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REVIEW ARTICLE

Paradoxical aortic stenosis: A systematic review☆

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Abstract Aortic stenosis (AS) is a complex systemic valvular and vascular disease with a high prevalence in developed countries. The new entity ''paradoxical low-flow, low-gradient aortic stenosis'' refers to cases in which patients have severe AS based on assessment of aortic valve area (AVA) ($\leq$1 cm^2) or indexed AVA ($\leq$0.6 cm^2/m^2), but paradoxically have a low mean transvalvular gradient (<40 mmHg) and a low stroke volume index ($\leq$35 ml/m^2), despite preserved left ventricular ejection fraction (>50%).

A search was carried out in the PubMed database on paradoxical AS for the period 2007-2014. A total of 57 articles were included for this review. The prevalence of paradoxical AS ranged from 3% to 35% of the population with severe degenerative AS. It was more frequent in females and in older patients. Paradoxical AS was associated with characteristic left ventricular remodeling as well as an increase in systemic arterial stiffness. It was noted that there may be errors and inaccuracies in the calculation of AVA by the continuity equation, which could erroneously suggest the paradoxical phenotype. There are new diagnostic methods to facilitate the study of AS, such as aortic valve calcium score, valvuloarterial impedance and the longitudinal mechanics of the left ventricle. With regard to its natural history, it is not clear whether paradoxical AS corresponds to an advance stage of the disease or if paradoxical AS patients have a distinct phenotype with specific characteristics. Valve replacement, either surgical or percutaneous, may be indicated in patients with severe and symptomatic paradoxical AS.

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PALAVRAS-CHAVE
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Estenose aórtica paradoxal – revisão sistemática

Resumo A estenose aórtica (EA) é uma doença valvular e vascular sistémica, com elevada prevalência nos países desenvolvidos. A nova entidade «EA grave paradoxal, baixo fluxo/baixo gradiente» refere-se aos casos em que os doentes apresentam EA grave com base na avaliação da área valvular aórtica (AVA) ($\leq 1\,cm^2$) ou AVA indexada ($\leq 0{,}6\,cm^2/m^2$), mas que paradoxalmente tenham um gradiente médio transvalvular baixo (< 40 mmHg), com baixo volume de ejeção sistólico indexado ($\leq 35\,ml/m^2$), apesar de uma fração de ejeção do ventrículo esquerdo preservada (> 50%).

Foi realizada uma pesquisa através da base de dados da *PubMed* sobre a EA paradoxal no período de 2007-2014. Para a presente revisão foram incluídos um total de 57 artigos.

A prevalência da EA paradoxal variou entre 3-35% da população com EA degenerativa grave. Foi mais frequente no género feminino e nos doentes com idade mais avançada, e esteve associada a uma remodelagem característica do ventrículo esquerdo, bem como a um aumento da rigidez vascular arterial sistémica. Assinala-se a possibilidade de erros e imprecisões no cálculo da AVA pela equação da continuidade, que podem sugerir o fenótipo paradoxal. Existem outros métodos de diagnóstico que podem auxiliar no estudo da EA, como o *score* de cálcio, a avaliação da impedância valvuloarterial e o estudo da mecânica longitudinal do ventrículo esquerdo. Relativamente à história natural, não é claro que a EA paradoxal corresponda a uma fase avançada da doença valvular aórtica, ou se representa um fenótipo distinto com especificidades próprias. A terapêutica de substituição valvular, cirúrgica ou percutânea, pode estar indicada no doente com EA paradoxal grave e sintomática.

List of abbreviations

AF	atrial fibrillation
AS	aortic stenosis
AVA	aortic valve area
AVAi	indexed aortic valve area
AVA_{proj}	projected aortic valve area
BNP	brain natriuretic peptide
BP	blood pressure
BSA	body surface area
CAD	coronary artery disease
CT	computed tomography
ELCo	energy loss coefficient
GLS	left ventricular global longitudinal strain
HR	heart rate
LF-LG-AS	low-flow, low-gradient aortic stenosis
LV	left ventricular
LVEF	left ventricular ejection fraction
LVOT	left ventricular outflow tract
MPG	mean pressure gradient between aorta and left ventricle
PFV	peak flow velocity
PVR	peripheral vascular resistance
SAC	systemic arterial compliance
SAVR	surgical aortic valve replacement
SVI	stroke volume index
TAVR	transcatheter aortic valve replacement
Zva	valvuloarterial impedance

Introduction

Aortic stenosis (AS) is the most common valve disease in Europe, and is most often due to degenerative etiology.[1] It is estimated to affect 2-7% of the population aged over 65 years.[2] Degenerative AS progresses slowly and is associated with various clinical manifestations including angina, syncope, cardiac rhythm disturbances, heart failure and sudden death.[1]

According to the European and American guidelines on valvular disease, severe AS is defined as aortic valve area (AVA) of $\leq$1 cm^2, mean pressure gradient (MPG) between aorta and left ventricle of $\geq$40 mmHg, or peak flow velocity (PFV) of $\geq$4 m/s, with normal cardiac output.[1,3]

In the absence of valve replacement, AS evolves to a form of heart failure with left ventricular (LV) dilatation and dysfunction. In this stage there is a reduction in transvalvular gradients, caused by diminished systolic flow through the aortic valve due to impaired LV systolic function. This entity, first described by Carabello et al. in 1980,[4] is termed low-flow, low-gradient aortic stenosis (LF-LG-AS). It is characterized by an AVA of $\leq$1 cm^2 or indexed AVA (AVAi) of $\leq$0.6 cm^2/m^2, MPG of <40 mmHg and left ventricular ejection fraction (LVEF) of $\leq$40%. Patients with LF-LG-AS account for only 5-10% of those with severe AS.[5–7]

In 2007, Hachicha et al.[8] described for the first time a form of AS with reduced systolic flow but, paradoxically, preserved LVEF. This new entity, which they termed paradoxical low-flow, low-gradient aortic stenosis, was defined as AVA of $\leq$1 cm^2, MPG of <40 mmHg, and stroke volume index (SVI) of