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# Congestive heart failure: treat the disease not the symptom - return to normalcy / Part II -- the experimental approach

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The report in this volume by Zhang and associates (1) applies an important 3-dimensional MRI tagging method to demonstrate that altering ventricular geometry by employing Dor procedure (as they interpreted this operation) in sheep in congestive heart failure increases systolic circumferential shortening in remote muscle. These experimental changes document the clinical improvement in remote muscle function reported world wide with LV restoration (2;3). Such application of advanced imaging methods allows studies to focus upon how interventions improve function by changing ventricular muscle deformation, that occurs sequentially during the cardiac twisting motion. Furthermore, this regional functional data allows differentiation from non functional remote regions that echocardiography shows are displaced without contracting, together with providing a time course for displaying how global function is affected by cardiac rebuilding.

## Normal and Abnormal Form

The surgical approach to congestive heart failure, like other operative objectives should treat the disease, not the symptom, and return structures toward normal as described by others (4) and became the title of my 2001 JCTVS Editorial (5). The geometric disease in ischemic dilated cardiomyopathy is the spherical chamber, which is different than the elliptical of conical normal heart shape (Figure 1). The symptom is the spherical chamber, whereby normal helical chamber develops a more circular configuration that may flatten fiber orientration and alter performance (6) (7).

Despite imaging advantages, the experimental design of this study has a major flaw, since baseline is ascribed to the infarction state, rather than to the normal heart. The authors held fast to repeated requests to supplement their data base with a design that introduces normality as a reconstructive guideline for operative interventions. It seems that, aside from supplying superb imaging technology, the surgical planning strategy must also recognize and codify normality (which exists before the infarction), show how disease distorts this (their preoperative control), identify how and why the intervention selected rebuilds normality, and relate results toward the limitations of the selected procedure. For example, if normality was not recaptured, the discussion should identify if this is a problem with the operation method, or related to timing of postoperative measurements.

## Border and Remote Muscle

Prior studies addressed the peri infarction border zone showing that the issue was impaired contractile function, rather than increased wall stress (8), and directed less attention toward the remote muscle that rapidly impairs function after anterior wall infarction in relation to ventricular shape (9). The tagging study in 2000 by Bogeart introduced the key link whereby border and remote muscle zones become combined culprits for dysfunction after ventricular volume is increased by anterior infarction (9). Zhang's study coalesces these data and is helpful in directing attention of cardiologists and surgeons toward malfunction of global muscle, whose recovery is quantified by returning deformation of the less efficient stretched muscle towards normal following ventricular restoration.

Kramer in 2002 (10) followed Boegart's approach and employed tagging methods to quantify remote muscle circumferential shortening improvement following restoration, compared the changes to control studies, showed this spatial configuration change (Figure 2a), and adhered to the aforementioned surgical study planning concept**.** Similar findings of remote muscle circumferential deformation improvement were recently reported by White's team at the Cleveland Clinic (11)**.** Editorial suggestions to include this information were not followed, so that a restricted background analysis underlies the manuscript's introduction statements about prior study limitations. Furthermore, non MRI studies by Taniguchi, codified improved velocity of remote muscle circumferential fiber shortening (12), showed regional stress, function, and remodeling improves after aneurysmectomy, and also demonstrated these results were not achieved by CABG alone, thereby answering the introduction's supposition that confounding effects of other procedures had not yet been addressed.

**Dilemma of abnormal shape**

Failure to achieve normal shape is the infrastructure of the limitations of a host of non reconstructive CHF therapies such as CABG, mitral valve rebuilding in ischemic cardiomyopathy, biventricular pacing, defibrillator devices and a spectrum of pharmacologic treatments that alter neuro endocrine factors, yet exclude addressing the scar nidus that underlies subsequent remote ventricular stretch. The sphere was retained in this study (Figure 2b), although slightly less circular. It seems the surgical objective should be to restore normality, rather than making the heart "less sick".

Certainly, the investigator is free to design each study and set goals that relate to how rebuilding improves function via the Starling relationship. However, the analysis should also echo the relationship of these objectives toward a) how their "Dor procedure" reproduces what was initially described, and b) define mechanisms that allow observed function to improve. Their goal of 50% surgical neck reduction to increase regional strain was achieved, but differs from Dor's objectives (to whom this operation is ascribed) that indicate "the endoventricular suture helps restore the curvature towards its shape before infarction, and helps in selection of the size, shape and orientation of the patch" (2).

These limitations are evident when current results in Fig 2b are compared to clinical findings of Kramer in Figure 2a, who also included preoperative normal configurations for comparison.  While the circular configurations are evident during infarction, a similar, but slightly less spherical shape followed this experiment, whereas the normal conical shape was achieved after clinical LV reconstruction.  Editorial suggestions to include an image of the control  natural ventricular shape  were declined;  inclusion of such a normal elliptical shape would a) allow contrast with the  circular or spherical chamber that develops after infarction, b) demonstrate the spherical configuration is relatively retained after experimental  patch placement, c) potentially  permit the authors and readers to question about  the role of geometry in determining function and d) possibly generate questions about what function could be expected if the rebuilding procedure  reconstructed the normal elliptical form rather than a smaller sphere.

**Importance of Normal Shape**

Unfortunately, the manuscript's statement that no one knows about optimal post operative shape skirts away from the beauty of understanding and driving toward rebuilding the normal shape.  Advantages of this configuration are evident from tagging MRI studies  of  Bogeart  (13) demonstrating  regional non uniformity of the normal left ventricle, whereby  deformation  accentuates as sequential normal heart motion progresses  from base to apex. Consequently, the stated "idealized LV wall geometry as a hemispherical shell" does not exist in the conical heart, and their relatively  spherical shaped  end point following LV rebuilding  (Figure 1b)  is clinically described as  a less ideal spherical box-like chamber (14) .

Reconstruction of a more normal elliptical shape aims toward Dor's objective of returning configuration towards its shape before infarction, and underlies development of clinically employed shaping devices and conically shaped mandrels. (15)  This normal form related endpoint has  led to placing the oblique patch above the scar to  reconstruct normal shape (16) as well as repeating this intervention in  ischemic non scarred septum muscle in dilated failing hearts in Russia (17) with similarly improved late results to those after scar exclusion, and underlies a recently posed question "is the goal to exclude  the disease or to rebuild form ?"(18)  Decisions toward this goal (Figure 3) evolved from recognizing higher late mortality in Dor's long term experience (19) after a  larger chamber was retained when excluding the scar was the anatomic reconstruction end point. This selection criteria led to postoperative retention of  more  dilated remote muscle, and  portended  higher late mortality, since volume is the surrogate for  survival after ischemic cardiac dilation (20).

Conceivably, the sphere shaped end point and functional results in this study might become the starting point for a new procedure, if these results are subsequently compared against rebuilding a conical chamber. If this approach is selected, new data that also includes control normal tagging data could simultaneously test how the each procedure restored normal function.

**Influence of Shape on Function**

The current recommendation to use a patch differs from concepts that non patch methods are preferable. One potential reason for this selection includes reduction of wall tension during patch placement into the fragile muscle within an akinetic segment containing trabecular scar. I suspect ventricular shape will become the vital surgical consideration, but subsequent functional studies are needed to determine if such decisions are related to patches (Dacron, pericardium or a flap of transmurally scarred muscle) or ventricular form. The normal elliptical spatial configuration relates to how the remaining fibers are oriented, and my suspicion is that creating a geometric change in fiber direction toward normal will become the endpoint that defines ultimate functional recovery.

The authors document how reconstruction changes in systolic and diastolic volume, and comment upon how it affects the Starling relationship. A form function relationship exists, so the shape influence upon fiber orientation will impact function at rest and during exercise, as shown by Sallin (6) and Ingels (7). This investigative team previously used diffusion tensor MRI analysis to determine whether the helical fiber orientation of the normal heart geometry is changed when this model of heart failure dilates ventricle and after restoration rebuilds cardiac structure (21). A control group was included in that study to properly respond to my principal objection to this report , but that report evaluated the unloaded, decompressed , non functioning heart and thus failed to determine if the stretch of disease a) changed fiber direction and b) could rebuilding restored the natural helical design that underlies the living heart's function.(22).

A basic anatomic concept of heart failure is that the dilated heart becomes spherical through a change in the radius of curvature within the ventricular wall. The currently reported functional analysis of improvement remote muscle systolic circumferential shortening implies the authors might consider repeating their prior MRI study and re-analyze, using the reported dilated chamber dimensions. Such a study would determine if the normal helical configuration is changed by infarction and restored by LV rebuilding, as well as if changes from an elliptical to a spherical fiber orientation altered function and then determine if changing fiber orientation would further improve deformation.

**Recovery Timing Evaluation**

The discussion suggests evaluations at a longer than 6 week recovery period may be needed, and subsequent changes may relate to repair of the collagen sheathing of myocytes where the half life of collagenase is 120 days (23). Recovery of neuro endocrine markers towards normal after longer intervals following ventricular volume reduction by LV restoration were recently reported from the Cleveland Clinic (24) and Japan (25) . Timing of functional evaluation may have important impact, since withdrawal of these neuro endocrine adaptive forces after stretch may explain the reported clinical change of pressure volume relationships following 4 months of decompression in a study that did not collect biochemical values (26). Perhaps future studies may harvest these biochemical markers at longer follow up intervals, compare them against the current spherical post operative shape, and against rebuilding a more conical configuration as shown in Figure 2a and b., and thus become a surrogate for avoiding more complex functional tests.

The role of LV rebuilding is linked to clinical recovery, and consistent with reports showing NYHA status and 6 minute walking tests improve (27) (3). Consequently, their conclusion comment that their study is the first to show the Dor procedure does anything seems a bit cavalier, especially since similar functional clinical findings were reported by Taniguchi in 1999 (28), Kramer in 2002 (29), and Carmichael from the Cleveland Clinic in 2006 (24). Ventricular shape should be considered with these changes in volume, since energy demands rise with exercise and stress is related to dimensional changes. Consequently, the radius of curvature underlying wall stress rises and is related to $\Pi R^3$ in a spherical chamber, but to $\Pi R^2$ in a cylinder. Conversely, wall stress falls in the conical heart; deformation increases and efficiency improves as muscle size anisotropically thickens as chamber dimension narrows toward the apex.

In conclusion, the starting point for evaluation for recovery must arise in the normal heart, not the damaged heart. This initiates with understanding normal form and function and avoiding comparisons against the wrong anatomy. This comparison initiates from a proper control data base so that the investigator and reader can understand that valid results garnered from starting with a sphere (which is the disease) and subsequently generated by a smaller sphere (following restoration) conveys an abnormal geometry based end point. Returning toward normal in both the operating room and the experimental laboratory will yield evaluation measurements that more closely shall define how our interventions work.

Figure Legends

Figure 1 The left image shows cardiac shape in the normal heart, with a conical or elliptical chamber. The right image shows a dilated failing heart with a spherical shape.

Figure 2 a) The left image shows of the spherical dilated cardiac patient with an anterior infarction, taken from the 2002 MRI tagging report by Kramer and associates(30). The right image shows how left ventricular rebuilding restored a conical left ventricular shape. 2 b) The left image shows is the experimental post infarction shape appearing in the report by Zhang (1), displaying the same spherical preoperative cardiac shape appearing in 2a displaying the pre operative clinical image. The right image in 2b shows that the postoperative volume is reduced, but the cardiac shape remains spherical, and continues to mirror the left image pre operative configuration in both the clinical and experimental study.

Figure 3

Comparison of treatment of the dilated ischemic cardiomyopathy (above) by addressing the disease (lower left) and leaving a spherical shape, or doing the SAVE of Pacopexy (18) (lower right) and rebuilding an elliptical shape. Note that the patch is placed into the septum that does not have scar, and the point of placement is above the scarred region in mid septum.

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Figure 1
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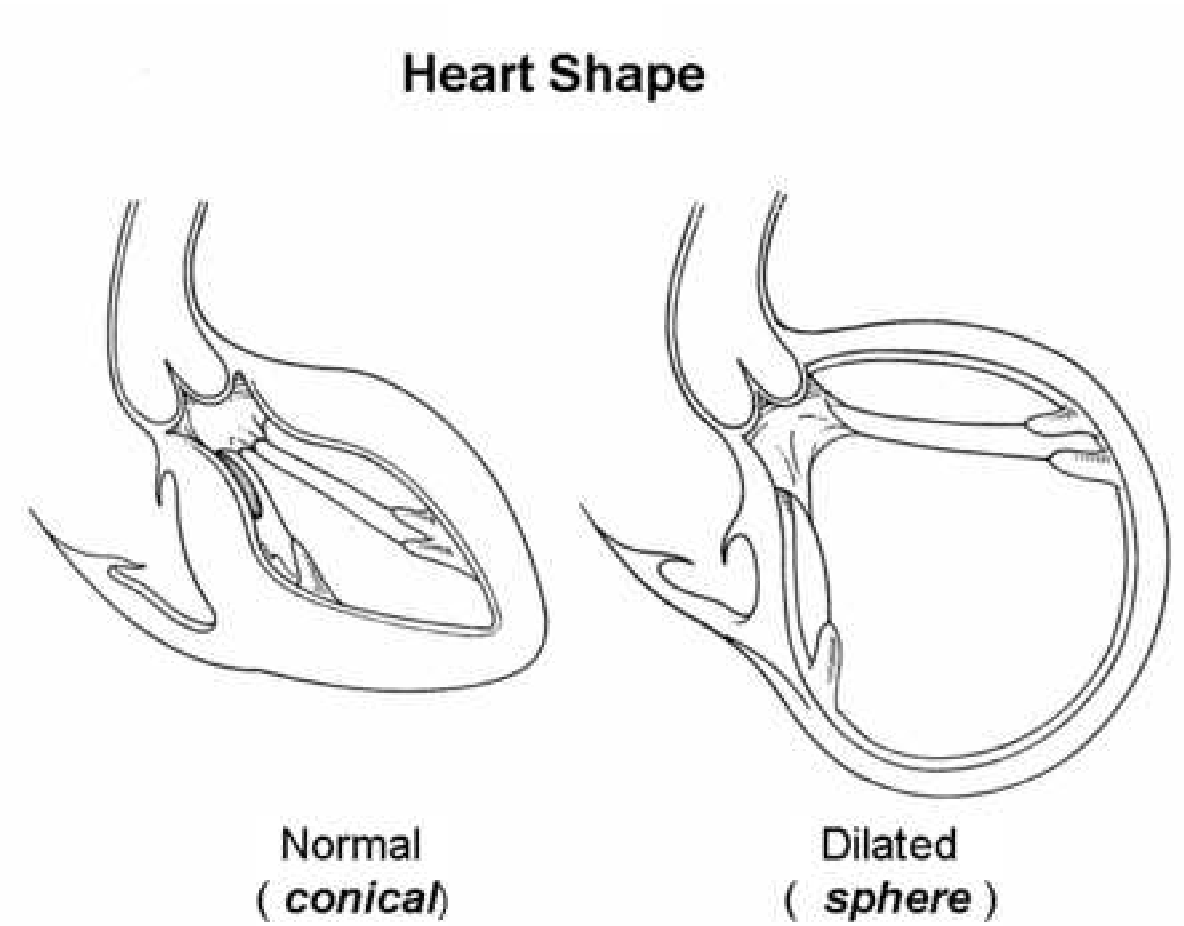

Figure 2

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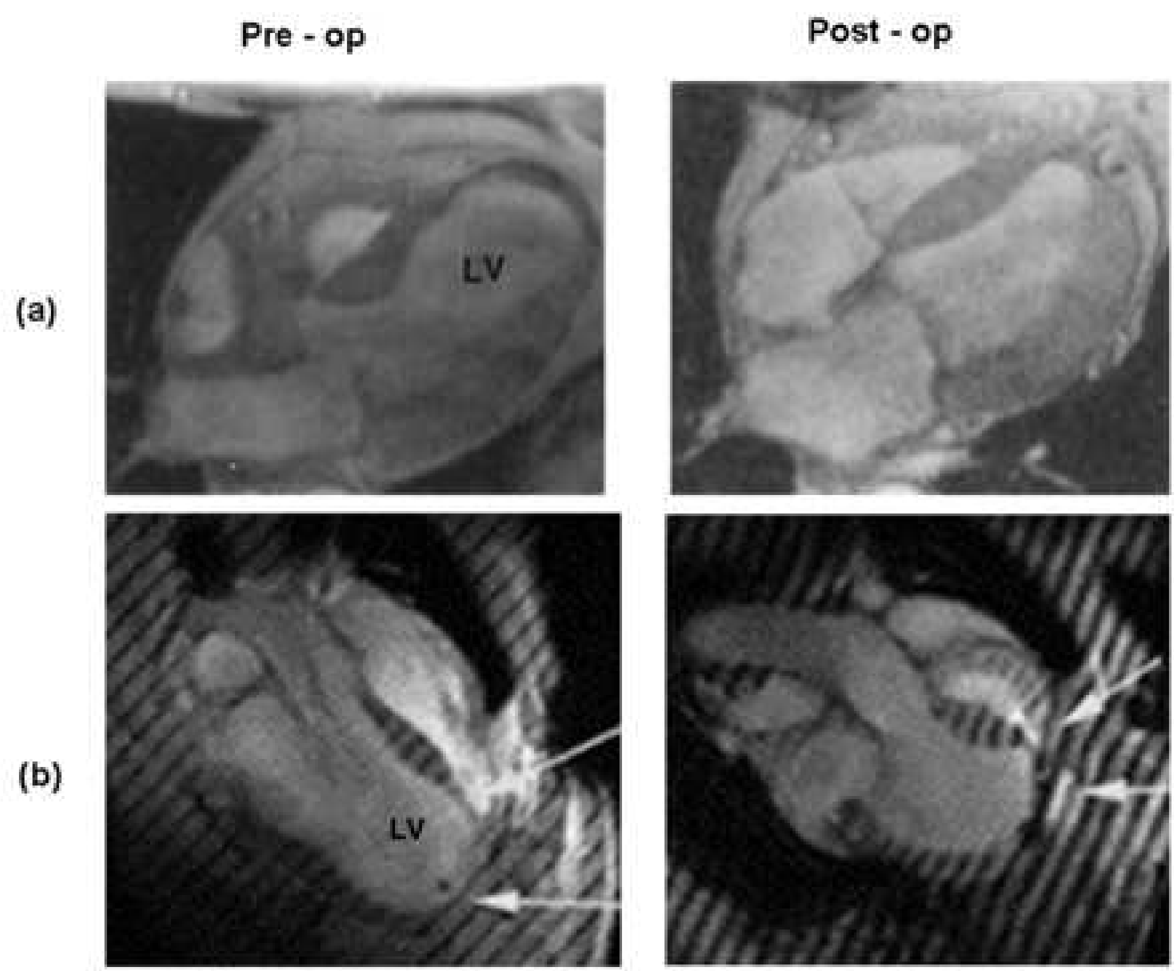

**Figure 3**
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