for R-PCI in the absence of shock, hemodynamic or electrical instability, or ongoing ischemia (40) should be revisited in future guidelines.

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REFERENCES


Carver et al. The REACT Trial: Longer-Term Follow-Up

Key Words: ST-segment elevation myocardial infarction • failed thrombolysis • rescue percutaneous coronary intervention.

APPENDIX

For a list of the REACT investigators, please see the online version of this article.