REVIEW ARTICLES

Aortic Valvular Heart Disease in the Adults

JORGE ORTEGA-GIL, MD*; JOSÉ M. RODRÍGUEZ CASTRO, MD†

Valvular Heart Disease (VHD) is an important cardiovascular problem in the adult population. The knowledge of the physiology involved, prompt recognition and diagnosis are of paramount importance for the primary care physician who is in the front line of patient care. This article is the second of a series of two that deals with valvular problems in the adults in concise and practical form (11). Each topic will be presented using the following format: description, etiology, pathophysiology, natural history, essential of diagnosis and management. In this second and final article we will discuss aortic valve disorders.

Key words: Aortic stenosis, Aortic regurgitation, Aortic insufficiency, Diagnosis, Management

Aortic Stenosis (AS)

Description

It is defined as a progressive obstruction of the left ventricular outflow tract (LVOT) creating a pressure difference between the left ventricle (LV) and the aorta. The obstruction may occur at the valve level (most common), below the valve and above the valve. If severe it is associated with significant morbidity and mortality. Typically symptoms includes: angina, syncope, heart failure and ultimately death if not treated.

Etiology

Patients with AS may be broadly classified in two categories: acquired and congenital.

Acquired AS

- Degenerative calcific AS: It is the most common cause of AS in US occurring in the 6th or 7th decade of life. It is characterized by calcium deposition at the fusion line of the valve leaflets. Degeneration (wear and tear) and probably atherosclerosis had also been implicated. There is now growing evidence that traditional risk factors of atherosclerotic vascular disease (hypertension, diabetes, dyslipidemia, smoking and end stage renal disease) are similar for AS and aortic sclerosis (1).
- Rheumatic AS: Infrequently seen in USA, often coexists with aortic regurgitation (AR) and mitral valve disease. Isolated AS suggests non rheumatic etiology. It results from adhesions and fusion of commissures and cusps and vascularization of the leaflets leading to retraction and stiffening of the free borders of the cusps. Calcium deposits are present in the pocket of the aortic cusps without affecting the commissures and the orifice is reduced to a small round or triangular opening resulting in a valve that is stenotic and regurgitant.

Congenital AS

- Bicuspid aortic valve (BAV): Predominates in men and is present in at least 1% of the population. Often have familial clustering consistent with an autosomal dominant inheritance. Severe stenosis develops must often in the 4th and 5th decade of life but occasionally develops earlier. BAV occurs in more than 50% of the patients with coarctation of the aorta. This simple focal lesion is related to problems of the entire arterial system and the term "diffuse arteriopathy" has been used. These patients are at risk of strokes (aneurysm of the circle of Willis), aortic aneurysm and dissection (2). The abnormal dome shaped architecture causes turbulent flow which traumatizes the leaflets leading to fibrosis, rigidity and calcification, resembling degenerative AS.
- Subvalvular AS: Is a congenital condition that may not be apparent at birth. Typically a fixed band like fibromuscular circumferential membrane is present

From the Section of Cardiology of the Department of Medicine of the UPR School of Medicine, *Professor of Medicine, †Fellow in Cardiology

Correspondence address: Dr. José M. Rodríguez Castro, Section of Cardiology, UPR School of Medicine, PO Box 365067, San Juan, Puerto Rico 00936-5067, e-mail: jovony@yahoo.com

in the LVOT below the aortic valve that eventually may cause AR. A tunnel like obstruction may be present in more severe cases. When associated with coarctation of the aorta it is termed Shone syndrome. This condition may be difficult to distinguish from hypertrophic cardiomyopathy and may recur after successful membrane resection.

- Supravalvular AS: It is very rare and may occur as a part of a congenital syndrome known as William's syndrome (elfin faces, mental retardation, hypercalcemia and peripheral pulmonary stenosis. Typically, a thrill on the right carotid artery can be palpated. .

In general, calcific AS is seen in patients that are older than 35 years old and results from calcification of a congenital or rheumatic valve or a normal valve that has undergone "degenerative" changes. Other rare causes of AS includes: Subacute Lupus Erythematosus (SLE), rheumatoid arthritis, homozygous type II hyperlipidemia, Paget's disease, infective endocarditis, ochronosis and radiation.

Pathophysiology

In AS, the obstruction worsens over many years (decades). A transvalvular pressure gradient develops between the LV and the ascending aorta. To maintain an effective cardiac output in the face of increased afterload, the left ventricle must generate higher systolic pressures, increasing in this way the LV wall stress. In response to this pressure overload the LV undergoes compensatory concentric hypertrophy allowing the wall stress to normalize (3) (LaPlace law: Wall stress = pressure **X** radius / wall thickness). However, these changes lead to a reduction in LV compliance affecting the early diastolic filling, making the left ventricular preload more dependent on atrial contraction. Over time the left ventricular afterload continues to increase and in order to maintain normal systolic function the LV uses two additional mechanisms: increase preload (Frank Starling curve) and increase myocardial contractility. When the preload reserve is no longer adequate (afterload / preload mismatch) or myocardial contractility is reduced the LV systolic function becomes abnormal. The pressures in all the chambers rise (both atria, both ventricles and the pulmonary vasculature) and symptoms of congestive heart failure (CHF) develops.

Natural history

Because a "good ventricle" can compensate the LVOT obstruction with hypertrophy, the AS in adults is characterized by a long latent phase in which the patient even with severe AS has no symptoms. Asymptomatic patients have a similar life expectancy as people without AS although there is marked individual variability in the length of the latent period and the rate of progression of disease. The aortic valve area (AVA) must be reduced to one fourth its normal size (which is 3.0 – 4.0 cm^2) before significant changes in the circulation occurs. See Table I, it classifies aortic stenosis according to aortic valve area and the mean transvalvular gradient. Studies indicate a decrease in AVA that ranges from (0.1 – 0.3) cm^2 and an increase in systolic peak gradient (SPG) of (10 – 15) mmHg per year (4). Once symptoms appear the survival rate decreases markedly, unless aortic valve replacement (AVR) is performed. After the onset of the classic triad: angina, syncope and systolic heart failure; each of these symptoms in order heralds an ominous prognosis. The average survival is 5, 3, and 2 years respectively (See Fig 1). Development of atrial fibrillation with loss of effective atrial contraction represents an ominous factor with an average survival time of 6 months (5).

Table 1. Classification of Aortic Stenosis

	AVA (cm^2)	MTG (mmHg)
Normal	2.4 – 4.0	0
Mild AS	> 1.5	0 - 20
Moderate AS	1.0 – 1.5	20 - 40
Severe AS	< 1.0	40 - 50
Critical AS	< 0.75	> 50

MTG = Mean Transvalvular Gradient. AVA = Aortic Value Area

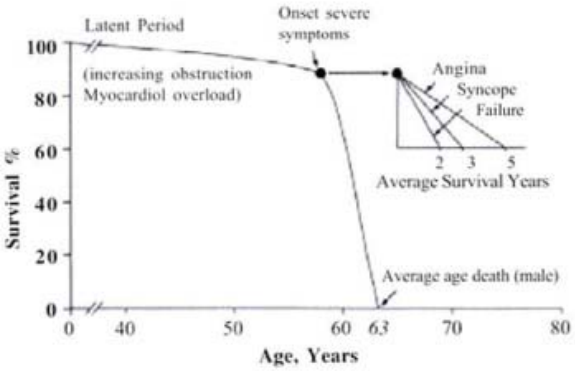


Figure 1. Natural History of Aortic Stenosis once Symptoms Develop. From Manual of Cardiovascular Disease.

Clinical Manifestations

- Angina: Patients with severe AS in the absence of epicardial coronary artery disease (CAD) may experience myocardial ischemia due to supply demand

imbalance caused by increase wall tension, reduced coronary blood flow (CBF) or abnormal distribution of CBF during exercise or tachycardia (6).

- Syncope or Presyncope: Precipitated by efforts which induce arterial vasodilation in the setting of a "fixed" cardiac output (CO) results in hypotension and reduction in cerebral perfusion (7).Syncope at rest is usually secondary to transient ventricular arrhythmias.
- Heart Failure: These symptoms may be caused by diastolic or systolic dysfunction or both.
- Lower Gastrointestinal Bleeding: Due to increased incidence of arteriovenous malformation, particularly related to right sided colonic angiodysplasia. Treatment with AVR prevents recurrent bleeding.

Physical findings

The most important physical findings in patients with severe AS include the following:

- *Pulsus parvus et tardus*. The small volume (parvus) and delayed (tardus) upstroke in the carotids arteries.
- A narrow arterial pulse pressure (if no concomitant hypertension or aortic regurgitation).
- The apical impulse is sustained non displaced and diffuse; often bifid as a result of a palpable S4.
- The aortic component of S2 diminishes and eventually it may disappear, resulting in a soft single S2 (loss of A2). S2 may be paradoxically splitted due to the prolonged duration of ejection through the severely narrowed valve.
- An S4 indicates increased strength of the atrial contraction.
- An S3 indicates poor LV systolic function.
- An ejection sound (ES) in patient with flexible valves (still mobile) can be seen in BAV. The typical murmur is a harsh late peaking crescendo-decrescendo (diamond shaped) systolic ejection murmur, loudest at the right upper sternal border that radiates to the neck. The longer the murmur the more severe the stenosis. *Gallavardin phenomenon* is an AS murmur transmitted in an altered form at the apex and easily mimics mitral regurgitation (MR).

Diagnostic techniques

Although ECG stress testing is contraindicated in the symptomatic patient with severe AS, a carefully supervised test in the asymptomatic patient may provide clinical useful information. The ECG usually demonstrates left atrial abnormality and left ventricular hypertrophy (LVH) with or without ST – T wave changes as show Fig 2. The Chest X Ray (CXR) may be normal or may become boot shaped because of concentric LVH. Calcifications of the aortic valve or aortic root may be present and post stenotic dilatation of the ascending aorta, as illustrated in Fig 2, may be evident . The 2 D Echo Doppler is the method of choice to establish the diagnosis of AS. It permits direct

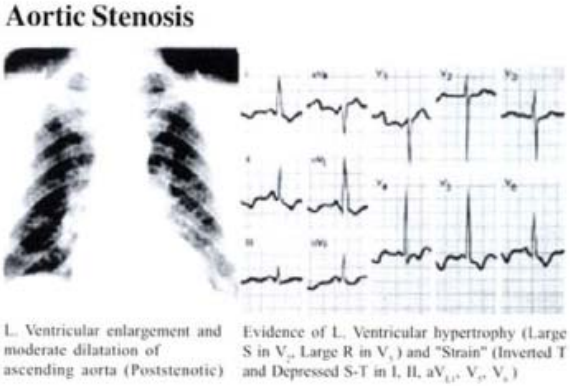


Figure 2. Aortic Stenosis: Chest X Rays and Electrocardiographic Changes. From F. Netter-CIBA Collection

visualization of the valve, measurement of the pressure difference or gradient across the valve, estimation of the valve area and assessment of the left ventricular systolic function. Cardiac catheterization is not needed for diagnosis. It provides an estimate of the valve area, transvalvular gradient and direct measurement of pulmonary pressures and hemodynamics. The pathophysiology and hemodynamics of AS are presented in Fig. 3. Cardiac catheterization is indicated in patients >35 years old or patients <35 years old with LV dysfunction or symptoms or signs suggesting CAD, and patients with 2 or more risks factors for premature CAD (7).

Two important considerations apply to the assessment of AS severity. First, AVA should be considered in relation to patient size. While a 1.0 cm^2 AVA may not reflect severe stenosis in a small patient, it may be associated with hemodynamic significance and symptoms in a larger person. Second, the gradients are affected by flow and may be low despite severe AS in the setting of LV systolic dysfunction. Doppler Echo during dobutamine infusion is useful to differentiate and guide therapy in such patients. Patients in whom the gradient increases with the dobutamine infusion are more likely to benefit from AVR. Those without increase in gradients despite the infusion (pseudostenosis) represent patients with marked irreversible systolic dysfunction without contractile reserve and does not benefit from surgical replacement.

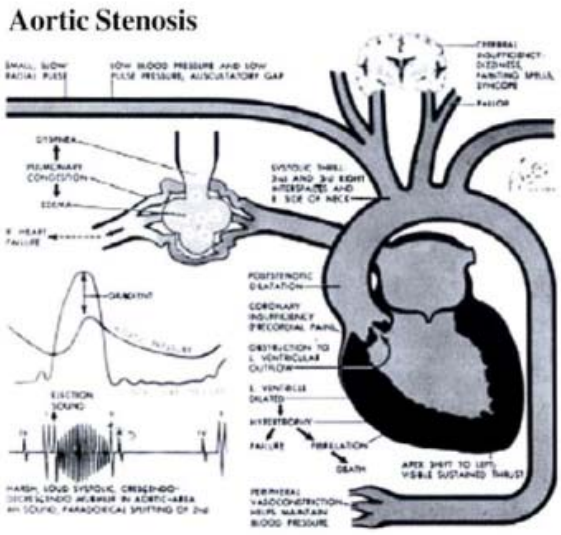


Figure 3. Aortic Stenosis: Pathophysiology and Hemodynamics. From F. Netter-CIBA Collection

Management

Patients with mild or moderate AS rarely have symptoms and do not require any specific medical therapy, except prophylaxis against infectious endocarditis. Some evidence have emerged regarding the statins use to slow the AS progression. Patients with mild AS generally does not has restriction for daily activities, but those with moderate AS should avoid moderate to severe physical exertion and competitive sports. Generally therapeutic decision making are based principally in the presence or absence of symptoms. The risk of sudden cardiac death (SCD) in asymptomatic patients with critical AS is less than 2% per year.

Many patients with severe AS develop symptoms within a few years. In the absence of serious comorbid condition, AVR is indicated in virtually all symptomatic patients with severe AS.

The use of ballon valvuloplasty in adults is not an effective long term treatment because of the high rate of restenosis and it does not prolong life. It is mainly used as a bridge in hemodynamically unstable patients who are at high risk for AVR or for palliation in patients with serious comorbid conditions, and patients who require urgent non cardiac surgery. The Ross procedure is a technique in wich the pulmonary valve of the patient is placed in the aortic position (autograft) and a homograft is placed in the pulmonary position. It does not require anticoagulation and the pulmonary autograft is capable of growing. Mostly reserved for children and women who like to become pregnant. Long term results are excellent.

In patients with severe AS who are waiting for surgery or those considered inoperable, the therapy is mainly directed to relief pulmonary congestion with cautious use of diuretics to avoid hypovolemia and hypotension. The use of vasodilators is contraindicated because reducing the systemic vascular resistance in the setting of a fixed cardiac output may cause syncope.

Aortic Regurgitation (AR)

Description

It is blood returning from the aorta back to the left ventricle during diastole. It results from failure of coaptation of the aortic valve leaflets, either because of valvular or aortic root disease. It is classified as chronic (compensated and decompensated) or acute and is very important to distinguish between them because they differ in the clinical presentation, natural history and treatment strategies

Etiology

AR has a surprisingly complex number of causes (Table 2). AR may be caused by intrinsic structural abnormalities

Table 2. Major Causes of Chronic Aortic Regurgitation

Annuloaortic ectasia	Behcet syndrome
Age related aortic dilatation	Hypertension
Cystic medial necrosis	Aortitis
(*Marfan's or isolated*)	(*syphilis, giant cell arteritis*)
Relapsing polychondritis	Congenital aortic regurgitation
Ehlers Danlos syndrome	Systemic lupus erythematosus
Drug induced valvulopathy	Rheumatoid arthritis
Whipple's disease	Bicuspid aortic valve
Crohn's disease	Trauma
Takayasu's arteritis	Endocarditis
Osteogenesis imperfecta	Rheumatic fever
Psoriatic Arthritis	Myxomatous degeneration
Ankylosing spondylitis	

of the aortic valve cusps and / or the wall of the aortic root. The latter represents the most common cause of chronic isolated severe AR in USA, secondary to age related degenerative or cystic medial necrosis. Between 40 to 60 % of surgical removed valves from patients with isolated severe AR are classified as idiopathic.

Pathophysiology

Chronic AR: It is a condition of chronic LV volume overload. The regurgitant volume increases the left ventricular end diastolic volume (LVEDV) but the left ventricle adapts to this increase in wall tension with eccentric hypertrophy. During this chronic compensated phase there is no significant increase in the end diastolic pressure (EDP) and the left ventricle is capable of preserving

forward stroke volume by producing a larger total stroke volume with each contractility (Frank Starling mechanism). The increased stroke volume results in bounding pulses with an increased systolic blood pressure (SBP). Peripheral vasodilatation and the large regurgitant flow result in a lower diastolic blood pressure (DBP) and a widened pulse pressure (SBP – DBP) a hallmark of chronic AR. However, over time the compliance of the LV reduces, progressive remodeling of the LV occurs leading to a chronic decompensated phase. This cause an increase in LVEDV with progressive cardiac dilatation causing a fall in ejection fraction and forward cardiac output.

Acute AR: In acute AR, the abrupt increase in large blood volume entering the non compliant LV results in sudden raise in LVEDP. The stroke volume and cardiac output (CO) decreases resulting in hypotension, pulmonary edema and rapid progression of hemodynamic collapse. Among the causes of acute AR are: acute infectious endocarditis, acute aortic dissection, traumatic rupture of the leaflets, acute prosthetic valve dysfunction and post aortic balloon valvuloplasty.

Natural History

Moderately severe chronic AR may be associated with a generally favorable prognosis for many years. Gradual deterioration of LV function may occur even during the asymptomatic phase and depressed LV function is among the most important determinants of mortality after AVR, particularly when the dysfunction does not improves after surgery.

Clinical Manifestations

The patients with chronic AR remain asymptomatic for many years until LV dysfunction supervenes. The main complains are: exertional dyspnea, orthopnea, paroxysmal nocturnal dyspnea, palpitations, angina (with or without epicardial coronary artery disease) mainly due to the increased in oxygen demand from the LV hypertrophy.

Physical Examination

- Bisferiens pulse: Double peak systolic impulse.
- Apical impulse is hyperdynamic and displaced downward and laterally signifying LV dilatation and hypertrophy.
- S1 is often normal but it might be muffled if PR interval is prolonged. The aortic component (A2) of the S2 may be decreased (with valvular disease) or increased (with aortic root disease).
- S3 may be present if dilatation of the LV occurs.
- A soft high pitched blowing diastolic decrescendo murmur best heard in the third left sternal border (if due to the valve) or the second right sternal border (if due to aortic root disease) at end of expiration with the patient sitting and leaning forward. The longer the murmur the more chronic and severe the AR.
- *Austin Flint murmur*: Low pitched mid and late diastolic murmur best heard at the apex due to the regurgitant aortic flow hitting the anterior mitral leaflet causing a relatively "mitral stenosis". This generally indicates the presence of severe AR.

In patients with chronic AR there is a wide pulse pressure due to elevated SBP created by an enhanced stroke volume and relatively low DBP created by the rapid run off of blood volume. This situation produces a myriad of peripheral physical stigmata. A partial list of these signs is included in Table 3.

In acute AR the apex is not lifted. The S1 may be soft due to the premature closure of the mitral valve (MV). The typical diastolic murmur of AR is shortened in duration, often difficult to heard, easily missed and peripheral signs are frequently absent.

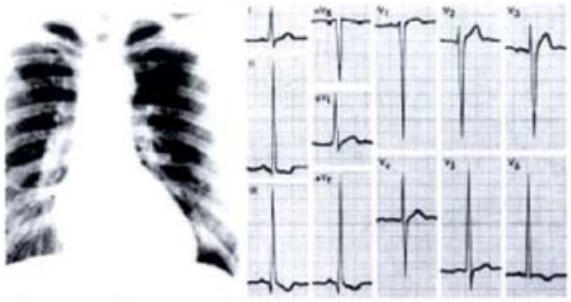
Table 3. Peripheral Physical Manifestations of Chronic Aortic Regurgitation

Name (*Eponym*)	Description
Becker sign	Arterial pulsations visible in the retinal arteries and pupils
Bisferiens pulse	Two palpable systolic impulses
Corrigan's pulse or Water Hammer	Rapid upstroke followed by marked and quick collapse
De Musset's sign	Synchronous head bobbing with each heart beat
Duroziez's sign	'to and Fro' (systolic and diastolic) murmur over the femoral artery when light compression with the diaphragm; but only systolic when compressed proximally and only diastolic when compressed distally
Hill sign	Popliteal cuff SBP exceeds brachial SBP at least 30 mmHg
Muller sign	Systolic pulsation of the uvula
Quincke's sign	Capillary pulsations visible in the lunula of the nailbed after holding the tip of the nail (best assessed by transmitting light through the patients fingertips)
Traube's sign	Pistol shot sounds over the femoral arteries in both systole and diastole

Diagnostic Techniques

- ECG: In chronic AR, LV hypertrophy, left axis deviation and left atrial abnormality are typical findings. The tall left precordial R waves may have associated peaked T waves, the "diastolic overload pattern" or the "strain pattern" with inverted T waves. In acute AR the ECG is notable for non specific ST- T wave abnormalities as illustrated in Fig. 4.
- CXR: Marked cardiomegaly in chronic AR with dilatation of the aortic knob. The *cor bovinum* of severe AR is the biggest and heaviest heart in cardiac pathology. In acute AR the heart looks with adequate size, but there is evidence of pulmonary congestion (See Fig 4).

Aortic Insufficiency



L. Ventricular Enlargement

L. Ventricular Hypertrophy and Dilatation: Increased Voltage of QRS in All Leads, Inverted T in Several

Figure 4. Aortic Regurgitation: Chest X Rays and Electrocardiographic Changes. From F. Netter-CIBA Collection

- Echocardiography: It is useful for determining the cause of AR, estimate its severity and asses overall LV size and function. There are several methods to estimate regurgitation volume and fraction and calculate the effective regurgitant orifice area. Transesophageal echocardiography (TEE) is used in cases of suspected valve ring abscess, to visualize congenital valvular abnormalities and to exclude aortic dissection.
- Cardiac catheterization: Usually the Echo/Doppler may determine the diagnosis and severity of AR. However, in questionable cases catheterization may be very helpful. Although CAD is much less prevalent in AR that it is in AS, coronary angiography is performed to asses the coronary anatomy if surgery is contemplated. In general coronary angiography is recommended in all patients with severe AR who are older than 50 years old and those with high risks factors (8). Aortography should be done to evaluate the degree of AR (angiographic grading scale). During cardiac catheterization, right heart hemodynamics measures are recommended (Fig. 5 illustrates the pathophysiology and hemodynamics of aortic insufficiency).

Aortic Insufficiency

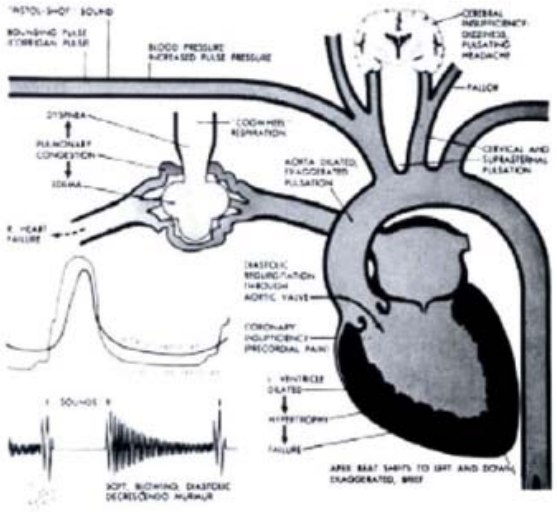


Figure 5. Aortic Regurgitation: Pathophysiology and Hemodynamics. From F. Netter-CIBA Collection

Management

Medical Therapy: Therapy is directed to slow the progression of LV dysfunction and limit LV dilatation. Vasodilators (ACE inhibitors, Calcium Channel blockers) form the mainstay of pharmacologic treatment in chronic AR. They are recommended in non surgical patients with severe chronic AR or asymptomatic patients with severe AR with LV dilatation and for patients with any degree of AR who have hypertension. The use of nifedipine in asymptomatic patients with severe AR and normal LV function can delay the need for surgery by 2 to 3 years (9). These patients need antibiotic prophylaxis for endocarditis. In acute AR the goal is hemodynamic stabilization before proceeding with surgical correction. This is achieved with intravenous vasodilators, diuretics and inotropic agents in severe cases. The intra aortic balloon pump (IABP) use is contraindicated in patients with moderate to severe AR.

Surgical Recommendations: There is no controversy with regard to AVR in symptomatic patients (NYHA class II-IV) and preserved LV systolic function. However controversy exists about the optimal timing of surgery in patients without symptoms and normal LV function.

Although AR should be corrected when more than mild symptoms develop there is compelling evidence that AR should be corrected before the onset of permanent LV damage even in asymptomatic patients. The extent of LV dilatation and dysfunction is crucial in the timing of surgery. Thus, to obtain a good outcome, AVR should be performed before the ejection fraction falls below 55% or the end systolic dimensions of the LV exceeds 55 mm (10).

Resumen

La enfermedad valvular del corazón (EVC) es un problema cardiovascular importante en la población adulta. El conocimiento de la fisiología envuelta, el reconocimiento y diagnóstico temprano es de suma importancia pare el médico primario que esta a cargo del manejo diario del paciente. Este artículo es el segundo de una serie de dos, en donde se discutirá la EVC en el adulto de una forma concisa y práctica (11). Cada tópico será presentado utilizando el siguiente formato: descripción, etiología, patofisiología, historia natural, herramientas diagnósticas y manejo. En éste segundo artículo discutiremos los trastornos de la válvula aórtica.

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