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Aortic Valve Disease: An Update

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ABSTRACT

Researchers also found that AS (also called a constriction of the orifice that limits anterograde flow through the AV) and AR (when blood flows backwards through the AV) Even though the pathology may not become obvious for many years, symptoms may not show up until the condition has developed to a severe state. When the problem has reached this point, the risk of morbidity and mortality associated with AVD is extremely considerable. Thus, to have better knowledge, we have reviewed AVD in terms of etiology, pathology, statistical studies, and evaluation criteria.
Key words: *AVD, AS, AR, Etiology, Pathology, Statistical, Evaluation criteria.*

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INTRODUCTION

Studies have also concluded that aortic stenosis (AS) and aortic regurgitation (AR), two illnesses that damage the aortic valve, pose a serious risk to the health of people all over the globe.[1] According to some estimates through studies, "1% of people younger than 55 years old and 6% of people older than 75 years old suffer from moderate or severe AS/AR".[2,3] Studies have also concluded that "when the leaflets of the valve become stiff, the orifice of the valve becomes smaller, leading to decreased anterograde flow during systole. Additionally, studies have demonstrated that the AVF's improper closure during diastole causes a retrograde blood flow from the aorta into the left ventricle, which results in AI".[5] The consequences of this include an increase in the LVEDV and an increase in the VWS.[4,5,6]

ETIOLOGY

Studies have also found that AS is an abnormal narrowing of the AV. Calcified (age-related) aortic stenosis and CBAV are two of the most common causes of this condition. Studies have also concluded that RHD is generally seen more often in less developed countries and is more commonly associated with the mitral valve. On the other hand, studies concluded that RHD may very infrequently be the cause of AS and/or AR. The cause of CAS, according to many studies, is thought to be progressive endothelial deterioration over the course of many years.[1,7,8] Studies have also found that the clinical manifestations of congenital AS appear 10 to 20 years sooner than those of calcific AS. Studies have also found that, in more than 90% of cases, BAV indicates CAS.[8] Studies have been showing "around 932 instances of IAV removed from individuals between the ages of 26 and 91 years old between the years of 1993 and 2004".[9]Studies have further concluded that AS is a disease that develops slowly.[10] Recent data suggest that "AS is linked to an increased risk of CE of 68% to 27%, and mortality of 36%".[11] With conservative treatment, the data from the PARTNER research suggest an annual mortality rate of fifty percent.[12] Studies have also found that AR may present itself in either a chronic or acute setting. In another study,one of the reasons for AAR is an AD that extends to the valve, and another cause is damage to the valve leaflets caused by viral or non-infectious endocarditis. The most common causes of CBVI, calcific disease, and Marfan syndrome are also the most common causes of CAR in developing countries.[4]

STATISTICAL STUDIES

Studies have also found that there is a greater prevalence of the condition known as AS among the elderly population, which includes those in their fifth to eighth decades of life. According to a study, "the incidence of AS was found to be 0.2% during the fifth decade of life, 1.3% during the sixth decade of life, 3.9% during the seventh decade of life, and 9.8% during the eighth decade of life respectively ".[1] It was found that the percentage of faulty valves went down with age in patients who had surgery for IAS, and a comparison of patients with congenital anatomical abnormalities of the AV to patients with normal

anatomy This was the case for those patients who had surgery for IAS.[1] Patients who had surgery and were under 50 years old had a bicuspid valve in two-thirds of the cases. In contrast, one-third of patients between the ages of 50 and 70 had unicuspid anatomy, while two-thirds of patients in this age range had bicuspid architecture, and one-third had normal tricuspid morphology. Sixty percent of patients with ages more than seventy years old had bicuspid valves, while forty percent had tricuspid valves. Studies have also found that there is an estimated prevalence of 4.9% for aortic regurgitation, which rises similarly with age up to the sixth decade, at which point it starts to fall. This rise in the prevalence of AR occurs with age. However, due to the fact that up to 75 percent of patients with AS may have some degree of AR that is not being reported, this number may be artificially low.[13,14]

EVALUATION OF AS [4]
Studies have shown that evaluation of aptients with AS defines 2 issues:-
1. SAS Patient
2. Improved by AVR

1. SAS Patient [4]
It has also been shown in studies that people with LVV-AS can be identified with high sensitivity but low specificity by using clinical criteria, ECG (LVH), or radiological criteria (calcification of the valve). An objective assessment of the severity of AS is thus necessary. [Table 1]

Criteria	Severe AS	Advantages	Disadvantages
Aortic surface area	≤ 1.0 cm^2	Measures effective AVA. However, this may also constitute a disadvantage because it does not measure anatomical AVA	Very sensitive to measurement errors
		Less flow-dependent compared with other measurements	
Indexed AVA to body surface area	≤ 0.6 cm^2/m^2	Useful for extreme heights/weights	Very sensitive to measurement errors
Mean transaortic pressure gradient	≥ 40 mmHg		Flow-dependent
			Requires correct alignment of Doppler signal with the flow direction
Peak transaortic flow velocity	≥ 4.0 m/s	Measures instantaneous velocity	Flow-dependent
		Best predictor of adverse events	Requires correct alignment of Doppler signal with the flow direction
Ratio between peak transaortic flow velocity and peak LVOT velocity	≤ 1/4	Good reproducibility (compared with AVA calculation)	Limited data on prognostic utility

Table 1: Currently Used Criteria for Sas [4]

Studies have also concluded that, "ECG criteria for SAS are not interchangeable and the criteria based on PG and velocities are highly dependent on blood flow, properly performed measurements using an integrative approach".[4] Studies also proved that a "gradient of 40 mmHg correlates to an AVA of 0.8 cm2 rather than 1 cm2, the latter being the usual diagnosis of SAS".[15] Researchers looked into this and found a "link between the mean transaortic pressure gradient (MTPG) and AVA in people with AS and normal LVEF".[16] Also, studies have shown that the AV's effective orifice area will be 1 cm2 at TFR of 125 mL/s, which is equal to a cardiac output of about 3 L/min, no matter how mild, moderate, or severe the AS . Additionally, studies also concluded that the MTPG is less than 40 mmHg for any severity of AS

(from moderate to severe, based on anatomical AVA) when the transaortic flow is less than 175 mL/min.[16] As a result, determining the SAS is particularly difficult in low-flow situations.[17]

2. Improved by AVR [4]

Studies have also concluded that "after a diagnosis of SAS has been made, the next step is to choose the patients who are candidates for AVR". [18,19] [Table 2]

Criteria	Level of recommendation		Differences between guidelines
	ESC/EACTS	AHA/ACC	
Severe AS with any symptoms clearly due to AS, based on history or unmasked by stress test	I	I	"High-gradient" in AHA/ACC guidelines
Asymptomatic severe AS with LVEF < 50%	I	I	
Severe AS and another indication for surgery (CABG, thoracic aorta, another valve)	I	I	
Asymptomatic severe AS where the systolic blood pressure does not increase by > 20 mmHg or drops compared with baseline during the treadmill test	IIa	IIa	AHA/ACC guidelines acknowledge the presence of fatigability during stress test as an indication for AVR
Moderate AS and another indication for surgery (CABG, thoracic aorta, another valve)	IIa	IIa	
Low-flow/low-gradient/low-LVEF severe AS with proof of contractile reserve presence	IIa	IIa	
Symptomatic low-flow/low-gradient/preserved LVEF severe AS after careful confirmation of severity	IIa	IIa	
Truly asymptomatic severe AS (no symptoms during treadmill test, no risk criteria) with preserved LVEF if the surgical risk is deemed low and the following criteria are also satisfied: Very severe AS (maximal velocity ≥ 5.5 m/s); Severe valvular calcification and increased maximal velocity by ≥ 0.3 m/s per year	IIa	IIa for velocity ≥ 5 m/s (see text)	AHA/ACC guideline: Velocity ≥ 5 m/s or mean gradient ≥ 60 mmHg AND severe calcifications; velocity 4 to 4.9 m/s or mean gradient 40 to 59 mmHg AND severe valvular calcification AND stress test demonstrating reduced tolerance or drop in blood pressure
		IIb for maximal velocity increase by ≥ 0.3 m/s per year	
Truly asymptomatic severe AS (no symptoms during treadmill test, no risk criteria) with preserved LVEF if the surgical risk is deemed low and 1 or more of the following criteria are also satisfied: Severely increased BNP/Nt-ProBNP levels at serial determinations and without an alternative explanation; increased transaortic pressure gradient at stress echocardiography by > 20 mmHg; excessive LV hypertrophy without an alternative explanation	IIb	-	This indication is not covered in the AHA/ACC guidelines
Low-flow/low-gradient/low-LVEF severe AS without contractile/flow reserve	IIb	-	This indication is not covered in the AHA/ACC guidelines

Table 2: Indication for AVR According To Guidelines [4]

Studies have also concluded that the "decision to perform AVR in patients with asymptomatic severe aortic stenosis (AS-AS) and preserved LVEF is highly controversial".[20,21] Studies further concluded that patients with AS-AS and LVEF had mortality rates of 3% and 26.4% at one year and five years, respectively. Furthermore, studies have concluded that a significant proportion of patients who were originally without symptoms, namely 46%, experienced the onset of symptoms during the subsequent 5 years.[22] Also, studies have shown that people with AS-AS and preserved LVEF who have very severe AS are more likely to have major adverse cardiovascular events (MACE) than people with severe AS and an

MTV of 4 to 5 m/s.[22] Specifically, studies also revealed that the "rate of MACE is twice as high in patients with very severe AS (96%) compared to those with severe AS (39%) over a period of 4 years." Studies also concluded that SAS is characterized by a MTV of 5.5 m/s. After a period of six years, almost all patients (97%) diagnosed with severe AS and a maximal velocity of less than five meters per second (m/s) had a significant negative MACE.[23] Recent research using patient registries indicated that SAVR resulted in an 86% decrease in mortality compared to the group of patients who were handled conservatively, following a 6-year follow-up period.[23] Studies also concluded that "the mortality rate was 2% in the surgical AVR group, compared to 32% in the conservatively managed group".[23] The research conducted a comparison between 102 patients who had surgical AVR and 95 patients who received conservative treatment. The results revealed that surgical AVR was linked to a significant 86% decrease in mortality. The current guidelines recommend a class IIa indication for AVR in patients with AS-AS and preserved LVEF.[4] However, this recommendation is contingent upon the center having a low estimated perioperative mortality rate. This categorization is derived from non-randomized data obtained only from a single center. The new guidelines also suggest a class IIa reason for AVR in people who have severe LF-AS and preserved LVEF. But studies also concluded that this was applicable only if it was shown that the symptoms were solely associated with AS.[4]

HIGH RISK CRITERIA (HRC) [4]

Studies have also concluded through various observational and retrospective data that it may be beneficial to take into account a number of risk factors for MACE and poor prognosis in these patients.[Table 3] Furthermore, studies also said that it is essential to emphasize that the sensitivity and specificity of these measures for the identification of patients who have a satisfactory post-operative prognosis are only about 80%. It is thus not possible to suggest that these measures be integrated into widespread clinical practice at this time; nonetheless, these parameters may be useful for individual decision-making in patients who are being considered for AVR. The prognostic importance of AVC and the hemodynamic response (HDR) during stress ECG are the two parameters that have been the subject of the most extensive amount of study.[4].

Test	High risk criteria
Electrocardiogram	Presence of LV hypertrophy with secondary ST segment deviation ("LV strain")
Blood tests	Highly increased BNP/Nt-ProBNP levels
Stress test	Unmasked symptoms: Fatigability/dyspnea at < 75 W, syncope/near syncope; angina
	Lack of increase in systolic blood pressure by > 20 mmHg (or decrease) with exercise
	Inducible myocardial ischemia (ST segment depression ≥ 2 mm)
	Severe ventricular arrhythmias (sustained VT, polymorphic VT, VF)
Conventional Doppler echocardiography	Very severe AS (AVA ≤ 0.6 cm; maximal velocity ≥ 5 m/s)
	LVEF < 50%
	Severe LV hypertrophy (≥ 15 mm)?
	Reduced LV longitudinal strain
	Zva ≥ 4.5 mmHg/mL per square meters
Dobutamine stress echocardiography (in low-flow, low-gradient, low LVEF)	Lack of contractile reserve
Exercise echocardiography (ergometric bicycle) - any severe AS	Increase in transvalvular pressure gradient by > 20 mmHg during exercise
	Inducible pulmonary hypertension during exercise (systolic pulmonary pressure ≥ 60 mmHg)
Documentation of valvular calcification	Presence of severe valvular calcifications: Qualitatively (radiology, conventional echocardiography); quantitatively (computed tomography): Calcium score ≥ 1651 Agatston units (lower in women *vs* men)

Table 3: HRC in AS-AS [4]

Studies have also concluded that the predictive significance of the change in TPG during exercise has also been proposed. Therefore, studies also concluded that "the rate of MACE is highest (100% at 2 years) in patients with a high RTPG (> 35 mmHg) that increases by more than 20 mmHg during exercise". Studies also concluded that "it is intermediate in patients whose TPG increases by less than 20% during exercise (50% at 2 years for patients with high RTPG and 20% at 2 years for patients with low TPG). The rate is lowest (10% at 2 years) in patients with a low TPG (≤ 35 mmHg) that increases by less than 20% during exercise".[24,25] On the other hand, studies have also concluded that there was a significant increase in the incidence of MACE in both of these groups.[4] This finding suggests that early AVR is beneficial in this population. This data implies that early AVR is useful in treating this population. Despite this, observational studies showed that medically treated patients were older and sicker, and up to 50% of these patients got a class I indication for AVR during follow-up. However, they were rejected for a number of reasons, which meant they were too sick to have either surgical or interventional AVR.[22,26]

EVALUATION OF AR [4]

Studies have concluded that evaluation of SAR by ECG includes:_

1. SAR Patient
2. Indication for AVR

1. SAR Patient

Studies have also concluded that the ECG is considered to be the most useful for detecting SAR [Table 4] .[27]

	Mild AR	Moderate AR	Severe AR
Ratio between the AR jet diameter and the LVOT diameter	< 25%	25%-64%	≥ 65%
Vena contracta (mm)	< 3	3-5.9	≥ 6
Regurgitant volume (mL/beat)	< 30	30-59	≥ 60
Regurgitant fraction	< 30%	30%-49%	≥ 50%
EROA (cm^2)	< 0.1	0.1-0.29	≥ 0.3
Diastolic backflow in the descending thoracic and/or abdominal aorta	Minimal	Less than holodiastolic	Holodiastolic (especially for backflow documented in the abdominal aorta)
Angiographic	1+	2+	3-4+
LV dilatation	No	No	Yes (mandatory for chronic severe AR)

Table 4: Criteria for Diagnosis of SAR [4]

2. Indication for AVR

Studies have also concluded that the gold standard of treatment for AR remains SAVR, which was developed in the old days. Studies have also found that surgical AV repair may be an option in some reputable centers for people with good anatomy, like an aortic root that is dilated or an aortic cusp that has prolapsed.[28,29] Studies have further concluded that TAVR has only been employed in these patients on a case-by-case basis so far, and its effectiveness in treating AR is very limited.[30] In addition, the majority of the data on the "prognosis of AR originates from studies that were published more than two decades ago and employed evaluation methods that are now considered to be archaic".[31] Studies have also concluded that a SA-AR needs emergency surgical treatment as soon as possible.[32][Table 5&6]

Criteria	Class of indication		Differences between guidelines
	ESC/EACTS	AHA/ACC	
Symptomatic severe AR (any LVEF)	I	I	
Asymptomatic severe AR with depressed LV function (LVEF < 50%)	I	I	
Severe AR in patients with another indication for cardiac surgery (*e.g.*, CABG, thoracic aorta, another valve)	I	I	
Asymptomatic severe AR with normal LVEF (> 50%) but with severe LV dilatation	IIa	IIa	Definition of severe LV dilatation: ESC/EACTS guideline: End-diastolic LV diameter > 70 mm, or end-systolic LV diameter > 50 mm (or > 25 mm/m^2); AHA/ACC guidelines: End-systolic LV diameter > 50 mm
Moderate AR in patients with another indication for cardiac surgery (*e.g.*, coronary bypass, thoracic aorta, another valve)	-	IIa	This indication is not covered in the ESC/EACTS guidelines
Severe AR with normal LVEF (> 50%) but with progressive LV dilatation (end-diastolic LV diameter > 65 mm) if the surgical risk is low	-	IIb	This indication is not covered in the ESC/EACTS guidelines

TABLE 5: Indication for AVR in car [4]

Class of indication	Guideline		Differences between guidelines
	ESC/ EACTS 2012	AHA/ACC 2016 Consensus on AHA/ACC 2014, and ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM 2010 Guidelines	
I	-	Asymptomatic bicuspid aortic valve with dilatation of Valsalva sinuses or the ascending thoracic aortic diameter > 55 mm	No class I indications in the 2012 ESC/EACTS guidelines
IIa	Bicuspid aortic valve with an ascending thoracic aortic diameter > 50 mm if the patient also has at least one of the followings: Family history of aortic dissection; documented increase in the aortic diameter > 2 mm/yr (assessed using the same imaging method, at the same level, and with comparative images available); arterial hypertension; coarctation of the aorta	Bicuspid aortic valve AND dilatation of the Valsalva sinuses or of the ascending thoracic aorta (> 50 mm) AND at least one of the following	
		Family history of aortic dissection	
		Documented increase in aortic diameter > 5 mm/yr	
		OR low surgical risk in an expert center	
	-	Replacement of the ascending aorta if the patient also has an indication for surgery for AS/AR, and the ascending aortic/Valsalva sinus diameter is > 45 mm	Not covered by the 2012 ESC guidelines

TABLE 6: Indication (BAV & ARD) [4]

PATHOLOGY

Studies have also concluded that progressive endothelial damage is what causes CAS. This damage may first cause inflammation, which may then lead to the invasion of macrophages and other kinds of inflammatory cells.[1] This leads to the development of profibrotic factors, which create a collagen matrix that, in a manner analogous to the formation of bone, ultimately turns into calcified tissue. Studies have also found that the "most common effects of AS are those that happen when there is less anterograde flow from the left ventricle into the aorta. This causes blood to build up in the LV and the P between the V and the A to rise. This backflow may be the cause of symptoms of HF, beginning with LAD and MR and ultimately leading to PE and HF on the right side of the heart. Studies have shown that symptoms often do not develop until the AV area has decreased to less than 1.0 cm. The aortic valve in a healthy individual measures between 3 and 4 cm. When a valve reaches a significant degree of stenosis, it makes it more difficult to maintain an acceptable cardiac output. Ischemia, arrhythmias, and decreased cerebral perfusion may be the results of the LV going through hypertrophy and remodeling, which may lead to increased LVOD. This, in addition to a decreased cardiac output, may also result in decreased brain perfusion".[1] Studies have also concluded that AR causes blood to flow backwards from the A into the LV, which leads to an increase LV volume and dilatation of chamber. On the other hand, studies also concluded that "this increase in CO causes distention and increased P in the PA, which in turn leads to an increase in PSP." [5] Additionally, studies concluded that this leads to worsening of AR, which may cause a rapid reduction in PSP and, in severe cases of the disease, CVS collapse.[33,34,35]

CONCLUSION

We come to the conclusion that AS, or AR, is linked with a poor prognosis, and both of these conditions constitute substantial threats to the health of the global population. So, after carefully selecting patients, both SAVR and TAVR may be utilized to treat AS. The gold standard of treatment for AR remains selective for aortic surgery. Only then can the clinician effectively identify those patients who are candidates for surgery. After that, the doctor will finally be able to correctly identify those patients who are candidates for surgery.

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