Index of Microvascular Resistance and Microvascular Obstruction in patients with Acute Myocardial Infarction

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To the editor: Despite timely reperfusion by primary percutaneous coronary intervention (PPCI), microvascular obstruction (MVO) occurs in up to 50% of ST-segment elevation myocardial infarction (STEMI) patients.(1) Its presence is associated with adverse left ventricular (LV) remodeling and worse clinical outcomes(1), and there is currently no effective therapy for reducing its burden. MVO can be detected by cardiovascular magnetic resonance (CMR), but this can only be performed after PPCI, when it may be too late implement potential therapies to minimize its deleterious effect.

In this regard, the index of microvascular resistance (IMR, defined as the product of the distal pressure and mean transit time of a saline bolus during maximum hyperaemia using a dual temperature and pressure wire) has been introduced as a method for evaluating the coronary microvascular circulation at the time of PPCI. However, not all studies have consistently shown a significant difference in IMR between those with and without MVO and were likely due to being underpowered. Therefore, we conducted a meta-analysis to investigate the role of IMR in detecting the presence of MVO at the time of PPCI in reperfused STEMI patients.

We searched MEDLINE and EMBASE databases up to June 2016. The inclusion criteria were those studies undertaking both IMR at the end of PPCI in STEMI patients and performing CMR to detect MVO. We only included studies reporting the mean IMR in patients with and without MVO. Further details of the studies included in this meta-analysis are available in the online appendix.

Six studies were included in the meta-analysis, comprising a total of 288 patients.(2-4) Further details of the 6 included studies are available in the online appendix. MVO data by CMR was available for 246 patients. MVO was present in 130/246 (53%) patients. The weighted mean IMR of the whole cohort was 38.6±30.6U (99%CI 33.5-43.6U). The weighted mean IMR in the 130 patients with MVO was 49.1±33.6U (99%CI 41.4-56.8U), whereas it was 26.7±21.5U (99%CI 21.6-32.0U)(P<0.0001; heterogeneity; Chi^2=4.31. df=5, P=0.51, I^2=0%) in 116 patients without MVO. The weighted mean difference in IMR between these 2 groups was 20.9U (99%CI 14.0-27.8U; I^2 =0%; P<0.00001)(Forest plot in Figure 1).

This study suggest that patients with a weighted mean IMR <32U (upper limit of the 99%CI in the group without MVO) were far less likely to have MVO, whereas patients with a weighted mean IMR >41U (lower limit of the 99%CI in the group with MVO) were much more likely to have MVO. Interestingly, a median IMR value of >40U was previously shown to be an independent predictor of death in a large study of 253 STEMI patients (hazard ratio 4.3, P 0.02) after a median follow-up of 2.8 years.(5) These IMR values are very close to the cut-off values we obtained from this meta-analysis using MVO by CMR as a surrogate.

Therefore, we would propose that when investigating a novel intervention for minimizing the burden of MVO, selecting patients with an IMR>41 U may help identify at the time of PPCI those very likely to have MVO and at risk of worse outcomes. This approach would identify those most likely to benefit from promising therapies such as an infusion of glycoprotein IIb/IIIa inhibitors and intracoronary thrombolysis. Furthermore, by only targeting

those with an IMR of >41 U at the end of the PPCI procedure, those at lower risk of MVO (IMR≤ 41U) will not be subjected to unnecessary risk of adverse events such as bleeding.

The main limitations of this study are patient-level data were not available to report on sensitivity and specificity of IMR to detect MVO. The SDs reported in some of these studies were quite wide and this highlights the heterogeneity present when measuring IMR. It is highly probable that the sensitivity and specificity of IMR to detect MVO would be affected as a result. However, our study is not suggesting that IMR measurement can dichotomise those with and without MVO but is providing an approach to identify those at high risk of having MVO in the cardiac catheterization laboratory and could be targeted in future studies. The interval between PPCI and CMR was different in each study and could have affected the detection of MVO. MVO detection was assessed on LGE images performed between 10 to 15 minutes post contrast in the majority of the studies but one study performed LGE between 5 to 10 minutes(3) and may have led to higher incidence of MVO in the later study.

In conclusion, IMR at the time of PPCI can identify those patients with MVO allowing the implementation of treatment to prevent this complication. We provide weighted mean IMR values in patients with MVO (49±33U) and without MVO (27±22U), information that may be used to estimate sample sizes when planning future studies to assess the efficacy of novel therapies for reducing MVO.

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Figure 1: Forest plot of IMR in patients with and without MVO by CMR

This is a Forest plot of the 6 studies included and shows the weighted mean IMR in those with and without MVO by CMR.