# Benefits of complete functional revascularization with PCI: 5 years results of SYNTAX II and ERACI IV trials

## Beneficios de la revascularización completa funcional en angioplastia: análisis de los resultados a 5 años de los estudios SYNTAX II y ERACI IV

*Revista Argentina de Cardioangiología Intervencionista 2021;12(4):208-209. https://doi.org/10.30567/RACI/202104/0208-0209*

During the last month of September, the long-term 5-year follow-up of the prospective registry SYNTAX II was published. This registry used a new drug-eluting stent (DES2) design followed by a revascularization strategy with FFR (fractional flow reserve) assessment to achieve the complete functional revascularization of every lesion with FFR, that is, all lesions considered "treatable" based on the severity seen on the angiography were assessed using the iFR or FFR indices. If lesions were not ischemic, they never received the DES (1-3).

The SYNTAX II had significant differences compared to the randomized SYNTAX I trial beyond the randomization, or not, of one or the other study and the different stent design. (1,3). In the SYNTAX I, first-generation DESs (DES1) were used, but the most important thing was the functional assessment-guided revascularization strategy of the SYNTAX II. Therefore, the objective was complete functional revascularization that has given us, interventional cardiologists, so many good results over the last 30 years (4) in comparative randomized clinical trials (RCT) with coronary artery bypass graft (CABG). In the SYNTAX I the revascularization strategy attempted to obtain complete angiographic and/or anatomical revascularization with angioplasty (1).

This guided angiography led to a significantly lower number of stents implanted per patient (4.04 vs 2.6 SYNTAX I vs II; $P$ <. 001, respectively); also, to the finding of much less 3-vessel disease (83.3% vs 37.2% in SYNTAX I vs II; $P$ <. 001, respectively).

The retrospective comparison with data from the SYNTAX I made at the 1-year follow-up confirmed a lower rate of major adverse cardiovascular events (MACE), also of each of its components (3).

At the 5-year follow-up (5), the MACE rate dropped 46%, while mortality rate dropped 43% in the SYNTAX II compared to the angioplasty arm of the SYNTAX I.

The fewer acute myocardial infarctions (AMI), new revascularizations (TVR), and stent thromboses reported also favored the SYNTAX II trial significantly ($P$ <. 001).

We should mention that by using fewer DESs we obtain a lower number of revascularizations, which validates the fact that functional revascularization should be the target of coronary angioplasty.

Also, the lesions assessed using functional tests confirmed that the number of patients with severe 3-vessel disease from the SYNTAX I trial was probable overestimated.

The use of second-generation DESs (DES2) could also be associated with better disease progression, although these devices are not always synonym of better results (6) like the recent results from the NOBLE and the EXCEL clinical trials (7-8) and meta-analysis (9) of RCTs of the left main coronary artery (LMCA) reveal. Surprisingly, the first RCTs that used DES1 were associated with better disease progression after 5 years regarding all-cause mortality (OR = 1.19, 0.83-1.71; CABG vs PCI in the PRECOMBAT trial, and LMCA subgroup of the SYNTAX I) compared to the RCTs that used DES2 (OR = 0.78, 0.62-0.99; CABG vs PCI in the NOBLE and the EXCEL trials).

During the recent SOLACI/CACI Congress, the final 5-year results of the still unpublished ERACI IV registry were presented.

This registry also used a functional assessment-guided revascularization strategy while always in observance of the protocol of the ERACI anatomical score (10) where the revascularization of all intermediate lesions (50% to 69% through visual estimation), and lesions found in small vessels is ill-advised.

Similarly, in bifurcation lesions, the investigators were encouraged to use a simple strategy like stenting the main vessel as the first attempt.

This ERACI IV trial has the same limitations as the SYNTAX II since neither one of them is a randomized clinical trial. The actual comparison should be made with the ERACI III trial conducted several years ago where the coadjuvant pharmacological strategy with more powerful thienopyridines (prasugrel or ticagrelor) (11-12) was not available and the stent used was also a first-generation DES (DES1).

Although the mid-term follow-up results have already been published (13), the 5-year data were presented for the first time during the SOLACI/CACI Congress (14). In this presentation it became clear that the final primary endpoint of MACE reduced significantly compared to the ERACI III (33.8% vs 18.7% ERACI III vs IV, respectively; $P$ <. 001), as well as each of the primary endpoint components (like AMI and TVR).

If we analyze the reduction of the primary endpoint in both the SYNTAX II and the ERACI IV registries, we will be able to see that this reduction was 46% and 44% respectively ($P$ <. 001) for both registries compared to previous studies.

Another significant finding of both the SYNTAX II and the ERACI IV trials was that only 21% and 28% of the patients were on a 5-year course of dual antiplatelet therapy, a fact that may very well be associated with noncardiac adverse events at the late follow-up of DES (15).

In conclusion, these findings stress the idea that, although the type of stent used is important, the rational strategy during revascularization seeks a complete functional and non-anatomical revascularization. A strategy that has somehow fallen into oblivion over the last few years but that would be associated with a more favorable late disease progression in patients treated with angioplasty and stenting.

The good results seen in the overall and cardiovascular mortality rates described after 5 years reported by the SYNTAX II trial (3) make us feel optimistic about future randomized comparisons between angioplasty vs CABG and/or optimal medical therapy. In sum,*"there seems to be light at the end of the tunnel... after the many obstacles we've had to overcome over the last few years..... (6-8,16)"*

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