Is it always a pleasure to measure pressure?

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Related article
by Błaziak et al.

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DOI: 10.33963/v.phj.103457

Received:
October 24, 2024

Accepted:
October 25, 2024

Early publication date:
November 6, 2024

In the current issue of the *Polish Heart Journal* Błaziak et al. [1] present an outcome meta-analysis of randomized studies that compared fractional flow reserve (FFR)-guided or angiography-guided revascularization in patients with chronic coronary syndrome or acute coronary syndrome (ACS). The main finding is that FFR-guided revascularization as compared to angiographic guidance, was associated with a significantly lower rate of myocardial infarction for the entire population (5.4% vs. 7.4%) and also for the acute coronary syndrome subset alone. These results were achieved with a significantly reduced revascularization rate.

The authors found no difference in all-cause mortality. Most of the deaths would likely be due to cardiovascular causes during the relatively short mean follow-up time of 13.3 months. However, the absolute number of deaths was relatively low (2.6 vs. 2.8%), making it unlikely that a difference in cardiovascular death could be detected even if this had been reported in the meta-analysis. Based on the main finding of the reduction in MI, it seems reasonable to perform FFR-guided percutaneous coronary intervention (PCI) in non-culprit lesions in ACS patients to improve prognosis. As expected, patients in the FFR arm received fewer stents than in the angiography arm, making it also plausible in the long-term to reduce the risk of stent-related problems.

Błaziak et al. state that "Recent ESC guidelines covering all types of ACS lowered recommendation for FFR use in the ST-segment elevation myocardial infarction (STEMI) to class III" [2]. However, it must be emphasized that these guidelines state that invasive epicardial functional assessment of non-culprit segments of the infarct-related artery is not recommended during the index procedure (class III C). This is easy to understand because it is well known that FFR in the infarct-related vessel during primary PCI is not to be performed since it may underestimate the severity of the lesion due to stunning and/or microvascular obstruction. It is a completely different thing to measure FFR in non-culprit vessels in remote segments of other main vessel areas. It is difficult to understand why FLOWER-MI was not included in this meta-analysis, since that study compared FFR-guided vs. angio-guided PCI in remote non-culprit lesions in patients with STEMI [3]. If the line of reasoning of not including patients with STEMI and multivessel disease (MVD) was chosen, it is also hard to understand why FRAME-AMI was included in the meta-analysis, where half of the patients presented with STEMI [4].

There has been some concern regarding the possible effect of general microcirculatory dysfunction in myocardial infarction on FFR measurements. However, it has been described that FFR is safe and reliable in evaluating non-culprit lesions, remote from the culprit main vessel area, during primary PCI as compared with repeated measurements at a later stage [5–7]. The recent European Society of Cardiology guidelines [2] state that it is recommended that PCI of the non-infarct related artery in STEMI patients is based on angiographic severity (class I B), based in large part on the convincing findings of the COMPLETE trial [8]. That trial showed that preventive stenting of non-culprit lesions

based on visual estimation of stenosis severity was superior to culprit lesion-only PCI in 4041 patients with STEMI and MVD and reduced the co-primary combined endpoint of death from cardiovascular causes or new myocardial infarction by 26% at 3 years of follow-up. The FIRE trial [9] included 1445 older (≥75 years of age) patients with NSTEMI or STEMI and showed a 36% reduction in the combined secondary endpoint of cardiovascular death or myocardial infarction by a physiology-guided, predominately FFR-based, complete revascularization strategy at one year of follow-up. However, the results of the FULL REVASC trial that included 1542 patients with a longer follow-up of 4.8 years suggested that routine FFR-guided non-culprit lesion PCI may not reduce the longer-term risk of all-cause death or myocardial infarction as compared to culprit lesion only PCI [10]. Taken together, a very recent individual patient meta-analysis of 1779 patients aged ≥75 years with STEMI and MVD demonstrated that the combined endpoint of death from cardiovascular causes or new myocardial infarction could be reduced by complete non-culprit revascularization as compared to culprit-only PCI [11]. The benefit of complete revascularization was maintained regardless of patients' receiving complete revascularization guided by angiography or by coronary physiology in this age group. Planned meta-analyses with the use of individual patient data from all age groups in 7 large, randomized studies in patients with STEMI and MVD may help to elucidate the clinical relevance of complete revascularization regarding hard end points. Results of the ongoing COMPLETE-2 (ClinicalTrials.gov number NCT0570135) and AIR-STEMI (ClinicalTrials.gov number NCT05818475) trials evaluating physiology-guided versus conventional angiography-guided non-culprit lesion revascularization in patients with acute myocardial infarction and MVD and focusing on the STEMI/NSTEMI and STEMI populations, respectively are also eagerly awaited [12].

The authors speculate that staged procedures in NSTEMI non-culprit lesions would result in fewer PCIs without the risk of false-negative FFR results. This is a valid point, but maybe not for that reason. It has been shown in cardiac magnetic resonance studies that in patients with NSTEMI, the PCI operator is incorrect regarding the correct culprit lesion in as many as 31% of the cases, and non-ischemic pathologies are detected in a further 15% of the patients [13, 14]. Therefore, in patients with NSTEMI and multivessel disease without clear electrocardiography or echocardiography changes, often with a minor or moderate troponine increase, we make an incorrect guess regarding the culprit lesion. Also, if we measure FFR in the culprit lesion where there is still some stunning or microvascular obstruction it might result in false negative values. Therefore, in those cases, there is a risk of leaving the true culprit lesion untreated. With that said and in conclusion, this meta-analysis confirms the European Society of Cardiology guidelines in that FFR-guided PCI in multivessel PCI is recommended in stable angina (class I A) and should be considered in NSTEMI (class IIa). Regarding STEMI with MVD the jury is still out, since only small studies so far have made direct comparisons between FFR-guided or angiography-guided PCI of non-culprit lesions in this patient group.

Article information

Conflict of interest: FB — received institutional grants for the FULL REVASC study from Boston Scientific and Abbott. FJ and SJ have nothing to declare.

Funding: None.

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