Culprit Vessel Versus Multivessel Intervention at the Time of Primary Percutaneous Coronary Intervention in Patients With ST-Segment–Elevation Myocardial Infarction and Multivessel Disease

Real-World Analysis of 3984 Patients in London

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Background—It is estimated that up to two thirds of patients presenting with ST-segment–elevation myocardial infarction have multivessel disease. The optimal strategy for treating nonculprit disease is currently under debate. This study provides a real-world analysis comparing a strategy of culprit-vessel intervention (CVI) versus multivessel intervention at the time of primary percutaneous coronary intervention in patients with ST-segment–elevation myocardial infarction.

Methods and Results—We compared CVI versus multivessel intervention in 3984 patients with multivessel disease undergoing primary percutaneous coronary intervention between 2004 and 2011 at all 8 tertiary cardiac centers in London. Multivariable-adjusted models were built to determine independent predictors for in-hospital major adverse cardiovascular events (MACEs) and all-cause mortality at 1 year. To reduce confounding and bias, propensity score methods were used. CVI was associated with reduced in-hospital MACE (4.6% versus 7.2%; \( P = 0.010 \)) and mortality at 1 year (7.4% versus 10.1%; \( P = 0.031 \)). CVI was an independent predictor for reduced in-hospital MACE (odds ratio, 0.49; 95% confidence interval [CI], 0.32–0.75; \( P < 0.001 \)) and survival at 1 year (hazard ratio, 0.47–0.91; \( P = 0.011 \)) in the complete cohort; and in 2821 patients in propensity-matched cohort (in-hospital MACE: odds ratio, 0.49; 95% CI, 0.32–0.76; \( P = 0.002 \); and 1-year survival: hazard ratio, 0.64; 95% CI, 0.45–0.90; \( P = 0.010 \)). Inverse probability treatment weighted analyses also confirmed CVI as an independent predictor for reduced in-hospital MACE (odds ratio, 0.38; 95% CI, 0.15–0.96; \( P = 0.040 \)) and survival at 1 year (hazard ratio, 0.44; 95% CI, 0.21–0.93; \( P = 0.033 \)).

Conclusions—In this observational analysis of patients with ST-segment–elevation myocardial infarction undergoing primary percutaneous coronary intervention, CVI was associated with increased survival at 1 year. Acknowledging the limitations with observational analyses, our findings support current recommended practice guidelines. (Circ Cardiovasc Qual Outcomes. 2014;7:936-943.)

Key Words: culprit artery ■ multivessel percutaneous coronary intervention ■ primary percutaneous coronary intervention ■ ST-segment elevation myocardial infarction
WHAT IS KNOWN

- Up to two thirds of patients presenting with acute ST-segment–elevation myocardial infarction undergoing primary percutaneous coronary intervention have multivessel disease.
- Currently available randomized and nonrandomized studies addressing the management of bystander disease in the setting of primary percutaneous coronary intervention have yielded conflicting results. Because of lack of robust evidence base, there is divergent clinical practice.
- Current guidelines discourage revascularization of non–infarct-related arteries at the time primary percutaneous coronary intervention except for patients in cardiogenic shock or in those with ongoing ischemia.

WHAT THE STUDY ADDS

- This observational study compares a strategy of culprit-only versus multivessel intervention at the time of primary percutaneous coronary intervention exclusively in patients with multivessel disease without outcardiac shock and bystander left main stem disease.
- Culprit-only intervention at the time of primary percutaneous coronary intervention was found to be associated with improved survival at 1 year, supporting current recommended practice guidelines.

The currently available randomized and nonrandomized studies addressing the management of bystander disease in the setting of PPCI have yielded conflicting results. Because of lack of robust evidence base, there is divergent clinical practice. Current guidelines discourage revascularization of non–infarct-related arteries at the time primary percutaneous coronary intervention except for patients in cardiogenic shock or in those with ongoing ischemia.

is independently associated with worse clinical outcomes. Thus, one may hypothesize that treating the bystander disease during the peri-infarct period may reduce the incidence of recurrent ischemia derived from nonculprit lesions, and this in turn could reduce overall ischemic burden and obviate the need for recurrent procedures. Conversely, assessment of bystander disease severity, both visually and functionally, may be difficult in the acute setting, and thus treating these stenoses may not be wholly justified at the time of index intervention. Furthermore, multivessel revascularization is associated with coronary microembolization, iatrogenic myocardial infarction (MI), coronary reserve reduction, and increased risk of contrast nephropathy. Thus, the optimum strategy for the treatment of bystander disease and whether it should be treated at the time of the index intervention continues to be debated.

The available randomized and nonrandomized studies addressing the management of bystander disease in the setting of PPCI have yielded conflicting results. Because of lack of robust evidence base, there is divergent clinical practice, and strategies used to treat these patients are summarized in Figure 1. Based on the available evidence, current American Heart Association/American College of Cardiology/European Society of Cardiology guidelines discourage PCI of non–infarct-related arteries at the time of PPCI in patients with STEMI except for patients in cardiogenic shock or in those with ongoing ischemia. There is still uncertainty as to whether multivessel coronary intervention at the time of PPCI for STEMI is beneficial. In this observational analysis, we compared culprit-vessel intervention (CVI) versus multivessel intervention (MVI) in patients with STEMI undergoing PPCI and its association with mortality at 1 year.

Methods

This was a retrospective observational cohort study to investigate the relationship between CVI versus MVI at the time of PPCI for patients presenting with STEMI and mortality at 1 year. Patients with cardiogenic shock were excluded from the analysis. Given that the presence of left main stem (LMS) disease may be an indication for surgical revascularization, patients with bystander LMS disease were also excluded from the analysis. We used merged data sets from local British Cardiac Intervention Society (BCIS) databases, which contribute to the BCIS national database. All data were collected prospectively.

BCIS-National Institute for Cardiovascular Outcomes Research Database

The BCIS-National Institute for Cardiovascular Outcomes Research database collects data from all hospitals in the United Kingdom that perform PCI, recording information about every procedure performed. Data are collected prospectively at each hospital, electronically encrypted and transferred online to a central database. Patients’ survival data are obtained by linkage of patients’ National Health Service numbers to the Office of National Statistics, which records the date of death for all patients.

Population Study and Design

We examined an observational cohort of consecutive patients treated with PCI between January 4, 2005, and November 18, 2011, at all 8 tertiary cardiac centers in London, United Kingdom. Patient and procedural details were recorded at the time of the procedure and during the admission into each center’s local BCIS database. Anonymous data sets with linked mortality data from the Office of National Statistics were merged for analysis. Initially, we identified 10,422 patients with STEMI that were treated with PPCI. Of these, 669 patients with cardiogenic shock and 376 patients with bystander LMS disease (>50% stenosis) were excluded. Of these, 3,984 patients had multivessel disease and were included in the final analysis.

Definitions and Clinical Outcomes

A diseased coronary artery was defined as any epicardial vessel with a stenosis ≥50%. Multivessel disease was defined as stenosis ≥50% in ≥2 epicardial coronary arteries. For in-hospital outcomes, we analyzed in-hospital major adverse cardiovascular events (MACEs), which was a composite of in-hospital reinfarction (new pathological Q waves in the distribution of the treated coronary artery with an increase of creatine kinase-MB to ≥2× the reference value or significant rise in troponin biomarkers), reintervention, cerebral vascular accident, and mortality. For long-term outcomes, we analyzed all-cause
mortality at 30 days and 1 year. CVI was defined as treatment of a single CVI, and MVI was defined as MVI at the time of PCI.

Ethics
All patient-identifiable information was removed before database merging and analysis. Because this analysis was performed on anonymized data from mandatory audit, the local ethics committee advised us that ethical approval was not required.

Statistical Analyses
Patients were divided into CVI and MVI groups. Noncategorical variables in our data set had a skewed distribution, and thus were summarized using median (lower and upper quartiles) and compared using the Mann–Whitney U test. Categorical variables were expressed as percentages and compared using the Z test. All statistical analyses were performed using MedCalc v12.1 (MedCalc Software, Ostend, Belgium) and R (Foundation for Statistical Computing, Vienna, Austria). Statistical significance was established at P<0.05 (2-tailed) for all tests.

Multivariable-Adjusted Models for Mortality
To determine independent predictors for mortality, Cox proportional hazards regression models were used to provide adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). The proportional hazards assumption was tested and verified with Schoenfeld residuals.

To guide selection of significant variables for the final multivariable model, we initially adjusted for age, sex, diabetes mellitus, glycoprotein 2b-3a inhibitor use, previous MI, previous history of revascularization, hypertension, hypercholesterolemia, renal disease, previous cerebrovascular accident, peripheral vascular disease, smoking, radial access, vessel involved on (LMS, left anterior descending artery, left circumflex artery, right coronary artery, graft), drug-eluting stent use, intra-aortic balloon pump use, inotropic support, intubation status, aspiration thrombectomy, severe left ventricular dysfunction, call-to-balloon time, and CVI using a stepwise variable selection process, where the entry criterion was P<0.05 and exit criterion was P>0.1. The following variables were included in the final multivariable model: age, sex, diabetes mellitus, glycoprotein 2b-3a inhibitor use, previous MI, previous history of revascularization, renal disease, radial access, drug-eluting stent use, intra-aortic balloon pump use, inotropic status, aspiration thrombectomy, and CVI. The number of variables was limited to 1 per ≥20 events to prevent overfitting of the model. Cumulative mortality rates were also presented as Kaplan–Meier curves and compared with the log-rank test.

Multivariable-Adjusted Models for In-Hospital Outcomes
To determine independent predictors for in-hospital outcomes, we used multivariable logistic regression models to provide adjusted odds ratios (ORs) with associated 95% CIs. We adjusted for all variables that were included in the Cox proportional hazards regression model (as above). The number of variables was limited to 1 per ≥20 events to prevent overfitting of the model. The goodness of fit was determined using the Hosmer–Lemeshow test and the discriminatory power using receiver operating characteristic curve analysis (c-statistic).15

Propensity Score Matching
To account for confounding and bias, propensity matching was performed for 3429 patients with multivessel disease. To derive propensity scores (PS), a logistic regression model was fit for revascularization strategy (MVI versus CVI) to patient demographics, clinical, anatomic and procedural variables. The ultimate goal of a propensity model is not to maximize the prediction of treatment status, but to reduce the bias in the estimated treatment effect,16 and variables that affect both treatment selection and outcome should be included.17 Therefore, the following variables were included in our propensity score model: age, sex, diabetes mellitus, glycoprotein 2b-3a inhibitor use, previous MI, previous history of revascularization, hypertension, hypercholesterolemia, renal disease, previous cerebrovascular accident, peripheral vascular disease, smoking, intra-aortic balloon pump use, drug-eluting stent use, and bystander coronary disease. A common limitation with propensity matching is that often the study population is considerably reduced, particularly when there is a large disparity in proportion of treated versus control subjects, for example, only 14% of patients with multivessel disease had MVI. To address this, we used 1:6 matching to use the larger patient pool.18 Propensity score matching was performed using nearest-neighbor matching and matching without replacement.17 Cumulative mortality rates were also presented as Kaplan–Meier curves and compared with a stratified log-rank test.

The propensity score models were assessed using the receiver operating characteristic curve analysis (c-statistic) and Hosmer–Lemeshow test. Covariate balance was assessed using absolute standardized differences in means for the propensity-matched cohorts, with differences <10% taken to indicate good balance.17 Cox proportional hazards regression models and logistic regression models were then applied to the propensity-matched cohorts adjusting for the significant covariates identified from multivariate models and PS (double-robust models).19

Inverse Probability Treatment Weighted Analysis
To further account for confounding and selection bias, an inverse probability treatment weighted (IPTW) analysis was conducted for all 3984 patients with multivessel disease. PS were determined for all patients as above. IPTW analysis uses weights based on the PS to create a population in which the distribution of measured baseline covariates is independent of treatment assignment. These weights (IPTW) were assigned to each patient with IPTWi=1/PSi for treated patients (MVI); and IPTW i=(1–PSi) for control patients (CVI).21 Finally, Cox proportional hazards regression and logistic regression models were used to determine the effect of CVI versus MVI incorporating significant covariates identified from the multivariate models and IPTW in the final model.

Results
Baseline Population and Procedural Characteristics
We analyzed 3984 consecutive patients who underwent PCI for STEMI across all 8 tertiary cardiac centers in London who had multivessel disease and did not present with cardiogenic shock and did not have bystander LMS disease. Of this patient population, 3429 patients were treated with CVI and 555 patients were treated with MVI. The patient characteristics are summarized in Table 1.

Unadjusted Mortality and In-Hospital Outcomes
In patients with multivessel disease, CVI was associated with lower mortality at 30 days (4.7% versus 7.7%; P=0.002); and at 1 year (7.4% versus 10.1%; P=0.031). When examining in-hospital outcomes, CVI was associated with lower in-hospital MACE (4.6% versus 7.2%; P=0.010) and this was driven by reduced reinfarction (0.2% versus 0.8%; P=0.017), reintervention (0.1% versus 1.1%; P<0.001), and mortality (3.5% versus 6.1%; P=0.005).

Cox Proportional Hazards Regression Models for Mortality
When adjusting for baseline clinical, anatomic, and procedural variables, multivariable-adjusted analyses identified CVI use as an independent predictor for mortality at 30 days (HR, 0.45; 95% CI, 0.31–0.64; P<0.001) and 1 year (HR, 0.65; 95% CI, 0.47–0.91; P=0.011). Although severe left ventricular dysfunction and call-to-balloon time were not identified as significant predictors in the stepwise variable selection process, when these 2 additional variables were forced into
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Table 1. Baseline Demographic and Procedural Characteristics for Total Study Population

<table>
<thead>
<tr>
<th>Clinical factors</th>
<th>All Patients With STEMI and MVD</th>
<th>CVI</th>
<th>MVI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 (52, 73)</td>
<td>62 (52, 73)</td>
<td>62 (53, 72)</td>
<td>0.676</td>
</tr>
<tr>
<td>Female</td>
<td>22.6</td>
<td>22.8</td>
<td>21.1</td>
<td>0.384</td>
</tr>
<tr>
<td>PVD</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>0.943</td>
</tr>
<tr>
<td>Renal disease*</td>
<td>1.8</td>
<td>1.7</td>
<td>2.6</td>
<td>0.202</td>
</tr>
<tr>
<td>previous CVA</td>
<td>2.3</td>
<td>2.2</td>
<td>2.7</td>
<td>0.529</td>
</tr>
<tr>
<td>Previous MI</td>
<td>21.0</td>
<td>20.4</td>
<td>24.9</td>
<td>0.019</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>15.0</td>
<td>14.9</td>
<td>15.7</td>
<td>0.634</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18.4</td>
<td>18.5</td>
<td>17.9</td>
<td>0.729</td>
</tr>
<tr>
<td>Hypertension</td>
<td>41.7</td>
<td>41.4</td>
<td>43.0</td>
<td>0.504</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>42.9</td>
<td>43.3</td>
<td>40.7</td>
<td>0.283</td>
</tr>
<tr>
<td>Smoking†</td>
<td>42.2</td>
<td>42.0</td>
<td>43.6</td>
<td>0.506</td>
</tr>
<tr>
<td>Intubated</td>
<td>3.1</td>
<td>3.2</td>
<td>2.3</td>
<td>0.270</td>
</tr>
<tr>
<td>Severe LV (EF≤30%)</td>
<td>16.1</td>
<td>16.8</td>
<td>12.5</td>
<td>0.104</td>
</tr>
<tr>
<td>Coronary anatomy ‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>86.5</td>
<td>86.6</td>
<td>85.9</td>
<td>0.697</td>
</tr>
<tr>
<td>LCx</td>
<td>65.1</td>
<td>64.4</td>
<td>69.2</td>
<td>0.028</td>
</tr>
<tr>
<td>RCA</td>
<td>82.8</td>
<td>83.6</td>
<td>77.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2 (2, 3)</td>
<td>2 (2, 3)</td>
<td>2 (2, 3)</td>
<td>0.273</td>
</tr>
<tr>
<td>Procedural characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Call to balloon, min</td>
<td>130                         (99, 207)</td>
<td>129</td>
<td>137</td>
<td>0.178</td>
</tr>
<tr>
<td>Radial access</td>
<td>23.3</td>
<td>23.5</td>
<td>21.9</td>
<td>0.417</td>
</tr>
<tr>
<td>GP2b/3a inhibitor</td>
<td>4.7</td>
<td>4.2</td>
<td>7.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DES use</td>
<td>28.8</td>
<td>29.5</td>
<td>24.7</td>
<td>0.021</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2 (2, 3)</td>
<td>2 (2, 3)</td>
<td>2 (2, 3)</td>
<td>0.273</td>
</tr>
<tr>
<td>Target vessel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LMS</td>
<td>2.4</td>
<td>0.8</td>
<td>12.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAD</td>
<td>41.9</td>
<td>36.6</td>
<td>74.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LCx</td>
<td>21.2</td>
<td>15.0</td>
<td>59.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RCA</td>
<td>47.5</td>
<td>45.3</td>
<td>60.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Graft</td>
<td>2.2</td>
<td>2.3</td>
<td>1.3</td>
<td>0.109</td>
</tr>
</tbody>
</table>

Discrete variables are presented as percentages and compared using the Z-test (2-tailed). Continuous data presented as medians (25% IQ, 75% IQ) and compared using the Mann–Whitney U test (2-tailed). CVA indicates cerebrovascular accident; CVI, culprit-vessel intervention; DES, drug-eluting stent; EF, ejection fraction; GP, glycoprotein; IAPB, intra-aortic balloon pump; IQ, interquartile; LAD, left anterior descending artery; LCx, left circumflex artery; MVD, multivessel disease; MVI, multivessel intervention; PVD, peripheral vascular disease; RCA, right coronary artery; and STEMI, ST-segment-elevation myocardial infarction. *Renal disease was defined as serum creatinine >200 mmol/L or renal replacement therapy. †Smoking was defined as smoking of ≥1 cigarettes/d and had smoked in the month preceding percutaneous coronary intervention. ‡A diseased epicardial coronary vessel was defined as having a >50% coronary stenosis by visual estimation.

In these analyses, CVI remained an independent predictor for mortality at 30 days (HR, 0.28; 95% CI, 0.14–0.55; P<0.001) and 1 year (HR, 0.46; 95% CI, 0.24–0.86; P=0.012). Patients with LMS culprits treated percutaneously often have features that preclude emergent bypass surgery and may be considered to represent the sicker population. A significantly greater proportion of patients in the MVI group had culprit LMS lesions, and this may have a confounding effect. However, when excluding all patients with culprit LMS lesions, CVI was still associated with lower mortality at 30 days (HR, 0.42; 95% CI, 0.29–0.60; P<0.001) and 1 year (HR, 0.63; 95% CI, 0.45–0.89; P=0.008).

**Logistic Regression Models for In-Hospital Outcomes**

When adjusting for baseline clinical, anatomic and procedural variables, multivariable-adjusted analyses identified CVI use as an independent predictor for MACE (OR, 0.49; 95% CI, 0.32–0.75; P<0.001). Examining individual components of MACE, CVI was also an independent predictor for in-hospital reinfarction (OR, 0.19; 95% CI, 0.05–0.74; P=0.016) and in-hospital mortality (OR, 0.41; 95% CI, 0.26–0.65; P<0.001), but not in-hospital reintervention (OR, 0.90; 95% CI, 0.31–2.66; P=0.853).

**Propensity-Matched Analyses**

Propensity score matching was performed on 3984 patients to adjust for differences in demographic, clinical, anatomic and procedural variables yielding a total of 2821 matched patients (2418 patients in the CVI group and 403 patients in the MVI group). The c-statistics for the propensity score model was 0.73 and Hosmer–Lemeshow test yielded a P=0.849. Table 2 illustrates that the baseline demographics, clinical, anatomic and procedural variables were well balanced in the propensity-matched cohorts and the absolute standardized differences were all <10% (Figure 2). In the propensity-matched cohorts, CVI use was associated with significantly lower inhospital MACE (4.2% versus 8.3%; P=0.025) and mortality at 30 days (4.2% versus 8.7%; P=0.025), and at 1 year (6.8% versus 10.2%; P=0.059). Multivariable-adjusted models (double-robust models) identified CVI as an independent predictor for in-hospital MACE (OR, 0.49; 95% CI, 0.32–0.76; P=0.002) and mortality at 30 days (HR, 0.44; 95% CI, 0.30–0.65; P<0.001) and 1 year (HR, 0.64; 95% CI, 0.45–0.90; P=0.010).

**IPTW Analyses**

Cox multivariate regression analysis incorporating IPTW were used to further provide an unbiased estimate of treatment effect and included all 3984 patients with multivessel disease. In these analyses, CVI was an independent predictor of in-hospital MACE (0.38; 95% CI, 0.15–0.96; P=0.012) and mortality at 30 days (HR, 0.44; 95% CI, 0.21–0.93; P=0.033) and 1 year (HR, 0.44; 95% CI, 0.21–0.93; P=0.033). These findings were consistent with those from the propensity-matched cohorts.

**Kaplan–Meier Survival Analyses**

The Kaplan–Meier survival curves for the total cohort, and propensity-matched cohorts are shown in Figure 3. All curves demonstrate a survival benefit with CVI.
Discussion

In patients presenting with STEMI undergoing PPCI, the optimal management of significant bystander coronary disease continues to be debated, reflecting the limited and conflicting available data in this field.9,10 Our study represents the largest reported analysis comparing CVI versus MVI in patients with STEMI and with the longest reported follow-up. We analyzed 3984 patients with STEMI and multivessel disease, and found CVI to be an independent predictor for reduced in-hospital MACE and survival at 1 year. Unlike previous observational analyses, when rigorously adjusting for measured confounders using propensity-matched analyses and IPTW analyses, CVI remained an independent predictor for reduced in-hospital MACE and survival at 1 year.

To date, the largest reported retrospective analysis is the US National Cardiovascular Data Registry, which included 28,936 STEMI patients (including patients with cardiogenic shock) and demonstrated no difference between CVI and MVI.22 A limitation of this study was it examined only in-hospital mortality, and long-term mortality data were not available. A meta-analysis of observational studies including >32,000 patients also found similar outcomes with either strategy.9 More recent analyses have found a strategy of CVI at the time of PPCI to be associated with improved outcomes.10,11 Other than a study from the New York PCI registry, which included a propensity-matched analysis (1006 patients) and concluded that only CVI should be performed at time of the index PPCI procedure,23 a common limitation of reported observational studies is that they have not adjusted for the presence of selection bias. However, in this study, only 87.5% of patients in the CVI group had multivessel disease.23 Although it may be possible to correct for this in the adjusted analyses, when comparing CVI versus MVI it would be important to examine outcomes specifically in patients with multivessel disease.

We found that CVI was independently associated with reduced in-hospital MACE. This was driven by reduced reinfarction and mortality. Patients in the MVI group, in whom revascularization of bystander nonculprit was performed,

Table 2. Distribution of Covariates in the Propensity-Matched Cohorts

<table>
<thead>
<tr>
<th>Clinical factors</th>
<th>Total (n=2821)</th>
<th>CVI (n=2418)</th>
<th>MVI (n=403)</th>
<th>P Value</th>
<th>Sdiff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 (61, 63)</td>
<td>62 (61, 63)</td>
<td>63 (61, 65)</td>
<td>0.540</td>
<td>0.5</td>
</tr>
<tr>
<td>Female</td>
<td>21.9</td>
<td>21.8</td>
<td>22.1</td>
<td>0.911</td>
<td>0.6</td>
</tr>
<tr>
<td>PVD</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>0.950</td>
<td>0.3</td>
</tr>
<tr>
<td>Renal disease</td>
<td>2.1</td>
<td>2.0</td>
<td>2.5</td>
<td>0.614</td>
<td>2.9</td>
</tr>
<tr>
<td>Previous CVA</td>
<td>2.6</td>
<td>2.5</td>
<td>3.0</td>
<td>0.594</td>
<td>2.8</td>
</tr>
<tr>
<td>Previous MI</td>
<td>22.2</td>
<td>21.8</td>
<td>24.8</td>
<td>0.177</td>
<td>7.1</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>14.7</td>
<td>14.6</td>
<td>15.4</td>
<td>0.664</td>
<td>2.3</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18.0</td>
<td>18.1</td>
<td>17.6</td>
<td>0.826</td>
<td>1.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>44.4</td>
<td>44.3</td>
<td>44.9</td>
<td>0.829</td>
<td>1.2</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>43.8</td>
<td>44.0</td>
<td>42.7</td>
<td>0.620</td>
<td>2.7</td>
</tr>
<tr>
<td>Smoking</td>
<td>42.0</td>
<td>42.0</td>
<td>42.3</td>
<td>0.925</td>
<td>0.5</td>
</tr>
<tr>
<td>Intubated</td>
<td>1.7</td>
<td>1.7</td>
<td>1.7</td>
<td>1.000</td>
<td>0.0</td>
</tr>
<tr>
<td>Severe LV (EF≤30%)</td>
<td>16.9</td>
<td>17.2</td>
<td>15.3</td>
<td>0.328</td>
<td>5.1</td>
</tr>
<tr>
<td>Coronary anatomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>85.5</td>
<td>85.5</td>
<td>85.1</td>
<td>0.827</td>
<td>1.2</td>
</tr>
<tr>
<td>LCx</td>
<td>67.9</td>
<td>67.4</td>
<td>71.0</td>
<td>0.157</td>
<td>7.7</td>
</tr>
<tr>
<td>RCA</td>
<td>80.9</td>
<td>81.4</td>
<td>77.7</td>
<td>0.085</td>
<td>9.3</td>
</tr>
<tr>
<td>No. of diseased vessels</td>
<td>2 (2, 3)</td>
<td>2 (2, 3)</td>
<td>2 (2, 3)</td>
<td>0.149</td>
<td>1.6</td>
</tr>
<tr>
<td>Procedural characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Call-to-balloon, min</td>
<td>129 (98, 207)</td>
<td>128 (98, 201)</td>
<td>137 (99, 237)</td>
<td>0.298</td>
<td>7.4</td>
</tr>
<tr>
<td>Radial access</td>
<td>24.8</td>
<td>24.9</td>
<td>24.1</td>
<td>0.709</td>
<td>2.0</td>
</tr>
<tr>
<td>IABP use</td>
<td>4.9</td>
<td>4.7</td>
<td>6.5</td>
<td>0.127</td>
<td>7.8</td>
</tr>
<tr>
<td>GP2b/3a inhibitor</td>
<td>72.5</td>
<td>72.2</td>
<td>74.2</td>
<td>0.399</td>
<td>4.6</td>
</tr>
<tr>
<td>Thrombectomy</td>
<td>27.3</td>
<td>27.7</td>
<td>25.3</td>
<td>0.300</td>
<td>5.5</td>
</tr>
<tr>
<td>DES use</td>
<td>45.7</td>
<td>45.4</td>
<td>47.4</td>
<td>0.450</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Discrete variables are presented as percentages and compared using the Z test (2-tailed). Continuous data presented as medians (25% IQ, 75% IQ) and compared using the Mann–Whitney U test (2-tailed). All variables were also compared using absolute standardized difference in mean (%; Sdiff). CVA indicates cerebrovascular accident; DES, drug-eluting stent; EF, ejection fraction; GP, glycoprotein; IABP, intra-aortic balloon pump; IQ, interquartile; LAD, left anterior descending artery; LCx, left circumflex artery; LV, left ventricular; MI, myocardial infarction; MVI, multivessel intervention; and RCA, right coronary artery.
had increased reinfarction rates, and this may reflect coronary microembolization and iatrogenic MI, all of which are associated with multivessel coronary intervention. Untreated coronary stenoses are often perceived as increasing overall ischemic burden, which may dictate treatment of nonculprit vessels at the time of index intervention. However, our findings suggest that leaving stable nonculprit disease at the time of index intervention does not seem to be associated with increased risk of in-hospital recurrent ischemic events.

Up until 2013, there were only 3 randomized studies examining different revascularization strategies in patients with STEMI and multivessel disease.24–26 These studies were limited by small sizes and lack of statistical power. The largest of these was a single-center study that included 214 patients. There was a significant reduction in MACEs during a mean follow-up of 2.5 years in the patients treated with complete revascularization (staged or complete during PPCI) compared with culprit-only revascularization. The end point was driven mainly by an increase in subsequent revascularization in the culprit-only arm. There was no difference between complete versus staged revascularization.26

In 2013, the Preventative Angioplasty in Myocardial Infarction (PRAMI) trial was published.27 This compared culprit-only versus complete revascularization (preventative PCI) at the time of PPCI in 465 patients with STEMI and multivessel disease. Preventative PCI was associated with a significant reduction in the primary endpoint, a composite of death from cardiac causes, nonfatal MI, or refractory angina (HR, 0.35; 95% CI, 0.21–0.58; P<0.001). The primary outcome was driven by reductions in nonfatal MI and refractory angina. Subsequent need for revascularization was not included in the primary outcome as this end point would be influenced by not performing PCI of nonculprit vessels and be dictated by the treatment strategy. However, refractory angina was included in the primary outcome, and one may also argue that this outcome measure may also be driven by stenoses, which had been left untreated in patients who did not undergo preventative PCI.

The more recently reported Complete Versus culprit-Lesion only PRimary PCI (CVLPRIT) trial compared a strategy of complete in-hospital revascularization with culprit-only PCI and subsequent revascularization based on recurrent (ischemia proven) symptoms in 296 patients with multivessel coronary disease at PPCI.28,29 This study found that a strategy of complete revascularization before discharge was associated with reduced composite risk of death, recurrent MI, heart failure, or ischemia-driven revascularization at 30 days (HR, 0.45; 95% CI, 0.24–0.84; P=0.009) and the results were sustained ≤1 year. However, there was no statistical significance when each component was analyzed separately. Furthermore, given that ischemia-driven revascularization may also be dictated by treatment strategy as it will be driven by untreated stenoses, its inclusion in the primary end point may make the results difficult to interpret. It must also be noted that 57% of the patients underwent multivessel revascularization at the time of the PPCI with the reminder receiving complete revascularization before discharge. An important question stemming from CVLPRIT is whether complete revascularization at the time of
PPCI or whether before hospital discharge is associated with better outcomes. Given the small study size, subgroup analyses addressing this question are likely to be underpowered.

The use of revascularization and refractory angina is well-established outcomes in cardiovascular studies, but these outcomes are all dictated by the treatment strategy and are difficult to interpret for patients treated with culprit-only revascularization in the setting of bystander coronary disease. This is also demonstrated by a more recent observational analysis of 1909 patients, where MVI was associated with reduced MACE rates, but this composite end point was driven by reduced reintervention rates. The difficulty in designing a randomized trial in this setting is further compounded by the fact that so many strategies and treatment options exist for these patients in every day clinical practice (Figure 1), and it may be difficult to incorporate and evaluate each strategy in a randomized control trial. Although the PRAMI and CVLPRIT trials have certainly added to the current evidence base, further studies are warranted to further refine our treatment strategies for STEMI patients with multivessel disease. The Complete versus Culprit-only Revascularization to Treat Multi-vessel Disease After Primary PCI for STEMI (COMPLETE) trial aims to compare a strategy of complete (including staged) versus culprit-only revascularization in reducing the composite outcome of CV death or MI in 3900 patients with multivessel disease at PPCI.

The main strength of this study is that it is the largest reported analysis comparing CVI versus MVI in STEMI patients with multivessel disease with the longest reported follow-up. Given that it is an observational analysis, there is likely to be confounding, but this was addressed by various analytical methods that account for measured confounding. Although observational analyses may be associated with under-reporting of complications, the figures reported in this study for the primary outcome of all-cause mortality can be considered as accurate because tracking using the Office of National Statistics is robust. Data for other clinical end points such as reinfarction and revascularization after hospital discharge were not available. This study has all the limitations of a registry and all the potential bias associated with nonrandomization and thus residual confounding cannot be excluded. Given that 14% of patients with multivessel disease underwent MVI, this would imply a strong selection process and may reflect the current guidelines for revascularization in STEMI. Furthermore, besides operator choice, clinical indications that may potentially drive MVI could not be deduced from the database, a common problem with observational studies of this nature. Furthermore, the nature and complexity of the bystander disease were not captured by the database, and this may be a factor dictating non-CVI at time of PPCI. Although patients with cardiogenic shock were excluded from the analysis, it is possible that periprocedural hemodynamic instability may have driven MVI. Although periprocedural hemodynamic data were not available, we did adjust for intra-aortic balloon pump use, intubation status, and inotropic support, which would otherwise account for hemodynamic instability and the sicker patient population. Despite our attempts to account for measured confounders, an important limitation of this study is the presence of unmeasured confounders. Data with regards to subsequent staged revascularization (both during the admission and as an elective staged procedure) for patients receiving CVI were not available from the database and thus comparison with CVI plus staged revascularization with MVI, which would be a clinically more meaningful analysis, was not possible. Data with regards to complete revascularization were not captured by the database. Nevertheless, the results of our study indicate that culprit-only revascularization at the time of PPCI is associated with better outcomes and support the current recommended practice guidelines.

Conclusions
In this observational analysis of patients with STEMI undergoing PPCI, CVI at the time of PPCI was independently associated with reduced 1-year mortality. These findings differ to recent randomized trial data. Although there are limitations of registry data, our findings support current recommended practice guidelines.

Sources of Funding
This work was supported by the National Institute of Health Research Cardiovascular Biomedical Research Unit of Royal Brompton and Harefield National Health Service Foundation Trust and Imperial College London.

Disclosures
None.

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Culprit Vessel Versus Multivessel Intervention at the Time of Primary Percutaneous Coronary Intervention in Patients With ST-Segment–Elevation Myocardial Infarction and Multivessel Disease: Real-World Analysis of 3984 Patients in London

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Circ Cardiovasc Qual Outcomes. 2014;7:936-943; originally published online November 4, 2014;
doi: 10.1161/CIRCOUTCOMES.114.001194

Circulation: Cardiovascular Quality and Outcomes is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-7705. Online ISSN: 1941-7713

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