Combining invasive coronary physiology with cardiovascular magnetic resonance for long-term risk-stratification in ST-segment Elevation Myocardial Infarction: ready for clinical application?

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Timely reperfusion of the occluded coronary artery by primary percutaneous coronary intervention (PPCI) is the most effective treatment for limiting myocardial infarct (MI) size and improving clinical outcomes in ST-segment elevation myocardial infarction (STEMI) patients. However, despite prompt and successful restoration of epicardial coronary blood flow in the infarct-related artery, the presence of acute myocardial reperfusion injury can attenuate the benefits of timely reperfusion and contribute up to 50% of the final infarct size in reperfused STEMI patients(1). A prognostically important component of acute myocardial reperfusion injury is coronary microvascular dysfunction (CMD)(2,3), and manifests as angiography no-reflow at time of PPCI, an increase in index microvascular resistance (IMR) on invasive coronary physiology, or the presence of microvascular obstruction (MVO) and intramyocardial hemorrhage (IMH) on cardiovascular magnetic resonance (CMR)(4).

Angiographic no-reflow (post-PCI Thrombolysis in Myocardial Infarction (TIMI) flow grade ≤ 2) has previously been shown to be a strong predictor of clinical outcomes in STEMI patients(4), and MVO and IMH are associated with larger MI size, adverse left ventricular (LV) remodelling, and worse clinical outcomes post-STEMI(5). IMR has recently attracted much interest as it can interrogate the coronary microvascular circulation immediately post-PPCI(4). An IMR>40U immediately post-PPCI in STEMI patients has consistently been shown to be strongly associated with MVO(6), IMH(7), adverse LV remodelling(7) and poorer long-term clinical outcomes(8,9).

Of note, both IMR and MVO has been shown to be dynamic in the first few days following PPCI. Cuculi et al(10) showed that there was a reduction in IMR from 37±22U to 31±21U within 24 hours in a small cohort of STEMI patients. Carrick et al(5) previously demonstrated that the extent of MVO by CMR remained similar from 4-12 hours post-PPCI to day 2 and then reduced in size by day 10. The dynamic nature of IMR and MVO, may therefore explain why the Oxford Acute Myocardial Infarction (OxAMI) investigators previously found

that up to a third of patients had discordance between IMR>40U at the time of PPCI and the presence of MVO by CMR within 48 hours(11).

In this issue of *JACC: Cardiovascular Imaging*, the OxAMI investigators have extended their studies to evaluate the long-term prognostic implications of CMD defined as high IMR (>40U) and/or the presence of MVO on CMR performed within 2 days(12). In a cohort of 198 STEMI patients, those with either IMR>40U or MVO (Group 2) had similar outcomes for the primary composite endpoint of all-cause mortality, new heart failure, cardiac arrest, sustained ventricular tachycardia/fibrillation and cardioverter defibrillator implantation at 1 year, when compared to those with IMR≤40U and no MVO (Group 1), whereas those with both IMR>40U and MVO (Group 3) had worse outcomes when compared to Groups 1 and 2(12). However, after long-term follow-up (median time of 40 months), those in Groups 2 and 3 experienced similarly poorer clinical outcomes than Group 1, and this was driven by new heart failure. The authors suggest that both IMR and MVO should be considered in the early risk-stratification of STEMI patients, so as to allow tailored additional therapy and/or closer follow-up to be implemented(12). Of note, patients with persistent angiographic no-reflow (13.6% of patients having post-PCI TIMI flow grade ≤ 2) were also included, and post-PCI TIMI flow was also a strong independent predictor of outcomes, after adjusting for high IMR and/or MVO. Therefore, an alternative approach could be that post-PCI TIMI flow, IMR and MVO could be used in a step-wise manner to identify a high-risk cohort in the first 48 hours post-PCI, and this may negate the need for all patients to have IMR and MVO assessment as illustrated in the hypothetical and pragmatic approach in Figure 1. IMR has previously been shown to have similar prognostic value as <50% ST-segment resolution (STR) on the electrocardiogram at 60 minutes(7), and whether <50% STR and/or MVO would have performed equally well to high IMR and/or MVO was not included in this study and it is plausible that <50% STR may be a suitable alternative, when IMR is not available or feasible.

Similarly, IMH may be an alternative to MVO to detect CMD by CMR post-STEMI, in cases when gadolinium contrast is contraindicated or scan time needs to be kept to a minimum(13).

The study by Scarsini et al(12) is of great interest and relevance given that optimizing risk-stratification of reperfused STEMI patients has been a topic of ongoing research. However, there are a few observations to take into consideration that may put their research findings into perspective. Undertaking both IMR and CMR in PPCI-treated STEMI patients to detect CMD may be challenging to implement in the clinical setting given that it depends on the availability of technical expertise and suitable facilities. More importantly, whether CMD should be defined in a dichotomised manner as IMR>40U and/or the presence of MVO is highly debatable. An alternative approach may have been to define "clinically important CMD" as IMR>40U and/or the presence of a prognostically significant extent of MVO. Last but not least, whether high IMR and/or MVO provide additive long-term prognostication value over existing clinical risk scores such as the Global Registry of Acute Coronary Events (GRACE) and TIMI STEMI risk scores was not evaluated in this study.

The clinical utility of performing either IMR immediately post-PPCI or CMR 2 days post-PPCI may not be so attractive for long-term risk-stratification unless treatments are available to target and reduce CMD and improve clinical outcomes in STEMI patients with IMR>40U or MVO, respectively(4). If the use of IMR is to only provide long-term risk stratification, the CMR risk score(14) which includes MI size, LV ejection fraction and MVO has already been shown to provide incremental prognostic value over clinical risk factors in reperfused STEMI patients. However, more work is required to assess whether a CMR-only approach or a hybrid approach (invasive coronary physiology + CMR) as used by Scarsini et al(12) performs better, and would be easier and more cost-effective for clinical implementation.

To conclude, the OxAMI investigators should be congratulated for their study, as it is the first to provide prognostic insights into combining invasive coronary physiology and CMR

for early risk stratification post-PPCI. Their study provides a platform for further research on how angiographic, electrocardiographic and invasive coronary physiology parameters, and CMR indices could add prognostic value to existing GRACE or TIMI STEMI risk scores to further streamline the risk-stratification of STEMI patients treated by PPCI.

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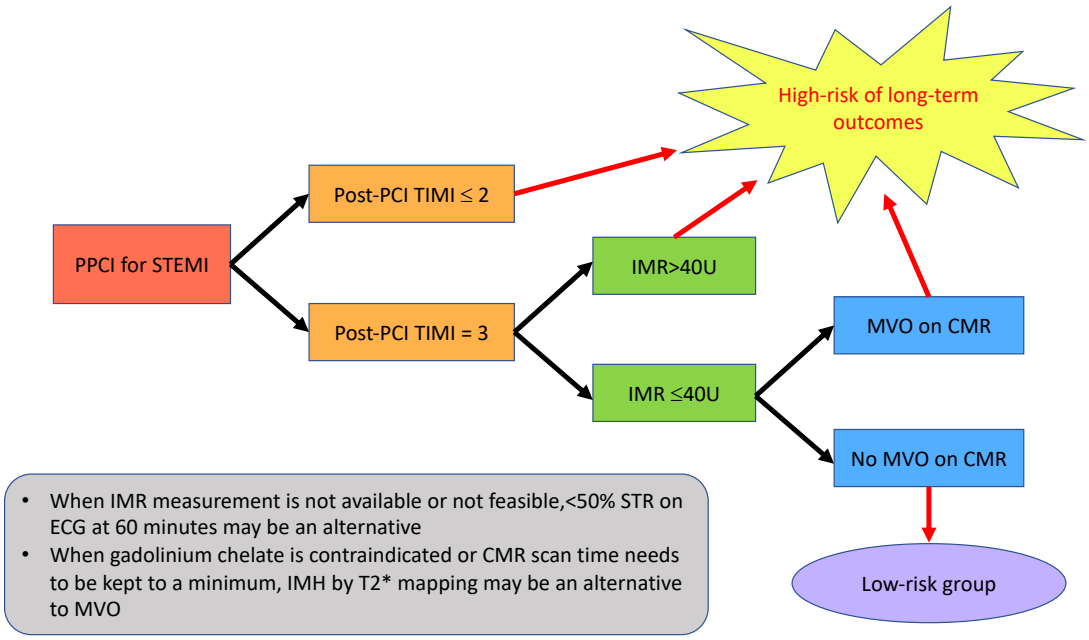
Figure 1: Hypothetical and pragmatic approach to risk-stratify STEMI patients based on the findings of the study by Scarsini et al (13).



PPCI: primary percutaneous coronary intervention; TIMI: Thrombolysis In Myocardial Infarction; IMR: index of microvascular resistance; MVO: microvascular obstruction; CMR: cardiovascular magnetic resonance; STR: ST-segment resolution; ECG: electrocardiography; IMH: intramyocardial haemorrhage