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Valve disease in women

Valvulopatías en la mujer

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INTRODUCTION

Valvular disease (VD) has a prevalence of 2.5% in the population, with an increase in degenerative etiologies and in older adults.[1] Women and men are equally likely to develop VD, with some sex-specific differences. In general, women suffer more mitral valve diseases, especially mitral valve prolapse (MVP) and rheumatic valve disease (RVD), and men have more aortic valve diseases, such as aortic insufficiency (AI) and aortic stenosis (AS).

AORTIC VALVE DISEASE (AVD)

Men are at higher risk of developing AS; it is more common in the elderly, mostly women. Women have less valvular calcium but more fibrosis. At presentation, they are older, hypertensive, with worse functional class but better left ventricular ejection fraction (LVEF) with hypertrophic ventricles. Greater low-flow, low-gradient paradoxical AS and less amyloidosis.[1,2] Aortic insufficiency is more frequent in men associated with bicuspids (BAV), with a 2% male/female ratio of 3:1. Women will develop more AS and men AI aneurysms, aortic dissection, and endocarditis.[2]

MITRAL VALVE DISEASE (MVD)

RVD is responsible for the most significant global burden of VMD and is more common among women in all age groups.[1] New mechanisms for the pathogenesis of VRD suggest that Prothymosin alpha, associated with Estrogen Receptor alpha activity, would have a role in the sexual predisposition of RVD, perhaps explaining the higher incidence of rheumatic valve disease in women.[3]

Mitral valve insufficiency (MVI) is women's most common valve pathology. It can be primary: rheumatic, valve prolapse (myxomatous degeneration, thickening of the leaflets), or secondary: due to alteration in the geometry of the left ventricle, due to ischemic heart disease, or other dilated heart diseases. Women have more symptoms of heart failure (CHF), their condition is underestimated, and fewer are referred for intervention.[1,2]

Mitral stenosis (MS) is more common in women; its etiology is rheumatic or degenerative, associated with calcification of the mitral annulus at an advanced age. Some cases are related to chest radiation, carcinoid heart disease, or inherited metabolic disorders. It is classified as severe when the mitral valve area is ≤ 1.5 cm^2.[1,3]

TRICUSPID VALVE DISEASE (TVD)

Tricuspid regurgitation (TR) can be due to primary causes (congenital, genetic, endocarditis, rheumatic compromise, or device-related anomalies) or secondary causes (right ventricular dilatation and dysfunction). TR is more common in women/men in a 1.6:1 ratio. Once it develops in them, it progresses more rapidly, possibly due to anatomical differences in the annulus more elastic, cellular, and smaller[1] than in men, that have myocardium fibers in the annulus.

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In women, secondary TR occurs at an older age than in men (72 [62-79] years vs 70 [61-77] years; p = 0.003) and is more symptomatic. The most common etiology in women is isolated TR or is related to left-sided valvular disease.[1] In the imaging evaluation of the severity of TR, the quantification of the size of the cardiac cavities, according to sex and body surface, must be considered. Sex-specific dimension data now exist for different cardiac imaging modalities.[4,5]

VALVE INTERVENTIONISM

AVD. Women treated with surgical aortic valve replacement (SAVR) are older than men, with more advanced disease and higher operative

Table 1: Valvular disease in pregnancy.

Physiological changes
Increased blood volume and preload, increased cardiac output and rate
Decreased vascular and pulmonary resistance. Decreased blood pressure
Hypercoagulability. Cavity dilation

Valve stenosis	Poorly tolerated when severe First-line beta-blockers and diuretics Consider valvuloplasty if medical therapy fails. If surgery is required, preferably in the 2nd trimester Fetal adverse events are increased (especially mortality) with surgery with the fetus *in utero* Gradients rise throughout pregnancy	**Aortic stenosis**	**Severe symptomatic aortic stenosis** **WHO class IV (pregnancy is contraindicated)**
			Congenital > AVB High risk in the 2nd and 3rd trimesters Adverse fetal events
		Mitral stenosis	**Severe mitral stenosis** **mWHO class IV (pregnancy is contraindicated)**
			Congenital, rheumatic High risk of supraventricular arrhythmias (atrial fibrillation) Adverse fetal events
		Pulmonary stenosis	Congenital Generally better tolerated The right ventricle should be monitored, and the appearance of symptoms
Valvular insufficiency	Better tolerated except when accompanied by severe ventricular dysfunction Symptoms of dyspnea and heart failure in advanced stages They tend to be more symptomatic at the end of pregnancy or postpartum (close monitoring for signs of overload in the early postpartum period)	**Aortic/mitral valve insufficiency**	Ideally, surgical management before pregnancy Avoid pregnancy if severe aortic/mitral regurgitation and LVEF < 30% Diuretic management, if required. Avoid surgery during pregnancy
		Pulmonary insufficiency	Congenital. Late postoperative of ROSS or tetralogy of Fallot Evaluate failure of the right ventricle

Table 1 continues: Valvular disease in pregnancy.

Prosthetic valves	Maternal and fetal adverse events (mainly with mechanical valves) Ideally, pregnancies with biological prostheses Preconception couple and family counseling consultation and clarify the risks Analyze time in therapeutic range adherence to Warfarin Weekly monitoring of defined anticoagulant therapy	**Biological valves**	Use of aspirin in pregnancy. Fewer complications than mechanical valves but higher than other cardiac pathologies in pregnancy. Fewer complications as long as the Bioprosthesis is functioning normally. Fewer complications as long as the Bioprosthesis is functioning normally
		Mechanical valves	**WHO class III mechanical valve (significant mortality and morbidity)**
			Warfarin associated with teratogenic effects but dose-dependent in the 1st trimester: **First trimester:** warfarin, if the dose is ≤ 5 mg/day, is the choice, or LMWH as an alternative, but always with measurement of activated anti-factor Xa levels* **Second trimester:** warfarin independent of dose **Third trimester:** dose-independent warfarin with the transition at 36 weeks to UFH by nomogram or LMWH based on activated anti-factor Xa levels* Vaginal delivery if at least two weeks of discontinuation of Warfarin and bridging suspension with UFH 4-6 hours before delivery

mWHO = modified obstetric risk classification World Health Organization. BAV = bicuspid aortic valve.
LMWH = low molecular weight heparin. UFH = unfractionated heparin.
* Recommended activated anti-factor X levels of 0.8 to 1 U/mL for the aortic valve and 1 to 1.2 U/mL for the mitral or tricuspid valve.

mortality. Female gender is considered an independent predictor of post-SAVR operative mortality and morbidity.[6] Transcatheter aortic valve implantation (TAVI) results by gender show no differences in implant success; the female sex was associated with increased vascular complications and major bleeding but a lower incidence of paravalvular leak, pacemaker, and better medium-term survival.[7]

MVD. The registries show that the women were taken significantly less or later to mitral surgery (repair/replacement). In degenerative MI, women are less frequently taken to repair (44 vs 31.9%, p = 0.001), with slightly lower long-term survival.[1]

In percutaneous therapy in severe functional MR with TEER (Transcatheter Edge-to-Edge Repair) with more MitraClip evidence, women represented only 36% of patients in the COAPT study and 25% in MITRA-FR, being younger, but with worse quality of life and functional capacity. TEER resulted in better clinical outcomes vs. medical therapy, regardless of gender; the reduction in CHF hospitalizations was less pronounced in women. Female gender was independently associated with a lower adjusted risk of death at two years (HR, 0.64; 95% CI, 0.46-0.90; p = 0.011).[1]

In RVD, the treatment of choice is mitral valvuloplasty with a catheter and a balloon, followed by valve surgery.[8]

TVD. Regarding the surgical results in tricuspid insufficiency (TI), the repair has higher survival, and there is no difference by sex in terms of results.[1]

PREGNANCY AND STROKE

Moderate or severe EV in pregnancy is complex and requires an experienced cardio-obstetric

multidisciplinary team. Significant MS and symptomatic severe AS are poorly tolerated. Percutaneous commissurotomy should be considered in MS with severe symptoms (NYHA III-IV) or pulmonary artery systolic pressure > 50 mmHg and unresponsive to medical treatment. Aortic balloon valvuloplasty can be regarded as salvage therapy in AS with severe symptoms despite medical treatment, and definitive interventions will be defined after delivery. Valvular insufficiencies are usually better tolerated, except when there is associated ventricular dysfunction.[9]

If valve surgery is required and the fetus is viable, a cesarean section will be performed, followed by valve surgery. Valve surgery with extracorporeal circulation with a fetus in utero has fetal mortality of 15-56%. Therefore, it should be restricted to situations with life-threatening risk for the mother and no percutaneous management option.

Pregnant women with mechanical prostheses are very complex since there is no ideal anticoagulant regimen, so it is necessary to weigh the risks for the mother and the fetus (Warfarin according to the dose or low molecular weight heparin but always with monitoring of antifactory Xa levels)[9,10] *(Table 1)*.

Women with VD have been underrepresented in studies and tend to be diagnosed and referred for interventions later, leading to adverse outcomes[1,2] summarizes the complex relationship between pregnancy and valvular heart disease.

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