Left Ventricular Outflow Tract Obstruction
Obstrucción del tracto de salida del ventrículo izquierdo

Alejandro Zuluaga Santamaría1
Natalia Aldana S.1
Carolina Gutiérrez M.2
Sebastián Bustamante Z.2
Paula C. Muñoz G.3
Nicolás Zuluaga M.3

Summary
The left ventricular outflow tract (LVOT) is the anatomic structure through which the left ventricular stroke volume passes towards the aorta. The LVOT consists of three components: subvalvular component, which is delimited by the membranous and basal muscular portions of the interventricular septum; valvular component (the aortic valve); and supravalvular component. This academic review evaluates different obstructive pathologies of the LVOT, including entities located at the aortic valve level (valvular), in the ascending aorta (supravalvular), and in the proximal portion of the LVOT (subvalvular).

Resumen
El tracto de salida del ventrículo izquierdo (TSVI) es la estructura anatómica a través de la cual sale el flujo sistólico del ventrículo izquierdo (VI) hacia la aorta. El TSVI está conformado por tres componentes: subvalvular, el cual es delimitado por el septo interventricular en sus porciones membranosas y muscular basal y la válvula anterior de la válvula mitral; el componente valvular, corresponde a la válvula aórtica, y el supravalvular. En esta revisión académica se evaluarán las patologías obstructivas del tracto de salida del ventrículo izquierdo, incluyendo entidades localizadas en el sector valvular aórtico (valvulares), en la aorta ascendente (supravalvulares) y en el tracto de salida del ventrículo izquierdo proximal al plano valvular (subvalvulares).

Subvalvular obstruction
The subvalvular left ventricular outflow tract (LVOT) is delimited by the interventricular septum in its basal membranous and muscular portion and fibrous continuity tissue between the aortic valves and the mitral valve (anterior valve to the mitral valve). Through these structures passes the systolic flow of the left ventricle before reaching the aortic valve. Both components are highly mobile so the subvalvular LVOT area may be modified during the cardiac cycle (1).

Aortic subvalvular obstruction may be the consequence of different pathophysiological mechanisms: dynamics, such as those that can present after mitral and aortic valve surgery; mixed, as usually occurs in hypertrophic cardiomyopathy and mechanisms in which a fixed anatomical substrate prevails as in the membranes or the diaphragms.

Hypertrophic cardiomyopathy (HCM)
The accepted clinical definition for HCM is left ventricular (LV) hypertrophy associated to a non-dilated ventricular chamber, a condition that can’t be explained by heart or systemic disease (2-5). HCM is caused by mutations in the genes encoding cardiac sarcomeres proteins. It is an autosomal dominant disease with variable expression and penetrance. The usual morphological phenotype is the thickening of the wall of the left ventricle. However, because of the multiplicity of genetic mutations and their transmission, the cardiac in-
volvement may vary and rarely appears with normal wall thickness of the LV or with compromise of the right ventricle (RV) (4). Accepted diagnostic criteria for HCM consist of a maximum wall thickness of LV ≥15 mm and a ratio between the thickness of the septal wall and that of the lower wall higher than 1.5. In children, a thickness of the wall ≥ 2 standard deviations above the mean (score z ≥2) is used (6). The clinical presentation of HCM is varied and in all age groups, the majority of patients have a normal life expectancy without disability or need for major therapeutic procedures. When manifestations occur clinical symptoms usually come in three forms: sudden death due to malignant arrhythmias (more common in children under 35 years and athletes), heart failure with exertional dyspnea and paroxysmal or chronic atrial fibrillation (6). The HCM has different subtypes: septal, asymmetric, midventricular, apical and concentric, among others (7,8).

The mechanism causing obstruction of the outflow tract of the LV at the HCM is mixed:

1. **Anatomical substrate**
   - Protrusion of the hypertrophic basal interventricular septum towards the exit tract (figure 1).
   - Anomalies of the valvular and subvalvular mitral apparatus, including elongated mitral valves, small mitral annulus or endocardial thickening of the ventricular surface of the anterior valve (9).
   - Subvalvular abnormalities include hypertrophy and variants in the papillary muscles, which can be bifid or have variation in the number of implantation, as in the case of short tendon cords or direct insertion of the papillary muscles in the mitral valves (10). The anterolateral displacement of the papillary muscles may contribute to the obstruction of the outflow tract. These alterations may produce obstruction even in patients with ventricular wall thickness very close to normal (11,12).

2. **Proposed dynamic mechanisms**
   - Protrusion of the hypertrophic septum generates acceleration of flow in the LVOT and reduction of lateral pressure, triggering a venturi effect that “attracts” the anterior valve of the mitral valve and causes it to contact the interventricular septum accentuating the obstructive effect. This phenomenon is known as systolic anterior movement (SAM) of the anterior valve of the mitral valve (Figure 1b and d). When SAM is present, it produces flow of mitral insufficiency (13-16).
   - The second mechanism suggests an abnormal ventricular morphology with an unusual relationship of the output and input tracts of the LV. A decrease in the aortomitral angle of the LVOT, including the degree of hypertrophy and the precise location of the thickening of the myocardium, evaluation of the valvular and subvalvular mitral apparatus and presence of myocardial fibrosis that is manifested in late enhancement images in inversion sequences (22). Cardiac MRI can also be used to measure the area of the hole of LVOTO, which is determined by transplanar flow planimetry using phase contrast sequences (figure 1f), which has demonstrated to be a reliable parameter for characterizing patients with obstructive HCM. Contrary to routinely used parameters on echocardiography, MRI is free of interobserver variability, conditions of image variability and is a non-invasive method (22-24). Measurement of the tract area by MRI is useful to define the degree of obstruction. An outflow tract <2.7 cm² during systole, with cardiac MR, has a sensitivity and specificity of 100% to differentiate obstructive and non-obstructive form of HCM (25,26). The main role of MRI in patients with HCM is to clarify the diagnosis and phenotype (6,27-31). In patients in whom echocardiography is inconclusive usually through poor acoustic window or when hypertrophy is located in regions that are not easily visualized by this method, cardiac MRI should be performed (6,32). Late enhancement sequences allow the identification of areas of myocardial fibrosis in patients with HCM. Patients with evidence of myocardial fibrosis and CMR have been associated with risk markers for sudden death, malignant ventricular arrhythmias and electrocardiographic disorders (33-38).

Obstruction of the left ventricular outflow tract (LVOTO) caused by SAM is found in one-third of patients with HCM at rest (13,15) and occurs in up to two thirds of symptomatic patients which have no obstruction at rest but do so during manoeuvres that reduce preload and afterload or increase contractility (20). LVOTO in patients with HCM is considered clinically significant when a gradient greater than 30 mm Hg at rest or greater than 50 mm Hg is encountered during manoeuvres by echocardiography, such as exercise, Valsalva or pharmacological stress (21). Surgical intervention is recommended in patients who have not responded to pharmacological management. Septal ablation with alcohol is recommended in patients who are not candidates for surgery and older patients regardless of whether or not they are candidates for surgical management (6).

Transthoracic (TT) or transesophageal (TE) echocardiography with Doppler is usually the first test performed when there is suspicion of LVOTO or HCM, for the identification and classification of the severity of subvalvular stenosis according to the pressure gradient. Cardiac MRI may provide important additional information to define in detail the anatomy of the LVOT, including the degree of hypertrophy and the precise location of the thickening of the myocardium, evaluation of the valvular and subvalvular mitral apparatus and presence of myocardial fibrosis that is manifested in late enhancement images in inversion sequences (22). Cardiac MRI can also be used to measure the area of the hole of LVOTO, which is determined by transplanar flow planimetry using phase contrast sequences (figure 1f), which has demonstrated to be a reliable parameter for characterizing patients with obstructive HCM. Contrary to routinely used parameters on echocardiography, MRI is free of interobserver variability, conditions of image variability and is a non-invasive method (22-24). Measurement of the tract area by MRI is useful to define the degree of obstruction. An outflow tract <2.7 cm² during systole, with cardiac MR, has a sensitivity and specificity of 100% to differentiate obstructive and non-obstructive form of HCM (25,26). The main role of MRI in patients with HCM is to clarify the diagnosis and phenotype (6,27-31). In patients in whom echocardiography is inconclusive usually through poor acoustic window or when hypertrophy is located in regions that are not easily visualized by this method, cardiac MRI should be performed (6,32). Late enhancement sequences allow the identification of areas of myocardial fibrosis in patients with HCM. Patients with evidence of myocardial fibrosis and CMR have been associated with risk markers for sudden death, malignant ventricular arrhythmias and electrocardiographic disorders (33-38).
**LVOTO by membranes, diaphragms and subvalvular infundibulum**

They may have different morphologies; the most frequent form is a fibroelastic tissue membrane or spine that extends from the endocardial surface of the basal septum and protrudes to the outflow tract, being able to extend to the base of the anterior valve of the Mitral valve (Figure 2). Indications for surgical treatment of patients with membranes, diaphragms or infundibuli of the ventricular outflow tract depend on the clinical manifestations, the gradient pressure and morphology of the lesions (1,12).

**LVOTO in patients after closure of ventricular septal defect (VSD)**

La obstrucción subvalvular también se ha informado luego del cierre del defecto de septo ventricular. Subvalvular obstruction has also been reported after surgical closure of ventricular septal defects and is believed to be due to proliferation of fibrotic tissue at turbulent flow sites (39). The membranes located immediately adjacent to the aortic valve or extending to the anterior Mitral valve are more likely to lead to progressive obstruction and aortic valve injury with insufficiency (Figure 3) (1,40).

**LVOTO after Mitral valve surgery**

In patients undergoing Mitral valve replacement, outflow tract obstruction is one of the postoperative complications (22). Obstruction occurs by a high profile protrusion of the prosthetic valve to the outflow tract or by an abnormal position of the prosthesis at the subvalvular level. If the prosthesis is not properly oriented, one of the ends can obstruct the LVOT (figure 4) (41).

**Sigmoid septum**

The interventricular sigmoid septum involves the protrusion of segments of the septum to the outflow tract of the LV and appears, usually, in elderly patients with a history of hypertension with low-grade concentric hypertrophy of the LV myocardium (thickness of the myocardium in diastole usually between 12 to 16 mm) (figure 5). The decrease in the aortoseptal angle Is typical of patients with sigmoid septum. Recently It has been proposed that the sigmoid configuration of the septum may lead to dynamic obstruction of the LVOT even without ventricular hypertrophy. In some cases the sigmoid septum may cause stenosis of the LVOT with dynamic obstruction and an increase in the pressure of the LV, especially if there is hypertrophy, physical exercise, general anaesthesia, acute myocardial infarction (AMI), dehydration or aggressive management of hypertension (42,43).

**Valve obstruction**

**Aortic valve stenosis**

Aortic stenosis is a common disease that usually affects older patients. There are two important factors that make it one of the most common valvulopathies: a. approximately 1-2 % of the population is born with a bicuspid aortic valve, which is prone to stenosis and b. aortic stenosis develops with age.

Calcified aortic stenosis was considered a degenerative lesion; However, it shares many characteristics with coronary artery
disease. Both are more common in men, older people, patients with hypercholesterolemia and both are derived from a chronic inflammatory process. Aortic stenosis differs from sclerosis due to the degree of valve involvement. In aortic sclerosis, the valves are abnormally thickened and the obstruction of the outflow tract is minimal. In contrast, in aortic stenosis the functional area of the leaflets has diminished sufficiently to cause measurable flow obstruction (44).

The bivalve aorta (Figure 6) occurs by abnormal valvulogenesis with the formation of a small cusp and a larger cusp, usually by congenital fusion of one of the valvular commissures. This disposition makes the valve more susceptible to trauma and finally leads to calcification and fibrosis. By the time the obstruction of the outflow tract causes significant symptoms, the valve is a rigid, calcified mass that makes it difficult to determine the etiology of this process. This type of valve configuration is usually not obstructive early. Valvular stenosis develops between the fourth and sixth decade of life and represents > 50% of cases of aortic stenosis disease in people under 70 years of age. The presence of a bivalve aortic valve is associated with an increase in the incidence of complications such as stenosis, insufficiency, endocarditis and aneurysmal dilatation of the aorta (1).

In developed countries, aortic stenosis is usually related to risk factors similar to those which cause atherosclerosis. Another major cause of aortic stenosis is rheumatic disease, which generates inflammatory adhesions of the valvular cusps that lead to fusion of the commissures and, consequently, to valve stenosis and/or regurgitation (45,46). As the compromise is greater, ventricular dysfunction occurs. Initially, the patients are asymptomatic and a systolic breath can be found in an incidental manner. As the disease progresses, the symptoms it produces are angina, dyspnea, syncope and, finally, heart failure. Once the symptoms appear, survival without surgical treatment is 2 to 3 years (45).

Doppler ultrasound can be performed in most patients, but the severity of the stenosis may be underestimated if the quality of the image is poor and is affected by technical factors. CT is useful for the quantification of valvular calcification (severe: > 1000 Agatston units) and in patients to whom they will practice transcatheter replacement, to undergo planimetry and take measurements of the valvular ring area, valve leaflet length and the distance from the ring to the coronary ostium; It is also sought to determine the dimensions of the aortic root, the severity of the vascular disease and the state of the coronary arteries (Figure 7) (47).

MRI allows a better characterization of the myocardium in patients with aortic stenosis and the detection of fibrosis with late enhancement sequences. A pattern of patched and subendocardial enhancement has been described, which predominates in basal segments. It has been shown that the late enhancement, as an indicator of myocardial fibrosis, is a factor of independent risk of mortality in patients with moderate or severe aortic stenosis, and is associated with a worse prognosis after valvular replacement (45, 48-50).
The severity of aortic valve stenosis is classified according to the following parameters (48):

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<th>Low</th>
<th>Moderate</th>
<th>Severe</th>
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<tr>
<td>Valve area (cm²)</td>
<td>1.6-2.0</td>
<td>10-2.5</td>
<td>&lt; 1.0</td>
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<td></td>
<td>2.0-2.9</td>
<td>3.0-3.9</td>
<td>4.0</td>
</tr>
<tr>
<td>Estimated gradient (mm Hg)</td>
<td>20-35</td>
<td>36-63</td>
<td>&gt; 64</td>
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Figure 5. Aortoseptal angle in patient with sigmoid septum. CMRI, SSFP (steady-state free precession) long axis projection of three chambers cine sequence. Basal septum protrusion (arrow) to the outflow tract in a patient with chronic hypertension, with aortoseptal angle and discreet concentric hypertrophy of the myocardium.

Figure 6. Cardiac CT in a patient with bivalve aorta without stenosis. 3D reconstruction in systole a) and diastole b).

Figure 7. 78-year-old patient with severe aortic valve stenosis. Patient in protocol for TAVI planning, cardio-triggered CT, a) orthogonal multi-planar reconstructions of the aortic valve in systole and b) of the valve ring, c) three-dimensional reconstruction with superior sight of the aortic valve in diastole, d) multi-planar reconstruction long axis of three chambers. Anatomically trivalent aortic valve patient, but with complete fusion of the right and left valves, which causes the valve to behave physiologically as a bivalve with semilunar opening in systole (a). A valvular area in systole is identified by planimetry of 0.9 cm² that correlates with severe stenosis. The extent of aortic valve calcification is identified through the outflow tract to the base of the anterior valve of the Mitral valve, a finding that must be reported since it significantly increases the risk of perforation in TAVI procedures (d).

Figure 8. 2 year old patient with Williams-Beuren syndrome with supravalvular aortic stenosis. Study of triggered cardio CT, sagittal reconstruction of the aorta and its root where aortic ascending stenosis from the sinotubular junction to the origin of the brachiocephalic trunk with decreased concentric vascular lumen is identified.
Supravalvular obstruction

Aortic supravalvular lesions are the rarest cause of LVOTO. They are characterized by a diffuse or focal stenosis that initiates at the sinotubular junction and occasionally extends throughout the ascending aorta. It rarely involves the aortic arch.

Aortic supravalvular stenosis is often associated with Williams-Beuren syndrome (Figure 8). This is an autosomal condition which occurs in 1 in 20,000 live births and in which 71% of the time there is supravalvular aortic stenosis; It is also accompanied by mental retardation, stenosis of the pulmonary arteries, prolapse and up to 50% of patients present aortic valve abnormalities, mainly aorta bivalve. This syndrome can be accompanied by alteration in the perfusion secondary to some degree of aortic valve adhesion in the sinotubular junction that restricts the diastolic filling of the coronary arteries (1).

Stenosis of the sinotubular region can be surgically extended when the patient has symptoms such as angina, dyspnea and syncope or when there is an average pressure gradient greater than 50 mm Hg (1).

Conclusion

Currently, cardiac magnetic resonance plays a leading role in the evaluation of patients with obstruction of the left ventricle, especially in the assessment of hypertrophic cardiomyopathies and in patients where echocardiography is unfinished or technically limited. The detection of myocardial fibrosis using late enhancement allows detecting those patients who are at increased risk of sudden death, malignant arrhythmias and electrocardiographic disorders.

References


Correspondence

Carolina Gutiérrez Márquez
CediMed
Calle 7 # 39-197
Medellín, Colombia
carogutmar@gmail.com

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