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Published in:
European Journal of Radiology

DOI:
[10.1016/j.ejrad.2020.108971](https://doi.org/10.1016/j.ejrad.2020.108971)

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Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Westenbrink, B. D., de Boer, R. A., & Vliegenthart, R. (2020). Aortic regurgitation, a forgotten valve disease in hypertrophic cardiomyopathy? *European Journal of Radiology*, 126, [108971].
<https://doi.org/10.1016/j.ejrad.2020.108971>

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Aortic regurgitation, a forgotten valve disease in hypertrophic cardiomyopathy?

Hypertrophic cardiomyopathy (HCM) is the most common inherited heart disease, and is usually defined as “the presence of increased left ventricular (LV) wall thickness, that is not solely explained by abnormal loading conditions” [1]. Most cases of HCM are caused by autosomal dominant mutations in sarcomeric proteins, supplemented with rare genetic, metabolic or infiltrative disorders [1]. Hypertrophy in HCM is often asymmetrical, mostly septal, and disproportionate septal hypertrophy may cause left ventricular outflow tract (LVOT) obstruction, in up to approximately 30 % of HCM patients. LVOT obstruction is not only related to the degree of septal hypertrophy, but also to anatomical variations in the size and shape of the mitral valve leaflets that promote systolic anterior motion (SAM) of the anterior mitral valve [2]. Accordingly, surgical treatment of patients with Hypertrophic Obstructive Cardiomyopathy (HOCM) often involves a combination of septal myectomy and mitral valve repair [1,2]. The genetic underpinnings of mitral valve abnormalities in sarcomeric HCM are not well described and seem to exceed a simple pressure driven movement, rather involving the valvular apparatus itself as well. It is possible that other heart valves display similar anatomical variations.

In this issue of the European Journal of Radiology Chen et al. sought to determine the incidence of aortic regurgitation (AR) in patients with HCM and also explore the potential mechanisms [3]. For this purpose a retrospective analysis of echocardiographic and cardiac magnetic resonance studies was performed in 105 patients with HCM, 50 patients with hypertension and 50 healthy controls. HCM was defined according to contemporary criteria [1], and 48 (46 %) HCM patients with a spontaneous or provoked gradient over the LVOT of > 30 mmHg were classified as HOCM. The presence and severity of AR was systematically evaluated as well. The authors developed a new method to define and quantify morphological changes to the subaortic complex in order to allow detailed exploration of putative mechanisms.

The most important finding of the study was that the incidence of AR was significantly higher in patients with HCM (36 %) compared to patients with hypertension (17 %) or healthy controls (10 %). Moreover, the incidence of AR was twice as high (52 %) in patients with HOCM compared to patients with HCM without obstruction (23 %). Interestingly, detailed analysis of the subaortic complex revealed a potential link between AR and the severity of LVOT obstruction. Indeed, protrusion of the intraventricular septum into the LVOT, length of the anterior mitral leaflet, systolic anterior motion of the mitral valve and the incidence of mitral regurgitation were all higher in patients with AR. Accordingly, the effective LVOT width during systole was significantly reduced in patients with AR. The parameters mentioned above were all univariate predictors of AR, while LVOT obstruction and advanced age were independent predictors of AR. In summary, the article by Chen et al. suggests that the incidence of AR is increased in patients with HOCM. Moreover, the mechanisms responsible for AR in HOCM appear to be related to structural changes within the subaortic complex.

The article by Chen et al. is provocative and challenges contemporary understanding of the pathophysiology of HOCM. In addition, the authors should be applauded for their new and intuitive method to quantify multiple aspects of the subaortic complex. This new method provides mechanistic insights into the development of AR that were not otherwise possible. For instance, the degree of protrusion of the intraventricular septum into the LVOT was associated with AR, whereas the position of the maximal septal wall thickness relative to the aortic valve was not. While the model requires prospective validation in other cohorts, it could have future diagnostic and therapeutic implications.

Despite its merits, several important questions remain. First, from a clinical perspective, AR has never been denoted as an important clinical problem in HOCM, and these results suggest it may have been overlooked for decades. The most intriguing question is related to the putative mechanisms of AR in HCM. The authors speculate that “changes to the subaortic complex and the velocity, direction, and dynamics of the systolic jet” are likely to contribute to the development of AR. But it is difficult to understand how systolic outflow tract obstruction would affect aortic valve patency during diastole. The authors suggest that asymmetric hypertrophy could cause distortions of the aortic annulus that impede valve closure, analogous to AR in patients with aortic root dilatation. Unfortunately, information on the size and shape of the aortic valve or morphological classifications of the aortic annulus that could support this hypothesis is not provided. A recent study in 2640 patients with HCM recently indicated that the incidence of anatomical variations to the aortic valve in HCM were comparable to the normal population [4]. However, the prevalence of aortic root dilatation has reported to be slightly higher in patients with HCM [5]. Another explanation proposed was that the high velocity jets in the LVOT could inflict repetitive trauma to the aortic valve. Evidence for this hypothesis can be sought in the univariate association between aortic valve thickening and the presence of AR. This association was, however, lost after correction for age, arguing against the hypothesis that aortic valve degeneration is accelerated in patients with HOCM. Finally, sarcomeric HCM is associated with a number of anatomical variations in cardiac structures including myofibrillar disarray, papillary muscle abnormalities and elongation of the mitral valve leaflets [1,2]. One might speculate that the increased incidence of AR in HOCM could reflect a currently overlooked anatomical variation related to the genetic cause.

The increased incidence of AR in HOCM is intriguing and in line with a previous report [6]. The clinical implications of this study should, however, be interpreted with caution. First, the degree of AR was mild at most, and partially diagnosed with CMR rather than echocardiography. While CMR-based quantitative assessment of the severity of AR can provide important diagnostic information [7], echocardiography remains the gold standard for the assessment of valvular heart disease [8]. In the current study, the CMR-based definition of AR relied on visualization of a signal void below the aortic valve in diastole. Unlike with Echocardiography, the size of the

dephasing void detected with CMR is an unreliable indicator of the severity of AR as it depends on multiple factors including flip angle and echo time [9]. It is therefore likely that the current CMR definition of AR resulted in an overestimation of the true incidence and the prognostic significance of AR. The authors rightfully argue that post-operative AR may reflect progression of previously unrecognized AR, urging vigilance during pre- and perioperative assessments. Of note, the incidence of post-operative AR using contemporary surgical techniques is very low [10]. Future prospective large (multicenter) studies that employ more rigorous methods to quantify the severity of AR are required to determine the true incidence of AR in patients with HOCM. Such studies will allow us to determine whether AR truly is a forgotten valve disease in patients with HCM.

Declaration of Competing Interest

None.

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