19. Little WC, Oh JK. Echocardiographic evaluation of diastolic function can be used to guide clinical care. Circulation 120: 802–809, 2009.

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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 of the onset of transmural 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...
characterized them with a logarithmic relation that contained the equilibrium volume, i.e., the volume (Vo) at zero transmural pressure. Contraction to an ESV < Vo stored elastic energy that had the potential to produce negative LV pressures and is, therefore, the criterion for suction (1–5, 11, 17). Thus a conceptual property, diastolic suction, is defined in terms of a physical property, equilibrium volume, independent of deactivation (16). The Nikolic analysis (11) is consistent with the knowledge of isolated muscle mechanics and extracellular structure (9, 13, 14, 15). The heart is thus characterized as an organ that is capable of using the property of suction to maintain a filling pressure that is in the physiological range and that does so by maintaining a low downstream pressure in the ventricle due to its elastic properties.

Whereas the Katz criterion (7), endorsed by Zhang et al. (24, 25), concludes that the ventricle is always a suction pump, we maintain that it acts as a suction pump only when ESV < Vo. Think about it! According to Zhang et al. (24, 25), a failing heart, where dP/dV is always less than zero during early filling, is a suction pump, despite the knowledge that in that heart, where the ESV is almost certainly greater than Vo, there is no elastic recoil and therefore no suction. We ask the reader, is that physiologically reasonable? Figure 2 illustrates our position. Does the new definition of equilibrium volume proposed by Zhang et al. (24, 25) contribute to the physiology of diastolic suction? We fail to see how.

The proposed Veq (24, 25) is not a physical property because it varies with the duration of diastole; at high heart rates it cannot even be identified! It has no relation to elastic recoil, since at the time in diastole after early filling has ceased, i.e., preceding the atrial contraction, ~80% of filling has occurred, relaxation is complete, and dP/dV is no longer negative.

The Katz/Zhang et al. (7, 24, 25) definition of diastolic suction is based on changes in LV volume and cavity pressure and is, therefore, related to the amount of LV early diastolic inflow. Early inflow on the other hand, is determined by the atriocinval pressure gradient, which depends on both active and passive properties of the LV and properties of the atrium. Thus, according to the Katz/Zhang et al. (7, 24) definition, LV suction, a property of the ventricle, is dependent on two different ventricular mechanisms as well as on atrial properties. We find this approach confusing and physiologically meaningless.

The Brecher/Nikolic definition of diastolic suction is related to the negative transmural LV pressure contracting below Vo and is determined solely by the characteristics of the left ventricular myocardium. In addition, Vo reflects the intrinsic properties of the LV structure and proportionally changes with normal growth of the LV, thus representing a normalizing parameter for comparing various ventricles either of different size or pathologically remodeled (8, 11). Note that Vo is not the unstressed volume (12).

In conclusion, we find that the ventricular volume during diastasis as defined by Zhang et al. (24), is not the physiological in vivo equilibrium volume and is clearly not related to diastolic suction.

DISCLOSURES

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

REFERENCES

18. Wang Z, Jalali F, Sun YH, Wang JJ, Parker KH, Tyberg JV. Assessment of left ventricular diastolic suction in dogs using wave

Fig. 2. P-V loops illustrating diastolic suction when ESV < 0. Loop A, ESV > V0, cannot reach a negative transmural pressure unless contractility increases and reduces ESV, leading to suction. Loop B has the potential ability to relax to negative Pt with the same filling volume as loop A and with lower mean LAP. Loop C has the ability to relax to even lower negative Pt. LV volume at the time of diastasis (A) is shown in each P-V loop, and clearly has no relationship to diastolic suction.
zhang et al. (10) and shmuylovich et al. (9) argue as follows:

the diastatic pressure-volume relationship is not
fundamental chamber properties in the form of passive stiff-
ness (10).

hence, concluding that equilibrium volume must be the
volume at diastasis is just one of several insights gained by a
kinematic perspective of diastole. it consolidates a range of
observations by providing consistency with and between
experiments, from the myofiber to the ventricle, and from ven-
tricular development to disease (2, 4, 6, 7, 9, 10).

references
1. chung cs, karananoglu m, kovács sj. duration of diastole and its
phases as a function of heart rate during supine bicycle exercise. am j
2. chung cs, kovács sj. physical determinants of left ventricular isovolu-
mic pressure decline: model prediction with in vivo validation. am j
physiol heart circ physiol 294: h1589–h1596, 2008.
3. hinken ac, solaro rj. a dominant role of cardiac molecular motors in
the intrinsic regulation of ventricular ejection and relaxation. physiology
4. rich mw, stützle n, kovács sj. prognostic value of diastolic filling
parameters derived using a novel image processing technique in patients
or > 70 years of age with congestive heart failure. am j cardiol 84: 82–86,
1999.
5. rosen bd, gerber bl, edvardsen t, castillo e, amado lc, nasir k,
kratchman dl, osmam nf, bluemke da, lima jac. late systolic
onset of regional lc relaxation demonstrated in three dimensional space
by mri tissue tagging. am j physiol heart circ physiol 287: h1740–
6. shmuylovich l, chung cs, kovács sj. point: left ventricular vol-
ume during diastasis is the physiological in vivo equilibrium vol-
ume and is related to diastolic suction. j appl physiol; doi:10.1152/
ajpphysiol.01399.2009.
7. stehle r, solzin j, iorga b, poggesi c. insights into the kinetics of ca2+
regulated contraction and relaxation from myofibril studies. eur j physiol
8. yellin e, nikolic sd. counterpoint: left ventricular volume dur-
ing diastasis is not the physiological in vivo equilibrium volume and
is not related to diastolic suction. j appl physiol; doi:10.1152/
ajpphysiol.01399.2009a.
9. yotti r, bermejo j, antoranz jc, rojo-álvarez jl, allue c, silva
j, desco mm, moreno m, garcia-fernandez ma. a non invasive
method for assessing diastolic suction into the clinical realm. ers
10. zhang w, kovács sj. the diastatic pressure-volume relationship is not
the same as the end-diastolic pressure-volume relationship. am j
physiol heart circ physiol 294: h2750–h2760, 2008.

rebuttal from yellin and nikolic
we are pleased that kovacs’ group has raised the importance of
clarifying the relation between diastolic suction and ventric-
ular equilibrium volume. there is, indeed, a need to translate
experimental studies of diastolic suction into the clinical realm.
zhang et al. (10) and shmuylovich et al. (9) argue as follows:
(i) on the basis of the katz criterion (5) onset of filling is caused

in key contrast to our view (6), yellin and nikolic suggest
that “lv volume clamping ... allows the ventricle to com-
tpletely relax without relengthening” (8). however, recent stud-
ies show strong coupling between cross-bridge deactivation/
relaxation and elastic recoil/relengthening. deactivation inde-
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indeed, the dynamic balance between stored elastic energy
and cross-bridge deactivation determines wall stress and re-
sulting decreasing chamber pressure (2, 3, 7). deactivation
alone cannot drop pressures fully. only motion, i.e., the ex-
pansion of the ventricle faster than it can fill, can generate the
atrioventricular pressure gradient to initiate suction. chamber
expansion would not occur if relaxation (cross-bridge uncou-
pling) were not coupled with release of stored elastic energy,
i.e., recoil.

yellin and nikolic’s assertion that diastasis “has no
relation to elastic recoil, since ... 80% of filling has oc-
curred” (8) ignores the kinematics. the fact that diastasis
follows recoil assures causality. atrial contraction and ven-
tricular systole displace the ventricle from equilibrium and
only during diastasis are forces, flows, and strains reequili-
brated (6). this is consistent with the fact that all hearts are

intensity analysis. am j physiol heart circ physiol 288: h1641–h1651,
2005.
19. yellin el, hori m, yoran c, sonnenblick eh, gabbay s, frater
rmw. left ventricular relaxation in the filling and non-ﬁlling intact
canine heart. am j physiol heart circ physiol 250: h620–h629, 1986.
20. yellin el, nikolic sd, frater rmw. left ventricular filling dynamics
21. yellin el, nikolic sd. diastolic suction and the dynamics of left
ventricular ﬁlling. in: left ventricular diastolic dysfunction and heart
failure, edited by gaasch wh, lewinter mm. philadelphia: lea and
22. yellin el, meinsen js. physiology of diastolic function and transmural
23. yotti r, bermejo j, antoranz jc, desco mm, cortina c, rojo-
álvarez jl, allue c, martin l, moreno m, serrano ja, munoz r,
garcia-fernandez ma. a noninvasive method for assessing diastic
suction in patients with dilated cardiomyopathy. circulation 112: 2921–
2929, 2005.
24. zhang w, chung cs, shmuylovich l, kovacs sj. viewpoint: is left
ventricular volume during diastasis the real equilibrium volume, and what
is its relationship to diastolic suction? j appl physiol 105: 1012–1014,
2008.
25. zhang w, chung cs, shmuylovich l, kovacs sj. last word on
viewpoint: is left ventricular volume during diastasis the real equilibrium
volume, and what is its relationship to diastolic suction? j appl physiol

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rebuttal from shmuylovich, chung, and kovacs

in key contrast to our view (6), yellin and nikolic suggest
that “lv volume clamping ... allows the ventricle to com-
tpletely relax without relengthening” (8). however, recent stud-
ies show strong coupling between cross-bridge deactivation/
relaxation and elastic recoil/relengthening. deactivation inde-
pendently accounts for only 3–5% of maximal force (i.e.,
pressure) decline after calcium activation, while the majority of
force (pressure) decline occurs with sarcomere relengthening
(7). this is in precise agreement with chamber mechanics,
where, during and after calcium sequestration (3), elastic recoil
(motion) is observed, manifesting as torsion during isovolumic
relaxation (5). this conceptual foundation motivated our
model that accurately predicts isovolumic pressure decline by
unifying recoil and deactivation (2).

indeed, the dynamic balance between stored elastic energy
and cross-bridge deactivation determines wall stress and re-
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alone cannot drop pressures fully. only motion, i.e., the ex-
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tricular systole displace the ventricle from equilibrium and
only during diastasis are forces, flows, and strains reequili-
brated (6). this is consistent with the fact that all hearts are

suction pumps, but does not imply that failing hearts cannot
be suction pumps; in fact, studies that quantify suction
demonstrate the opposite (4, 9).

yellin and nikolic note the intrinsic variability of diastasis
(8). at low heart rates diastasis is unambiguous, but diastasis
can vary from beat-to-beat and may be masked by atrial
contraction (1). variation in diastatic pressure and volume is
due to load, atrial properties, and ventricular properties,
but that does not negate the functional role of diastasis as the
equilibrium volume. ventricular and atrial tone, contractility,
and load balance at diastasis are dynamic physiological
variables. thus equilibrium volume must also be dynamic. in fact,
quantifying diastatic pressure and volume variation provides
fundamental chamber properties in the form of passive stiff-
ness (10).

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volume at diastasis is just one of several insights gained by a
kinematic perspective of diastole. it consolidates a range of
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