



# The relationship between structure and function: why does reshaping the left ventricle surgically not always result in functional improvement?

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## Abstract

Surgical strategies recently introduced to improve ventricular function have been based on the concepts of reduction of ventricular diameter, synchronization of myocardial activity, passive support of diastolic ventricular shape, and active support of systolic ventricular constriction. They have depended on several established theoretical assumptions, not all of which are totally valid. Clinical results have proved markedly variable. This is especially true for procedures designed to reduce the radius of the left ventricle. Some have reported up to 80% mortality, whereas others achieve results comparable with those for heart transplantation. Because of this, the method runs the risk to be rejected, or else, its more widespread application will be postponed until essential details concerning the basic concepts have been elucidated. It is these details which we discuss in this review.

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## 1. Introduction

The ventricular walls have a basically fasciculated structure, although there are no naturally occurring boundaries between the fascicles and tracts of myocardial fibres which can be demonstrated

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by careful dissection. Despite this essential uniformity in anatomical structure, well-demonstrated disparities in wall stress, in decline of mechanical activity, in radius of curvature, and in mural thickness, justify the functional consideration of the ventricular walls as being composed of several units, each with its own physiology and pathophysiology. The intricate structure merges to build up a dualistic function with a prevailing constrictive contractile activity and a less forceful opposing force generator, which is likely to confine systolic thickening of the ventricular wall.

## **2. Structure conditions function**

In the past, the ventricular musculature has been unrolled as if it were a biventricular continuum. This artificially imposed concept of structure cannot be reconciled with the reality of the three-dimensional arrangement of the ventricular mass. If, however, the myocardium functions as a subdivided system, we need to determine how the pumps, each with their own solitary cavity, exhibit segmental gradients in wall stress and duration of activation, and variable angles of wall curvature and thickness. We need to decide whether retardation in relaxation, and any disparity in function of the ventricular wall, are pathologic flaws or essential components of normality.

At present, however, there is no clinical diagnostic tool with which these questions are investigated. Preterminal heart failure is usually treated by heart transplantation, artificial hearts, and assist devices. Any questions concerning the structure of the failing heart are treated as academic rather than potentially therapeutic. This era of the “throw away attitude” may soon be over, if not only for economic reasons. Heart-saving strategies are in demand. However, we do not yet know to what degree global ventricular surgical mutilation, and segmental repair strategies, are compatible with improved function of the ventricular pump. For this gap to close detailed information is required concerning segmental function of the ventricular walls. In this review, therefore, we consider first the existing conceptual deficiencies, and then speculate about the knowledge required to increase the efficiency of potential heart-saving strategies.

Since the time of Frank, the hollow ventricular mass has usually been considered by physiologists as nothing but a pump, able to constrict actively, and to be dilated by its filling pressure [1]. It has been recognized to have some inborn active or passive elastic restoring forces [2–4]. More recent insights have taught us that, in health and disease, the heart exhibits an inhomogeneous pattern of wall stress and strain [5–12].

The therapy of chronic heart failure has attained a new quality. By a bold surgical stroke, Batista ventured to reduce the size of the left ventricle, and hence to remodel its shape [13,14] assuming that its size-related mural stress is the crucial determinant of the heart's ultimate fate. Long-term results are markedly variable. The fact that part of the more than 1000 patients who have undergone surgery are either still alive, or have lived for months or years with an improved quality of life, questions the significance of the intricate spiralling path of the individual myocardial fibres within the ventricular wall. The very success of the procedure also rules out the tendency of the dissected myocardium to develop arrhythmias and nociceptive reflex mechanisms, such as the Bezold–Jarish reflex, which was supposed to critically depress contractile function following myocardial mechanical trauma, to be triggered by surgical radius reduction. In contrast, the critically disabled myocardium seems to tolerate well extended ventricular incisions, spacious resections, and encroaching transmural sutures

on the left ventricular wall, and global ventricular function is improved, unless coronary perfusion is essentially disabled by the intervention.

Despite the success, however, mortality reported by various teams has varied between 25% and 80% [10,15–28]. In those who are most successful, the mortality at 1 year is comparable to the standards expected for cardiac transplantation. In other groups survival, or deterioration, or death, seem to be a matter of hazard. Important pathomechanisms have been ignored or underestimated, or indeed, have yet to be defined, which might critically interfere with the surgical procedure? This situation raises fundamental ethical questions about the acceptability of surgery on the solitary indication of ventricular dilation.

### *2.1. The trouble with Laplace's law*

There has been much recent discussion concerning Laplace's law [29–31]. While we can accept that the law yields a rough approximation concerning global ventricular wall stress, we should remember that it hardly holds true with respect to local stress. In fact, there is no tool presently available with which to measure ventricular wall stress globally! We should be concerned about the limitations of the law when applied to both the normal and the diseased heart, and in particular to the surgically remodelled left ventricle. According to the law of Laplace, wall stress is determined by the intraventricular pressure, regional wall thickness, and the radius of curvature. Discontinuities in the radius of curvature, and in thickness of the left ventricular wall, however, are obvious, and vary characteristically with different diseases, although they may be so discrete that they escape observation by clinical routine ventricular imaging.

### *2.2. The non-tangential alignment of myocardial fibres*

When Laplace's law is applied to the beating heart, it is usually tacitly assumed that the force vector yielded by the myocardial meshwork is oriented in the centripetal direction. No consideration is given to the possibility of forces exerted in other directions. So as to substantiate this assumption, Frank asserted [1], erroneously, that the weave of the individual fibres is solely aligned parallel, and tangential, to the ventricular surface.

There is a wealth of anatomical work devoted to the study of fibre orientation with respect to the longitudinal and transversal axes of the ventricles [32–41]. Any centripetal inclination of the fibres with respect to mural thickness has received little attention [7,29,33,42,43].

By extending old techniques for anatomical dissection [4,44,45], and expunging the erroneous concepts of Torrent-Guasp concerning anatomically discrete planes of cleavage [46], the process of peeling [47] has confirmed the existence of an obliquely orientated meshwork of fibres extending between the endocardium and the epicardium [44]. These peeling studies have revealed greater angles of inclination in the subendocardium than in the outer layers, and a particular irregularity in the midportion of the ventricle, where the basal and apical components merge and intertwine [7,8,33,48].

The studies have confirmed the concept proposed by Streeter for myocardial architecture [39], displaying layered fibres rotating upon a transmural axis. The studies expand the original concept of Streeter, since they permit analysis of the whole heart, including the septum and the right ventricle. They overcome the deficiencies in the concept of Streeter, and the "rope-model" of Torrent-Guasp

[46], by acknowledging and quantifying the transmurally arranged oblique fibres of the myocardial meshwork.

### 2.3. Ventricular “wringing”

Strongest evidence for the organization of the ventricular muscle in units is the intricate rotation inherent in the contraction of the left ventricle. Stuber et al. [12] have shown that, in health, the left ventricle rotates during the period of ejection, performing a wringing motion, clockwise, at the base and counterclockwise at the apex. In the normal heart, the maximum torsion of the apex relative to the base is  $\sim 6.5^\circ$ , but in patients suffering from aortic stenosis it almost doubles to  $\sim 12^\circ$ .

The late systolic backswing [12,49–51], which is necessary to bring all components of the ventricle back to the initial position, must be due to passive elastic restoring forces, unless we assume the persistence of some active restoring forces. If such forces exist, they may well be found in an oblique transmural arrangement of fibres [7,33,42,52]. The physiological and pathophysiological function of the cardiac wringing motion is unknown. Any contribution to ventricular emptying is implausible because the angles of rotation are too small. Nor can there be a contribution to early ventricular filling, because rotation reverses during iso-volumic relaxation. Anyway, it seems to be essential to the extent that it undergoes measurable alterations in the state of global ventricular disease [12]. Recently, shear stress acting on the coronary vascular bed, and on the myocardial matrix itself, has attracted some interest as part of a mechanism for interstitial transport mechanisms [47,53–55].

### 2.4. Layered shear strain

Global ventricular wringing is associated with shear strain of the layered myocardial fibres, at least in the inner and outer layers, since the fibres in the circular middle layers are parallel to the direction of rotation.

When histological sections are cut parallel to the main alignment of the fibres, they look like a dense rail network. The net is arranged so that it sustains three-dimensional displacement with only modest lengthening or shortening of any single fibre. The netted structure, for instance, explains the seemingly unleashed realignment of primarily oblique longitudinal fibres to the circular orientation which was described by Greenbaum et al. [35] in the hypertrophic heart. The amount of necessary change in the length of single fibres depends on the primary orientation of the fibre, and the degree of shear of the tissue block under consideration. Its side effect results from the fact that any major stretch or release applied to a contracting bundle of fibres modifies the time course of contraction [55–59]. This could mean that the active state in any contractile pathway is also controlled by forces yielded by neighbours coupled in parallel or series. During surgery aimed to reduce left ventricular radius, the surgeon must keep in mind the potential of disturbing segmental contractility when applying techniques of resection which require an extended realignment of the myocardial tissues. The original procedure introduced by Batista involved asymmetrical resection, and demanded considerable topographic readaptation. And, indeed, in patients undergoing surgery in this fashion, we demonstrated a weak trend to a more marked drop in mesh tension in the close vicinity of the surgical wound than in other patients who underwent an essentially symmetrical resection [25]. In the latter patients [25,60], the resected segments were wider than in the former group [47]. Admittedly,

another reason for this difference may have been the improved myocardial protection provided for the latter group of patients [25,60].

### 2.5. *The cardiac paracrine activity*

Another linkage between contractile function and the wringing motion of the heart could be an effect of squeezing the coronary and lymphatic vessels, and stretching the myocytes. This might stimulate the autocrine activity of the myocytes and the endothelium, triggering the release of transmitters from the myocardium or endothelium into the fibrous myocardial matrix [47,52–54,61–64]. It is, indeed, most appealing to suggest that the physiological shear stress, and with it endothelial NOS-activity, are impaired when the cardiac pattern of motion is jeopardized, be the amplitude of movement attenuated or amplified.

### 2.6. *Are basic structures and functions invariably impaired by the strategies for cardiac salvage?*

In partial ventriculectomy, resection takes place most frequently at the obtuse margin, where the radius of curvature is small in the normal left ventricle, but which becomes ballooned in dilated cardiomyopathy. Resection, therefore, is performed on a ventricular segment which, according to the law of Laplace, has also been the site of major mural stress overload. The apex is typically widely resected because it is rounded in the diseased heart, and hence, overloaded. By measuring focal tension within the myocardial mesh [65], we have shown that partial ventriculectomy unloads the ventricular wall by up to one-third. Comparing our results obtained during measurements performed with Dr. Batista in Curitiba [65] with those obtained during operations performed by Dr. Konertz in Berlin, we have noticed an important difference. In one-quarter of the sites of measurement in Curitiba, an unexpected increase, rather than a decrease, was noted in local myocardial mesh-tension after partial left ventriculectomy. In those patients, the resection had been performed following the original asymmetric technique. In contrast, in patients undergoing surgery in Berlin, an increase in mesh-tension was found in only one out of 38 sites of measurement. In these patients, a symmetrical segment, shaped as a figure of eight, had been resected from the interpapillary region. From this experience, we infer that the shape and topography of resection has a major impact on the resulting redistribution of wall stress.

Furthermore, a more pronounced reduction in the postoperative levels of force we found in Curitiba although a wider area was resected in the patients undergoing surgery in Berlin. Probably the levels of force measured immediately postoperatively are influenced also by the surgical procedure, including the effect of transient ischemia. A very careful protocol of myocardial protection is used in Berlin, whereas the procedure as initially performed in Curitiba on the beating heart consisted of an alternating series of ventricular fibrillations, electrical defibrillations, cardiac arrest induced by repeated intracoronary potassium injections, and repeated haemorrhage from coronary arteries, the latter event causing intermittent falls in coronary arterial pressure.

## 3. **Some obvious mechanisms causing failure of partial ventriculectomy**

*Overcorrection of compliance:* There is, as yet, no unanimously accepted methodology for partial left ventriculectomy. The site of resection, as well as the shape and size of the resected segments, are

as judged by the surgeon. And so, surgical reduction continues to be a most variable, and sometimes a hazardous, intervention.

We have seen patients suffering from left ventricular diastolic heart failure mediated by overcorrection. We saw one young lady dying from lung oedema within the first 24 h following moderate replacement of fluids simply because the intensivist was not aware of her overcorrected left ventricular compliance.

*Undercorrection:* It is part of the learning curve of most surgical teams to start with resections which are too faint-hearted. This applies to the size of the resected segment, as well as to its topography. Newcomers focus on the dilated apex leaving untouched the midportion and the base. This is “virtual volume reduction surgery” which provides a cosmetic increase in ejection fraction, but has only a minor impact on myocardial consumption of oxygen [11,66].

The aim is to correct left ventricular diameter, from base to apex, rather than to shorten the long axis of the ventricle. If this is not achieved the ventricle will continue to dilate. Ultimately, mitral valve incompetence will dominate the natural history of the disease. To make the difference very clear, not volume reduction surgery but radius reduction surgery is the target procedure.

*Asymmetrical resection and distopical readaptation:* According to Batista’s original description [13,14], the incision is asymmetrical, resulting in a longer posterior than anterior lip of the wound. When both lips are reconstituted by the suture, wall segments are unified which were not originally linked. Some areas are stretched more than others, some areas are compressed by the suture. Hence, the resulting damage to the tissues widens the scar [67], which extends beyond the suture line and forms an unpredictably shaped and extended block of connective tissue. The garland-like edge of the scar reflects the inhomogeneous repartition of stress acting on the remaining wall segments and/or an inadequate focal vascularization. In contrast, the symmetrical technique of resection [24,25] readapts the basal to the basal level of the left ventricle, and the apical to the apical level.

*Impairment of the inner layers of the left ventricular wall:* Particularly delicate parts of the heart are its subendocardial layers. In the human heart, the inner layers are extensively trabeculated. This is not the case in the hearts of quadruples, the inner surfaces of which are smooth. The trabeculated inner layers are supposed to pull down the annulus of the mitral valve in apical direction during systole, thus widening the atrium and enhancing its filling by suction [68]. Partial ventriculectomy fixes the inner layers from base to apex to the subjacent middle layers. The ensuing restriction in freedom of motion may be involved in the formation of the extended area of endocardial trauma and scarring which we found at autopsy in three human hearts which survived the intervention for at least several months. These extended endocardial scars were the potential origin of arterial embolization, the interference of which after partial ventriculectomy is probably underestimated.

*Deficit in coronary arterial perfusion:* In three hearts obtained from long-term survivors, we performed a postmortem dissection with special reference to the scar and the alignment of the myocardial fibres around the scar. In all hearts, we found an asymmetrical scar, diverging markedly from the epicardium to the endocardium. Its fibrotic edges extended beyond the main suture line by between 2 mm and 2 cm, so that the edges of the scar did not parallel the suture line. From these observations, we infer that wall stress around the suture line deviates both in amount and direction from its original alignment, thus jeopardizing coronary perfusion. Coronary arteries may be kinked or virtually occluded [69]. Circumscribed areas around the wound may be excluded from coronary arterial perfusion which, previously, were part of the “offstream” area of the resected marginal coronary artery.

*Dearth of myocytes:* A significant amount of contractile mass is resected while the heart is in a state of dilation and hypertrophy. After intervention, wall stress is attenuated. The trigger for myocardial hypertrophy is thereby annulled. The remaining myocytes may regain their original length and thickness while shrinking. However, the absolute number of myocytes had been reduced. Does this mean that ventricular size keeps shrinking to an excess. To our knowledge, no case has been reported of a heart which shrank to death. In contrast, there is a wealth of experimental work done on normal hearts which were reduced in radius, and, which survived and grew back to normal size within several weeks. This shows that any remodelling of the left ventricle is likely to be triggered by haemodynamic requirements rather than by an intrinsic pattern of standard-shaped myocytes.

*Arrhythmias:* There are no figures available as to the percentage of sudden deaths which must be attributed to ventricular fibrillation. Small number of patients (eight) have been studied by body surface mapping and QT variability analysis [70–73]. In a group of more than 40 patients, Konertz et al. [24,25] have implanted defibrillators. It is their opinion that malignant arrhythmias are overestimated, at least in the group of patients with non-ischaemic heart failure suffering from idiopathic dilated cardiomyopathy. In the group of primarily ischaemic patients, nonetheless, they found a high incidence of life threatening arrhythmias after partial ventriculectomy.

*Wall thickness pump failure:* Comparing two hearts using electron beam tomography in systole and diastole before and after partial ventriculectomy we could show that patients survived, and markedly improved in left ventricular function when the left ventricular wall was able essentially to increase in thickness. Other patients developed low cardiac output failure, and required insertion of a left ventricular assist device. Eventually, they died because they were unable to develop after ventricular radius reduction the necessary increase in wall thickness, neither in the mean, nor during systole.

*Persistence of the primary disease or addiction:* There are no data available about the percentage of viral infections or immunological diseases contributing to the population of patients undergoing radius reduction surgery. Particularly deceiving results in cachectic patients suggests that in those patients who were unable to profit from the intervention, the primary disease might have continued to degrade the remaining myocardium.

In principal, the same applies to heavy smokers and alcoholics who are unable to abstain from addiction. We dissected the heart of a 50 year old man who died 9 months after partial ventriculectomy in left heart failure caused by alcoholic dilated cardiomyopathy [74]. He had resisted all attempts to make him abstain from alcohol.

*Inadequate postoperative care:* At the junction of surgery, anaesthesiology and cardiology, namely in the Intensive Care Unit, the patient faces some potential additional dangers. A particular problem is the postoperative regulation of volume in the face of an abruptly decreased left ventricular compliance. Given the various potential mechanisms which can lead to postoperative deterioration, the optimal regimen for any individual patient remains to be established.

#### 4. Summary and outlook

Most patients who are referred to surgery for heart preserving surgery are insufficiently defined in terms of their primary disease, the function of the prospectively remaining myocardium, and their

global physical reserve. The most important diagnostic tool is to assess the reserve for wall thickness pump activity under hypovolaemic conditions. The manoeuvre simulates the working conditions of the shrunken heart after the intervention. Hibernating wall segments [69,75] can be differentiated from scars by positive inotropic medication. Furthermore, the pattern of coronary vascularization needs to be assessed. Pulmonary hypertension complicates the process of postoperative recovery, and is a particular point of concern in the Intensive Care Unit. The search for the primary disease, and its state of healing at the time of the intervention, require greater diagnostic endeavour. The routine implantation of defibrillators will probably become standard at least in those patients with ischaemic hearts, in whom the incidence of postoperative ventricular fibrillation turns out to be high. The proper procedure of reshaping the dilated ventricle has to be standardized by it by resecting a segment, girding it with a circular intramural suture, or wrapping it with a jacket. To redeem cardiac surgeons from justified queries from ethical committees, clinical and basic research should be united to address the outstanding problems in concerted fashion.

A most promising approach is off-pump partial ventriculectomy using the ventricular plication technique. It is performed on the closed heart while beating. Using aspirator cups of variable shape and size, the segment to be plicated is individually tailored. The most functionally efficient position is selected by repeated test aspirations, which are easily tolerated. Ultimately, a new suture technique permits preservation of the coronary arteries in the plicated area and its surroundings.

## **5. Summary**

Surgical strategies recently introduced to improve ventricular function have been based on the concepts of reduction of ventricular diameter, synchronization of myocardial activity, passive support of diastolic ventricular shape, and active support of systolic ventricular constriction. They have depended on several established theoretical assumptions, not all of which are totally valid.

Clinical results have proved markedly variable. This is especially true for procedures designed to reduce the radius of the left ventricle. Some have reported up to 80% mortality, whereas others achieve results comparable with those for heart transplantation. Because of this, the method runs the risk to be rejected, or else, its more widespread application will be postponed until essential details concerning the basic concepts have been elucidated. It is these details which we discuss in this review.

The substrate presently offered to the surgeon is essentially undefined, while the surgical methods have still to be standardized. Diagnostic work-up does not match the requirements of the available therapeutic options. Individual patients with dilated cardiomyopathy are rarely specified in terms of the basic disease, or its state of progress. Detailed knowledge is presently lacking concerning the tolerance of the heart to destruction of its internal structure, its electrical vulnerability, and the effect of disturbances of its autocrinal activities.

Some most unfavourable conditions which militate presently against successful implementation of partial left ventriculectomy are exposed in the present review. Successful strategies for surgery designed to reduce ventricular radius require an adequate understanding of their potential side effects on ventricular structure and function. It will be necessary to standardize pre-, intra- and postoperative diagnostic monitoring. Detailed knowledge is essential concerning the primary disease, and its effect on ventricular function. Surgical methodology must be standardized, thus permitting multicentric

comparisons of strategies, ultimately leading to adoption of an optimal therapy tailored to the needs of the individual patient.

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