CONTROVERSY

In Severe Aortic Stenosis Without Left Ventricular Dysfunction, do not Wait for Symptoms to Develop

En la estenosis aórtica grave sin disfunción ventricular no hay que esperar la aparición de síntomas

AGONIST

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INTRODUCTION

Severe aortic stenosis is the valvular heart disease most frequently undergoing valve replacement in middle- and high-income countries. (1) The risk factors for developing aortic stenosis are similar to traditional cardiovascular risk factors. (2) However, randomized trials have not demonstrated that medical treatment with drugs such as statins reduces disease progression. (3) Nowadays we count with two mechanical treatments for severe aortic stenosis: surgical aortic valve replacement (SAVR) and transcatheter aortic valve implantation (TAVI). In our environment, the indication of SAVR or TAVI is based on high-certainty guidelines developed for Latin America, where TAVI via transfemoral access is indicated mainly in the elderly. (4)

There is international consensus that severe symptomatic aortic stenosis (either with dyspnea, angina, heart failure, or syncope), or the presence of left ventricular dysfunction (left ventricular ejection fraction < 50%), or the requirement for other heart surgery, are strong indications for aortic valve replacement. (5,6) We will now examine the logical arguments behind the suggestion that limiting the scope of the intervention to those with a more advanced stage or more symptoms may not be the most prudent course of action.

PHILOSOPHICAL ARGUMENT

Severe aortic stenosis is a progressive disease that will progress to sudden cardiac death or heart failure without treatment, which in the best scenario will allow treatment before it is too late. There are many examples in medicine where, in progressive, non-reversible, lethal, and potentially treatable diseases, no symptoms or irreversible damage are expected before indicating an aggressive treatment. Would you wait for a stage I lung cancer to progress to stage II or III before initiating treatment, or would you prefer to treat it as soon as possible? Would you wait for a patient diagnosed with 90% obstruction in the left main coronary artery to have symptoms before treating it? You probably would not wait in either scenario because they are both progressive, non-reversible diseases with high mortality risk, as severe aortic stenosis.

ASYMPTOMATIC IS NOT SYNONYMOUS OF LOW RISK.

There must be no physician who has not wondered why, with the same degree of disease, some patients have symptoms while others are asymptomatic. Two patients may have the same level of aortic stenosis (for example, two men of the same age with aortic stenosis and preserved left ventricular ejection fraction, aortic valve area of 0.7 cm^2 and no other comorbidities). One complains of functional class III dyspnea, while the other has no symptoms and is living a normal life. It is probable that there are biological factors contributing to this phenomenon, but they are not currently relevant as they are not yet understood. We can ascertain that a significant number of patients receive timely treatment due to the early development of symptoms. Conversely, those who have not yet exhibited any symptoms may have to wait for structural damage to be treated. Sudden cardiac death may be the first manifestation in asymptomatic patients. The annual risk of sudden cardiac death in asymptomatic patients is about 1%; during follow-up, half of the deaths occur in asymptomatic patients. (7)

STRUCTURAL DAMAGE MEANS WE ARE TOO LATE

Phillipe Genereaux et al. developed a staging system for severe aortic stenosis. (8) This system is stratified in stages from 0 to 4. Stage 0 is the absence of any type of structural damage, Stage 1 represents the presence of incipient damage, which progresses to increasingly significant damage. Stage 4 is associated with a notable decline in left ventricular systolic function.

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While it is true that the more advanced the structural damage, the lower the probability of regression, there is no guarantee that less advanced stages will revert to stage 0 following the intervention. It has been postulated that the lack of regression of structural damage justifies the worse outcome following the intervention, including cases of sudden cardiac death. (9) On the other hand, the presence of structural damage increases the risk of the procedure. (10) Then, why must we wait for structural damage in asymptomatic patients? The most frequently cited arguments are the risk of the intervention and the durability of the implanted prosthetic heart valve.

PERIPROCEDURAL RISK

Despite following the highest standards, some patients will die or suffer adverse events related to the intervention. They would have probably lived longer if they had not undergone the procedure. However, a proportion of these patients may experience detrimental effects as a result of waiting for symptoms to manifest. This includes, but is not limited to, the mentioned 1% annual risk of sudden cardiac death. (7)

The results have significantly improved in the last decades for SAVR and in the last years for TAVI. The contemporary mortality for both procedures in referral centers is near 1% in low-risk patients. (11,12) We could say that the risk of periprocedural mortality is comparable to the risk of sudden cardiac death within the following year.

Other serious adverse events can occur in the periprocedural period, such as stroke, myocardial infarction and infections, among others. It is very difficult to define the importance of these events compared to the risk of continuing to wait, but the fact that most patients undergo the procedure without significant complications has led many physicians and patients to consider early intervention as a viable option.

DURABILITY OF THE PROCEDURE

A highly experienced mentor once provided me with me the best way to explain to a patient that the prosthetic heart valve has limited durability: “While replacements are available for your problem, the original components are not”.

The evidence shows that the risk of reintervention is relatively low. For SAVR with contemporary prosthetic heart valves, the risk of reintervention is 1.9% at 10 years and 15% at 20 years (5.6% and 46%, respectively, in patients < 60 years). (13) While long-term data for TAVI is not currently available, the evidence from randomized studies (with follow-up periods of 5 to 10 years) indicates that these prosthetic heart valves perform similarly to those used in SAVR. In any case, the indication for TAVI in our environment is restricted to patients with low life expectancy, who are those > 75 years, or younger patients with high surgical risk. (4)

EVIDENCE

If all this makes sense, it should be reflected in the evidence. Multiple meta-analyses of observational studies have shown a marked reduction in mortality with early intervention (from 50% to 70%). (7) However, as these are observational studies, the results are subjected to an inevitable and unwavering risk of selection bias and multiple confounders. Therefore, this evidence does not provide sufficient certainty to change clinical practice if it cannot be reproduced by randomized trials. There are two randomized studies in this regard, the Conventional Treatment in Very Severe Aortic Stenosis (RECOVERY) trial, (14) and the Aortic Valve Replacement vs. Conservative Treatment in Asymptomatic Severe Aortic Stenosis (AVATAR) trial. (15)

The RECOVERY study enrolled 145 patients with severe aortic stenosis (aortic valve area ≤ 0.75 cm^2, aortic jet velocity 5.1 m/s) in South Korea and randomly assigned them to SAVR or conservative treatment. At a median follow-up period of 6.2 years, there was a reduction in the primary composite event of operative death and death from cardiovascular causes at follow-up from 15% to 1%, with a hazard ratio (HR) of 0.09, and 95% confidence interval (95% CI) of 0.01-0.67. It should be noted that the study included patients with a significantly elevated transvalvular gradient, that stress testing was not systematically performed, and that the patients’ risk was very low (EuroSCORE II 0.9%) with a perioperative mortality of 0%. The most important limitation was the small number of primary events (12 in total).

The AVATAR study evaluated a composite endpoint of all-cause death, myocardial infarction, stroke, and unplanned hospitalization for heart failure. With a median follow-up of 32 months, a 64% reduction in the primary event was observed (HR 0.46, 95% CI 0.23-0.90). This study included a population with less severe valvular heart disease (mean aortic jet velocity of 4.5 m/s) and all the patients underwent exercise stress testing. One limitation is the shorter follow-up period compared to the RECOVERY trial.

Both randomized studies confirm that in the mid-term the balance would be in favor of intervention in asymptomatic patients, consistent with previous observational evidence. Although it will be 10 to 20 years before we have enough data to get the full picture, we do know that patients who have undergone SAVR with contemporary prosthetic heart valves rarely need reintervention, and the short-term benefit appears to be significant in relative terms. We are also waiting for the results of at least five additional randomized studies evaluating the same research question. (16)

RECOMMENDATIONS IN ASYMPTOMATIC PATIENTS

There are indications for intervention beyond patients presenting with symptoms or those with systolic ventricular dysfunction. These include: 1) a systolic

blood pressure drop ≥10 mm Hg on exercise; 2) a peak aortic jet velocity ≥ 5.0 m/s; 3) an increase in aortic jet velocity of ≥ 0.3 m/s per year in serial testing; and 4) an increase in serum B-type natriuretic peptide level of > 3 times normal in serial testing. (5,6) These recommendations are weak (class IIa for the American or European guideline systems) and are supported by evidence that has demonstrated an adverse prognostic impact despite being asymptomatic patients. Furthermore, patients must be at low risk to be eligible for these indications.

It should be noted that both the American and European guidelines were developed prior to the publication of RECOVERY and AVATAR trials.

CONCLUSIONS

Patients with asymptomatic severe aortic stenosis without systolic dysfunction are at increased risk of morbidity and mortality. Waiting for symptoms to develop puts the patient at increased risk of sudden cardiac death, potentially irreversible structural damage and increased risk in case of intervention. The perioperative mortality rate for both SAVR and TAVI has decreased significantly in recent years as well as the number of patients requiring reintervention during follow-up in more contemporary series. The evidence on this research question, originally derived from observational studies and later from randomized trials with consistent findings, suggests that there is an important benefit in terms of the rate of events, including mid-term mortality. While the guidelines have already established certain indications for intervening asymptomatic patients and there are multiple ongoing trials, it is possible that they will change favoring early intervention when these new trials are integrated into the already published randomized studies.

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ANTAGONIST

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Aortic stenosis is a progressive disease with high morbidity and mortality. The onset of symptoms represents a significant shift in its prognosis, with a one-year mortality rate of around 25% in the absence of valve intervention. (1) Recent evidence has confirmed that even pre-symptomatic severe aortic stenosis and moderate aortic stenosis have a poor prognosis, and that the progressive nature of the disease requires an analysis that must go beyond the divisions imposed by hemodynamic classifications. Nevertheless, it would be an error to assume that, due to the elevated risk of complications associated with severe aortic steno-

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sis, early intervention should be the indication for all patients. How high is the risk of the disease and how high is the risk of its treatment? It is essential to consider this interplay of forces each time we evaluate a patient with severe aortic stenosis who is not yet symptomatic.

In the setting of symptomatic patient, the indication for intervention is clear, although underutilized. On the other hand, in the setting of patients with severe aortic stenosis who do not present symptoms and who are periodically monitored (watchful waiting or conservative treatment), the low rate of major events has supported this approach. We could ask ourselves whether, based on the current evidence, we are exposing patients with asymptomatic severe aortic stenosis to an unacceptably high risk by delaying surgical indication unnecessarily.

First, we need to make sure that the severity of aortic stenosis has been adequately estimated. Secondly, the patient must be undoubtedly asymptomatic, since failure to recognize symptoms is a common scenario that implies a more adverse prognosis than in truly asymptomatic patients. Adaptation and the indolent nature of the disease lead in some cases to a gradual reduction in physical demands which result in lack of awareness of exercise-induced symptoms. Therefore, exercise stress echocardiography is suggested to unmask symptoms in patients with severe aortic stenosis, although its usefulness in elderly patients is less clear. (2,3) In elderly patients, decreased mobility and the presence of comorbidities that can mask symptoms until very advanced stages of the disease, makes the detection of symptoms more complex.

There are methods as cardiac magnetic resonance imaging which can demonstrate interstitial ventricular fibrosis, global longitudinal strain which detects myocardial dysfunction before left ventricular ejection fraction falls, and serum markers (as natriuretic peptides, troponin, etc.) which reflect myocardial damage and overload that occur before the onset of symptoms. Furthermore, in some cases the damage is not reversed even after aortic valve intervention. The presence, extent and reversibility of cardiac damage, particularly fibrosis, inflammation and oxidative stress, play an important role in the prognosis of the disease. In this scenario, the possibility of delaying disease progression and evaluating early treatment of diastolic dysfunction in aortic stenosis with drugs currently available in heart failure treatment, such as sodium-glucose cotransporter 2 inhibitors, is being considered. (4) In the coming years we will learn the effectiveness of new pharmacological strategies designed to mitigate or slow irreversible cardiac remodeling associated with aortic stenosis and its associated ventricular dysfunction. This knowledge will inform the optimal timing for implementing intervention.

Severe aortic stenosis includes risk subgroups, such as those with very severe or critical aortic stenosis (peak velocity > 5m/s), those with concomitant coronary artery disease and/or with rapid hemodynamic progression in whom current guidelines suggest early intervention. We will therefore focus our discussion on those with severe but not critical aortic stenosis, with preserved ventricular function and with an anticipated rate of hemodynamic progression. This is usually a younger and lower risk population within the universe of severe aortic stenosis. In this scenario, how long is it better to wait than to intervene?

Is it time to intervene all severe aortic stenosis regardless of symptoms and ventricular function? One might be inclined to respond in the affirmative. However, in our environment it is sensible to say not yet. The following paragraphs will attempt to identify the rationale behind this cautious warning.

Recent evidence appears to indicate that early SAVR may be a beneficial approach for patients with severe aortic stenosis. The results of the RECOVERY and AVATAR trials support SAVR in patients with asymptomatic severe aortic stenosis. This patient population was notably younger than the typical patient with severe aortic stenosis, and their surgical risk very low (EuroSCORE II of 0.9% in the RECOVERY trial and STS score of 1.7% in the AVATAR trial). (5,6) These findings cannot be applied to elderly patients due to the higher risk of surgical complications, and the competitive risks between the prognosis of aortic stenosis and the impact of comorbidities and frailty. In addition, these findings cannot be applied to TAVI because there is currently no information from randomized studies in asymptomatic patients. Nevertheless, it is important to analyze these studies beyond their conclusions, and to determine their applicable in our real world.

In the RECOVERY study, which included 145 asymptomatic patients < 80 years (mean age 63.4 years) with very severe aortic stenosis, the incidence of the composite end point of death due to SAVR or cardiovascular death was significantly higher in the conservative arm (21%) than in those assigned to early SAVR (7%), HR 0.33; 95% CI 0.12-0.90. It should not be overlooked that the mean peak aortic jet velocity was 5.1m/s (most patients had critical aortic stenosis), that there was a 74% crossover from the conservative arm to SAVR during follow-up, and the most remarkable aspect: the operative mortality of SAVR (in patients undergoing elective surgery and even emergency surgery who crossed over from the conservative arm to the SAVR arm) was 0%. This result surely reflects the excellence of the participating centers, but considerably reduces the external validity of the study. In the conservative group, the cumulative incidence of sudden cardiac death was 4% at 4 years. (5) It should also be noted that given the advanced stage of aortic stenosis, many patients met the criteria for a class IIa indication for elective SAVR. (7)

The AVATAR study included 157 patients (mean age 67 years) and demonstrated that early SAVR reduced the composite primary end point of death, myo-

Table. Published national results of SAVR in patients with symptomatic severe aortic stenosis

	n	Number of centers	Patients´ age (years)	Year	Risk	Isolated AVR	Surgical priority	Postoperative complications	In-hospital mortality	30-day mortality	Mortality by surgical risk
ESMUCICA valvular heart disease patients (9)	241	4 (>300 surgical procedures/ year)	65.8 ± 12	1997			Elective: 90% Urgent: 10%	61.5% (mainly AF and LCO)	(7.9% in text, 8.3% in abstract)	Not reported	Low: 3.8% Moderate: 9.1% High: 27.3%
CONAREC XVI (10)	359	49 (with residency program or similar)	64.8 ± 12.4	2008	EuroSCORE 3.51%-6.51%	100%	Elective: 89% Urgent: 10% Emergency: 0.8%	Elderly: 29.2% LCOS: 17.2% Reoperation: 5.8%	8.9%	Not reported	
David et al. (11)	125	2	71 (36-91)	2015-2017	103 p STS<4 22 p STS 4-7%	70%	Elective: 85.6%	Stroke: 1.6% Reoperation: 2.4%	2.4%	Not reported	
Borracci et al. (12)	422	Universitary centers	69.1 ± 11	2012-2017	EuroSCORE 2 (0.5-32.1) 75% <2.5%	100%	Not reported	Reoperation: 0.9%	3.6%	3.8%	
Stutzbach et al. (14)	934	1 (>300 surgical procedures/ year)	63.5 ± 13	1996-2001	Parsonnet 8.2 ± 3.3	52%	Elective: 83.3% Urgent:14.4% Emergency: 2.2%	AF: 26.5% LCOS: 24.5% Reoperation: 7.9%	5.5%	Elective: 3.1% Overall: 5.5%	Low: 0% Moderate: 2.6% High: 4%
Piccinini et al. (15)	87	1 (>300 surgical procedures/ year)	83 ± 2.5	1997-2008	Logistic EuroSCORE 12.4% ± 15%	100%	Elective: 72%	Stroke: 3% AF: 28% Reoperation: 5%		Elective: 9.5% Urgent: 12.5%	Low: 7.1% Moderate: 15.4% High: 5%
Navia et al. (16)	520	1 (>300 surgical procedures/ year)	76.8 ± 4.7	2010-2017	STS 2.5%±1.2	60.2%	Elective: 100%	AF: 33.7% LCOS: 6.3% Reoperation: 3.5%	3.1%	5.1%	Low: 2.7% Moderate: 5.3%
Fortunato et al. (17)	97	1 (>300 surgical procedures/ year)	79.4 ± 6.18	2007-2017	STS PROM 5.1% (4.4-6)	37%	Elective: 66% Urgent: 32% Emergency: 2.1%	AF: 44.5%	Not reported	5.1%	

AF: atrial fibrillation; AVR: aortic valve replacement; LCOS: low cardiac output syndrome; MV: mechanical ventilation

cardial infarction, stroke or hospitalization for heart failure compared to conservative treatment (HR 0.46; 95% CI, 0.23-0.90; p = 0.02). Operative mortality of SAVR was 1.4%. (6) A recent meta-analysis including these 2 studies and 10 observational studies evaluating SAVR vs. conservative treatment in asymptomatic patients showed a lower overall mortality rate for early SAVR compared to the conservative arm, mainly determined by the results of the 2 aforementioned studies. (8) The risk of stroke and myocardial infarction was similar between both groups. However, there was great heterogeneity in the magnitude of the effect across the included studies (pooled OR 0.40; 95% CI 0.35 - 0.45, $p < 0.01$; $I^2 = 61\%$), without being able to rule out bias. Among the numerous limitations reported, the meta-analysis included open studies which indicated conservative treatment in older and sicker patients, and the impossibility of extrapolating the results to elder patients, to TAVI and to patients with bicuspid aortic valve. The results of several ongoing studies (EARLY-TAVR, EaSY-AS, etc.) are still pending to reinforce the evidence.

In the meantime, we should not simply support an indication for early SAVR by extrapolating the surgical results of the AVATAR and RECOVERY studies to our reality. Although we may feel tempted, it would

not be correct to assume that the external validity of these results is applicable to our complex and heterogeneous local environment. It is essential to have a clear understanding of the surgical mortality rate in our country and the significant constraints on the population's access to surgical or interventional treatment at centers of excellence before extending an indication of this magnitude. Are we aware of the mortality rates of SAVR and TAVI in our country?

The risk of morbidity and mortality associated with SAVR varies widely. There are few contemporary publications in our environment reporting on the mortality of SAVR and even fewer have evaluated mortality in asymptomatic patients. Most publications include patients with symptomatic severe aortic stenosis and very few have updated information (Table). The statistics from the ESMUCICA II study (9) and the CONAREC XVI Registry (10) were gathered over 15 years ago and primarily focus on patients who have undergone coronary artery surgery. In both cases mortality rates of SAVR is high, even in high-volume centers. (9) The multicenter CONAREC XVI registry, which included 359 patients with a mean age of 64.8 years, reported an overall in-hospital mortality of 8.9%. (10) David et al. reported the series with the lowest in-hospital mortality of SAVR (2.4%) in symptomatic severe aortic stenosis with mainly elective procedures in patients with low and intermediate surgical risk (age 71 years). (11) Borracci et al. included 422 consecutive patients operated on with isolated aortic stenosis (age 69 years, left ventricular ejection fraction 58%) with an in-hospital mortality of 3.6%. (12) In the subgroup with low anticipated mortality according to EuroSCORE II, the observed mortality was 1.6%. In a meta-analysis by Borracci et al. which included 1192 low- and moderate-risk patients intervened in university centers, in-hospital mortality after SAVR was 3.1%. (13) In our environment, mortality in elder patients undergoing SAVR is > 3% in the rest of the published studies. (14–17) These publications mostly reflect the results of high-volume centers, with a high rate of publications, which do not necessarily represent the reality of most surgical centers in our country.

In this scenario, TAVI would be a particularly attractive option because it is less invasive than surgery considering that these patients are asymptomatic. However, there is no evidence from randomized studies yet. Moreover, there are few local publications on TAVI in low surgical risk populations. Caponi et al. published a series of 200 patients with symptomatic severe aortic stenosis and moderate to high surgical risk (logistic EuroSCORE =18) undergoing TAVI via the transfemoral access (2009-2016) at a university center. Total in-hospital mortality was 3.5% and 1-year mortality was 11.5%. (18) Progressive training in the technique, combined with the availability of better prostheses, were associated with a lower rate of complications and a lower rate of mortality over time. Boissonnet et al. published a systematic review of 1156 patients (81 years) who underwent TAVI in South America (2008-2015) with an in-hospital mortality of 8.1% and 30-day mortality of 12.5%. (19) More recently, other authors have reported 30-day mortality rates < 5.5% with transfemoral TAVI in low or moderate surgical risk patients. (20) Nau et al. published the results of 770 patients who received TAVI (81 years) in high-volume centers mainly via the transfemoral access (80% with self-expandable valves). In-hospital mortality rate for low, intermediate and high-risk patients categorized by the STS PROM score was 3.9%, 5.9% and 9.6%, respectively. (21) The persistently high rate of pacemaker requirement, coupled with the paravalvular leak, the paucity of data regarding prosthetic durability in younger patients, and the mortality rate associated with the procedure, which has not yet reached 0-1%, make this option inadvisable for the time being.

Therefore, the little that we do know reflects a very different scenario from that of the randomized trials, with a mortality associated with SAVR or TAVI that is at least double or triple that of the AVATAR and RECOVERY trials. In addition, we should keep in mind that, so far, we have only talked about operative mortality and acute periprocedural complications. The studies do not emphasize the incidence of long-term complications of a prosthetic heart valve, or they do not provide much information about them. Even in patients who survive surgery and do not develop perioperative complications, prosthetic heart valves are associated with significant long-term morbidity. The expected complications include paravalvular leak, prosthesis-patient mismatch, pacemaker requirement (mainly in TAVI), prosthetic dysfunction, thrombus formation, thromboembolism, infective endocarditis and problems associated with anticoagulation (bleeding, resistance, etc.). Although the incidence of complications depends on the type of prosthesis, significant complications occur at a rate of approximately 3% per year and procedure-related death rate is 1% per year.

We all know that symptomatic patients who do not receive treatment for aortic stenosis have an ominous prognosis. (22,23) However, real-life studies and registries from the surgical and TAVI eras are still reporting that a high proportion of patients with an indication for surgery or TAVI do not receive adequate treatment. Likewise, frailty, a variable that increases morbidity and mortality, is also not properly assessed in patients with aortic stenosis. Undertreatment is associated with age, comorbidities, reduced left ventricular ejection fraction, perceived surgical risk by the treating physician, and lack of knowledge of the disease. Valvular intervention (either surgical or percutaneous implantation) is appropriate only in patients who are likely to have benefit from the procedure. Treating patients for whom the intervention is futile further overburdens a limited health care sys-

tem and is associated with an incorrect assessment of the patient's benefit and life expectancy prior to the intervention. Despite the efforts to educate the medical system about the benefits of treating patients with symptomatic severe aortic stenosis, there is still an underutilization of surgical and/or TAVI treatment even in scenarios where the prognosis without treatment is unfavorable. (24) Furthermore, the availability of a Heart Team or working group on valvular diseases remains limited in our environment. Additionally, there is a lack of periodic publication of statistics on mortality associated with procedures. Therefore, a reasonable strategy may be to start by improving these aspects in order to make progress in the prognosis and management of patients with severe aortic stenosis in our environment before extending the indication to other less certain scenarios.

In conclusion, when weighing the benefits and risks of a decision for early intervention, the weight of uncertainty and lack of knowledge of local outcomes must be measured in terms of in-hospital mortality for SAVR and TAVI in patients with asymptomatic severe aortic stenosis. In centers of excellence with mortality rates for elective SAVR close to 0%, young patients could choose the early intervention strategy, but this is not the prevailing reality in the local setting. Moreover, valve replacement does not fully eliminate the risk of sudden cardiac death and is also associated with non-negligible complications typical of prosthetic heart valves. Therefore, even if surgical mortality can be minimized, the combined risk of the procedure and late complications of a prosthetic heart valve may outweigh the possibility of preventing sudden cardiac death in some asymptomatic patients with severe aortic stenosis.

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AGONIST REPLY

I agree with many aspects and disagree with very few points. I agree that the subgroup of asymptomatic patients with more critical or rapidly progressive aortic stenosis should benefit from early intervention. For early intervention, I also agree that the center must have morbidity and mortality rates that meet international standards for both TAVI and SAVR. However, the fact that a randomized study (e.g., the RECOVERY trial) has reported 0% of in-hospital mortality in 75 consecutive patients does not mean that the early intervention can only be applied to a center with 0% mortality in its "real-life" reports. It is quite possible that many centers in our environment have an in-hospital mortality for SAVR or TAVI close to 0 or 1% in the last 75 consecutive low-risk patients with a low burden of comorbidities as those "highly selected" for randomized studies such as the RECOVERY study. Furthermore, the references regarding TAVI-related mortality in our environment come from the beginning of the programs (2009) until 5 to 10 years ago and do not represent the results presented in scientific events or contemporary quality audits.

The area where we do not agree is in what to do with asymptomatic and severe, but not critical, aortic stenosis. We know that many patients can wait until symptoms develop; the issue is that we do not know who should not wait. When we prescribe statins in secondary prevention, we know that most patients will not derive any benefit, but as we do not know who will benefit from statin therapy, we prescribe statins to all those who are at risk. Until evidence demonstrating who does not benefit from statin therapy is available, we will continue prescribing statins to all patients in secondary prevention. The same is true in this scenario: just because some patients do not benefit does not mean that we should not offer early intervention to all those who are eligible. To date, randomized studies, consistent with previous observational evidence, suggest benefit from early intervention in these patients. It is important to note that these studies have limitations, primarily due to the low event rates and medium-term follow-up periods. These limitations will be further elucidated with the publication of the multiple ongoing randomized trials in the coming years.

Pablo Lamelas

ANTAGONIST REPLY

Over the past few decades, we have witnessed a revolutionary shift in the field of aortic stenosis, with improvements in its diagnosis, risk stratification and treatment. Early intervention in asymptomatic stages is a topic of current debate. However, we do not know the mortality and morbidity rates of SAVR in most centers in our environment, and we often want to assume that the results of a few international centers of excellence are the overall national results.

As mentioned above, although there is evidence from 2 randomized clinical trials in favor of this strategy, they lack external validity in our setting. One of the aforementioned studies evaluated the intervention in patients with critical aortic stenosis, which is a current indication in the guidelines, and reported a mortality rate of 0%. The other study included patients younger than the usual ones with this disease with results favoring early SAVR and surgical mortality rate < 1.5%. I must keep on emphasizing that these findings cannot be yet applied to elderly patients, to surgical centers with mortality rates > 1.5%, or to TAVI, for which there is still no evidence.

How many of us work in centers that have sustained and published mortality rate <1.5% following SAVR?

We will not be in a position to extend the intervention to asymptomatic severe or moderate aortic stenosis without left ventricular dysfunction until we have access to the information on local surgical results that are similar or close to those of the aforementioned studies. We must always have a clear understanding of the local reality in order to improve it and act accordingly. This will be the first step in enabling us to provide truly beneficial care to our patients.

María Celeste Carrero