Viewpoint: Is Left Ventricular Volume During Diastasis the Real Equilibrium Volume and, What is its Relationship to Diastolic Suction?

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Short Title: Diastasis defines ventricular equilibrium

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“Whatever role cardiac suction of venous blood may play in determining circulatory dynamics, no one can deny that mention of this term (diastolic suction) has proven a most effective method of raising blood pressure in several generations of cardiovascular physiologists”

–GA Brecher 1958

Defining Suction: A Persistent Problem

Recent articles(31,32) illustrate the challenge in providing a self consistent definition of ventricular suction. Conceptually different definitions are treated equivalently despite the fact that they lead to disparate conclusions. We discuss various definitions of suction, their physiological implications, and propose a unifying concept based on an in-vivo definition that requires a new perspective on the meaning of diastolic equilibrium volume.

The History of Diastolic Suction

The experimental observation of diastolic suction or “vis a fronte” (a force acting from in front) dates back nearly 2 millennia to Galen, who concluded that the heart can fill itself(26). However, controversy regarding diastolic suction(7) has persisted. Brecher noted(5) experimental evidence of diastolic suction by showing that excised beating animal hearts submerged in fluid draw fluid back into the ventricle after systole. Numerous investigators have described similar events(2,3,8,28-30,32), but quantification of diastolic suction had to wait until the pioneering work of Louis Katz in 1930(17).
Katz observed that in early diastole, turtle ventricular pressure ($P_{LV}$) decreases simultaneously with increasing ventricular volume ($V_{LV}$). This observation provided a conceptually simple and elegant quantitative definition of ventricular diastolic suction, namely, that diastolic suction is present when:

$$\frac{dP_{LV}}{dV_{LV}} < 0$$ \hspace{1cm} [1]

This definition is a ‘relative’ index, as it depends only on intraventricular pressure and volume changes, and therefore is independent of ‘absolute’ ventricular pressures or volumes. That $\frac{dP_{LV}}{dV_{LV}} < 0$ after mitral valve opening is well established(8,29) and depends on the endocardium mechanically recoiling faster than blood can fill the chamber which has been observed even in the developing zebrafish heart(9). Filling involves more than the lumped ‘ventricular perspective’ of Equation 1. However, when going beyond the ‘ventricular perspective’, the source of filling must be considered with care, because the atrium rather than the atmosphere represents the source for filling, and flow requires generation of a pressure gradient. During early-rapid ventricular filling the atrium is a passive conduit and atrial pressure always decreases immediately after MVO. Therefore as LV pressure decreases below atrial pressure inscribing the atrioventricular pressure gradient, it accelerates flow into the chamber. Indeed, a consistent definition of diastolic suction, incorporating the atrium, recognizes the role of atrioventricular gradients(1,12,18,32). Since all ventricles generate atrioventricular gradients in early diastole it follows that all ventricles must operate as suction pumps in early diastole.

**Diastolic Suction, Sub-atmospheric Pressure and the Open-Chest Equilibrium Volume**
While early diastolic intraventricular and atrioventricular gradients causally guarantee LV generated diastolic suction, alternative definitions regarding suction exist in both physiology and clinical echocardiography (31,32). One alternative definition stems from pioneering experimental work by Nikolic et al (21). They occluded the mitral valve at various filling volumes and determined the minimum pressure reached by fully relaxed canine ventricles in an open chest, open pericardial setting. They defined the development of subatmospheric pressures as evidence of suction. Therefore suction exists only when:

\[ P_{LV} < P_{atmospheric} \] [2]

The post-occlusion asymptotic pressures were the fully relaxed chamber pressures for the particular volume at which occlusion occurred. The lower the volume when the mitral valve is occluded, the stronger the suction force is, as shown by the more negative fully relaxed pressure. The asymptotic P-V points generated a nonlinear relationship that was fit logarithmically (see Figure 1). The occlusion volume, where the corresponding relaxed pressure was atmospheric, defined the open-chest equilibrium volume (14,15,21,27). Accordingly, ventricles achieving end-systolic volumes below this equilibrium volume were defined as suction pumps.

While the experimental definition proposed by Nikolic is widely accepted (10,25,28), others have also measured equilibrium volume (20,21,27). In particular, the \( P_{atmospheric} \) definition has been applied in the closed-chest, in-vivo setting, generating controversy regarding diastolic suction. Levine et al (20), defined diastolic suction by Equation 2 and concluded that intact closed-chest ventricles did not generate suction after bed-rest associated atrophy because their end-systolic volumes were higher than the equilibrium volume. Rankin et al (25), and others using the closed-chest measurements (10,28), concluded that \textit{in-vivo} hearts, in general, do not
exhibit diastolic suction. These conclusions are inconsistent with the work of Katz. Thus, while it is proper to consider the volume at which relaxed ventricular pressure is atmospheric in the open-chest setting, in the *in-vivo* closed-chest setting this choice may be less applicable.

**Physiologic Mechanisms Responsible for Diastolic Suction**

Irrespective of how diastolic suction and equilibrium volumes are defined in pressure-volume terms, there is general agreement that the hypothesized causal mechanisms for ventricular diastolic suction are similar. All definitions assume that ventricular recoil, and associated torsion as quantified by MRI (6) is powered by stored elastic strain energy(18,21,30). Recent experiments indicate that proteins such as titin, acting as a bi-directional, linear spring, together with extracellular matrix and microtubules, etc. play roles in generating elastic recoil(11,24). Deactivation (crossbridge uncoupling) unmasks stored elastic strain energy and leads to decreased elastic wall-stress, wall-torsion and ventricular chamber pressure (by Laplace's law). Abnormal crossbridge deactivation, has been associated with (clinically defined) delayed relaxation(16), and has been shown to prevent the recoil (release of stored strain) of myofibrils(24).

**Difficulties with Suction Relative to the Atmosphere**

There are some issues with the application of the $P_{\text{atmospheric}}$ definition (Equation 2). To put these in context, we note that that the absolute pressure ($P_{LV}<P_{\text{atmospheric}}$) condition utilizes a presumption of zero transmural wall-stress, where transmural forces are balanced because the transmural pressure gradient vanishes(2,3,5,21,28). However, in the closed-chest setting, $P_{LV}=P_{\text{atmospheric}}$ does not imply zero transmural pressure gradient, since pericardial pressure is usually not atmospheric(13). Finally, and most importantly, while the $P_{LV}<P_{\text{atmospheric}}$ definition
assumes a zero wall-stress state, Omens and Fung showed that fully relaxed ventricles, with zero transmural pressure gradient, possess stored elastic strain(22). Therefore, the zero transmural wall-stress condition is unlikely to exist even when the chamber is fully relaxed, and in order for transmural pressure gradients to play a role in-vivo, they must be great enough to overcome the residual wall-stress present.

One way to resolve the difficulties of defining suction relative to atmospheric pressure is to adhere to Katz’s definition: a ‘relative’ definition that remains applicable regardless of atmospheric pressures, external pressure conditions such as diving or high altitudes(4,19), and experimental conditions such as an open chest preparation.

**The distinction between a transmural force balance and zero force**

It is appropriate to define diastolic suction as Nikolic and others have, relative to an equilibrium volume, but this volume must reflect a mechanical equilibrium. Despite the presence of non-zero residual intra-myocardial stress(23), all forces are balanced and the chamber remains static (non-moving), during diastasis. In other words, mechanical and kinematic equilibrium is achieved when all residual forces and stresses (including pressure in the atrium, residual stress in the wall, etc.) are balanced, rather than only when the transmural forces or transmural pressure gradients are zero. This distinction is physiologically realistic, it is unambiguous, and its consequences (static vs. moving) are easily discernable. Defining the equilibrium volume of the ventricle as a state of mechanical equilibrium, defined by a zero-motion (static) condition over a finite time interval, rather than a zero-force condition, yields:

\[ V_{eq} = V_{diastasis} \]  \[3\]

In analogy to the Nikolic et al determinations of equilibrium volume and suction, Equation 3
implies the presence of diastolic suction only if the end-systolic volume (ESV) is below the diastasis volume (equilibrium volume). In general, ESV is always $<\text{diastatic volume}$ and thus, because $\frac{dP}{dV}<0$ as the ventricle initiates filling (E-wave), our definition of equilibrium volume being the diastatic volume is consistent with Katz’ definition of diastolic suction and is consistent with the conclusion that diastolic suction is present when ESV $<\text{equilibrium volume}$. In a temporal sense, abatement of the $\frac{dP}{dV}<0$ suction mechanism (release of stored elastic strain) allows the chamber to settle down to its ‘equilibrium’ or force-balanced state. In our view Equation 3 is the functional \textit{in-vivo} closed-chest equilibrium volume, because it defines an easily discernible mechanical equilibrium, resolves (‘relative’ vs. ‘absolute’) inconsistencies between various definitions, and does not require a zero transmural pressure gradient.

**Conclusions**

Prior conceptual and experimental results regarding diastolic suction and the equilibrium volume of the LV have been interpreted inconsistently. To resolve the inconsistencies generated by different (‘absolute’ vs. ‘relative’) definitions and different (closed-chest vs. open chest) preparations, we advocate $\frac{dP_{LV}}{dV_{LV}}<0$ as the necessary and sufficient condition for definition of diastolic suction. This definition (ventricular recoil) follows not only from physiologic constraints but from kinematic considerations (the release of stored elastic strain). This definition guarantees that suction manifests only when ESV $<$ $V_{eq}$ and naturally leads to the kinematics-based definition that after the recoil process has terminated, the chamber settles down to the LV volume at diastasis, which must be the functional, in-vivo equilibrium volume.
References


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Figure Caption

**Figure 1.** Experimental, open chest canine P-V data for equilibrium volume determination using the pioneering mitral valve occluder method of Nikolic et al (21). In their study, the completion of suction initiated filling, i.e. the transition from kinematics to statics defines the equilibrium state. Solid line, normal pressure volume loop for one diastole. Points 1-6 represent a sequence of fully relaxed LVP at variable filling volumes, which were achieved via an electronically controlled mitral valve occulder. The fully relaxed pressure and the corresponding volume (data points 1 to 7) were fit logarithmically. Open chest equilibrium volume $V_{eq}$ is the intersection of the dashed (logarithmic) curve and the volume axis (pointed out by arrow), and corresponds to the LV volume when the fully relaxed LVP = 0. End systolic volume ($V_{ES}$) is also marked by arrow on the figure. [Figure from (21), used with permission.] See text for details.

Supplemental Video Caption

Left ventriculogram with normal ejection fraction and Normal sinus rhythm demonstrating diastasis. Diastasis is a transient physical state of the chamber, (lasting for about 150 ms in this case). During diastasis, LV wall motion AND transmitral flow are both absent. Hence, the ventricle is in static equilibrium, since all the forces on the ventricle are balanced, although the forces are not zero. Note the Doppler A-wave as the brief entry of unopacified atrial blood through the mitral valve, just prior to systole.
Figure 1. Experimental, open chest canine P-V data for equilibrium volume determination using the pioneering mitral valve occluder method of Nikolic et al (21). In their study, the completion of suction initiated filling, i.e. the transition from kinematics to statics defines the equilibrium state. Solid line, normal pressure volume loop for one diastole. Points 1-6 represent a sequence of fully relaxed LVP at variable filling volumes, which were achieved via an electronically controlled mitral valve occluder. The fully relaxed pressure and the corresponding volume (data points 1 to 7) were fit logarithmically. Open chest equilibrium volume $V_{eq}$ is the intersection of the dashed (logarithmic) curve and the volume axis (pointed out by arrow), and corresponds to the LV volume when the fully relaxed LVP = 0. End systolic volume ($V_{es}$) is also marked by arrow on the figure. [Figure from (21), used with permission.] See text for details.