ASSESSMENT OF RESPONSE TO HEART FAILURE THERAPY: VENTRICULAR VOLUME CHANGES VERSUS SHAPE CHANGES.

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Background:

The prolate ellipsoid left ventricular geometry is crucial for its unique contraction and relaxation patterns. Perturbations in optimal cardiac function preceding overt heart failure ensue when this ellipsoid shape assumes a more spherical configuration. This stage of spherical configuration, prior to overt dilatation, is when therapy should be intensified. The dynamic shape changes during the cardiac cycle of systole and diastole in valvular regurgitations when ventricular volumes are within normal range have proved that shape changes are clearly dissociated from volume changes in the early stages. In the scenario of advanced heart failure, several therapeutic interventions have been tried with variable success. These therapies aim at decreasing the ventricular equator, and hence its volume. However, the ventricular shape may still be spherical leading to suboptimal function. The aim in any therapy for heart failure should be therefore to achieve near normal left ventricular anatomy and physiology, with shape assessment as the surrogate marker of therapeutic success.

Normal left ventricular geometry and function:

The normal left ventricular shape is a prolate ellipsoid with its long axis directed from apex to base, and its inflow and outflow being in continuity. Hence, entry of blood and exit is virtually through the same orifice, which makes its flow through the left ventricle bi-directional. This bi directional flow is required to generate a systolic blood pressure of

120 mm Hg in order to propel blood through the entire systemic circulation. This geometry is an adaptation to evolution and assumption of an erect posture. The amphibian has a spherical ventricle, man has an ellipsoid systemic ventricle and the giraffe has an extreme ellipsoid (almost cylindrical) ventricle which is required to generate a systolic blood pressure of 300 mm Hg[1].

This unique mode of left ventricular function is by torsion for both emptying and filling. It is the function of the angular orientation of the oblique muscular fibers, which are unique to the left ventricle. In systole, the apex and the base twist in opposite directions causing a wringing effect enhancing ventricular ejection. In diastole, LV torsion occurs in the reverse direction-both the apex and the base twist in reverse of the systolic twist. This untwisting augments LV filling by a suction effect. The orientation of the oblique myocardial fibers is thus decisive of ventricular shape and function[2,3]. By changing from a relatively globular to an elongated shape during systole, the LV ejects a greater volume per unit of fiber shortening than would be achieved if the chamber adhered to a constant shape throughout the cardiac cycle. In addition chamber elongation reduces the mid wall radius of curvature and thus decreases systolic wall stress. From its end systolic configuration, the ventricle can accommodate rapid early diastolic filling by shape change to a more spherical geometry without depending on equally rapid sarcomere elongation.

Perturbations in left ventricular geometry and function with the advent of heart failure:

In heart failure, dilatation of the cardiac chambers leads to perturbations in the LV ellipsoid geometry. At the base, dilatation leads to straightening of the LV inflow and outflow with increases in the angle between them, thus distorting the mitral aortic continuity. The oblique fibers from mid-wall to apex become more horizontal. A theoretical analysis can demonstrate that an oblique fiber angle on a surface with a certain radius of curvature can attain a narrower angle, as the surface projects onto one with a larger radius of curvature as in a dilated spherical ventricle. For example, for a normal 60^0 fiber angle, increase in short axis dimension of the ellipsoid by 3 centimeters can decrease the fiber angle by 10^0 that is from $60^0$to 50^0. Minor fiber angle changes of 5^0 to 10^0 can substantially affect ventricular torsion and performance[4]. Sallin and co-workers[5] demonstrated that a myofiber contraction of 15% in a ventricle with a normal short/ long axis ratio (sphericity index) of 0.5(ellipsoid shape), generated an ejection fraction of 62%. At the same 15% fiber contraction, the ejection fraction fell below 40% if the sphericity index approached 1 (spherical shape) and went up to ≥ 80% if the sphericity index approached 0(extreme ellipsoid).

In a spherical dilated heart, due to horizontal orientation of the fibers, both systole and diastole are affected.

Here, the LV shape changes during filling require greater and more rapid wall distension leading to increased diastolic wall stress and increased filling pressures.

Stroke volume is compromised due to maintenance of a more spherical shape leading to increased systolic wall stress.

Significance of left ventricular shape changes in heart failure:

Heart failure is a syndrome complex, being the net result of various pathological mechanisms which cause cardiac sphericity and dilatation. The left ventricular end diastolic and end systolic volumes have long been studied as surrogate markers of survival in assessing the impact of heart failure therapies[6]. In normal and diseased states, the ventricle exhibits dynamic changes both in shape and volume throughout the cardiac cycle. If ventricular shape were simply tied to ventricular volume, in a manner analogous to an inflatable balloon, no difference could be expected in the dynamics between the two states. In the normal LV, its eccentricity index , which is its short axis to long axis ratio increases during ejection and decreases during filling. In other words, the ventricle becomes more spherical during diastole and more ellipsoid during systole. In conditions of valvular regurgitations where ventricular volumes were matched between patients and normal controls, the dynamic shape changes were studied extensively employing many techniques[7]. In aortic regurgitation, the end diastolic eccentricity was lesser than that of controls as were the end systolic eccentricity indices. The ventricle had a more spherical shape during diastole and systole when compared to the normal ventricle. In mitral regurgitation, the end diastolic eccentricity was lesser with a more spherical shape as compared to the normal ventricle. But the end systolic eccentricity was greater than normal. During ejection, the ventricle became more ellipsoid than normal in mitral regurgitation. Thus, the shape changes cannot be predicted from diastolic and systolic cavity volumes alone but also depends on the nature of ventricular loading during ejection. In hearts with reduced ejection fractions and overt ventricular dilatation, shape changes are minimal as the systolic eccentricity is reduced, with the ventricle being more

globular in systole and diastole. The increases in systolic eccentricity are seen only in hearts with ejection fractions > 50%[8].

The symptoms of heart failure develop when the ellipsoid left ventricular geometry changes to a more spherical one, even prior to overt ventricular dilatation. Sabbah et al [9] have shown that symptoms of heart failure develop when the sphericity index (long axis: short axis ratio) of the ventricle decreases even prior to overt ventricular dilatation. Tishcler et al [10] have shown that when patients with heart failure were subjected to exercise testing, the patients whose sphericity indices increased on exercise had lesser exercise capacity. This highlights that obliquity of left ventricular myofibers are a pre requisite for optimal ventricular emptying and filling. Left ventricular sphericity and dilatation can themselves lead to abnormalities of the mitral valve causing progressive mitral regurgitation which worsens ventricular dilatation[11]. The stage of heart failure with increased ventricular sphericity without overt dilatation, according to us forms the ideal substrate for intensive therapy targeted at decreasing sphericity, which may prevent overt ventricular dilatation.

Assessment of ventricular shape changes:

The assessment of ventricular volumes has been achieved by various invasive and non invasive techniques. Left ventricular contrast ventriculography can accurately assess volumes by the Dodge formula. Ventricular volumes can also be accurately calculated by 3D Echocardiography and Cardiac magnetic resonance.

Several techniques have been employed to assess ventricular shape. The invasive and non invasive methods are by centerline method, Fourier shape analysis and the eccentricity index or sphericity index. However, the centerline and Fourier shape analysis are

cumbersome, time consuming and therefore cannot be used for LV shape analysis in large populations. The eccentricity index is a simple, reproducible method of LV shape assessment and can be applied to non invasive techniques like 2D Echocardiography. This index is calculated as the ventricular short axis(distance between the papillary muscles in the para sternal short axis view) divided by the long axis(in the 4 chamber view, from the mitral valve tips to the apex). When the value approaches zero, the shape is ellipsoid. When the value approaches 1, the shape is spherical[12].

Therapeutic modalities for reversing ventricular shape and volume:

The major objective of treatment of heart failure is to blunt mechanisms that contribute to pathological cardiac remodeling. Following a myocardial infarction, ventricular remodeling is related to the amount of myocardial fibrosis leading to dilatation of the remaining contractile myocardium. In dilated cardiomyopathy adverse remodeling occurs as a result of various disease processes by various mechanisms including apoptosis. Strategies that reduce afterload and block the beta-adrenergic and renin-angiotensin-aldosterone axes aim to delay or even reverse maladaptive remodeling in the early stage, which is assessed by decrease in ventricular volumes and increases in EF.

Revascularization by percutaneous intervention or surgery (CABG) is an adjunct to standard heart failure therapy in a specific population with demonstrable reversible ischemia and ventricular dysfunction. When patients with advanced heart failure were studied in a large randomized study, beneficial decreases in ventricular volumes were found to be achieved by revascularization alone, compared to revascularization and surgical ventricular restoration [13]. However, recent data[14] suggests that ventricular re shaping by the coapsys device as an adjunct to surgical revascularization(Coronary

Artery Bypass Graft) in patients with functional mitral regurgitation had better survival outcomes and significant decreases in mitral regurgitation as compared to CABG alone. Here too the importance of modifying the ventricular shape by reshaping the mitral annulus has been proved to result in survival benefits over and above that resulting from revascularization alone. The use of coapsys device and the myosplint device have beneficial short term results with respect to reverse remodeling and subjective clinical improvements in advanced heart failure patients who are not eligible for cardiac transplantation[15]. These results highlight the benefits of modifying ventricular shape as opposed to decreasing ventricular volumes without significant modification of ventricular shape. The surgical techniques for restoring ventricular geometry have evolved from mere reductions in volume to restoring an ellipsoid geometry[16, 17]. The existing techniques can be improvised by the assessment of ventricular shape and modifications to existing therapies can be applied in order to achieve near normal ventricular shape in tandem with decreases in ventricular volume.

Conclusions:

It is essential to assess the ventricular shape changes in systole and diastole in heart failure. The ventricular shape changes to a more spherical configuration in the stage prior to overt dilatation forms the ideal substrate for intensive anti failure therapy. The use of the eccentricity index is therefore invaluable in assessing clinical response to therapy.

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