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Aortic Stenosis and Stressed Heart Morphology

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Abstract

Myocardial geometric remodeling is a response to increased stress which includes increased afterload situations during clinical conditions. In this review, we have focused on early and late geometric features in aortic stenosis, importance of recognition of these findings and consequences due to progression of valve disease. We have also pointed out the similarities in early focal and global myocardial geometric remodeling in acute and chronic conditions as hypertension and acute stress cardiomypathy which are associated with myocardial functional and geometric response to acute or chronic stress exposure and relevant increased afterload. In aortic stenosis, target organ involvement in disease progression has been evaluated and discussed in the report. In addition to quantitative evaluation of valve disease, importance of myocardial involvement and global assessment of patients with aortic stenosis also have been mentioned in the report. Finally, we have discussed the importance of global myocardial geometric changes and timing for surgery before development of heart failure in this specific group of patients.

Keywords

Aortic Stenosis, Basal Septal Hypertrophy, Left Ventricular Hypertrophy, Hypertension, Acute Stress Cardiomyopathy

1. Introduction

Aortic stenosis has become a relatively common disease which is associated with major morbidity, mortality, and health economic costs, however, it has not established any medical approach to slow its progressive course [1]. Aortic stenosis produces a mechanical reason for increased afterload and results in compensatory left ventricular

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hypertrophy (LVH) to normalize the wall stress due to pressure-overload [2]. Cardiac ultrasonography is the basic equipment for better understanding of the disease course and for the follow-up progression stages [3]. Novel therapeutic strategies can be used for documentation of target organ damage and can provide a documentation of the details of disease progression [4]. Failure in establishment of the universal markers regarding the stages of progression of the disease course may lead to a difficulty to predict disease progression. Optimal timing of valve surgery could be affected negatively by lack of assessment of myocardial involvement. Nevertheless, determination of myocardial involvement in aortic stenosis is tremendously important [5].

Secondary LVH due to increased afterload develops most frequently in aort stenosis and hypertension. In addition to precise measurements for detection of severity of aortic valve disease by transvalvular blood flow Doppler velocity and the additional measurements [4], quantitative assessment of target tissue involvement in regards to detection of LVH that is the main compensatory mechanism for normalization of intracardiac pressure overload in the process of aortic stenosis provides an additional information to evaluate patients effectively [6]. For this purpose, quantification of LV contractility using cardiac imaging has long been used to detect the severity of myocardial diseases. We and the others previously pointed out that tissue Doppler imaging is an informative ultrasound modality that records regional diastolic and systolic intervals within the myocardial tissue or annulus of valves and allows to evaluate functions of both intervals [7] [8].

Longitudinal LV function is quantified by mitral annular excursion and function of longitudinal myocardial fibers can be detected by tissue Doppler in the early stage of aortic stenosis [9]. The disease progression effects on LV myocardial involvement and increased myocardial mass is associated with adverse outcomes [10]. Aortic stenosis may lead to physiological hypertrophy in the early stage of disease. Takeda *et al*. [9] documented that mitral lateral annular excursion in mild to moderate aortic stenosis is comparable to that in normal subjects and that long axis excursion is in a relation with both LV mass index and the grade of aortic stenosis. Aortic stenosis possibly results in physiological hypertrophy in the earlier stage before developing LV dysfunction. In this study, however, both lateral and septal side of mitral annulus became more dysfunctional in terms of abnormal long axis excursion with progression of disease. However, both primary valve pathology leading to increased afterload as well as increased myocardial mass may together contribute to the main adverse outcome due to pathologic hypertrophy in advance, then finally heart failure develops in aortic stenosis [1] [10]. Therefore, timing of valve surgery is crucial to prevent the progression of pathologic process which mentioned above.

2. Therapeutical Approach to Aortic Stenosis

There was no certainly validated medical therapy in this disease. Surgical aortic valve replacement has been recognized to be the definitive therapy (which improves survival considerably) in severe aortic stenosis since more than 40 years. In the most recent period, operative mortality of isolated aortic valve replacement for aortic stenosis has been detected approximately 1% - 3% in low-risk patients who are younger than 70 years and approximately 4% - 8% in selected older adults [11]-[13].

Numerous observational studies have consistently demonstrated that corrective surgery in symptomatic patients have shown an improvement in quality of life and a substantial increase in survival rates. It is broadly accepted and documented that aortic valve replacement provides survival benefit for selected asymptomatic patients, when compared to conservative management [14] [15]. Several considerations should be remembered before surgical correction of aortic stenosis including the choice of the valve type as mechanical valve or bioprosthetic valve, stented, stentless valves, aortic homografts and cadaveric recovered autografts.

More recently, transcatheter aortic valve implantation has been produced as a feasible option in patients with high surgical risk using either a retrograde transfemoral transsubclavian or direct aortic approach or anantegrade, transapical access [16] [17]. 30-day mortality has been found to be 5% and 15% which is acceptable when compared to the risk predicted by the logistic EuroSCORE (varying between 20% and 35%) [18]. One major concern is the high rate of paravalvular regurgitation which is detected in 85% of the patients and this consequence requires careful follow-up as well as critical evaluation. Despite promising 3 - 5 year results, longstanding usefulness of these valves with a consideration on the effects of crimping should be elucidated [17].

On the other hand, it is well known that hypertension and cardiomyopathy even in earlier stages are associated with pathological hypertrophy [19]-[21]. Novel cardiac imaging provided quantified data regarding the LV geometry besides the functional data regarding the level of myocardial tissue involvement in aortic stenosis. Real-time three dimensional cardiac imaging documented the regional details of secondary LVH and provided to

differentiate from primary cardiomyopathy. We previously showed using real-time 3 dimensional cardiac imaging that diminished regional intracavity volume in LV base possibly due to predominant involvement of myocardial tissue which is the regional geometric feature of secondary LVH due to both aortic stenosis and hypertension [22].

We previously demonstrated that focal hypertrophy of LV base or basal septal hypertrophy (BSH) is related to high pressure-heart rate product stress induction in hypertension and discussed the importance of exaggerated hypertension under stress [23]-[25]. We observed that BSH in hypertension is associated with stress-induced hypercontractility of hypertrophied LV base using tissue Doppler imaging [26]. While stress exposure in hypertension is associated with vasoconstriction and relevant increased afterload, aortic stenosis directly blocks LV ejection and leads to increased afterload. BSH could be observed in patients with aortic stenosis (**Figure 1**, **Figure 2**) similar to hypertension and acute stress cardiomyopathy. This support the notion that BSH could possibly be a part of early LV remodeling in clinical situations with increased afterload including hypertension, aortic stenosis and acute stress cardiomyopathy [27].

In fact, both regional predominant and hypercontractile response of LV base to stress is a part of the clinical spectrum in acute stress cardiomyopathy with decreased midapical contractility with a relatively larger mida-

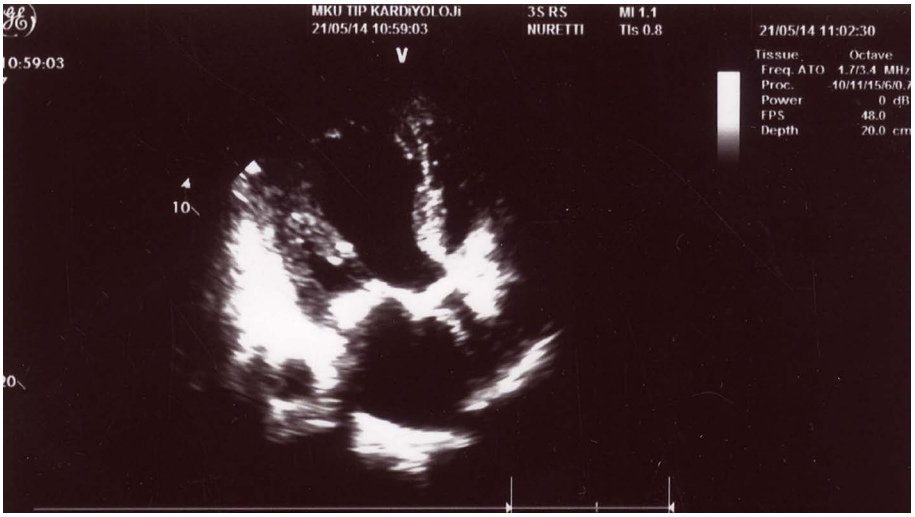

Figure 1. Echocardiographic image of a patient with severely calcified aortic stenotic valve and predominant septal base (1.25 cm) compared to other segments.

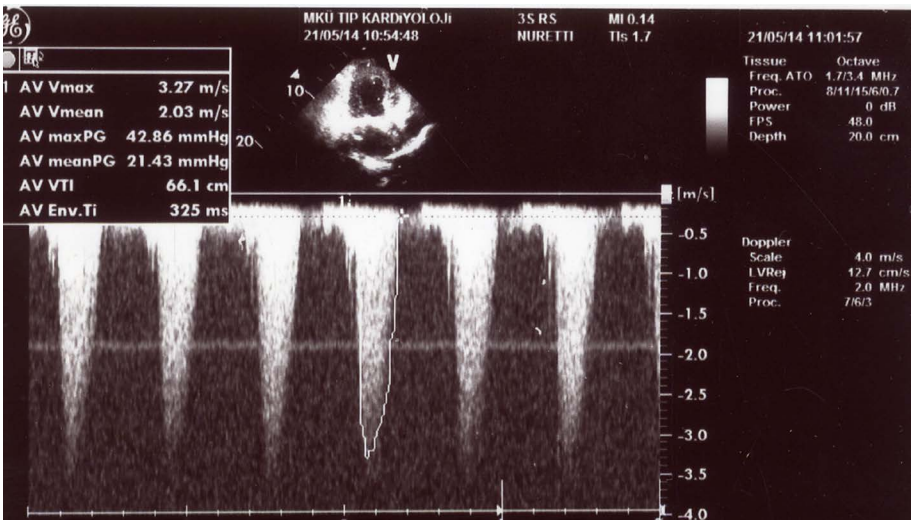

Figure 2. The image of increased transvalvular aortic gradient measurements of the same patient with moderate aortic valve stenosis (peak jet velocity: 3.27 m/s, max. peak gradient: 42 mmHg and max. mean gradient: 21.45 mmHg).

pical region that obviously has greater wall stress according to the Laplace Law during stress exposure [28] [29]. BSH is not only a specific geometric and functional features of LV base with segmental diminished cavity in the clinical conditions, but also a geometric description of myocardium in the increased afterload situations. Because of this specific interesting clinical observation which represents a conjunction in different diseases, as mentioned above, we described the stressed heart morphology and suggested that this geometric and functional similarity of LV base of the heart may represent a morphologic conjunction on LV geometry in clinical conditions with acute stress or chronic stress due to increased afterload in hypertension [29].

Focal hypertrophy of LV base (**Figure 3**) in aortic stenosis is a consistent finding with histopathologic data which shows predominant sympathetic innervation of base of the heart [30] [31]. Physiological LVH in the earlier stage of aortic stenosis is transformed to pathologic hypertrophy with development of LV dysfunction [9]. Similar to aortic stenosis, hypertension results in LVH before development heart failure and LVH is related to sympathetic hyperactivity which suggests that this produces a trophic effects, then norepinephrine release is associated with the development of hypertensive LVH [32]. In hypertensive patients, we showed using complex mitral annulus geometry and dynamics with reconstruction methodology that systolic function is preserved in hypertensive LVH differently from cardiomyopathy by real-time 3 dimensional echocardiography [33]. It was also shown preserved LV function using tissue Doppler imaging [34].

Before heart failure development, preserved LV function can explain the rationale acceptable contractile reserve under stress and stress-mediated hypercontractility of LV base in patients with hypertension. A comprehensive study on the pressure-overload model revealed the consistent finding with preserved LV function [35]. In this study, cardiac energy metabolism was preserved at the LVH stage before heart failure development in Dahl salt-sensitive rats. In fact, stress-induced dynamic LV outflow tract obstruction could be related to hyperdynamic focal myocardial tissue of LV septum which is the closest part to LV outflow tract [23] [26]. Septal alcohol ablation as used in hypertrophic cardiomyopathy was reported to be effective in a case with hypertension-mediated severe hypertrophy of LV base and relevant severe LV outflow tract obstruction [36]. Interestingly, predominant hypertrophy of septal base with hypercontractility was described as the part of diagnostic features in acute stress cardiomyopathy [28]. In this syndrome, dominant septal hypertrophy with hypercontractility and relevant LV intracavitary obstruction were documented as well [37].

Consistently, dynamic LV outflow obstruction which is likely to be related to stressed heart morphology [29] could be detected in patients with aortic stenosis as well [38]. Progressive increased afterload with development of valve disease in aortic stenosis is related to LVH, early adaptation pattern to normalize increased mechanic stress exposure. However, ongoing longstanding pathology could lead to deterioration of preserved LV function and development of abnormal myocardial function in aortic stenosis. Ejection fraction in daily clinical evaluation of patients is a powerful prognostic marker in aortic stenosis and transition from preserved LV function to LV systolic dysfunction is associated with a poor prognosis and high greater mortality [39]. Furthermore, timing for

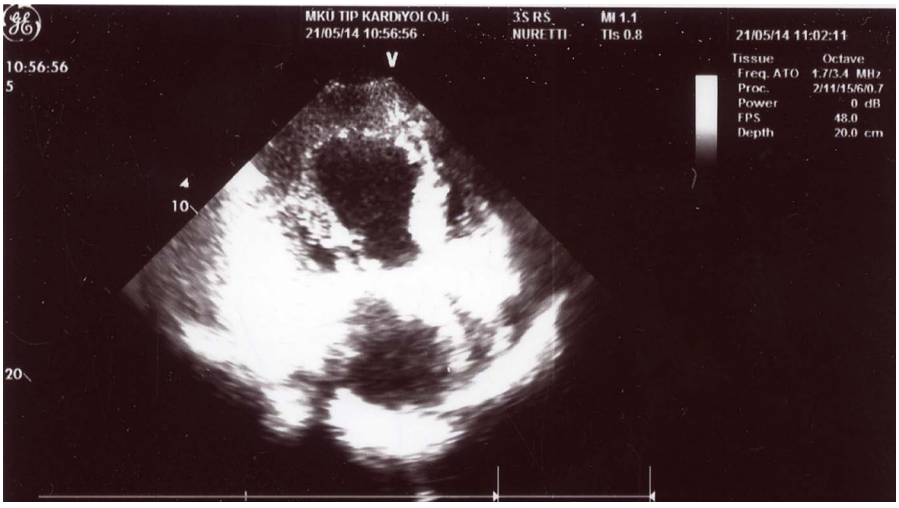

Figure 3. Systolic LV image shows stressed heart morphology with predominant LV base and relatively larger midapical LV cavity of the same patient.

surgery is missed and pathogenetic process is progressed in aortic stenosis, symptoms become more common dramatically after deterioration of myocardial function and adverse events occur more frequently [40].

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