

CORONARY ARTERY-BYPASS GRAFT OR PERCUTANEOUS CORONARY INTERVENTION FOR LEFT MAIN CORONARY ARTERY LESIONS: AN ONGOING DISCUSSION

CIRUGÍA DE REVASCULARIZACIÓN O INTERVENCIONISMO EN LESIONES DE TRONCO DE LA ARTERIA CORONARIA IZQUIERDA: UN DEBATE EN CURSO

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Thirty-five years after the introduction of coronary angioplasty by Andreas Gruntzig in 1977, the controversy between percutaneous coronary intervention (PCI) and Coronary Artery Bypass Graft (CABG) remains firmly installed in the international cardiology community. Successive generations of coronary stents, and the emergence of new and more potent drugs that complement its mechanical action, pave the way for the increasingly aggressive and radical positioning of PCI. Scores of various clinical trials have been designed and published in these decades attempting to show the superiority of this technique, at least in more simple subsets of patients. But its great Achilles' heel remains the high selectivity of these, with very broad exclusion criteria, which have led to randomization processes, from which very high percentages of patients have been excluded, and it is a very important limitation for

the generalization of its conclusions.

Thus, it is not difficult to explain the high impact that the SYNTAX trial¹ has had in the last five years, in which, for the first time in literature; the results in the most complex groups of three-vessel disease (3VD) and left main (LM) coronary disease are compared. By a strict and objective (though undeniably complex) index of lesions, recruitment close to 100% was generated, and even those nonrandomized patients were entered into specific subsets of monitoring to broaden the spectrum of possible conclusions. In this way, an unusual universe of patients –without distinction– was generated, with different treatments in international centers of well-known expertise and level of results, and they have received follow up during five years with all the guarantees of a very rigorous and strict methodological scrutiny.

It could be argued that the technology used in the Taxus stent is now outdated. But thanks to the relentless technological advances, it is unthinkable that any prospective design, at five years, as the SYNTAX, can reach the end of its period of performance and analysis without being liable to such objections. On the other hand, it is also true that the CABG sub-population

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has not received, but in limited percentages, the kind of procedures that could currently be considered "state of the art", according to the most recent and relevant scientific information. Indeed, only 27% of patients received double mammary artery and only 15% were revascularized without extracorporeal circulation.

Although the most disturbing surgical indicator was a higher incidence of cerebrovascular accidents (CVA) (2.2 vs. 0.6%), it follows that, if revascularization with multiple arterial pedicles and beating-heart surgery (without cannulation maneuvers and clamping of the aorta) had been used more often, the incidence of this complication could have been lower, without affecting revascularization quality and a long term excellent functional expectation²⁻⁴.

If one considers that only 88% of CABG patients received acetylsalicylic acid, and 19%, clopidogrel or another thienopyridine; versus 96 and 97% respectively, in the PCI group; and that 50% of postsurgical CVAs occurred after the first 30 days, it is easy to conclude that prevention of this complication in the CABG group was not the most appropriate⁵.

Apart from all other considerations, in the SYNTAX trial, PCI failed to reach criteria for "non inferiority" compared with CABG, so all subsequent sub-analysis, at 2 and 5 years, can only be considered "observational" or "hypothesis-generating only"⁶. Its results should be interpreted in light of the trial design limitations: most CABG adverse events occur early, just within the first year of analysis, whereas many PCI adverse events continue to occur later⁵, so the benefits of CABG, in terms of survival, usually appear after 3 to 5 years⁷.

At 3 years, a slight benefit of CABG in terms of mortality was found (6.7 vs. 8.6%, $p=0.21$)⁸. But compared with the results at one year, the difference in CVA risk was no longer significant (3.4 vs. 2.1%, $p=0.07$), while the incidence of myocardial infarction (3.6 vs. 7.1%, $p=0.002$) and revascularization (11 vs. 21%, $p=0.001$), showed increasing differences. So, the incidence of major adverse cardiac and cerebrovascular events (MACCE) was significantly lower for CABG (20 vs. 28%, $p=0.001$).

There were however, some rather striking differences. In the 3VD subgroup, the benefits of CABG over PCI were more noticeable. By contrast, in the LM subgroup there was no difference in terms of mortality (8.4 vs. 7.3%, $p=0.64$) or myocardial infarction (4.1 vs. 6.9%, $p=0.14$). But a higher incidence of CVA in the CABG group (4 vs. 1.2%, $p=0.02$), downplayed the reduced need for revascularization (12 vs. 20%, $p=0.004$), from what can be inferred that at least in some cases of LM disease, PCI can produce equivalent results, if

not superior, to those of CABG. When this LM disease group was subdivided according the SYNTAX-score, the difference in mortality in favor of PCI was limited to subgroups of low and intermediate risk (0-22 and 23-32), but in the high risk segment with SYNTAX score higher than 32, PCI mortality doubled that of CABG (13.4 vs. 7.6%), while tripling the incidence of new revascularization (28 vs. 9% $p=0.001$). These results allow us to hypothesize that in the absence of severe 3VD, less complex LM lesions can lead to more flow competition for vascular grafts and predispose its occlusion. By contrast, when complex injuries from the three coronary systems are added to the LM lesion, generating a SYNTAX score greater than 32, the picture is reversed and CABG shows a better performance.

If taken together, both randomized patients and those entered in the sub-registries (CABG or PCI), almost 80% of those with 3VD and two thirds of those with LM disease show a clear benefit in terms of survival and a reduced need for repeating revascularization procedures with CABG treatment compared to PCI procedures, which explains that CABG remains the treatment of choice for most of these patients⁹.

The results at 4 years^{10,11}, showed that these trends continued without much variation, and the results of the final evaluation at 5 years will be presented at the end of 2012.

Other studies apart from SYNTAX provide information to determine the best treatment in unprotected LM disease. One of them is the PRECOMBAT trial¹², conducted in Korea, where 600 patients were randomized to CABG or PCI. This is a population with a SYNTAX-score and a EuroSCORE somewhat below SYNTAX, in which the incidence of MACCE was lower after CABG (8.1 vs. 12.2%), figures that are almost equal when the repeated revascularization factor is suppressed (4.4 vs. 4.7%). Unlike SYNTAX, in this relatively low-risk population, there was no increased operative mortality after CABG, and a similar incidence of CVA was also proved (0.7 vs. 0.4%), which is also lower than in SYNTAX.

In light of these facts, it is difficult to accept some overzealous but unfounded interpretations¹³, such as these statements "... it would take a very unlikely 50% increase in mortality in the stent arm of the upcoming randomized trials before CABG becomes close to an unequivocal treatment choice... Most of my patients would rather have 2, 3, or even 5 stent procedures to avoid 1 bypass surgery". Statements as proactive and as risky like these deserve to be neglected by the scientific community. The main target of our work –the

patient— deserves to receive dispassionate and objective information on the current state of the knowledge available as well as the safety of our most selfless and wise therapeutic recommendation.

Currently a new clinical trial is underway, the EXCEL trial¹⁴ that will randomize for CABG or PCI (everolimus stents) 2,600 patients with unprotected LM disease and SYNTAX score lower than 33, with up to three years follow up in 165 centers and 18 countries. As in SYNTAX, about 1,000 nonrandomized patients will be followed in parallel registries. But unlike SYNTAX, only myocardial infarction, CVA and death will be considered as primary major events. Repetitive revascularization will be considered as a secondary endpoint, with the argument that it is not an irreversible event. The first cases in Europe were recruited in late 2010 and in the U.S., a year later, so one will have to wait a little longer to have the information and analysis.

In summary, one can say that until the present time, there is no basis to change the current recommendations stated in American and European guidelines on criteria for revascularization in stable angina. The former¹⁵ state that for isolated LM disease or those associated with 1 or 2 VD with low SYNTAX score, CABG is rated appropriate and the results of PCI remain "uncertain". In LM diseases with 3VD, chronic occlusions or high SYNTAX score, CABG is rated appropriate and PCI inappropriate. The latter¹⁶ assign CABG a IA indication for any LM disease, isolated or associated with coronary lesions in any of the three systems, regardless of the morphology and location of the trunk lesion, while PCI is considered class IIAB indication in patients with ostial or intermediate trunk disease, and class IIbB indication for lesions located in its bifurcation, with or without distal LM disease and SYNTAX score ≤ 32 . At the same time it is contraindicated in LM disease with lesion of two or three vessels, and SYNTAX score ≥ 33 (Class IIIB indication).

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