

Best percutaneous coronary intervention approach for small caliber coronary arteries

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Percutaneous coronary intervention (PCI) of small coronary arteries represents a difficult task for the operator. Treating small vessels has become very common and is currently estimated to account for 30–40% of all coronary procedures (1–3). Yet, to date there is very limited evidence to assist in choosing the best strategy for treating these patients.

What we do know is that patients with small vessel disease often have other comorbidities such as diabetes mellitus, multi vessel disease and often longer lesions. All of which harbor higher risk for poor outcome. We also know that interventions in small coronary vessels are often challenging and associated with a higher rate of restenosis and therefore also a higher rate of repeat revascularizations regardless of the chosen technique for treatment (4,5).

Accelerated late lumen loss is partly explained by the fact that the rate of neointimal hyperplasia is equal in small and large vessels and thus the relative lumen reduction is more pronounced in small vessels per a fixed amount of hyperplasia, i.e., if the neointimal hyperplasia is 0.5 mm in a 4.0-mm the minimal lumen diameter will be 3.0 mm while in a 2.3-mm vessel it will be only 1.3 mm (6).

When analyzing data on small caliber vessels we face the issue of definition. While some trials used the cutoff of 3 mm to define small coronary artery vessels others define it as 2.5 mm. We believe that most operators would consider a small vessel to be under 2.5 mm. Also, there is a great variation in vessel size estimation compared to core lab QCA analyses.

Five different interventions [sirolimus-eluting stents (SES), paclitaxel-eluting stents (PES), bare metal stents (BMS), drug coated balloons (DCB), and balloon angioplasty (BA)] were evaluated before for the treatment of small coronary arteries. However the amount of good

quality data from randomized trials is scarce and some interventions were never assessed in a head to head trial. Moreover trials incorporating the use of drug eluting stents have only used first generation stents which are known to be inferior to currently used DESs with regards to target lesion restenosis in larger vessels.

And so when attempting to treat small vessel lesions we find ourselves in uncharted waters since these lesions are not only ill defined but are also notoriously known to be technically challenging and with higher rates of restenosis. Previously published trials are insufficient in helping the operator to reach a sound, evidence based decision which would most likely lead to the best result as good data are lacking and some of the techniques used in these trials are becoming obsolete.

The meta-analysis published by Siontis *et al.* seeks to address this situation (7). A total of 19 randomized clinical trials evaluating the five mentioned interventions with 5,072 patients, were analyzed with long-term angiographic data available from 16 trials including 4,349 patients.

The primary angiographic outcome measure was percentage diameter stenosis at follow-up. This had been chosen under the correct assumption that the treatment of small vessel disease may have a limited clinical effect which is therefore hard to measure and may lead to under detection of some real differences.

In this analysis early generation SES were found to be the most effective treatment in terms of percentage diameter stenosis, followed by PES and DCB. Both BMS and BA provided poorer clinical and angiographic results. Even when binary restenosis rates are considered, SES remains the best-ranked intervention, while BMS and BA the worst.

It is important to note that none of the analyzed trials included new-generation DES. This is due to a current lack of trials dealing with this subject. While the authors' assumption that the previously proven superiority of new generation stents over first generation stents in lower rates of stent thrombosis and repeat revascularizations will remain or even be greater in small coronary vessels is quite logical it has not been proven yet and remains to be established in the future (8).

SES and PES were associated with a significant reduction in percentage diameter stenosis compared with DCB. But, only two relatively small studies evaluated the efficacy of DCB in small vessels (9,10). One of which was terminated early since the very early generation DCB used failed to reduce neointimal proliferation. The specific use of modern DCB in small vessels had not been evaluated. Accordingly it is probably wrong to deduce precise decisions with regards to the efficacy of DCBs from these trials. Moreover in both afore mentioned trials DCB were compared with PES rendering all conclusions regarding SES to be based on indirect evidence.

This meta-analysis emphasizes the fact that BA should not be used for the treatment of small vessels as it scored the lowest scores of all five techniques. As noticed before the trials incorporated in the meta-analysis compared BA to BMS and not to newer techniques such as DES or DCBs.

In conclusion this meta-analysis addresses an important issue that had not been clarified before. Indeed the treatment of lesions in small coronary arteries could be very demanding and the need for sound data is obvious. This work highlights two very important points:

- (I) The use of DES is probably superior to other interventions;
- (II) BA should be avoided as it resulted in the lowest rankings.

Unfortunately the main downfall of this analysis is the lack of sufficient evidence regarding modern era equipment. Since no trials using new-generation DES were included, first-generation DES are no longer in use and the two trials considering DCBs were small and used early generation models—we believe that the information regarding these major, current tools and the conclusions made with regards to them are somewhat obscure.

While it may be true that newer generation DESs and balloons will perform better than the older ones, we must wait for the appropriate data to be published before we embrace that assumption, until then we will keep wading through uncharted waters.

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Footnote

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Comment on: Siontis GC, Piccolo R, Praz F, *et al.* Percutaneous Coronary Interventions for the Treatment of Stenoses in Small Coronary Arteries: A Network Meta-Analysis. *JACC Cardiovasc Interv* 2016;9:1324-34.

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