**Long Term Follow-Up of the Randomized Trial of Complete Versus Lesion-Only Revascularization in Patients Undergoing Primary Percutaneous Coronary Intervention for STEMI and Multivessel Disease - The CvLPRIT Trial**

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**Abstract**

**BACKGROUND:** Randomised trials have shown complete revascularisation in STEMI patients with multivessel disease results in lower MACE (all-cause death, MI, Ischaemia-driven revascularisation, heart failure).

**OBJECTIVES:** This follow-up study set out to determine if the benefits of complete revascularisation are sustained long term.

**METHODS:** CvLPRIT was a randomised trial of complete inpatient revascularisation versus infarct-related artery revascularisation only at the index admission. Randomised patients have been followed longer-term. The components of the original primary endpoint were collected from physical and electronic patient records, and from local databases for all readmissions.

**RESULTS:** The median follow-up (achieved in >90% patients) from randomisation to first event or last follow-up is 5.6 years (0-7.3 years). The primary MACE endpoint rate at this time point was 24.0% in the complete revascularisation group but 37.7% of the IRA-only group (HR=0.57, 95% CI = 0.37 – 0.87, p=0.0079).

The composite endpoint of all-cause death/MI was 10.0% in complete revascularisation group versus 18.5% in the IRA-only group (HR=0.47, 95% CI=0.25 – 0.89, p=0.0175). In a landmark analysis (from 12 months to final follow-up) there was no significant difference between MACE, death/MI and individual components of the primary endpoint.

**CONCLUSIONS:** Long term follow-up of the CvLPRIT trial shows that the significantly lower rate of MACE in the complete revascularisation group, previously seen at 12 months, is sustained to a median of 5.6 years. A significant difference in composite all-cause death/MI favouring the complete revascularisation was also observed. These data support the longer term safety and efficacy of complete revascularisation in multivessel STEMI patients.

**Condensed Abstract.** The CvLPRIT trial showed lower MACE (all-cause death, MI, ischaemia-driven revascularisation and heart failure) at 12 months with complete revascularisation in patients presenting with STEMI and mutivessel disease compared with infarct-related artery (IRA)-only PCI. This longer-term follow up aims to determine whether there is a sustained benefit in terms of MACE reduction with complete revascularisation. At a median follow-up of 5.6 years, the composite endpoint of all-cause death/MI was 10.0% in complete revascularisation group versus 18.5% in the IRA-only group (HR=0.47, 95% CI=0.25 – 0.89, p=0.0175). These data support the longer-term safety and efficacy of complete revascularisation in multivessel STEMI patients.

**Keywords**

Complete revascularisation, non-infarct related lesion, ST-Elevation Myocardial infarction, Multivessel disease, Primary Percutaneous Coronary Intervention.

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**Abbreviations**

STEMI = ST-Elevation Myocaridal Infarction.

P-PCI = Primary Percutaneous Coronary Intervention.

MVD = Multi-vessel disease

IRA = Infarct-related artery

N-IRA = Non-infarct-related artery

MACE = Major Adverse Cardiovascular Events

MI = Myocardial Infarction

PCI = Percutaneous Coronary Intervention

IDR = Ischaemia-driven revascularisation

CR = complete revascularisation

TVR = Target-vessel revascularisation

TLR = Target-lesion revascularisation

CV = cardiovascular

TLF = Target Lesion failure

MRI = Magnetic Resonance Imaging

**Introduction**

How best to manage multivessel disease (MVD) found during primary-PCI (P-PCI) for ST elevation myocardial infarction (STEMI) remains unresolved. Atheromatous disease in the non-infarct related artery (N-IRA) is seen in 30%-50% of STEMI patients (1-4). Those patients with STEMI plus other N-IRA disease have worse outcomes (3,5). Older observational, registry data suggested complete revascularisation may not be beneficial (6,7) but 4 recent small- to medium-sized randomized trials all showed similar, highly significant improvements in short term (12 -24 month) outcomes for complete versus culprit-only intervention (8-11). In all of the trials beneficial clinical outcomes were essentially driven by reduction in overall composite MACE, and while all MACE components fell, lower rates of repeat revascularisation were consistently seen.

Outcome data for all studies extends only to the original reported follow-up time (12-24 months). In the trials the divergence in Kaplan Meier curves for complete versus culprit only was seen early and appeared to be being maintained to trials end. Since no long-term follow-data have previously been published we believed it important to determine longer term patient outcomes.

The aim of this study was, for the first time, to determine if there is a sustained benefit in favour of multi-vessel PCI in the longer term.

**Methods**

The CvLPRIT Trial (9) was undertaken in 7 UK sites. The sample size was based on data published by Politi et al (12). Study rationale, design, and power calculation have been previously published (13). The first patient was randomised in May 2011, recruitment was for 2 years and so the last recruited patient was randomised in May 2013. 12 month follow up was completed in May 2014. The primary outcome analysis for the trial was published in 2015 (9).

For this long-term follow-up, patient level data were collected from the individual centres over the time period extending from the 12 month original follow-up (range May 2012-2014) until August 2018. This latter date was arbitrarily chosen as it exceeded 5 year follow-up of the last patient randomised to the CvLPRIT trial. Consent for long-term patient data collection was covered under the original Ethics Committee application and original consent.

Each centre was contacted and provided with an individual list of their patients’ trial ID numbers and a list of events for any of these patients that had occurred in the 12 months (and so reported in the main trial paper). Hospital electronic databases and case notes were interrogated to identify any new MACE event occurring since trial completion at 12 months. If the patient was flagged as having had a MACE event after 12 months then a case report form (based on those from the original trial) was generated by the centre.

The primary outcome was the occurrence of MACE event and secondary outcomes included composite of death/myocardial Infarction, components of MACE, and others.

**Statistical analyses**

Time-to-event data were plotted using Kaplan-Meier method and compared between groups using log-rank test. Kaplan-Meier curves were generated to represent the following:

1. MACE events from randomisation to final patient long term follow up date (time-to-first event analysis including all patients, intention to treat population).
2. Landmark analyses of MACE events from 12 months to final follow-up.

Event tables were generated for:

1. Time-to-first event analysis of all MACE and its component endpoints for all patients from randomisation until follow-up.
2. Ischaemia-driven revascularisation in all patients from 12 months post-randomisation until end of follow-up including those that had a non-fatal MACE event in the first 12 months.
3. Additional, subsequent MACE events in patients who had had a non-fatal event in the first 12 months (first event per patient).

Cox proportional hazard models were used to derive hazard ratios (HR) and 2-sided 95% CIs. Landmark analysis was from 12 months. Continuous data were expressed as mean (SD) or median (IQ range) and compared using t-test or Wilcoxon test as appropriate. Binary event outcomes were expressed as number (%) of patients and comparisons done using the chi-squared or Fishers Exact test.

**Results**

The original trial recruited 296 patients, with 150 randomised to complete revascularisation and 146 randomised to IRA-only PCI. The original demographic data for the two groups are shown in Supplementary Table 1. Secondary prevention medication at time of discharge, important in the context of longer term follow-up, is shown in Supplementary Table 2. The 12-month MACE and its components from the original paper are shown in Supplementary Table 3 (9).

At 12 months follow-up, 288 patients were still alive (2 deaths in the CR group and 6 deaths in the IRA-only revascularization). The original CONSORT diagram showed that there were 11 patients lost to follow-up in the complete revascularisation group and 8 patients lost to follow-up in the IRA-only group. After 12 months, the follow-up data could not be obtained for 1 patient from the complete revascularisation group and 4 patients from the IRA-only group despite multiple contact attempts. Thus, long-term follow-up data (beyond the completion of the CvLPRIT trial) was available for 272 patients (91.9% of original randomised cohort; 91.8% of patients undergoing CR and 92.0% of IRA-only PCI patients). (Figure 1). The median time of follow-up from randomisation to final follow-up was 5.6 years (range 0 years – 7.3 years).

## **Intention to Treat Analysis from Randomisation to long-term follow-up**

The time-to-first event analysis of all patients included in the long-term follow-up is shown in Figure 2. At a median time of 5.6 years, the composite MACE rate was 25.3% in the complete revascularisation group and 37.7% in the IRA-only group (HR=0.57, 95% CI = 0.37 – 0.87, p=0.0079).

The individual components of the primary endpoint are shown in Table 1. While no individual component drove the primary endpoint, the composite endpoint demonstrated a significant difference in favour of complete revascularisation.

When the secondary composite of ‘death/myocardial Infarction’ was analysed, this showed a significantly lower rate in the complete revascularisation group; 10.0% compared to 18.5% in the IRA-only group and (HR=0.47, 95% CI=0.25 – 0.89, p=0.0175).

Rates of ischaemia-driven revascularisation were not significantly different between groups (complete revascularisation = 11.3%; IRA-only = 13.0%, HR=0.76, 95% CI=0.40 – 1.49, p=0.4447) in this long term analysis.

## **Landmark analysis of intention-to-treat population from 12 months to end of follow-up**

We found that beyond 12-months there remains a non-significant trend towards a lower event rate for the primary composite endpoint of MACE in the complete revascularisation group. The MACE rate from 12-months to end of long-term follow-up in the intention-to-treat population is 17.2% in the complete revascularisation group and 23.3% in the IRA-only group (HR=0.72, 95%CI=0.40-1.27, p=0.248) (Figure3, Table 2)

As shown in Table 2, the individual components of the primary endpoint are similar between the complete and the IRA-only group revascularisation groups. The secondary composite endpoint of death/MI was also similar between both groups (complete revascularisation = 8.9%, IRA-only= 16.5%, HR=0.53, 95%CI=0.25 – 1.12, p=0.0905) but trending towards complete revascularisation.

## **Revascularisation in patients following 12-month follow-up**

From the 12-month landmark analysis, the rates of ischaemia driven revascularisation (IDR) were similar between the complete-revascularisation and the IRA-only group after the initially reported 12-month follow-up period (Table 5). Specifically, in the complete revascularisation group this was 8.1% and the IRA group IDR 6.8% (HR=1.12, 95% CI=0.44 – 3.04, p=0.7694).

In terms of total number of ischaemia-driven revascularisations (for example if a patient initially presented with MI and went on to revascularisation as a result) after 12 months, rates were also similar between IRA-only and complete revascularisation groups (complete revascularisation group 13/148, 8.8%; IRA-only group 14/140, 10.0%, p=0.736), see Table 3.

Figure 4 shows IDR rates in each treatment group both before and after 12-month post-randomisation. We observed that there continues to be a requirement for ischaemia-driven revascularisation in those patients who received complete revascularisation. This is equally distributed between IRA and N-IRA lesions.

Table 3 shows whether in each group the IDR was to the target or non-target vessel- indicating likely in-stent restenosis or stent thrombosis, or a de-novo lesion. In the IRA-group TVR indicates need for revascularisation in the treated IRA-lesion/vessel, while in the complete revascularisation group TVR can include any vessel that was stented, and thus distinction is made between TVR and de-novo lesion (i.e. non-TVR)

There was an even split within the complete revascularisation group, with 6 of 13 cases of IDR due to TVR, and the other 7 non-TVR/de-novo lesions. Within the IRA-only group, predominantly ischaemia-driven revascularisation was performed i.e in a non-culprit lesion, (11 of 14 IDR cases non-target vessel revascularisation).

Within the reported ischaemia-driven revascularisation events, there was only 1 report of stent thrombosis in the longer-term follow-up period. This occurred in a patient randomised to the complete revascularisation group, with stent thrombosis occurring in the treated culprit-lesion.

## **Subsequent MACE events in Patients with a prior non-fatal event in the first 12 months**

Of the 38 patients who had a non-fatal event in the first 12 months, 11 patients had a subsequent event from 12 months until the end of follow-up. Table 4 shows these events. In total, there were 3 events in the complete revascularisation group (23.1%) and 8 events in the IRA-only group (32%). Within the complete revascularisation group, there were 2 deaths and one myocardial infarction (that was fatal). Similar rates of death and MI were observed between the 2 groups. In the IRA-only group, there were 2 patients who required ischaemia-driven revascularisation in a non-MI setting.

**Discussion**

The major and novel findings of this long-term follow up of the CvLPRIT trial are as follows: 1.The MACE event rate curves remain separated to a median time point of 5.6 years (max 7.3 years). 2. A highly significant difference in MACE rates between the complete revascularisation undertaken at the time of the primary PCI and infarct related artery only groups revascularisation persist at longer term follow-up. 3. There was no in-group difference in MACE between 12 months post randomisation and long-term follow-up. 4. While individual components of the MACE were not significantly different individually, all were numerically lower in the favour complete revascularisation group. 5. Rate of combined hard end point of death/MI was significantly different between the two groups (favouring complete revascularisation) at longer term follow up. 6. Ischaemia driven revascularisation rates were low during extended follow-up, with no difference between groups beyond 12 months. In the complete group, repeat intervention was equally split between culprit and non-culprit treated vessels while in the incomplete group, repeat revascularisation was due mostly to ischaemia-driven intervention to non-culprit vessels.

These long-term data are novel and thought-provoking. Until now there have been no published longer-term follow up data in patients randomised at the time of P-PCI to either complete or infarct-related artery only intervention. To date, unpublished data presented at EURO-PCR 2018 by the COMPARE ACUTE (11) study group suggest that the difference in outcomes seen at 12 months are maintained to 2 years. It is interesting that the curves both in that study and in our current extended follow-up study remain separated over a longer period. Similarly, the median follow-up of DANAMI-3-PRIMULTI trial was 27 months, with longest follow-up of 4 years, and this also showed a sustained lower rate of MACE following complete revascularisation (10), but this was not planned long-term follow up as such. All of these data suggest that lower rates of events seen within 12 months do translate into longer term benefit, predominantly through non-attenuation of benefit. Our data, showing a highly significant difference in the longer term without safety concerns, supports the current ESC Guidelines, and the focused update of the ACC guidelines, which indicate that complete revascularisation within the hospital admission should be at least considered in this patient group (IIa A and Class IIb respectively) (14,15).

It remains unclear exactly how early complete revascularisation could lead to longer term benefit. We postulate that early complete revascularisation in the STEMI patient with multivessel disease benefits may be due to both improvement in collateral flow to the peri-infarct ischaemic territory, and to the proactive management of N-IRA lesions, in the context of a pan-inflammatory paradigm. Certainly, given that both the MRI and nuclear medicine sub-studies of CVLPRIT (16,17) showed no difference in ischaemic burden between the groups at 1 week and 6 weeks respectively, the benefit we have demonstrated does not appear to be explained simply in terms of ischaemic burden being dealt with prophylactically in the complete group. It is important to state that the groups in CvLPRIT were evenly matched so an excess of events could be only due to the randomised treatments. Stenting has become a robust procedure with low stent-associated complications, reducing degradation of event benefit in the complete revascularisation arm.

The driver of the overall benefit we observe from complete revascularisation remains speculative, but may become clearer after publication of larger trials such as COMPLETE (NCT01740479) and FULL REVASC (NCT0286219). Meta-analyses of the recent smaller trials do, however, confirm significant benefit in terms of hard end points (18,19). In this context our new finding of significant benefit from a combined death/MI endpoint at longer term follow up suggests that the original trial was indeed underpowered for hard end points and that in the longer term hard end point combinations may become important. This is a novel observation supporting a complete revascularisation strategy, and is the first time that a benefit, judged by hard end points, has been seen in a single trial. While this is clearly the combination of 0-12 months (NS) and 12 month to follow-up (NS in landmark 0.0819 Table 2), and despite the small numbers, these are not small differences (approximately 50%). The contribution to this reduction in combined hard end point is shared between death and MI with the greater impact perhaps from MI (Tables 1 and 2).

It should be noted that while there appear to be no cases of heart failure during follow-up, in fact the 3 cases that did occur were not counted in the analyses as these were not hierarchical first events. In addition, the robust diagnosis of heart failure can be challenging.

Revascularisation rates are low in both groups in our study and remain low over extended follow-up. From 12 months onwards, the rates of revascularisation are similar between the IRA-only and complete revascularisation groups. Although in the IRA-only group revascularisation after 12 months is mainly N-IRA PCI, by contrast in the complete revascularisation group it is split between de-novo intervention and repeat revascularisation to the originally treated vessels. The overall numbers remain low, however and do not indicate that there is risk of excess requirement for repeat PCI in the complete revascularisation group-contemporary stenting is a robust procedure. For example, it is established that current restenosis rates for third generation drug-eluting stents are very low at <5% [eg real-world follow-up of patient treated with Everolimus-Eluting Synergy Stent from the SCARR registry showed restenosis rate at 1 year of 1.1% and stent thrombosis 0.4% (20)]. Longer-term rates of restenosis in second generation drug-eluting stent are also very low. In the NOBORI-2 study demonstrates 5-year rates of TLF of 7.3% in non-diabetic patients and 12.4% in diabetic patients (21). Similarly, the DUTCH PEERS (TWENTE II) study showed low rates of target vessel revascularisation and stent thrombosis at 5 years with Promus Element and Resolute Integrity drug- eluting stents (22)]. The 5-year results of the EXAMINATION trial demonstrated that definite stent thrombosis at 5 years in patients treated with EES-stents in STEMI patients was 2%, with target-lesion revascularisation of 4% and overall revascularisation rate of 12% (23). The findings are commensurate with the current presented analysis of the CvLPRIT study, in which the minimum follow-up was 5.6 years. Hence, this analysis confirms the robust outcome and longer-term safety of performing PCI to non-culprit lesions. Trials of prophylactic interventional treatment of coronary lesions must be predicated on demonstrable good outcomes. If a trial such as CvLPRIT had been undertaken 10 years earlier the outcomes (with the then high rates of stent thrombosis and in-stent restenosis) might well look very different, with early benefits offset by high stent event rates.

It should be highlighted that in the original paper the rate of IDR in the IRA-only group mostly drove the primary endpoint difference, which is not the case in this time frame.

Our data suggest that total revascularisation, known to have benefits in various cohorts with coronary artery disease (24), should now probably be considered the standard of care in suitable STEMI patients with multivessel disease. While the individual trials were small, the meta-analyses with their low I2 statistic are compelling, especially since they show a lack of significant harm (no contrast-induced nephropathy, no excess bleeding), and the novel data in this report should add to the evidence base that complete revascularisation appears better for the patient in the longer term as well as previously shown short term.

**Limitations**

The essential limitations in this study include all those published in the original trial (9). Specifically, the numbers remain small and therefore need interpreting cautiously despite the high significance and low HRs For this study there is always the chance that, despite methodological rigor, patient some events may have been missed, but this was mitigated by achieving patient level data from the original recruiting centres by the local investigators and original trial research nurses. The forms used were based on trial event capture forms to ensure cross checking and that event details (such as repeat revascularisation) were cross checked.

As with any longer term follow-up study, the use of all-cause mortality as opposed to cardiovascular mortality may affect interpretation of the results. However, full data could not be obtained on the cause of death and hence CV mortality could not be reported in this study.

The assessment of repeat revascularisation procedures were limited to angiographic and PCI procedural descriptions from case note-based angiography reports, as was the assessment as to whether there was TLR/TVR/non-TVR or stent thrombosis.

Finally, whilst high levels of secondary prevention were administered at discharge we have not adjudicated this at long-term follow-up.

**Conclusions**

Long term follow-up of the CvLPRIT trial shows that the significantly lower rate of MACE in the complete revascularisation group, previously seen at 12 months, is sustained to a median of 5.6 years. A significant difference in composite all-cause death/MI favouring the complete revascularisation was also observed. These data support the longer term safety and efficacy of complete revascularisation in multivessel STEMI patients.

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**Conflicts of Interest**

**None of the authors indicate any conflicts of interest in relation to this work**

**Perspectives**

**Competency in Medical Knowledge:** There are sustained long term benefits for complete revascularisation complete revascularisation in patients presenting with STEMI and mutli-vessel disease, with reduction in MACE and long-term composite of death/MI.

**Competency in Patient Care:** Patients presenting with STEMI and evidence of multi-vessel disease should undergo PCI of N-IRA lesions in addition to treatment of the infarct related artery.

**Translational Outlook 1:** Further larger studies are required to determine the optimal timing of N-IRA lesion treatment (either at time of PPCI, during in-patient admission or as a staged outpatient procedure).

**Translational Outlook 2:** Determine which N-IRA lesions require treatment to confer benefit in terms of mortality and recurrent MI reduction may also be a focus of future research, as to date anatomical and physiological assessment has not yielded any subgroup with demonstrable benefit. In particular, whether targeting N-IRA PCI to vulnerable plaque lesions determined by OCT, VH-IVUS or NIRS could identify such lesions.

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**Table Legends**

**Table 1:** Individual components of MACE - Randomisation to end of long-term follow-up**.**

**Table 2:** Components of MACE in landmark analysis - from 12 months to end-of-follow-up**.** *NB: 24 individuals excluded as withdrew consent at 12 months (12 from each treatment group; 8 IRA and 11 Complete from initial trial; Additional 4 IRA and 1 complete who did not consent beyond 12 months). p from log-rank test.*

**Table 3:** Ischaemia Driven Revascularisation beyond 12 months in all patients surviving beyond 12 months. *For IRA-only group, TVR refers to revascularisation required in the culprit-only artery. For Complete revascularisation group, TVR refers to revascularisation required in any vessel that was treated with PCI during index admission.*

**Table 4:** Subsequent events during long-term follow-up in those patients with a non-fatal event in the first 12 months post-randomisation (first event only per patient).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table 1: Individual components of MACE - Randomisation to end of long-term follow-up** | | | | |
| **Event** | **Complete N=150 (%)** | **IRA only N=146 (%)** | **HR (95% CI)** | **p** |
| Total MACE | 36 (24.0) | 55 (37.7) | 0.57 (0.37, 0.87) | 0.008 |
| Death (All-cause) | 9 (6) | 15 (10.3) | 0.51 (0.22, 1.16) | 0.100 |
| Recurrent MI | 6 (4) | 12 (8.2) | 0.43 (0.16, 1.15) | 0.084 |
| Heart Failure | 4 (2.7) | 9 (6.2) | 0.42 (0.13, 1.37) | 0.138 |
| Ischaemia-Driven Revascularization | 17 (11.3) | 19 (13.0) | 0.76 (0.40, 1.49) | 0.445 |
| Death/MI | 15 (10) | 27 (18.5) | 0.47 (0.25, 0.89) | 0.018 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Table 2: Components of MACE in landmark analysis - from 12 months to end-of-follow-up** | | | | |
| **Event** | **Complete N=123 (%)** | **IRA only N=103 (%)** | **HR (95% CI)** | **p** |
| Total MACE | 21 (17.1) | 24 (23.3) | 0.71 (0.40, 1.27) | 0.248 |
| Death (All-cause) | 7 (5.7) | 9 (8.7) | 0.63 (0.23, 1.68) | 0.348 |
| Recurrent MI | 4 (3.3) | 8 (7.8) | 0.41 (0.12, 1.36) | 0.133 |
| Heart Failure | 0 (0) | 0 (0) | NA | NA |
| Ischaemia-Driven Revascularization | 10 (8.1) | 7 (6.8) | 1.12 (0.44, 3.04) | 0.769 |
| Death/MI | 11 (8.9) | 17 (16.5) | 0.53 (0.25, 1.12) | 0.091 |
| *NB: 24 individuals excluded as withdrew consent at 12 months (12 from each treatment group; 8 IRA and 11 Complete from initial trial; Additional 4 IRA and 1 complete who did not consent beyond 12 months)* | | | | |
| p from log-rank test |  |  |  |  |

**Table 3: Ischaemia Driven Revascularisation beyond 12 months in all patients surviving beyond 12 months.**

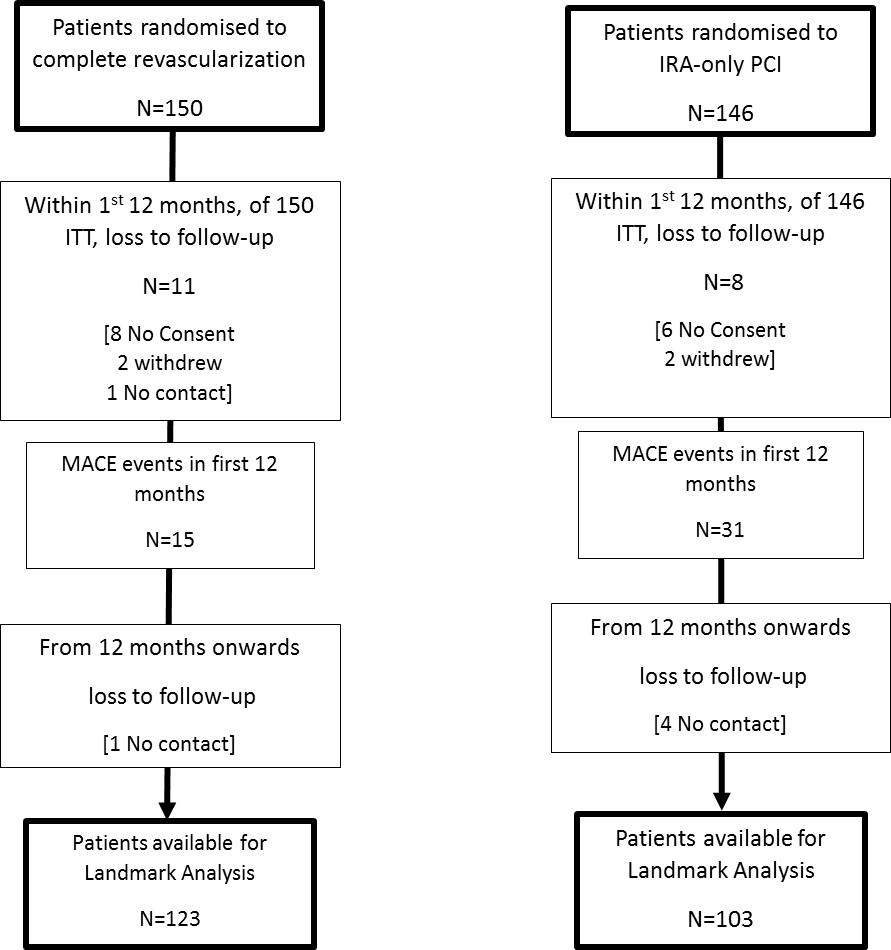
|  |  |  |  |
| --- | --- | --- | --- |
|  | Complete Revascularisation (n=148) | IRA-only PCI (n=140) | p-value |
| TVR | 6 (4.1%) | 3 (2.1%) | 0.346 |
| Non-TVR | 7 (4.7%) | 11 (7.9%) | 0.279 |
| Total IDR | 13 (8.8%) | 14 (10.0%) | 0.736 |

*For IRA-only group, TVR refers to revascularisation required in the culprit-only artery. For Complete revascularisation group, TVR refers to revascularisation required in any vessel that was treated with PCI during index admission.*

**Table 4: Subsequent events during long-term follow-up in those patients with a non-fatal event in the first 12 months post-randomisation (first event only per patient).**

|  |  |  |
| --- | --- | --- |
|  | **Complete Revascularisation (n=13)** | **IRA-Only PCI (n=25)** |
| Death | 2 (15.4%) | 5 (20%) |
| Myocardial Infarction | 1 (7.7%) | 1 (4%) |
| Ischaemia-driven Revascularisation | 0 | 2 (8%) |
| Heart Failure | 0 | 0 |
| **MACE events from 12 months until end of follow-up** | **3 (23.1%)** | **8 (32%)** |

**Figure 1: Flow Diagram for long-term follow-up and landmark analyses of CvLPRIT trial**

****

**Figure 2**

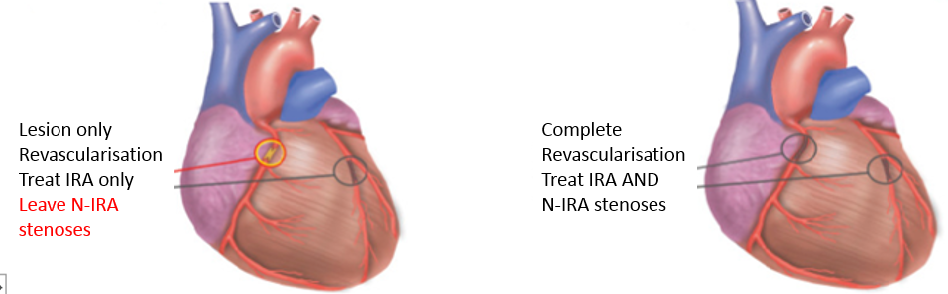
**MACE for Randomisation to long-term follow-up (First event, intention to treat analysis)**



**Figure 3 Landmark analysis in patients from 12 months to follow up (Intention-to-treat analysis)**



**Figure 4. Revascularisation during follow-up according to randomisation group and artery treated (IR or N-IR) during 2 periods of follow-up (randomisation till 12 months and 12 months till last follow-up, n= number of lesions present)**



|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **IRA only treatment** | X |  |  | **Complete revascularisation** |  |  |
|  | N-IRA  255 | IRA  146 |  |  | N-IRA  251 | IRA  150 |
| **IDR**  Rand – 12 mo | 11 | 1 |  | **IDR**  Rand – 12 mo | 5 | 2 |
| **IDR**  12 mo follow up | 11 | 3 |  | **IDR**  12 mo follow up | 7 | 6 |
| **TOTAL** | 22 | 4 |  | **TOTAL** | 12 | 8 |

**Central Illustration.**

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**Supplemental Material**

**This section contains the following supplementary tables:**

**Supplementary Table 1 Demographics of the two groups.**

**Supplementary Table 2 Secondary prevention medication at discharge**

**Supplementary Table 3: MACE rate at 12-months and its components from original CvLPRIT paper**

**Supplemental Material**

**Supplementary Table 1 Demographics of the two groups. (Taken from (9))**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Complete Revascularization (n = 150)** | **IRA-Only Revascularization (n = 146)** |  | **p Value** |
| Age, years |  |  |  | 64.6 ± 11.2 | 65.3 ± 11.9 |  | 0.57 |
| Male |  |  |  | 128 (85.3) | 112 (76.7) |  | 0.06 |
| Treated diabetes |  |  |  | 19/147 (12.9) | 20/140 (14.3) |  | 0.74 |
| Treated hypertension |  |  |  | 54/147 (36.6) | 51/140 (36.4) |  | 0.96 |
| Treated hypercholesterolemia |  |  |  | 41/147 (27.9) | 34/140 (24.3) |  | 0.49 |
| Current smoker |  |  |  | 50/146 (34.3) | 37/138 (26.8) |  | 0.17 |
| Previous MI |  |  |  | 7/147 (4.8) | 5/140 (3.6) |  | 0.62 |
| Previous PCI |  |  |  | 6/147 (4.1) | 3/140 (2.1) |  | 0.50 |
| Killip class II/III on admission |  |  |  | 10/147 (6.8) | 13/139 (9.4) |  | 0.43 |
| GFR <30 ml/min |  |  |  | 1/140 (0.7) | 1/137 (0.7) |  | 1.00 |
| Anterior MI |  |  |  | 54/150 (36.0) | 52/146 (35.6) |  | 0.94 |
| IRA site (selected CASS) |  |  |  |  |  |  |  |
| 1 Proximal RCA |  |  |  | 29 (19.3) | 30 (20.5) |  |  |
| 2 Mid RCA |  |  |  | 23 (15.3) | 24 (16.4) |  | 0.82 |
| 11 LMS |  |  |  | 0 | 0 |  |  |
| 12 Proximal LAD |  |  |  | 29 (19.3) | 31 (21.2) |  |  |
| 13 Mid LAD |  |  |  | 22 (14.7) | 16 (11.0) |  |  |
| 18 Proximal Cx |  |  |  | 9 (6.0) | 13 (8.9) |  |  |
| Other |  |  |  | 38 (25.3) | 32 (21.9) |  |  |
| N-IRA anatomic site (selected CASS) |  |  |  |  |  |  |  |
| 1 Proximal RCA |  |  |  | 23 (15.3) | 22 (15.1) |  |  |
| 2 Mid RCA |  |  |  | 24 (16.0) | 23 (15.8) |  | 0.96 |
| 11 LMS |  |  |  | 1 (0.7) | 2 (1.4) |  |  |
| 12 Proximal LAD |  |  |  | 27 (18.0) | 21 (14.4) |  |  |
| 13 Mid LAD |  |  |  | 44 (29.3) | 49 (33.6) |  |  |
| 18 Proximal Cx |  |  |  | 20 (13.3) | 20 (13.7) |  |  |
| Other |  |  |  | 11 (7.3) | 9 (6.2) |  |  |
| N-IRA stenoses >70% |  |  |  | 131 (87.3) | 118 (80.8) |  | 0.12 |
| 2-Vessel disease |  |  |  | 119 (79.3) | 110 (75.3) |  |  |
| 3-Vessel disease |  |  |  | 31 (20.7) | 36 (24.7) |  | 0.41 |
| Symptom to balloon time, min |  |  |  | 182 (115-282) | 159 (119-265) |  | 0.41 |
| Maximum HS-TnT elevation |  |  |  | 985 (629-1,625) | 1073 (509-1,824) |  | 0.96 |
| EF (by CMR), % |  |  |  | 45.8 ± 9.8 (n = 100) | 45.1 ± 9.5 (n = 103) |  | 0.57 |
| Balloon pump |  |  |  | 2 (1) | 1 (0.6) |  | 1.00 |
| Radial approach |  |  |  | 112/146 (76.7) | 102/140 (72.9) |  | 0.45 |

Values are mean ± SD, n (%), n/N (%), or median (interquartile range).

CASS = [Coronary Artery](https://www.sciencedirect.com/topics/medicine-and-dentistry/coronary-circulation) Scoring System; CMR = cardiac magnetic resonance; Cx = circumflex; EF = [ejection fraction](https://www.sciencedirect.com/topics/medicine-and-dentistry/ejection-fraction); GFR = glomerular filtration rate; HS-TnT = high-sensitivity [troponin T](https://www.sciencedirect.com/topics/medicine-and-dentistry/troponin-t); IQR = interquartile range; IRA = infarct-related artery; LAD = [left anterior descending](https://www.sciencedirect.com/topics/medicine-and-dentistry/anterior-interventricular-branch-of-left-coronary-artery); LMS = left main stem; MI = [myocardial infarction](https://www.sciencedirect.com/topics/medicine-and-dentistry/myocardial-infarction); N-IRA = noninfarct-related artery; PCI = [percutaneous coronary intervention](https://www.sciencedirect.com/topics/medicine-and-dentistry/percutaneous-coronary-intervention); RCA = [right coronary artery](https://www.sciencedirect.com/topics/medicine-and-dentistry/right-coronary-artery).

**Supplementary Table 2 Secondary prevention medication at discharge**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Complete Revascularization (n = 150)** |  |  |  | **IRA-Only Revascularization (n = 146)** | **p Value** |
| ASA |  | 141/142 (99.3) |  |  |  | 131/135 (97.0) | 0.16 |
| Plus clopidogrel |  | 59/144 (41.0) |  |  |  | 54/138 (39.1) | 0.75 |
| Plus ticagrelor |  | 19/144 (13.2) |  |  |  | 18/135 (13.3) | 0.97 |
| Plus prasugrel |  | 58/144 (40.3) |  |  |  | 64/138 (46.4) | 0.30 |
| Plus warfarin |  | 1/147 (0.7) |  |  |  | 2/138 (1.5) | 0.61 |
| GPI |  | 46/145 (31.7) |  |  |  | 44/139 (31.7) | 0.99 |
| Bivalirudin |  | 79/139 (56.8) |  |  |  | 65/128 (50.8) | 0.32 |
| TIMI flow grade 0/1 on arrival |  | 120/147 (81.6) |  |  |  | 118/140 (84.3) | 0.55 |
| Thrombus aspiration catheter used |  | 93/145 (64.1) |  |  |  | 105/140 (75.0) | 0.047 |
| DES |  | 141/147 (95.9) |  |  |  | 127/140 (90.7) | 0.08 |
| Stents per patient |  | 3 (2–4) |  |  |  | 1 (1–2) | <0.0001 |
| Total procedure time, min |  | 55 (38–74) |  |  |  | 41 (30–55.5) | <0.0001 |
| Total contrast used, ml |  | 250 (190–330) |  |  |  | 190 (150–250) | <0.0001 |
| Beta-blocker |  | 137/147 (93.2) |  |  |  | 126/135 (93.3) | 0.96 |
| ACEI/ARB |  | 142/147 (96.6) |  |  |  | 129/135 (95.6) | 0.65 |
| Statin |  | 146/146 (100) |  |  |  | 133/135 (98.5) | 0.14 |
| Aldosterone antagonist |  | 9/147 (6.1) |  |  |  | 8/135 (5.9) | 0.95 |
| Other antianginal agent |  | 55/147 (37.4) |  |  |  | 49/135 (36.3) | 0.85 |
| Loop diuretic agent |  | 15/147 (10.2) |  |  |  | 17/135 (12.6) | 0.53 |

Values are n/N (%) or median (interquartile range).

ACEI/ARB = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; ASA = [acetylsalicylic acid](https://www.sciencedirect.com/topics/nursing-and-health-professions/aspirin); DES = drug-eluting stent(s); GPI = [glycoprotein IIb/IIIa inhibitor](https://www.sciencedirect.com/topics/medicine-and-dentistry/glycoprotein-iib-iiia-inhibitors); IRA = infarct-related artery; TIMI = [Thrombolysis](https://www.sciencedirect.com/topics/medicine-and-dentistry/thrombolysis) In [Myocardial Infarction](https://www.sciencedirect.com/topics/medicine-and-dentistry/myocardial-infarction).

**Supplementary Table 3: MACE rate at 12-months and its components from original CvLPRIT paper (9)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Event | Complete  N=150 (%) | IRA only  N=146 (%) | HR(95% ci) | p |
| Total MACE | 15 (10.0) | 31 (21.2) | 0.45 (0.24,0.84) | 0.009 |
| Death (All-cause) | 2(1.3) | 6 (4.1) | 0.32 (0.06,1.60) | 0.14 |
| Recurrent MI | 2 (1.3) | 4 (2.7) | 0.48 (0.09,2.62) | 0.39 |
| Heart Failure | 4 (2.7) | 9 (6.2) | 0.43 (0.13,1.39) | 0.14 |
| Repeat Revascularization | 7 (4.7) | 12 (8.2) | 0.55 (0.22,1.39) | 0.2 |