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Point:Counterpoint: Left ventricular volume during diastasis is/is not the physiological in vivo equilibrium volume and is/is not related to diastolic suction

POINT: LEFT VENTRICULAR VOLUME DURING DIASTASIS IS THE PHYSIOLOGICAL IN VIVO EQUILIBRIUM VOLUME AND IS RELATED TO DIASTOLIC SUCTION

> "*Once you eliminate the impossible, whatever remains, no matter how improbable, must be the truth.*" (Sherlock Holmes; Ref. 6a)

The truth regarding ventricular equilibrium and diastolic suction has been elusive since Galen (26) observed blood moving into the ventricle with a force "vis a fronte." The continued debate (29) justifies that we readdress the conceptual (i.e., kinematic) basis of ventricular equilibrium and diastolic suction.

Equilibrium at diastasis. We propose a physiologically intuitive, functional equilibrium: diastasis. When ventricular filling commences, the chamber expands (recoils) faster than it can fill and aspirates blood from the atrium by rapidly decreasing chamber pressure with simultaneous volume expansion $dP/dV < 0$ (10, 15). Wall recoil requires a net restoring force generated by the integrated action of loaded elastic elements seeking to return to their equilibrium dimension (2, 8, 12–14). As ventricular filling (Doppler E-wave) continues, the elastic elements approach their equilibrium dimension and elastic forces decrease. Once diastasis is reached, there is no wall motion, no atrioventricular pressure gradient, no flow, and no change in volume or pressure (19). Thus at diastasis, all forces and strains must be balanced (they are not zero), and there is no net force or wall motion. Hence, diastasis must be the in vivo equilibrium volume, and every ventricle approaches diastasis by suction initiated filling.

Kinematics of equilibrium. Before the contributors to ventricular elastic properties, such as titin, collagen, and visceral pericardium (12–14, 23) were appreciated, Brecher et al.(3) defined ventricular elastic equilibrium volume intuitively as the volume where the ventricle's "transmural pressure is zero ($\Delta P = 0$) and no stress is applied on its structural elements."

On the basis of this definition, Nikolic, Yellin, and others used elegant experimental techniques to show that the ventricle generates subatmospheric filling pressures only when the end-systolic volume (ESV) is below a certain value, Vo (21). This value was taken to be the Brecher defined [$\Delta P = 0$] equilibrium volume and reinforced the traditional view that suction only occurs when ventricular ESV<Vo.

In contrast, more recent work by Omens and Fung (22) and Balaban (14) shows that even when fully relaxed, the LV wall has residual stress. This presence of residual stresses negates Brecher's implied connection between $\Delta P = 0$ and a state where "no stress is applied" on ventricular elastic elements. Because the fully relaxed ventricle's thick walls maintain residual stress (22), the requirement that transmural pressures vanish ($\Delta P = 0$), need not be invoked to achieve equilibrium.

Toward equilibrium. Attainment of diastasis requires ventricular recoil, driven in part, by molecular elastic elements (5, 13, 14) releasing elastic strain stored during systole. If we assume Vo is equilibrium, a serious kinematic inconsistency arises if Vo<ESV. In this setting the elastic elements would remain displaced above their equilibrium position and would be expected to exert force opposing chamber enlargement at the start of filling. However, as the mitral valve opens and filling commences, there is always a net expansive force responsible for recoil of the ventricular tissue. An atrial "push" cannot account for this force, because it would cause LV pressure to increase immediately on mitral-valve opening. Relaxation of the LV tissue by itself cannot account for this force either, because relaxation only relieves a compressive force, but does not generate motion. When elastic elements are displaced above equilibrium (Fig. 1), it is not clear what provides the expansive force opposing the early filling-related

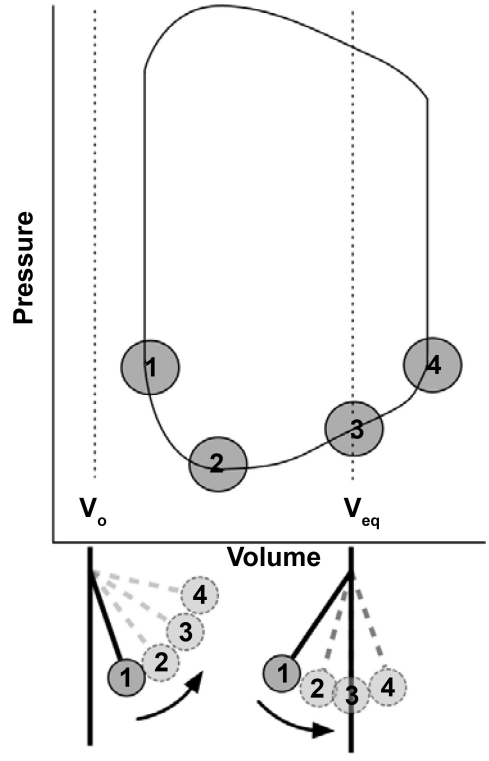

Fig. 1. Pressure-volume (P-V) loop and the kinematics/energetics of filling. Schematic P-V loop indicating *1*) end-systolic volume (ESV) at mitral valve opening, *2*) minimum left ventricular (LV) pressure, *3*) diastasis, and *4*) end-diastolic volume. Vertical dashed lines denote alternative locations of equilibrium volume (Vo defined by $\Delta P = 0$; Veq defined as volume at diastasis). If Vo is the equilibrium volume and Vo < ESV, then elastic elements are displaced further from equilibrium as filling continues. Idealized via an oscillator (pendulum, *bottom left*), the displacement of the pendulum away from vertical equilibrium represents the displacement of lumped ventricular elastic elements from ventricular equilibrium volume. If diastasis is the equilibrium volume, then ESV is always less than Veq and the displaced elastic elements are unmasked by the relaxation process and passively return toward equilibrium as early filling progresses. (Idealized via a pendulum, *bottom right*). Atrial filling displaces elastic elements beyond equilibrium, and this stored elastic energy powers late diastolic mitral regurgitation if 1st degree AV block is present. Numeric labels of pendulum position correspond to PV loop labeling. See POINT for details.

compressive elastic forces. It is also unclear what mechanism prevents the ventricle from shrinking toward its equilibrium volume when diastasis is reached in the case of Vo<ESV.

This inconsistency is avoided by rejecting Vo determined by $\Delta P = 0$ and accepting diastasis as the equilibrium volume. When ventricular volume exceeds diastatic volume, the chamber does oppose this volumetric enlargement with a net compressive force. This force can be appreciated in the presence of 1st degree AV block, for example, where one observes late diastolic mitral regurgitation (1) and a decline in LVP toward equilibrium, despite $\Delta P \neq 0$. By accepting diastasis as in-vivo equilibrium, late diastolic mitral regurgitation is the predictable result of displaced elastic elements that recoil toward diastasis and return the ventricle toward its equilibrium volume. Importantly, this type of spontaneous pressure decline after early rapid filling is not observed naturally unless the ventricular volume exceeds the volume at diastasis.

Relation between equilibrium at diastasis and suction. Accepting diastasis as the equilibrium volume means that for all ventricles the elastic elements are displaced at end systole, and it is the recoil of these elastic elements towards equilibrium that initiates filling with $dP/dV < 0$ and drives the ventricle toward diastasis. Elastic recoil moves the wall so the chamber expands faster than it can fill (10, 15), powers torsion (8, 24), and generates the negative atrioventricular pressure gradient that initiates the Doppler E-wave (7, 9). Thus ventricular suction, including the intraventricular pressure gradient (7) must always be present as a result of the recoil of displaced elastic elements returning toward equilibrium. Suction and its link to recoil toward equilibrium as a diastolic mechanism is included in the current American Society of Echocardiography standards (20).

It should be noted that suction requires only that the receiving chamber drop its pressure below the source pressure, and does not require negative transmural pressures. Brecher recognized this, saying plainly that "it was thought that only the occurrence of negative intraventricular transmural pressure could be taken as evidence for the existence of ventricular diastolic vis a fronte. A brief consideration of the physical forces will show that this conclusion is fallacious" (4). Consider a compressed turkey baster submerged in any depth of water; the baster always returns to its equilibrium position even though the pressure never falls below atmospheric. The elastic recoil of the baster is analogous to the kinematics of the heart at low or high pressure environments and the motion observed in excised hearts (2).

Suction and its (patho)physiological importance. Yellin et al. (27) suggested that a definition of diastolic suction based on $dP/dV < 0$ has little "utilitarian value," because it means that every ventricle initiates early rapid filling by being a suction pump (27).

However, the utilitarian value of suction is enhanced by the recognition of its general applicability and quantification. Indeed its physiological value is enhanced when one assesses its effectiveness on a continuum. For example, work by Yotti (28) and a related editorial by Little (18) suggests that diagnosing and quantifying suction via pressure gradients is important in understanding pathophysiology. Dilated ventricles are poor suction pumps, aspirating a relatively small volume in early filling and compensating with atrial contraction and a resting tachycardia to maintain cardiac output. Healthy ventricles store (and release) greater amounts of elastic energy during systole (and diastole) and are therefore more effective suction pumps. Thus the importance of suction is revealed through mechanistic understanding of how it is modulated, how it determines the contour of the E-wave (16, 17) and how a lack of suction affects patients clinically and physiologically (19, 20).

Understanding the conceptual basis of equilibrium volume and LV suction has expanded our knowledge of cardiovascular physiology, both transiently (5, 6) and at the organ level (25, 30). As noted above (18, 19), considering diastasis as the equilibrium state and appreciating how suction initiated filling leads the chamber toward equilibrium sheds new light on diastolic function and dysfunction from the embryo (10) to the clinic (11, 20).

Thus we conclude that the truth, no matter how improbable, must be that diastasis is the physiological in vivo equilibrium volume and requires diastolic suction as the mechanism by which it can be achieved.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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COUNTERPOINT: LEFT VENTRICULAR VOLUME DURING DIASTASIS IS NOT THE PHYSIOLOGICAL IN VIVO EQUILIBRIUM VOLUME AND IS NOT RELATED TO DIASTOLIC SUCTION

We agree with a recent Viewpoint paper (24) that reconciliation among different approaches to diastolic suction (18, 23) is required, but we do not agree that Zhang et al. (24, 25) resolve the issues by creating a conceptually new equilibrium volume, Veq, based on a vague time in late diastole. In this Point:Counterpoint discussion we welcome the opportunity to evaluate the different approaches and to respond to their mistaken interpretation of our research pertaining to the definition and interpretation of the ventricular equilibrium volume and its relation to diastolic suction (24, 25). We will demonstrate that Veq has no physiological relation to diastolic suction. We will also critically evaluate alternative approaches to defining diastolic suction. More comprehensive discussions may be found in review papers from our lab (20–22).

Katz (7) refuted the prevailing view that the energy for filling came entirely from the pressure in the atrium by demonstrating, in the isolated turtle heart, that the relaxing ventricle is not entirely passive but plays a role in filling because at the onset of transmitral flow, ventricular volume increased while ventricular pressure decreased, i.e., $dP/dV < 0$. Katz (7) then concluded that the heart was a suction pump. Although he recognized that two mechanisms are involved, he did not separate the effects of the pressure fall due to the relaxing myocardium from the pressure rise due to the expanding elastic chamber.

Brecher et al. (1–5) recognized that potential energy could be stored during contraction due to elastic elements that can be stretched and to those that can be compressed (5). He investigated the role of elastic recoil in the open chest canine preparation able to prevent inflow and to allow the ventricle to deactivate in the absence of filling. Among Brecher et al's. observations and conclusions were that volume clamping could lead to negative transmural LV pressures; decreasing the ESV leads to a greater negative pressure; and elastic recoil contributes to the negative pressure (1–5). They then introduced the concept of equilibrium volume as the volume (Vo) of the ventricle at zero transmural pressure (Pt). Suction due to elastic recoil occurred when ESV$<$Vo. Brecher and Kissen (2) constructed the passive LV pressure-volume relation of the heart arrested in diastole: the positive portion by saline infusion and the negative portion by aspiration. The intersection of the curve with the volume axis defined Vo (2). To overcome the nonphysiological use of aspiration, Tyberg et al. (17) obtained the negative P-V points in the beating LV by volume clamping when the ESV was below Vo, thus producing a physiologically meaningful negative pressure.

LV volume clamping itself does not create suction; it unmasks the effects of stretching the myocardium during filling and allows the ventricle to completely relax without relengthening. If elastic fibers have stored energy by contracting below the equilibrium volume, the elongating forces in the wall must be balanced by a chamber pressure that is less than the external, i.e., when transmural pressure is negative, $Pt < 0$. In the open chest preparation where the external pressure is atmospheric, the internal pressure must be less than zero, $LVP < 0$. We note also that, in contrast to the assertion by Zhang et al. (24, 25), this explanation is valid in both the open and closed chest preparations.

In our lab, we continued the investigation of diastolic suction in what are arguably the definitive studies that separated the effects of filling from the effects of relaxation (6, 10, 11, 19). Nikolic et al. (11) used a remote controlled mitral valve that allowed controlled amounts of filling under various physiological conditions, studied the passive properties of the fully relaxed LV in both the positive and negative domains, and