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Research Paper

Computerizing the Anatomically Smart Left Ventricle: How its Shape-factor based Index relates to its Contractile Performance - Depicting New Quantitative Trends in Medicine

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ABSTRACT

The human body is so smart that anatomists and physiologists, physicians and surgeons have not been able to adequately configure it. So then let us start with anatomy, and look into the heart's left ventricle (LV) as an example of how its intrinsically optimal shape efficiently contributes to its physiological performance. This will show us how mathematical formulation and computation of the LV shape-based contractility index can enable (i) assessment of its performance, and (ii) also precise medical diagnostics of a cardiomyopathic heart.

THIS ARTICLE COMPRISES OF THE FOLLOWING TWO SECTIONS

I. How the Left Ventricle's intrinsic ellipsoidal Anatomical shape is decisive for its Contractility performance. The shape of the left ventricle (LV) is of clinical relevance for prognosis and diagnosis of heart patients. We are defining the Shape Factor (S) of a left ventricular model derived from its imaging data. From medical imaging data, we are analyzing and showing that a normal LV is ellipsoidal in shape, relative to a pathological (poorly contracting) LV, and hence has a better shape factor value. Then, we are developing the LV shape-based contractility index, by which it can be seen that a more spherically shaped and less-ellipsoidal shaped LV is associated with a poor contractile weak and failing heart.

II. How Cardiomyopathy affects LV Shape and Contractile Function, as represented by LV Sphericity Index. We are defining the Sphericity Index (SI), which is also related to its shape factor (S). We are showing a normal LV to be more ellipsoidal than a cardiomyopathic LV, and hence having a lesser value of SI. Then we are showing that a normal LV becomes even more ellipsoidal as it contracts from end-diastole to end-systole, compared to an ischemic dilated cardiomyopathic LV. Hence, a bigger value of SI from end-diastole to end-systole can imply a well contracting LV, whereas a smaller value of SI can suggest a poorly contracting and pathological LV. This is how the sphericity index can enable us to detect a diseased LV, and even make a case for surgical restoration of its contractility.

These two sections are depicting new trends in medicine, by which we can make use of the anatomical shapes of the LV (defined by shape factor and sphericity index) to characterize its contractile performance, and to also diagnose a cardiomyopathic (poorly contracting) LV. So together these two sections can depict new quantitative trends in medicine, by means of mathematical anatomical modeling.

KEYWORDS: Cardiomyopathy, Biomechanics, Cardiac contractility index, Sphericity index, LV Shape factor.

INTRODUCTION

We have been talking about designing and digitizing smart cities and hospitals. But we need to recognize that the human body is intrinsically much smarter than everything that we can design. Only now by employing computerized imaging and modeling, can we determine how the human body anatomy is intrinsically optimally designed to take care of its physiological functions. So, let us now explore this long overdue computational configuration of the human body anatomy and its relationship to physiology.

Let us start with looking into the heart left ventricle's anatomical shape, as an example of how its intrinsically optimal shape contributes to its efficiently performing its physiological contractile function. For this purpose, we have formulated the LV shape-based contractility index and providing its application in reliable medical diagnostics.

I. HOW THE LEFT VENTRICLE'S INTRINSIC ANATOMICAL SHAPE IS DECISIVE FOR ITS CONTRACTILE PERFORMANCE

Contractility is the key mechanism of the left ventricular pumping role, and this is primarily due its ellipsoidal shape. So, let us look into how this happens to be.

In **figure 1**, we are depicting the heart anatomy with its four chambers, right atrium, right ventricle, left atrium and left ventricle. We can notice that the left ventricle (LV) looks ellipsoidal in shape.

1.1 Left Ventricular Model Geometry and its Shape Factor

The shape of the left ventricle (LV) is of clinical relevance for prognosis and diagnosis of heart patients. We can show that a normal LV is more ellipsoidal in shape, and that a more spherically shaped and less-ellipsoidal shaped LV is associated with a failing heart [1]. In figure 2, we are depicting the LV simulating geometrical model, as a prelate spheroid truncated 50% of the distance from equator to base. The LV shape, as in figure 2, can be defined by the major and minor radii of its two surfaces: the endocardium of the LV and the septum, and a surface defined by the epicardium of the free wall. The overall longitudinal distance from the base to apex BA (=3LA/2) is thus 1.5 times the major radius of the ellipse.

The simulated LV's geometrical parameters SA = AP/2, and LA = BA/1.5, where BA (the LV long axis) is defined as the longest distance from the apex to the base of the LV, as measured on the four-chamber MRI view of the heart; AP is defined as the widest LV minor axis. The measurements of AP and BA based on 2-D CMR imaging are shown in figure 6.

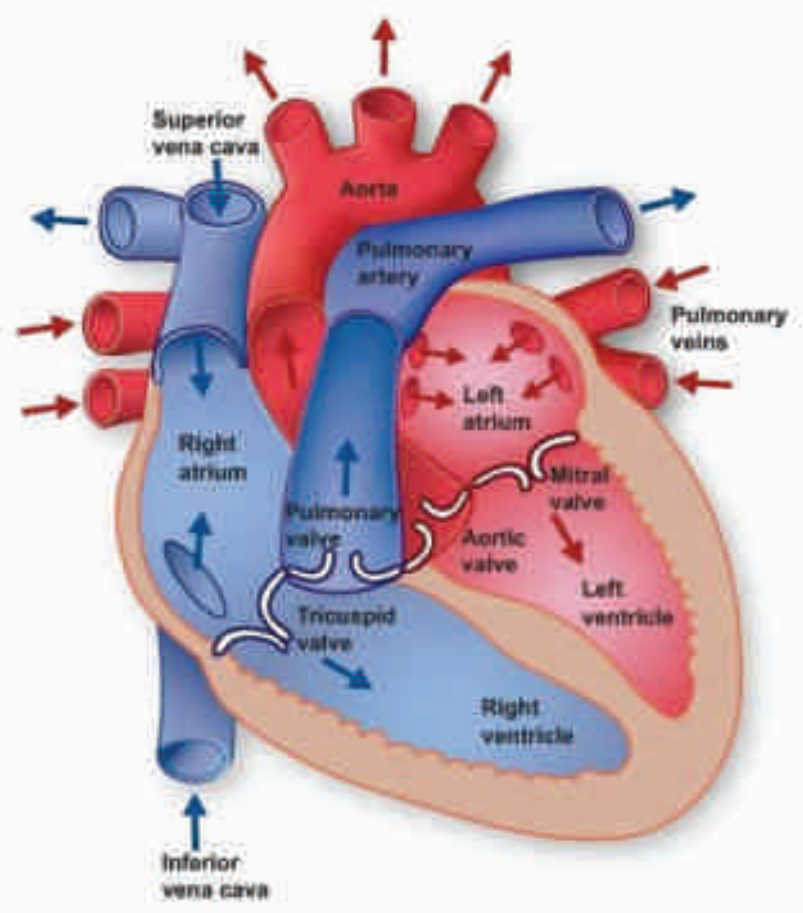

Figure 1: Picture of the heart, showing its four chambers, the valves, and the connecting blood vessels

The left ventricle's myocardial wall has helically wound fibers. So, when these fibers are activated and contract, it causes twisting of the left ventricle from bottom upwards. This in turn generates LV wall stress, and raises the intra-LV pressure to finally result in LV output into the aorta. Now this would not be possible if the left ventricle was cylindrically shaped. **We can thereby also recognize that the LV wall stress development is the basis of LV contractility.**

Based on **figure 2**, let us define the

LV shape factor: S = SA/LA (1)

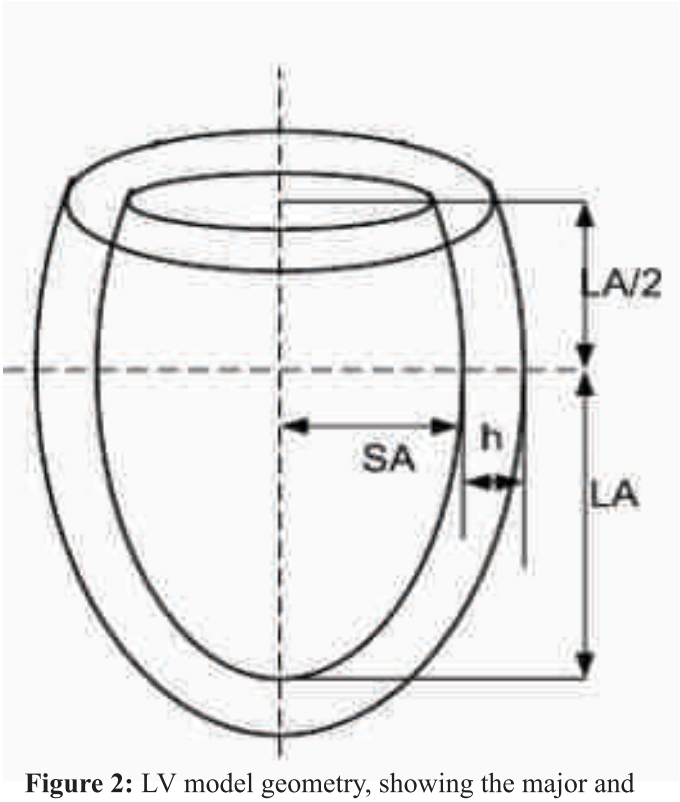

Figure 2: LV model geometry, showing the major and minor radii of the inner surface of the LV (LA & SA) and the wall-thickness (h). Based on this figure, we define LV shape factor S = SA/LA. Also, AP = 2 SA, and BA = 1.5 LA; Sphericity Index = AP/BA = 1.3 S, or S = 0.77 SI.

This LV shape factor value can be developed from heart imaging, as shown in figure 6.

The left ventricular cavity and wall volumes are calculated from the epicardial anterior-posterior (AP) and base-apex lengths according to the equations:

$$Vm = 9\pi[2\,LA \times SA + SA^2]h/8 \qquad (2)$$

$$V = 9\pi SA^2 LA/8 \qquad (3)$$

wherein V is LV volume, VM is myocardial volume, h is wall-thickness, LA and SA are endocardial major and minor radii. From these two equations, we can determine the values of SA and LA, and hence of the Shape Factor S = SA/LA. Now we are showing below how LVs with higher values of the shape factor (S) are poorly contracting LVs, and can be designated to be at risk of heart failure.

1.2 Left Ventricular Model Wall Stress

For an ellipsoidal shell, the circumferential wall stress$_\theta\sigma$ (referred to as σ) at the waist of the LV ellipsoidal model, is given by Mirsky [2], as:

$$\sigma = P\frac{SA}{h}\left[1-\frac{SA(SA/LA)^2}{(2SA+h)}\right] = P\frac{SA}{h}\left[1-\frac{(SA/h)(SA/LA)^2}{2(SA/h)+1}\right] \qquad (4)$$

From equations (2 & 3), we obtain, by putting S=SA/LA,

$$\frac{SA}{h} = \frac{V}{V_M}(2+\frac{SA}{LA}) = \frac{V}{V_M}(2+S) = \frac{2+S}{V^*} \qquad (5)$$

where S=SA/LA constitutes the LV shape factor, and V*= VM /V.

Combining equations (4) and (5), we can express the normalized LV wall stress $_*\sigma(=\sigma/P)$, as:

$$\sigma^* = \frac{2+S}{V^*}\left[1-\frac{S^2(2+S)}{2(2+S)+V^*}\right] = f(V^*,S) \qquad (6)$$

Equation (6) provides σ^*as a function of S, for a given V*. This is our non-invasively obtainable, pressure-normalized LV wall stress, in terms of S and V*. Now, as we have indicated above, the LV wall stress development is the basis of providing LV contractility. Hence this normalized LV wall stresscan also be associated with and be a measure of LV contractility.

1.3 Noninvasive Cardiac Contractility Index, based on normalized LV wall stress (σ^*)

Our concept of a LV shape-based contractility index is that it is a measure of the capacity of the LV myocardial sarcomere to contract and generate wall-stress that will adequately raise intra-LV pressure to eject the blood. Now since the LV wall stress depends on its shape (as per equation 6), hence the LV contractile capacity also depends on the LV shape. This is verily the rationale behind the LV shape-based contractility index. Based on clinical observations, a healthy LV shape

factor is more akin to the optimal-ellipsoidal shape factor, with a lesser value of S. However, it transforms into a more spherical shape with a greater value of S in a poorly contracting LV as well as in LV failure. Hence, our LV shape-based contractility index, expressed as $d\sigma^*/dt_{max}$ (based on equation 6) is meant to quantitatively express this clinical observation.

Noninvasive cardiac contractility index: Conventionally, the LV contractility is measured in terms of the LV pressure as dP/dt_{max}. Now in our paper [3], we had approximated the LV as a thick-wall spherical shell, consisting of incompressible, elastic material. We employed the maximum circumferential wall stress (σ_θ) at the endocardium, to obtain:

$$\sigma_\theta(r_i) = P\left[\frac{r_i^3/r_e^3 + 1/2}{1 - r_i^3/r_e^3}\right] \qquad [7]$$

where r_i and r_e are the inner and outer radii, and P is LV intracavitary pressure [3].

By normalizing the wall stress to LV intra-cavitary pressure (P), we obtained:

$$\sigma^*(r) = \frac{\sigma_\theta}{P} = \frac{r_i^3}{r_e^3 - r_i^3}\left(1 + \frac{r_e^3}{2r^3}\right) \qquad [8]$$

Since the maximum wall stress occurs at the inner endocardial wall, we have:

$$\sigma^*(r = r_i) = \left(\frac{P/(V_m + V) + 1/2}{1 - P/(V_m + V)}\right) = \left(\frac{3V + V_m}{2V_m}\right) = \left(\frac{3V}{2V_m} + \frac{1}{2}\right) \qquad [9]$$

where P is LV intra-cavitary pressure; σ_θ is the wall stress;

V(= $4\pi r_i^3/3$) denotes LV volume; Vm (= $4\pi(r_e^3 - r_i^3)/3$) denotes LV myocardial volume; ri and re are the inner and outer radii of the LV, respectively. By differentiating equation (9) with respect to time, we get:

$$d\sigma^*/dt_{max} = \left|\frac{d(\sigma_\theta/P)}{dt}\right|_{max} = \frac{3}{2V_m}\left|\left(\frac{dV}{dt}\right)\right|_{max} \qquad [10]$$

From equation (10), this **non-invasive cardiac contractility index** is also seen to represent the maximal flow rate from the ventricle (cardiac output) normalized to myocardial volume (or mass). This index is easily measured non-invasively, i.e. from echocardiography or magnetic resonance imaging, as explained in [3].

We have validated $d\sigma^*/dt_{max}$ against (i) the traditional invasively obtained contractility index dP/dt_{max} , (ii) maximum LV active elastance $E_{a,max}$, and (iii) end-systolic elastance Ees, in subjects with disparate ventricular function, as depicted in **Figure 3.**

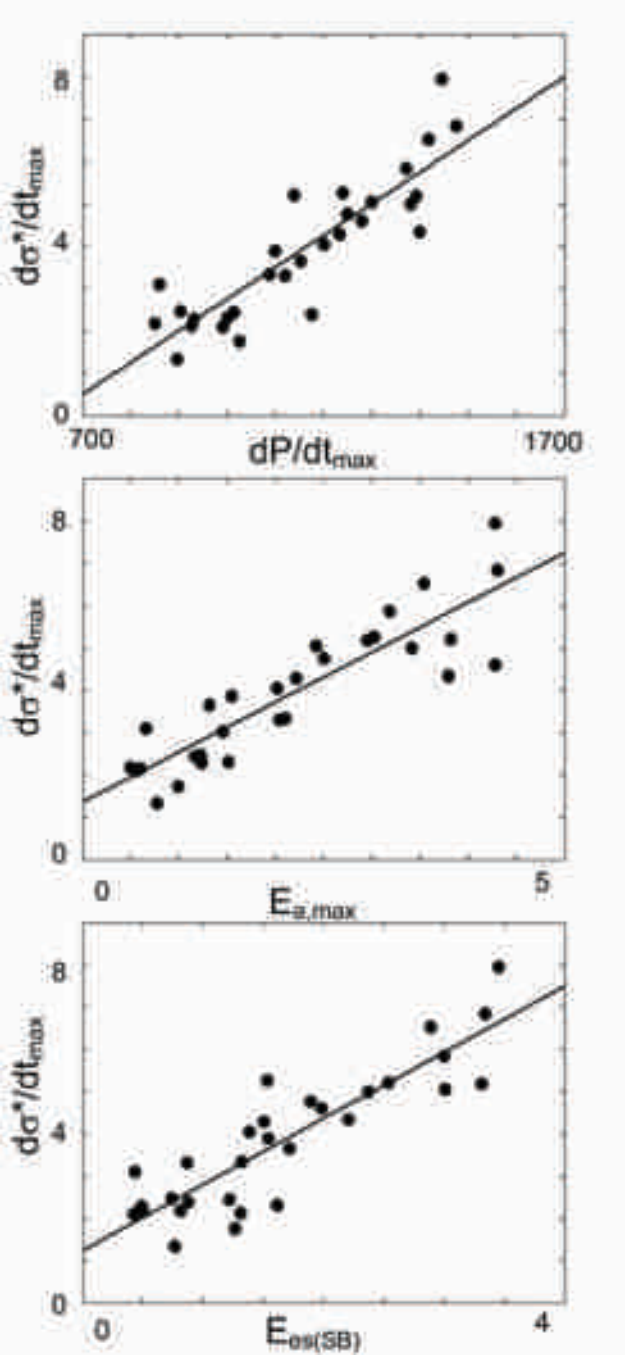

Figure 3: Linear regression analysis demonstrates good correlation between $d\sigma^*/dt_{max}$ and dP/dt_{max}: [$d\sigma^*/dt_{max}$ = $0.0075dP/dt_{max}$-4.70, r=0.88; top figure], between $d\sigma^*/dt_{max}$ and $E_{a,max}$ [$d\sigma^*/dt_{max}$ = $1.20E_{a,max}$+1.40, r=0.89; middle figure], and between $d\sigma^*/dt_{max}$ and $E_{es(SB)}$ [$d\sigma^*/dt_{max}$ = $1.60E_{es(SB)}$+1.20, r=0.88; bottom figure].

Now in contrast to the normalized LV wall stress σ^* given by Eq (10), our σ^* given by Eq (6) incorporates the ellipsoidal shape of the LV. In Figure 3, we have shown how $d\sigma^*/dt_{max}$ based on Eq (10) can provide such a good correlation with the traditional contractility index dP/dt_{max}, to serve as a non-

invasive contractility index. So we can now assume that $d\sigma^*/dt_{max}$ based on Eq (6) can in fact provide as good or even better correlation with dP/dt_{max} , to hence serve as a more relevant non-invasive contractility index.

1.4 Optimal LV Shape Factor and Corresponding Shape Factor Index

Let us designate the optimal shape factor S (=SA/LA) to be that value for which the generated normalized wall stress σ^* for a given LV volume (at the start of ejection V=Vse=Ved) is maximum for a specific value of V*. The concept of optimizing the shape factor is based on the format of LV pressure $P=\sigma/\sigma^*$. During systole, the interaction of the actin-myosin filaments causes contraction of the myocardial fibers and generation of myocardial wall stress (σ). The resultant LV pressure (P) generation is given by σ/σ^*, where (as can be seen from equation 6) σ^* is purely dependent on LV geometry and is a function of the shape factor (S) and volume ratio (V*).

Now for a particular V*, as S increases (i.e., as the LV becomes more spherical and less ellipsoidal),σ^* decreases, and hence the LV pressure increases. For an adequate amount of LV wall stress (σ) generated, we want the LV pressure to be maintained low, so that its oxygen demand is kept low. **Hence, we want that (for a specific V*)σ^* to be as high as possible and correspondingly S to be as low as possible, i.e., the LV must be more ellipsoidal in shape[1].**

So, from equation (6), we can maximize σ^* with respect to S, as:

$$\frac{d\sigma^*}{dS} = \frac{1}{V^{*\frac{2}{3}}} - \frac{\frac{1}{3}\left[(8S+12)V^{*\frac{2}{3}} - (4S^2+2S)\left(\frac{1}{3}V^{*-\frac{1}{3}}\right)\right] - (8S^2+6S+2)V^{*\frac{2}{3}}}{(V^{*\frac{2}{3}}+4+2S)^2} = 0 \quad [11]$$

Simplifying equation (7), we have:

$$6S^2+(4V^{*\frac{2}{3}}+3)S^2+(2V^{*\frac{2}{3}}+5)S+4V^{*\frac{2}{3}}+4)S-(V^{*\frac{2}{3}}+4)^2=0 \quad [12]$$

from which we obtain the expression of the Optimal shape factor S^{op}as a function of V*, as

$$S^{op} = 0.053V^* + 0.39 \quad [13]$$

This equation can be referred to as the **optimal Shape Factor Index** for maximizing LV contractility σ^*. If we substitute expression (13) into $d^2\sigma^*/dS^2$ we get $d^2\sigma^*/dS^2$ to be negative. In other words, this optimal S function (of V*) maximizes σ^*, in accordance with our rationale. The value of $S > S^{op}$ is associated with a poor contractile heart. The significance of expression (13) is that one can adjudge the cardiac health state of a patient merely in terms of how close the shape-factor S (=SA/LA) corresponding to a patient's V* value (at the start of ejection) is to the optimal value. We do not even need to compute σ^* or $d\sigma^*/dt$ in order to evaluate how efficiently a particular LV is pumping.

Now let us define **LV shape-factor based contractility index in anon-dimensional form** at the start of ejection (se), as follows:

$$SFI2 = (S_{se} - S_{se}^{op}) / S_{se}^{op} \quad [14]$$

where S_{se} is the measured shape factor value at the start of ejection (i.e., at end-diastole), $S_{se}^{op}$is the corresponding optimal value at the start-of-ejection. So, as SFI2 value increases, the LV contractility becomes poorer; in other words, lower the value of SFI2, the better the contractility of the subject.

Now this SFI2 index, based on equation (14), is applied clinically, and the calculated SFI2 and S_{se} values for the clinical patient data (of V*and ejection fraction EF) are shown in **Table 1**. It is seen that the value of SFI2 is obtained to be (i) 0.21 for subject HEL, with EF 0.36, (ii) 0.057 for subject DDM, with EF 0.66, and (iii) 0.11 for subject SKS with EF 0.24. Note that of the 3 subjects, the patient DDM (who did not have myocardial infarct or coronary arterial disease) has the highest EF, and correspondingly SFI2 is minimum for DDM. The details of the Clinical studies, measurements and the ethics approval are provided in our paper [1].

Table 1: Clinical history, calculated Sse and SFI2 from subjects (HEL, DDM, and SKS).

Subject	Disease	S_{se}	V^*	SFI2	EF
HEL	MI, DVD	0.56	1.4	0.21	0.36
DDM	DVD, HTN	0.48	1.15	0.057	0.66
SKS	TVD	0.55	2.1	0.11	0.24

Now let us look at **Figure 4**, in which the three cases of Table 1 are depicted on the (S-V*) plane. Based on this figure 4, we can postulate that if the shape factor S is located in the A zone, it can have a tolerable shape to provide a reasonable LV contractility; then the B zone can represent a poorly contracting LV, while the C zone can represent a failing heart.

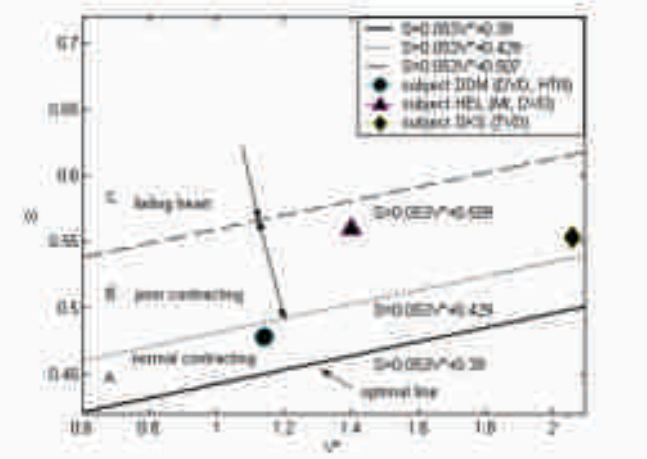

Figure 4: We can postulate LVs to be normal contracting, poorly contracting and failing heart, as illustrated in the above figure. Subject DDM, shown on the S-V* plane; can hence be depicted to have normally contracting heart. On the other hand, subjects HEL and SKS have poorly contracting hearts.The corresponding SFI2 values of these 3 subjects are

shown in Table 1, based on the location of the calculated (S, V*) plots on this plot. This figure is adopted from our paper [1].

1.5 Clinical Studies showing association of LV shape with contractility:

Now to further validate our association of LV ellipsoidal shape with its better contractility, we have performed clinical studies, which are described in detail in our paper [1]. Conventionally, as we have indicated above, the LV contractility is measured as dP/dt_{max}

Ten other patients (with coronary and/or valvular disease), with EF=0.49±0.13 and dP/dt_{max} =1183±62 mmHg/s were classified into **Group 2**, having mean-age of 57.4 years. Finally, we have **Group 3** of hospitalized patients (of having EF=0.38±0.12 and dP/dt_{max} =948±78 mmHg/s) with poor (clinically assessed) contractility. These subjects are listed in **Table 2.**

Now in **figure 5**, we take the average values of V(se) and S(se) for each group, and then show how the corresponding LV shape looks like, for these three groups. It is seen that Group 1 LV (on the left of figure 5) has normal contractility, with lowest

Table 2: Clinically monitored Data and Computed Parameters for Three Groups: Group1 (normal contractility), Group2 (inadequate contractility) and Group 3 (poor contractility).

	Group 1	Group 2	Group 3
Age (years)	58.70±6.65	57.40±5.85	58.20±9.11
dP/dt_{max}	1406.00±51.00	1183.00±62.00*	948.00±78.00*
HR (beats/min)	72.69±9.20	67.70±10.04	74.02±10.09
V_M (ml)	146.00±43.00	189.00±78.00	216.00±80.00*
V(se) (ml)	119.26±31.75	148.70±68.32	177.41±90.00
V(ee) (ml)	43.64±9.87	79.45±53.75*	116.73±54.01*
EF	0.63±0.05	0.49±0.13*	0.38±0.12.00*

In this study, ten subjects, with EF=0.63±0.05 dP/dt_{max} and =1406±51 mmHg/s were selected to comprise **Group1.** They did not use nicotine, caffeine or alcohol. The age profiles were similar and their anthropometric data, blood pressure, heart rate and ejection fraction (EF) were within the expected range.

value of S(se) and SFI2. Group 2 LV (in the middle) has poor contractility, while Group 3 LV (on the right) represents a failing heart, with the highest value of S(se) and SFI2. Now we can also see that the left Group 1 LV has a distinct ellipsoidal shape, while the middle Group 2 is less ellipsoidal, and the

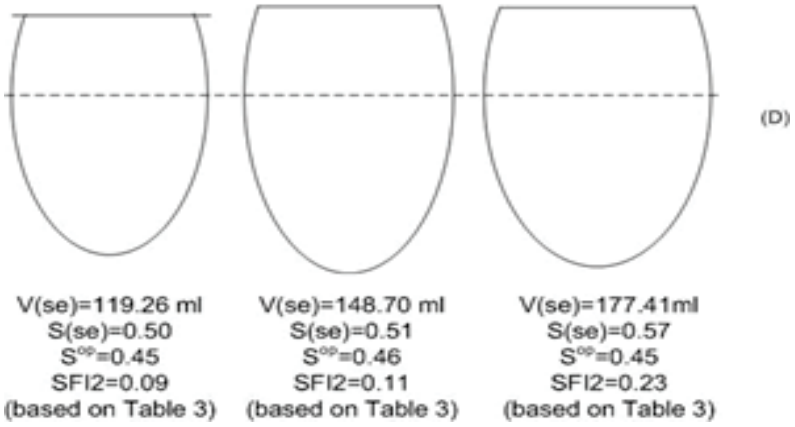

Figure 5: This figure provides the means values of V(SE), S(SE), Sop, and SFI2. The Sop is calculated using equation (13), and SFI2 is calculated using equation (14). This figure clearly demonstrates that a more-spherical shape, with higher values of S and SFI2, is associated with poor systolic function and decreased contractility of the LV. This figure is adopted from our paper [1].

right Group 3 LV is more spherically shaped. Thus, it is clearly demonstrated that a more-spherical shaped LV, with higher values of S and SFI2, is associated with poor systolic function and decreased contractility of the LV.

We can see that we can detect a poorly contracting LV based on the shape-factor based contractility index SFI2, showing how the LV's intrinsically optimal anatomical shape meant to make it contract optimally.

II. HOW CARDIOMYOPATHY AFFECTS LV SHAPE AND CONTRACTILE FUNCTION, AS REPRESENTED BY LV SPHERICITY INDEX

Now let us go one step further, and depict what happens when the LV contracts and how its geometrical shape changes, for a normal LV and a cardiomyopathic LV whose wall has been damaged, i.e., become ischemic by poor coronary perfusion due to stenotic coronary arteries.

Cardiomyopathy refers to diseases of the heart muscle. These diseases enlarge the heart muscle or make it thicker and more rigid than normal. In some cases, scar tissue replaces the muscle tissue. Myocardial ischemia and infarction can cause ischemic dilated cardiomyopathy (IDCM), and associated changes in left ventricular shape (regional curvatures), myocardial wall stress, and contractility cardiomyopathy. Cardiomyopathy causes measurable deterioration of myocardial function, and can lead to heart failure.

Heart failure (HF) is generally defined as the inability of the heart to supply sufficient blood flow to meet the body's needs. Common causes of heart failure include myocardial infarction (heart attacks) and other forms of ischemic heart disease and cardiomyopathy.

II.1 Defining Sphericity Index

Now then let us designate a 'sphericity index' to categorize such pathological LVs that can result in heart failure. So based on the above Figure 2, let us designate the endocardial minor axis dimension (SA) and major axis dimension (LA), shape factor (S), eccentricity (E) and **Sphericity Index** (SI) as follows:

$$SA = AP/2; \quad LA = BA/1.5; \quad S = SA/LA; \quad E = \left(\frac{BA^2 - AP^2}{BA^2}\right)^{0.5}; \quad SI = AP/BA \quad [15]$$

$$SI = AP/BA = 2\,SA/\,1.5\,LA = 1.3\,S \quad [16]$$

where BA (the LV long axis) is defined as the longest distance from the apex to the base of the LV, as measured on the four-chamber MRI view of the heart; AP is defined as the widest LV minor axis. A small value of SI implies an ellipsoidal LV, whereas a higher value of SI is associated with a cardiomyopathic LV. **We can also note that the sphericity index (SI) is closely related to the shape factor (S).**

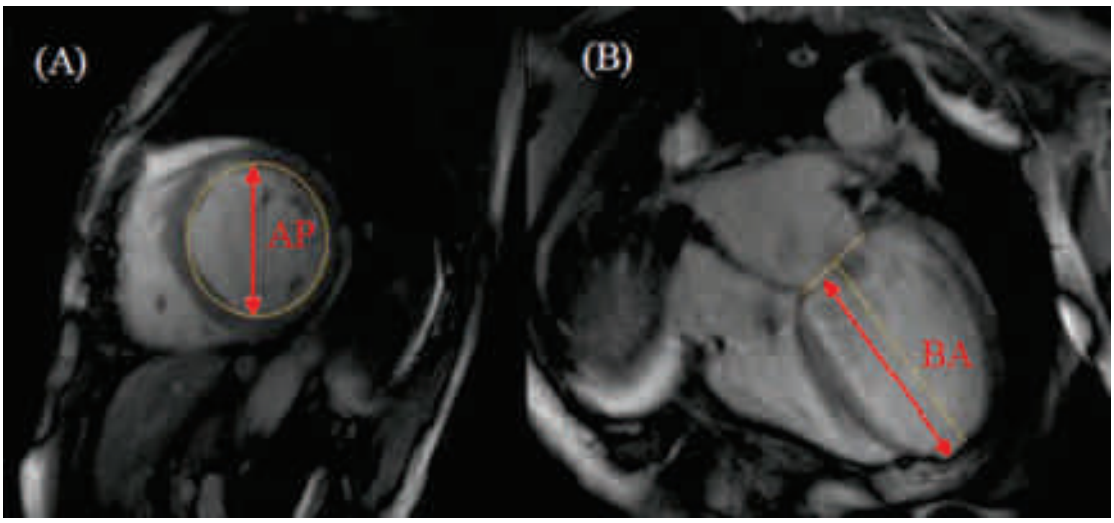

Figure 6. Short-axis (panel A) and long-axis (panel B) magnetic resonance images of a patient. The Anterior-posterior (AP) and base-apex (BA) were measured from 2-D CMR imaging. The shape factor S, eccentricity index E, and sphericity index (SI) can then be calculated from Equations(15) and (16). This figure is adopted from our work in [5].

Now we are providing the below **Figure 6**,showing how to define the Sphericity Index (based on equation 15), from MRI images of a patient.

II.2 Study of how IDCM affects the left ventricle performance

Our analysis of how IDCM affects the LV is based on the study of ten normal subjects and ten IDCM patients. All of these subjects underwent diagnostic MRI scan. None of the normal subjects had: (i) significant valvular or congenital cardiac disease, (ii) history of myocardial infarction, (iii) coronary artery lesions, or (iv) abnormal left ventricular pressure, end-diastolic volume or ejection fraction. Our paper [4] provides

the details of (i) MRI scanning for acquisition of LV geometry, (ii) Data processing, and (iii) LV geometry reconstruction using customized software.

Table 3 provides the characteristics of subjects studied, including the mean values (and variations) of their diastolic and systolic pressures, heart rate, cardiac index, end-diastolic volume index, end-systolic volume index, ejection fraction, sphericity index (SI) at end-diastole, and contractility index (given by Eq 10). It is seen that IDCM patients had (i) increased values of end-diastolic volume index and end-systolic volume index, (ii) higher value of sphericity index (SI), (iii) decreased value of ejection fraction (EF). and (iv) much lower value of left) at end-diastole. It can be clearly seen that the normal LV is distinctly ellipsoidal and can hence have a low value of SI (and S); on the other hand, while the IDCM LV is spherically shaped and can have a bigger value of SI (and S).

Now let us see how intensely the normal LV contracts and changes its shape to become even more ellipsoidal. In other words, it goes from a low SI (≈ 0.78) at ED to a much lesser SI (≈ 0.57) at ES. On the other hand, the IDCM LV goes from SI ≈ 0.96 at ED to SI ≈ 0.82.So for the normal LV, the change in SI from ED to ES is ≈ 0.14.

Table 3: Characteristics of normal control and ischemic dilated cardiomyopathy (IDCM) patients. This table is adopted from [4].

	Control (n = 10)	*IDCM* (n = 10)	*p value*
Age (years)	39 ± 17	52 ± 9	0.05
Weight (kg)	67 ± 15	71 ± 16	0.57
Height (cm)	169 ± 8	164 ± 8	0.18
Diastolic pressure (mmHg)	73 ± 12	70 ± 9	0.54
Systolic pressure (mmHg)	122 ± 17	113 ± 12	0.19
Heart rate, HR (beats/min)	70 ± 9	81 ± 18	0.10
Cardiac index, CI (ml/m^2)	3.3 ± 0.4	2.3 ± 0.4	<0.001
End-diastolic volume index, EDVI (ml/m^2)	73 ± 10	144 ± 27	<0.001
End-systolic volume index, ESVI (ml/m^2)	26 ± 6	114 ± 32	<0.001
Ejection fraction, EF (%)	65 ± 5	22 ± 9	<0.001
Sphericity index, SI	0.52 ± 0.06	0.62 ± 0.08	<0.05
Cardiac contractility index, $(d\sigma^*/dt)_{max}$ (s^{-1})	5.7 ± 1.3	2.4 ± 0.9	<0.001

IDCM, ischemic dilated cardiomyopathy; Cardiac contractility index (=*1.5(dV/dt)max/Vm*), where *(dV/dt)max* is maximum volume rate, and *Vm* is the myocardial volume.

cardiac contractility index. This table clearly shows the relevance of SI and its association with EF and cardiac contractility index.

II.3 LV Geometry Reconstruction, and depicting normal LV and IDCM LV

Figure 7 illustrates the shapes of typical normal and IDCM LVs reconstructed by using software from their MRI images. The details of the clinical studies (data processing, LV geometry reconstruction, and committee approval), are provided in our paper [4].It is seen that a normal LV (in the bottom row of the figure) becomes more ellipsoidal as it contracts from end-diastole to end-systole, compared to an ischemic dilated cardiomyopathy (IDCM).

There are other notable shape-based features that we can recognize from figure 7. Let us look at the reconstructed geometries of the normal LV (bottom left) and IDCM LV (top

We can now formulate a Nondimensional SI %Change Index (SIPCI), $\Delta SI/ SI_{ED} x 100$, the percentage change in SI from end-diastole to end-systole ΔSI, as given by:

$$SIPCI = \Delta SI_{(ED\ to\ ES)}/SI_{ED} = [SI_{ED} - SI_{ES}] / SI_{ED} \times 100\ \% \quad (17)$$

A bigger value of Δ SI can imply a well contracting LV becoming more ellipsoidal from end-diastole to end-systole, whereas a smaller value of Δ SI can suggest a poorly contracting and pathological LV, as illustrated in figure 6. In fact, since the Sphericity Index (SI) is closely related to the Shape factor (S), we can also format a **Nondimensional Shape Factor (S)% change index,** $\Delta S/S_{ED} x\ 100$, as given by

$$SCPI = \Delta S_{(ED\ to\ ES)}/S_{ED} = [S_{ED} - S_{ES}]/ S_{ED} \times 100\ \% \quad (18)$$

to detect a pathological cardiomyopathic LV related to a smaller value of ΔS from ED to ES.

Now based on Eq. 17 (and 18) the value of SIPCI (and SPCI)

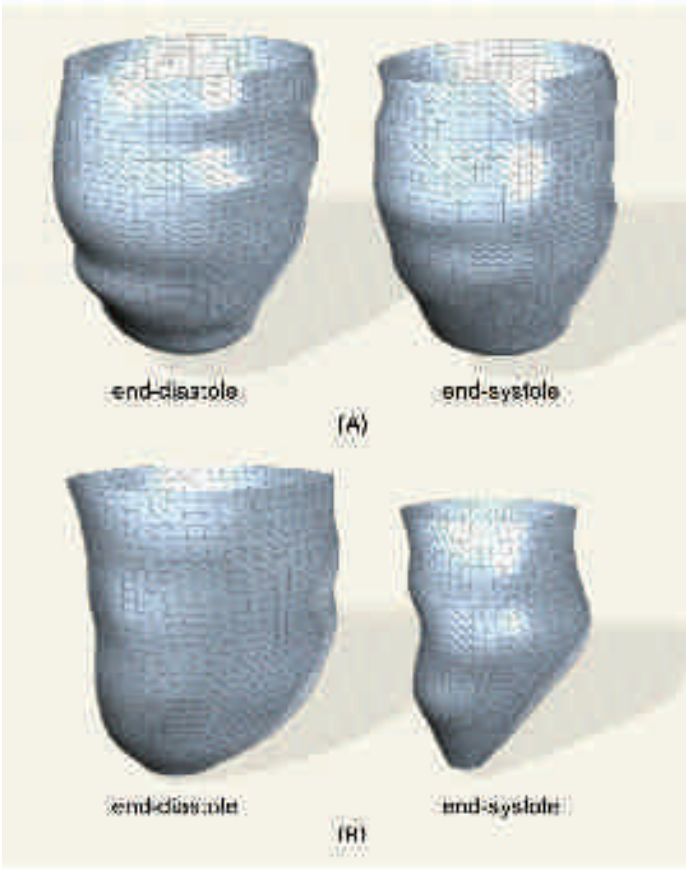

Figure 7.Three-dimensional reconstruction of LV endocardial surface at end-diastole and end-systole for (A) IDCM and (B) normal. This figure shows how the normal LV can more effectively contract from ED to ES by immensely decreasing its Sphericity Index (or S), compared to the IDCM LV. This figure is adopted from our paper [4].

for the normal LV in Fig 7 is very big≈27 % . On the other for the IDCM LV, the value of SIPCI (and SPCI) for the normal LV in Fig 7 is ≈ 16 %. This shows the effectiveness of these two indices in distinctly separating normal LVs from IDCM LVs. Now based on this effectiveness of SPCI, we need to determine its values for a wide range of normal and IDCM subjects, so as to be able to provide clear differential diagnostics.

III. CONCLUDING COMMENTS

This paper presents the novelty of our work on the formulation of LV shape-factor based indices to (i) depict the contractile performance of LVs, and (ii) detect cardiomyopathic LVs, thereby depicting new quantitative trends in medicine.

In Section I, we started with the formulation of non-invasively obtainable, pressure-normalized LV wall stress σ^*in terms of shape factor (S) and V*, in Eq (6). We can thereby employ the non-invasive contractility index $d\sigma^*/dt_{max}$ to provide a good substitute of the invasive contractility index dP/dt_{max}. Then by maximizing σ^* with respect to S, we derived the expression for S^{op} as a function of V* .From that, we derived the formula for the non-dimensional shape-factor based contractility index SFI2, which was employed to detect a poorly contracting LV. Thus, it is clearly demonstrated that a more-spherical shaped LV, with higher values of S and SFI2, is associated with poor systolic function and decreased contractility of the LV. This shows how the LV's intrinsically optimal anatomical shape is designed to make it contract optimally.

In Section II, we started with the formulation of LV geometry-based Sphericity Index SI, which is closely related to the shape factor S. We then showed that IDCM patients had (i) higher value of sphericity index (SI), (ii) decreased value of ejection fraction (EF), and (iii) much lower value of cardiac contractility index. Then most importantly, we displayed in Fig 7, the 3-d reconstructed LV endocardial surfaces at end-diastole and end-systole for IDCM and normal LVs. From this figure, we determined the values of SI (and S) in ED and ES, and changes in SI from ED to ES. We then formulated the SIPCI (and SPCI) indexes, and showed that the value of SIPCI (and SPCI) for the normal LV is very big≈ 27 %, compared with a much lower value of ≈ 16 % for the IDCM LV. This shows the effectiveness of these two indices in distinctly separating the normal LV from IDCM LV.

This is an illustration of how computerization and digitization of LV anatomical shape can be applied to LV physiology and pathological characterization. This can represent new quantitative trends in cardiology and medicine. It shows how simple computations of intrinsically optimal geometries of the left ventricle can teach us quantitative cardiology, leading to more precise medical diagnostics.

IV. REFERENCES

1. Zhong L, Ghista DN, Ng EYK, Lim ST, Chua T, Lee CN; Left Ventricular Shape-based Contractility Index, *Journal of Biomechanics*2006 ;39: 2397-2409,

2. Mirsky I, Basic terminology and formulae for left ventricular wall stress, in Cardiac Mechanics, ed Mirsky I, Ghista DN, Sandler H, Wiley New York, 3-10, 1973.

3. Zhong L , Tan RS, Ghista DN, Ng E. Y-K, Chua LP, Kassab GS; Validation of a novel noninvasive cardiac index of left ventricular contractility in patients, *Am J Physiol Heart Circ Physio*l2007;292:H2764-2772.

4. Zhong L, Su Y, Yeo SY, Tan RS, Ghista DN, Kassab GS; Left ventricular regional wall curvedness and wall stress in patients with ischemic dilated cardiomyopathy. *Am J Physiol Heart Circ Physiol* 2009;296:H573-H584

5. ZhongL, SolaS, TanRS, LeTT, GhistaDN, KurraV, NaviaJL, KassabG.; Effects of Surgical Ventricular Restorationon LV Contractility assessed by a novel Contractility index in patients with Ischemic cardiomyopathy", AmJ Cardiology, 2009;103(5):674-679.