Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial

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Aims
To examine the incidence of and propensity for non-culprit interventions performed at the time of the primary percutaneous coronary intervention (PCI) and its association with 90-day outcomes.

Methods and results
We examined the incidence, propensity for, and associated 90-day outcomes following non-culprit interventions performed at the time of primary PCI among ST-elevation myocardial infarction patients with multi-vessel coronary artery disease (MVD). Of the 5373 patients who underwent primary PCI in the APEX-AMI trial, 2201 had MVD. Of those, 217 (9.9%) underwent non-infarct-related arteries (IRA) PCI, whereas 1984 (90.1%) underwent PCI of the IRA alone. Ninety-day death and death/CHF/shock were higher in the non-IRA group compared with the IRA-only PCI group (12.5 vs. 5.6%, \(P\) (log-rank) = 0.001 and 17.4 vs. 12.0%, \(P\) (log-rank) = 0.020, respectively). After adjusting for patient and procedural characteristics as well as propensity for performing non-IRA PCI, this procedure remained independently associated with an increased hazard of 90-day mortality [adjusted hazard ratio 2.44, 95% CI (1.55–3.83), \(P\) < 0.001].

Conclusion
Non-culprit coronary interventions were performed at the time of primary PCI in 10% of MVD patients and were significantly associated with increased mortality. Our data support current guideline recommendations discouraging the performance of such procedures in stable primary PCI patients. Prospective randomized study of this issue may be warranted.

Keywords
Non-culprit coronary artery • Primary percutaneous coronary intervention • Myocardial infarction

Introduction
Multi-vessel coronary artery disease (CAD) occurs in 40–65% of patients undergoing primary percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) and is associated with adverse prognosis.1–4 Guidelines from both the European Society of Cardiology (ESC) and the American College of Cardiology/American Heart Association (ACC/AHA) discourage PCI of non-infarct-related arteries (non-IRA) at the time of primary or rescue PCI in stable STEMI patients (class III ACC/AHA).5–7 These recommendations, however, are based on Level C evidence derived from observational studies and clinical trials with limited power, emphasizing the mismatch that can exist between specific guideline recommendations and the underlying weight of data.7 As much of this evidence emerged from an era preceding routine stenting, platelet glycoprotein inhibition and clopidogrel pre-treatment, its relevance to contemporary practice and guidelines is frequently questioned.8–14

In order to examine this issue, we interrogated the Assessment of Pexelizumab in Acute Myocardial Infarction (APEX-AMI) trial.
which provides a large and well-characterized cohort of contemporary STEMI patients treated with primary PCI at experienced centres around the world. The trial protocol asserted compliance with ESC and ACC/AHA guidelines and it thus provides an appropriate vantage point from which to judge adherence to these guidelines in electrocardiographically high risk but generally stable patients. Using prospectively collected site-reported data, we identified all APEX-AMI subjects with multi-vessel disease (MVD) who underwent PCI in a non-IRA. We describe herein correlates and propensity for non-IRA PCI in the APEX-AMI trial and the associated 90-day outcomes.

Methods

The design and the primary results of the APEX-AMI trial have been published previously. Briefly, patients 18 years of age or older presenting within 6 h of symptoms were included if they were expected to undergo primary PCI and were required to have high-risk electrocardiographic characteristics. These included at least 2 mm ST-elevation in two anterior lateral leads or at least 3 mm ST-elevation in two inferior leads coupled with ST-depression in two contiguous anterior leads for a total of 8 mm or more or a new left-bundle branch block with at least 1 mm concordant ST-elevation. Patients were excluded if they were undergoing rescue PCI, had isolated inferior MI, were pregnant or breastfeeding, had known or suspected complement deficiency or active serious infection, or had other serious medical conditions likely to alter their recovery.

Patients received either an intravenous bolus followed by an infusion of pexelizumab or placebo, while concomitant medications and subsequent cardiac procedures were left to the discretion of the attending physician. Because no effect with pexelizumab was demonstrated, the treatment arms for this analysis were pooled. Percutaneous coronary intervention operators were strongly encouraged to comply with contemporaneous acute STEMI treatment guidelines established by the ESC and ACC/AHA. The choice of coronary intervention with balloon angioplasty or stenting and type of stent was left to the discretion of the interventional cardiologist.

Angiographic data were obtained visually by PCI operators at the investigative site. Mandatory data fields included the identification of the infarct-related coronary artery, its pre-intervention flow, and the maximum percent stenosis [in left main (LM), left anterior descending (LAD), left circumflex (LCx), right coronary artery (RCA)]. Flow in the IRA was graded using the thrombolysis in myocardial infarction (TIMI) flow grade, LAD as the IRA (for 90-day death/CHF/shock only), sytostolic blood pressure, heart rate, MI location, Killip class for the qualifying event, serum creatinine, SST-segment deviation on the baseline ECG, any CHF or cardiogenic shock prior to first balloon inflation, pre-PCI TIMI flow grade, LAD as the IRA (for 90-day death/CHF/shock only), and time from symptom onset to first balloon inflation.

A wide range of patient and procedural characteristics were considered in determining the factors associated with performing a non-IRA PCI and included age, body weight, heart rate, systolic blood pressure, Killip class, MI location, hypertension, history of CHF, diabetes mellitus, smoking status, SST-segment deviation on the baseline ECG, region (North America, Western Europe, Eastern Europe, and Australia/New Zealand), LAD-IRA, time from symptom onset to first balloon inflation, and any CHF or cardiogenic shock prior to first balloon inflation. Significant predictors were identified using backward stepwise selection and are reported as adjusted odds ratio (OR) with 95% CI. Predicted probabilities from the non-parsimonious propensity model for non-IRA PCI were generated and included in the clinical outcome models in an attempt to account for the selection bias in the decision to perform non-IRA PCI.

Finally, we examined whether outcomes varied with the volume of non-IRA PCIs performed in the enrolling sites. Specifically, sites were grouped into tertiles according to their non-IRA PCI rate. Ninety-day clinical outcomes for all patients were compared across the tertiles of non-IRA PCI site volume. All statistical tests were two-sided with 5% level of significance, and the analyses were performed using SAS 9.1 (SAS Institute, Cary, NC, USA).

Clinical outcomes

The endpoints of this study included 90-day mortality and the 90-day composite of death, congestive heart failure (CHF), and cardiogenic shock. Congestive heart failure and cardiogenic shock were centrally adjudicated by a clinical events committee (CEC) blinded to treatment assignment and details of the PCI. A detailed description of the endpoints has been previously published.

Statistical methods

Baseline patient characteristics, procedural features, and clinical outcomes were reported for the study cohort and according to occurrence of non-IRA intervention (non-IRA vs. IRA-only PCI). Percentages were presented for discrete variables and medians with 25th and 75th percentiles for continuous variables; differences between groups were tested with $\chi^2$ tests and Wilcoxon rank-sum tests, respectively. Kaplan–Meier curves according to intervention type (non-IRA vs. IRA-only PCI) were presented for 90-day death and composite of death/CHF/shock after first balloon inflation with the $P$-value for the pairwise log-rank test. Cox proportional hazards models were developed for 90-day mortality and 90-day death/CHF/shock after first balloon inflation. Independent predictors, reported as adjusted hazard ratios (HR) with 95% confidence intervals (CI), included age, sex (for 90-day death/CHF/shock only), systolic blood pressure, heart rate, MI location, Killip class for the qualifying event, serum creatinine, SST-segment deviation on the baseline ECG, any CHF or cardiogenic shock prior to first balloon inflation, pre-PCI TIMI flow grade, LAD as the IRA (for 90-day death/CHF/shock only), and time from symptom onset to first balloon inflation.

Results

Of 5745 patients enrolled in the APEX-AMI trial, 372 did not undergo primary PCI procedure. Among the remaining 5373 patients, 2201 (41%) had a significant stenosis in a coronary territory other than that of the culprit lesion, i.e. MVD: 217 [9.9%, 95% CI (8.6%, 11.1%)] of these patients underwent a non-IRA PCI, whereas 1984 patients (90.1%) had PCI confined to the IRA territory. The remaining 3172 (59%) patients had single-vessel CAD and therefore had PCI in the culprit artery only (Figure 1). Single-vessel CAD patients had significantly lower 90-day mortality than their counterparts with MVD [3.1 vs. 6.3%, $P$ (log-rank) < 0.001].
Patient and procedural characteristics are presented according to the performance or not of non-IRA PCI (Table 1). Patients undergoing non-IRA PCI had lower systolic blood pressure and were less likely to have inferior MI, hypertension, or diabetes. They were more likely to have the LAD as their culprit IRA and to receive GPI and drug-eluting stents. Although the prevalence of MVD across geographic regions was similar, a larger proportion of MVD patients received a non-IRA PCI in North America (12.6%) and Western Europe (10.5%) compared with those enrolled in other regions (Eastern Europe, 6.6%; Australia/New Zealand, 6.1%; P = 0.001). There were no differences in the peak cardiac biomarkers between the different groups [median peak CK 9.7 (25th, 75th percentiles: 5.0, 18.1) and 9.3 (5.0, 20.2) times the upper limit of normal for IRA-only and non-IRA PCI, respectively, P = 0.739]. Also, patients undergoing NIRA PCI had significantly longer procedure time compared with IRA-only PCI patients (56 vs. 42 min, P < 0.001). There was no statistically significant difference in GUSTO severe bleeding between the NIRA PCI and IRA-only PCI groups (1.8 vs. 0.6%, respectively, P = 0.065).

Patient and procedural characteristics that were significantly associated with non-IRA PCI was non-inferior MI [Χ² = 7.18; adjusted OR: 1.50, 95% CI (1.11–2.01), P = 0.007], whereas diabetes mellitus [Χ² = 9.37; 0.50 (0.32–0.78), P = 0.002] and undergoing PCI in a region other than North America [Χ² = 18.69; Western Europe: 0.78 (0.56–1.08); Eastern Europe: 0.46 (0.31–0.68); Australia/New Zealand: 0.43 (0.23–0.80), P < 0.001] were associated with a lower likelihood of undergoing a non-IRA PCI.

The anatomic distribution of the IRA is shown in the centre of Figure 2 in order to evaluate its relationship to the subsequent territory of non-IRA PCI. Non-IRA intervention was most common when the LAD was the culprit artery followed by the RCA and LCx. Non-IRA interventions were performed most commonly in the LCx (n = 103) and least commonly in the LAD (n = 49).

Clinical outcomes

The 90-day death rate was significantly higher in those undergoing non-IRA PCI compared with those undergoing IRA-only PCI alone [12.5 vs. 5.6%; P (log-rank) < 0.001 (Figure 3)]. Similarly, the composite endpoint of death, CHF, and shock from randomization to Day 90 was 18.9 vs. 13.1%, P (log-rank) = 0.011. When we excluded those who developed adjudicated endpoints of CHF or shock prior to the index PCI (n = 24 in IRA-only PCI and n = 4 in non-IRA PCI), the composite endpoint remained higher in non-IRA PCI patients (death/CHF/shock: 17.4 vs. 12.0%, P (log-rank) = 0.020 (Figure 4)). In 29 additional instances (26 in IRA-only PCI and 3 in non-IRA PCI), investigators identified patients with CHF or shock developing prior to PCI but subsequent CEC review concluded the events did not fulfill the CEC endpoint definitions. The additional exclusion of these subjects from our analysis did not substantially change our results (data not shown). Non-IRA PCI remained associated with an increased hazard of 90-day mortality [adjusted HR 2.44, 95% CI (1.55–3.83), P < 0.001] and 90-day death/CHF/shock, although not reaching statistical significance, [adjusted HR 1.39, 95% CI (0.96–2.01), P = 0.083] after adjustment for patient and procedural characteristics and the propensity for performing non-IRA PCI (Figure 5).

The examination of outcomes according to tertiles of non-IRA PCI practice revealed that the numerically lowest 90-day event rates were seen in the tertile with lowest non-IRA PCI rate. However, neither death nor the composite endpoint differed significantly across the tertiles [Table 2; 90-day death, P (interaction) = 0.132; 90-day death/CHF/shock, P (interaction) = 0.243]. No important differences in patient characteristics were observed across tertiles (data not shown).

Discussion

We observed that PCI in non-infarct coronary vessels was performed coincident with primary PCI in approximately 1 in 10 patients who had site-identified multi-vessel CAD despite guidelines that discourage this practice. The frequency of this practice varied considerably between geographic regions. Further, we found that discretionary PCI of a non-IRA coincident with a primary PCI procedure is associated with worse clinical outcome including a two-fold increase in 90-day death. This association remained robust even after adjustment for known covariates.

The prevalence of MVD in the APEX-AMI trial was 41%, comparable to previous reports that observed prevalence ranging from 40 to 65%.3–5 In the early 1990s, Moreno et al.3 noted that MVD patients undergoing primary angioplasty for STEMI at a single centre had a higher rate of in-hospital mortality than did those with single-vessel disease. Similarly, in the multi-centre Thrombolysis and Angioplasty in Myocardial Infarction study that incorporated routine early post-fibrinolytic cardiac catheterization, patients with MVD had lower left ventricular ejection fraction and higher in-hospital mortality.4 Our contemporary data are concordant with these historic data: we observed 90-day mortality rates of 6.3% in MVD patients vs. 3.1% in those with single-vessel CAD.

Previous studies examining the safety of non-IRA PCI at the time of the primary PCI procedure have shown mixed results and been heterogeneous, utilizing balloon angioplasty, bare metal stents as well as drug-eluting stents. In our review of the literature of eight studies published or presented at scientific meetings between 2001 and 2008, we identified data on only 456 patients receiving non-IRA intervention at the time of the primary PCI.3–5,14–19 In the only randomized trial published, 52 patients received complete PCI in non-IRA PCI compared with those undergoing IRA-only PCI alone [12.5 vs. 5.6%; P (log-rank) < 0.001 (Figure 3)]. Similarly, the composite endpoint of death, CHF, and shock from randomization to Day 90 was 18.9 vs. 13.1%, P (log-rank) = 0.011. When we excluded those who developed adjudicated endpoints of CHF or shock prior to the index PCI (n = 24 in IRA-only PCI and n = 4 in non-IRA PCI), the composite endpoint remained higher in non-IRA PCI patients (death/CHF/shock: 17.4 vs. 12.0%, P (log-rank) = 0.020 (Figure 4)). In 29 additional instances (26 in IRA-only PCI and 3 in non-IRA PCI), investigators identified patients with CHF or shock developing prior to PCI but subsequent CEC review concluded the events did not fulfill the CEC endpoint definitions. The additional exclusion of these subjects from our analysis did not substantially change our results (data not shown). Non-IRA PCI remained associated with an increased hazard of 90-day mortality [adjusted HR 2.44, 95% CI (1.55–3.83), P < 0.001] and 90-day death/CHF/shock, although not reaching statistical significance, [adjusted HR 1.39, 95% CI (0.96–2.01), P = 0.083] after adjustment for patient and procedural characteristics and the propensity for performing non-IRA PCI (Figure 5).

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revascularization vs. 17 patients who received culprit-only revascularization, Di Mario et al.9 showed that there was no excess in-hospital or 1-year MACE (defined as death, repeat MI, urgent PTCA, or CABG) associated with complete revascularization. In a retrospective analysis, Corpus et al.8 showed that the 26 patients undergoing non-IRA PCI at the time of the primary PCI procedure had higher in-hospital mortality and higher MACE (repeat MI, target vessel revascularization, CABG, death) at 1-year. Most recently, Feng, Qarawani, and Khattab showed that multi-vessel revascularization at the time of primary PCI was not associated with increased 30-day to 1-year mortality in 225 patients.10,12,14 Our cohort of 217 patients undergoing non-IRA PCI is the largest yet studied. Moreover, our results are more generalizable to a relatively high-risk STEMI population as patients in the current study had very few exclusion criteria and were treated at experienced PCI centres within 6 h of symptom onset in a contemporary multi-centre international trial environment.

Current ESC and ACC/AHA STEMI guidelines discourage operators from performing PCI in non-IRA targets at the time of primary PCI for STEMI unless haemodynamic compromise or cardiogenic shock is present.5,6 Most patients (90.1%) with multi-vessel CAD enrolled in the APEX-AMI trial appear to have been treated in accord with these guidelines. However, in 9.9% of our multi-vessel cohort, operators chose to treat non-IRA targets during the primary PCI procedure. These procedures may have been triggered in some cases by transient haemodynamic instability developing during or immediately following treatment of the IRA, and thus be potentially compliant with guidelines. Few clinical

### Table 1  Selected patient and procedural characteristics in patients with multi-vessel disease according to infarct-related artery only percutaneous coronary intervention and non-infarct-related artery percutaneous coronary intervention

<table>
<thead>
<tr>
<th>All MVD</th>
<th>IRA-only PCI</th>
<th>Non-IRA PCI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2201</td>
<td>1984</td>
<td>217</td>
</tr>
<tr>
<td>Age, year, median (25th, 75th percentile)</td>
<td>64 (55, 73)</td>
<td>64 (55, 73)</td>
<td>64 (53, 74)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>20.8</td>
<td>20.6</td>
<td>22.6</td>
</tr>
<tr>
<td>Weight, kg, median (25th, 75th percentile)</td>
<td>80 (70, 90)</td>
<td>80 (70, 90)</td>
<td>80 (72, 90)</td>
</tr>
<tr>
<td>Heart rate, b.p.m., median (25th, 75th percentile)</td>
<td>75 (65, 87)</td>
<td>75 (64, 87)</td>
<td>77 (67, 88)</td>
</tr>
<tr>
<td>Systolic BP, mmHg, median (25th, 75th percentile)</td>
<td>134 (116, 150)</td>
<td>134 (117, 150)</td>
<td>130 (112, 148)</td>
</tr>
<tr>
<td>Killip class &gt;1 (%)</td>
<td>11.6</td>
<td>11.4</td>
<td>13.8</td>
</tr>
<tr>
<td>Inferior MI (%)</td>
<td>44.7</td>
<td>45.5</td>
<td>37.0</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>54.8</td>
<td>55.6</td>
<td>47.5</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>15.5</td>
<td>15.9</td>
<td>12.4</td>
</tr>
<tr>
<td>Prior PCI (%)</td>
<td>11.5</td>
<td>11.7</td>
<td>9.7</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>3.6</td>
<td>4.0</td>
<td>0.5</td>
</tr>
<tr>
<td>Prior CHF (%)</td>
<td>4.0</td>
<td>3.9</td>
<td>4.6</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>19.2</td>
<td>20.0</td>
<td>11.5</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>39.7</td>
<td>39.9</td>
<td>38.2</td>
</tr>
<tr>
<td>Creatinine clearance, mL/min, median (25th, 75th percentile)</td>
<td>77.9 (59.8, 100.8)</td>
<td>78.4 (59.9, 100.7)</td>
<td>74.0 (58.6, 101.1)</td>
</tr>
<tr>
<td>SST-segment deviation on baseline ECG, mm, median (25th, 75th percentile)</td>
<td>13.5 (9.5, 19.0)</td>
<td>13.5 (9.5, 19)</td>
<td>13.5 (9.5, 18.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IRA (%)</th>
<th></th>
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<tbody>
<tr>
<td>LAD</td>
<td>49.0</td>
</tr>
<tr>
<td>LCX</td>
<td>12.3</td>
</tr>
<tr>
<td>RCA</td>
<td>38.5</td>
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<table>
<thead>
<tr>
<th>Extent of multi-vessel disease (%)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Two-vessel disease</td>
<td>67.7</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>31.2</td>
</tr>
</tbody>
</table>

| Time from symptom onset to PCI, h, median (25th, 75th percentile) | 3.4 (2.6, 4.7) | 3.4 (2.6, 4.7) | 3.5 (2.7, 4.9) | 0.277 |
| In-hospital GPI use (%)           | 72.6       | 71.9         | 78.8         | 0.030 |
| Stent (%)                         | 94.7       | 94.6        | 95.9        | 0.436 |
| DES, % of stents                  | 38.0       | 36.6        | 50.7        | <0.001 |
| BMS, % of stents                  | 54.6       | 56.1        | 40.6        | |
| LOS, days, median (25th, 75th percentile) | 6 (4, 9) | 6 (4, 9) | 6 (4, 9.5) | 0.203 |
| LOS (in in-hospital survivors), days, median (25th, 75th percentile) | 6 (5, 9) | 6 (5, 9) | 6 (4, 9) | 0.710 |

LOS, length of stay.
trial databases capture and characterize intra-procedural haemodynamic instability, while pre- and post-procedural data elements describing the haemodynamic state were obtained in the APEX-AMI trial, no data fields described intra-procedural status. Notwithstanding this uncertainty, the considerable regional variability in non-IRA PCI rates we observed indicates that other discretionary modulators were likely at play.

What other factors might influence this aspect of interventional practice? Economic incentives and process-of-care pressures targeting hospital length-of-stay would favour complete initial revascularization over a staged approach. It has been shown that improvement in care is associated with a decrease in the average length of hospital stay after AMI. However, no differences in length of stay were observed in our study. Many operators are also likely to recognize the adverse prognosis implied by the presence of MVD, and some may with good intention seek to reduce risk in this subset by treating non-IRA targets that are perceived to be a likely substrate for recurrent ischaemia or infarction. Advances in PCI technology may also contribute to discretionary non-IRA PCI. Existing guidelines addressing the specific issue of non-IRA PCI have been substantially influenced by lessons learned in the pre-stent, pre-GPI, and pre-thienopyridine era in which abrupt vessel closure could occur unpredictably leading to transmural ischaemia and infarction. Routine use of stents and contemporary antithrombotic regimens, however, have made intra-procedural and early post-procedural abrupt coronary occlusion less likely and may have instilled operator confidence that contemporary non-IRA PCI undertaken with coincident primary PCI is acceptably safe.

Examining the Kaplan–Meier analysis of mortality (Figure 3) reveals a gradual divergence of curves in which most of the differential death occurs well beyond the peri-procedural period, in a phase when STEMI patients are frequently under the care of others or perhaps have been discharged from hospital. In larger institutions typical of APEX-AMI sites, death occurring well after the initial primary PCI procedure, even if communicated to the original interventionalist, is unlikely to be attributed to a specific strategy employed during the original procedure.

If the hazard of non-IRA PCI that is suggested by our primary analysis (adjusted estimate of HR for 90-day death 2.44) is due merely to association with unmeasured high-risk patient characteristics (such as intra-procedural haemodynamic instability), we reasoned that mortality among the totality of multi-vessel subjects might be favourably affected by site-specific higher rates of therapeutically effective non-IRA PCI. The analysis of multi-vessel outcomes by tertile of non-IRA PCI site volume provides some insight in this regard. The observed absolute difference in mortality between lowest and highest non-IRA PCI site tertiles, while not significantly different, was 2% (5.4 vs. 7.4%), whereas the expected difference in mortality in each tertile was 1.6%. Although this secondary analysis is limited in power, its findings are most

Figure 2 Distribution of IRA and non-IRA in patients undergoing non-IRA PCI. The centre pie represents all patients who underwent non-IRA PCI (n = 217). Of these patients undergoing non-IRA PCI, 10 had the non-IRA intervention in two locations and one patient had three non-IRA locations.

Figure 3 Kaplan–Meier curve of 90-day mortality in patients with non-IRA PCI vs. IRA-only PCI.
compatible with a causal relationship linking non-IRA PCI and excess mortality.

**Limitations**

By design our trial only included electrocardiographically high-risk STEMI patients presenting within 6 h of symptom onset. Our findings may not apply to STEMI patients not meeting the APEX-AMI trial inclusion criteria; however, they were broadly inclusive and patients tended to be treated comprehensively with contemporary evidence-based agents. Our subjects were treated exclusively in high-volume experienced PCI centres with median time from symptom onset to PCI of 3.3 h. While transient intra-procedural haemodynamic disturbances may not have been captured, when
we excluded from our analysis patients with either adjudicated or non-adjudicated shock or CHF developing prior to PCI, those undergoing non-IRA PCI still had substantially worse 90-day clinical outcomes. Finally, the angiographic analysis in our study was conducted at the investigative site and we are unable to provide the location of the interventions within the non-IRAs in patients with MVD.

Conclusions
In the largest report of its kind to date, we have shown that non-culprit coronary interventions was performed concurrent with primary PCI in 10% of a contemporary STEMI cohort treated at experienced and high-volume PCI centres. This practice was associated with adverse outcome including excess death. Although our non-randomized analysis cannot conclusively demonstrate a causal relationship, the data strongly support current guideline recommendations discouraging non-IRA PCI procedures performed at the time of primary PCI when patients are haemodynamically stable. Prospective randomized study of this issue may be warranted.

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