EDITORIAL

# Surgical aortic valve replacement plus coronary artery bypass grafting remains as the current best option of treatment for severe aortic stenosis concomitant with stable coronary artery disease

*" He who influences the thinking of his time, influences all the moments that follow him. Leave your opinion for eternity."*

*- Hypatia of Alexandria –*

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***Palabras clave:*** **Estenosis aórtica; Enfermedad arterial coronaria; Reemplazo valvular aórtico quirúrgico (SAVR); Implante valvular aórtico transcatéter (TAVI); Guías clínicas.**

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In a recently published meta-analysis in the J Thorac Cardiovasc Surg, the authors compare two types of treatment for aortic stenosis concomitant with coronary artery disease, both of them with surgical indication [1]. One is [SAVR (surgical aortic valve replacement) plus CABG (coronary artery bypass grafting)] being considered as the standard, and the other [TAVI (transcatheter aortic valve implantation) plus PCI (percutaneous coronary intervention)] being considered as useful.

In the cited meta-analysis, two randomized controlled trials and 6 observational studies were included, with a total number of 104, 220 patients. Out of them, 5004 underwent TAVI plus PCI, and 99, 216 received SAVR plus CABG. The weighted mean follow-up was 30.2 months. All-cause mortality was higher for TAVI plus PCI (HR, 1.35; 95% CI, 1.11-1.65; p = 0.003). Coronary reintervention was also higher in TAVI plus PCI group (HR, 4.14; 95% CI, 1.74-9.86; p = 0.001). Permanent pacemaker implantation at 30 days after procedure was unfavorable for the interventional group (OR, 3.79; 95% CI, 1.61-8.95; p = 0.002). Vascular complications were much higher in TAVI plus PCI (OR, 6.97; 95% CI, 1.85-26.30; p = 0.004). The only favorable item for TAVI plus PCI was 30-day acute kidney injury rate (OR, 0.32; 95% CI, 0.20-0.50; p = 0.0001). In turn, rehospitalization, myocardial infarction, stroke, and 30-day mortality rates were very similar for both groups. Finally, authors conclude and highlight the fact that TAVR plus PCI is associated with greater all-cause mortality at follow-up [1].

In this paper, we will discuss some observed changing patterns of treatment for severe AS with concomitant stable CAD in the last years. Over the past two decades the scope of the new technologies has consistently expended. The idea has become widely accepted, thus affecting the decision-making process at all levels. In fact, the choice of competitive strategies for the years ahead requires that they be considered in the context of newly emerging realities. Nevertheless, in an era of total and almost religious reliance on technology as the major problem solver, coupled with an increasing awareness of its doubtful efficacy in view of the patient costs, small wonder that we sense a need to examine a comprehensive view of this type of management.

In order to gain understanding of this complex evolving treatment as a whole, we attempt to integrate the interrelationship between AS and CAD according to the current guidelines recommendations.

Hence, it is clear we are facing too many issues of great concern. TAVI indications have a large number of grey zones in the current guidelines. The same applies to PCI indica-

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tions, which have been under the debate since the current American and European guidelines were respectively released [2-5].

It is very well known that TAVI and PCI have their own limitations. However, it seems that all implications have not been completely stressed to their due levels of importance. Speaking about the current guidelines for valvular heart disease, there are several concerns with this regard [6,7].

The current 2020 ACC/ACC clinical practice guidelines for the management of the patient with valvular heart disease states:

***High risk patients:***

TAVI is indicated when high-risk is present. It means at least one of the following conditions: STS-PROM > 8%, frailty index ≥2, severe compromise of 1 or 2 organs which will not improve after surgery, or possible impediment to carrying out the surgical procedure. In this specific group, TAVI is indicated as Class I while SAVR is ruled out.

***Other than high risk patients:***

The indication is based on the patient's age: < 65 years, SAVR (Class I); 65-80 years, SAVR or TAVI (Class I), and > 80 years: TAVI (Class I) or SAVR (2A). The problem with this indication is that no article into the American guidelines supporting it had a mean age of <79 years [2]. With the exception of PARTNER 3 and Evolut low risk trials, no other study fulfills this requirement so far. Average patient age in PARTNER 3 and Evolut low risk trials was 73 and 74 years, respectively. Follow-up extension was 1-year in PARNTER-3, and 2-years in Evolut low risk [8].

Considering all the aforementioned, although PARTNER 3 showed that TAVI is noninferior to SAVR at low risk, the main problem is that there are insufficient data regarding the duration of TAVI in this group, beyond 2 years [9].

In other words, we currently do not have sufficient data to justify the use and support long-term durability of TAVI in patients under 73 years of age. Therefore, recommendation Class I for TAVI in patients between 65 and 80 years of age, as mentioned in the American guidelines for the management of VHD [2], it does not have sufficient scientific support.

In addition, the complications linked to the use of TAVI should be emphasized, such as permanent pacemaker implantation (at from 25.9% in the SURTAVI study 30-days after procedure to 10.9% reported by the STS-ACC TVT Registry, vs. 2.7% in SAVR [ 6]; subclinical valve thrombosis (12% in Sapien XT, S3, and Lotus, 8.3% in CoreValve, and only 7.4% in SAVR) [6], and paravalvular leaks (from 8.1% to 1.7% at 30 days post TAVI, among others [10]. ]. These facts render a much more important context of TAVI, when applied to low-risk patients.

The European guidelines for VHD seem more concordant with reality, giving a recommendation Class IA, in TAVI for patients with ≥ 75 years-old, or in those who are high risk (STS-PROM/EuroSCORE II >8%), or unsuitable for surgery [3].

Considering the criteria for stable coronary artery disease. In the 2018 European guidelines for coronary revascularization, for left main (LM) coronary stenosis, the recommendations are fundamentally based on the Syntax Score (0-22, low risk; 23-32, intermediate risk; ≥33, high risk). PCI has an indication I for low risk, IIa for intermediate risk, and III for high risk. CABG has an I indication for all scores.

In patients with multivessel disease (MVD), patients without diabetes mellitus with any Syntax score, CABG has a recommendation Class I. PCI is an indication IA with Syntax score 0-22. Patients with diabetes, CABG is Class IA for any Syntax score. PCI is Class IIb with Syntax score 0-22.

For one or two-vessels, if no proximal lesion in left anterior descending (LAD) coronary artery is present, PCI is preferred (IB). If proximal lesion present in LAD, CABG (IB) has a slight advantage over PCI (IC) [5,11].

However, it must be remembered that after the scandal with the Excel trial [12-19], the EACTS withdrew its support for the LM stenosis chapter in these European guidelines, in Dec 2019 [19]. Therefore, despite the wide use of the Syntax score in daily practice and decision-making process, officially speaking, this chapter in LM coronary stenosis is not currently valid. The rest remains with no changes.

Details within the current 2021 American guidelines for coronary revascularization need to be addressed [4]. The main problem with these guidelines is that, in stable CAD, they have downgraded the recommendation for CABG in MVD to IIb, based mainly on data coming from the ISCHEMIA trial. In this study, no difference was found, in terms of risk reduction of ischemic events cardiovascular events or death from any cause at 3.2 years of follow-up between the invasive strategy (PCI or CABG) and optimal medical treatment [20]. However, there are some details that must be emphasized. In this study, only 39.6% (940/2371) of the patients classified in the invasive group had 3-vessel disease. At the same time, only 36.2% had a proximal LAD lesion. Additionally, 3.8% had LM disease. Overall, 74.2% of cases underwent PCI while only 25.8% for CABG. In the invasive arm, only 19.2% underwent CABG as a non-randomized outcome; that is, only as a result of not being a PCI candidate. Therefore, the results for PCI cannot be extrapolated to CABG. In MVD, the comparison with OMT is applicable to PCI, but not to CABG. This special subset of patients who underwent CABG in ISCHEMIA is not representative of typical patients undergoing CABG in real life (MVD, LAD proximal stenosis, low LVEF) [21]. Also, the current indications for LM in this guideline must be revisited, as an important bias can be observed in the Bayesian analysis [22]. Thus, the opposition of various medical associations and societies to these clinical guidelines regarding the indications for CABG for MVD has been published in various documents [23,24].

Furthermore, are the aforementioned practical considerations applicable to specific patients with severe AS and concomitant CAD?

The 2020 American guidelines: for VHD consider:
In patients undergoing TAVI with significant left main or proximal CAD with or without angina, revascularization by PCI before TAVI is reasonable as recommendation Class IIa.

For severe AS and significant CAD, involving complex bifurcation left main or multivessel CAD with a SYNTAX score >33, SAVR and CABG are reasonable and preferred over TAVI and PCI, as recommendation Class IIa.

The remaining question is the management of MVD with Syntax score ≤ 33. If we apply the same concept of simple CAD without concomitant disease, then if we rule out PCI as I for Syntax score of 0-22 (becomes IIa with AS), IIb for 23-32, and III for ≥33. CABG I any item. Currently, CABG represents a recommendation IIa in every item. Of course, there is no reason to catalogue CABG + SAVR as Class IIa, since all of them are Class I (SAVR or CABG) when applied to each one separately [4].

If these details are accurate, it can be asserted according to the 2020 American guidelines for VHD, the proposed management is as follows (**Table 1**):

***Table 1. Recommendations for severe aortic stenosis plus coronary artery disease according to 2020 ACC/AHA guidelines for the management of VHD [2].***

| PATOLOGICAL CONDITION | PROCEDURE | RECOMMENDATION |
|---|---|---|
| Aortic stenosis + LM and/or MVD (Syntax score 0-22) | TAVI + PCI | Class IIa |
| Aortic stenosis + LM and/or MVD (Syntax score 23-32) | TAVI + PCI | Class IIb |
| Aortic Stenosis + LM and/or MVD (Syntax score 23-32) | SAVR + CABG | Class IIa |
| Aortic stenosis + LM and/or MVD (Syntax score ≥ 33) | SAVR + CABG | Class IIa |
| Aortic stenosis + LM and/or MVD (any Syntax score) | SAVR + CABG | Class IIa |

*All cases are for severe aortic stenosis. CABG: Coronary artery bypass grafting, LM: Left main coronary stenosis, MVD: Multivessel disease (commonly 3-vessel disease), PCI: Percutaneous coronary interventions, SAVR: Surgical aortic valve replacement, TAVI: Transcatheter aortic valve implantation,VHD: Valvular heart disease.*

In the European guidelines, recommendations for management of CAD in patients with VHD indicates that in patients with a primary indication for VHD surgery and CAD with coronary artery diameter stenosis ≥70%, CABG is a recommendation Class I. In addition, PCI is IIa in the same context.

If CAD diameter is between 50-70%, then CABG is Class IIa. In symptomatic patients not appropriate for surgery by the Heart Team, PCI (first) and TAVI (afterwards) should be considered [5]. Summarizing, according to the 2021 European guidelines for VHD, the proposed management is as follows (**Table 2**):

***Table 1. Recommendations for severe aortic stenosis plus coronary artery disease according to 2021 ESC/EACTS guidelines for the management of VHD [3].***

| PATOLOGICAL CONDITION | PROCEDURE | RECOMMENDATION |
|---|---|---|
| Aortic stenosis + CAD ≥ 70% | SAVR + CABG | Class I |
| Aortic stenosis + CAD ≥ 70% | TAVI + PCI | Class IIa |
| Aortic stenosis + CAD 50-70% | SAVR + CABG | Class IIa |

*All cases are for severe aortic stenosis.* ***No Syntax score is considered.*** *CABG: Coronary artery bypass grafting, CAD: Coronary artery disease, PCI: Percutaneous coronary interventions, SAVR: Surgical aortic valve replacement, TAVI: Transcatheter aortic valve implantation,VHD: Valvular heart disease.*

We should highlight the fact that if we could first consider perfect processes, this permitting us to build a model, to which we could try afterwards to fit a best. All above notwithstanding, not it is always possible to avoid the complications of performing one procedure or another.

With all this as a framework of reference, this article has been just released, in which mortality from any cause, coronary reintervention, permanent pacemaker, and vascular complications were higher for TAVI + PCI. Freedom from renal failure at 30-days after procedure was the sole favorable factor for TAVI + PCI. Finally, authors conclude and highlight the fact that TAVR + PCI is associated with greater all-cause mortality at follow-up [1].

In closing, the binomial composed of TAVI + PCI as the first option for cases with severe aortic stenosis and CAD should remain relegated to recommendation Class IIa, as indicated in the 2021 European guidelines for patient management with VHD. It is obvious that the condition indicating the utilization of TAVI + PCI instead of SAVR + CABG cannot be fulfilled, owing to the reasons already mentioned. It must be said that these very sophisticated processes are not far from actual practice in the real world. Thus, it is interesting to try to evaluate the cost we have to pay for this complexity. Additionally, indications based primarily on the Syntax Score, such as the 2020 American guidelines for the management of VHD, remain to be validated.

Finally, because of the trend showed into this paper, it becomes imperative that the treatment of the severe AS concomitant with stable CAD assumes even greater importance as a necessary long-term planning objective, whatever the selected percutaneous or surgical approach.

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