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Systolic Indices of Cardiac Contractility: Modeling and Analysis using Pressure-Volume Loop

Filip Konecny

ABSTRACT

Modeling cardiac contractility in pre-clinical catheterization laboratory settings remains an important task to collect results under controlled hemodynamic conditions, while providing an assessment of systolic and diastolic indices. Diligent hemodynamic monitoring with acute-based pressure-volume modeling uncovers early indicators of heart failure (HF). In this article, basic procedural assessments are outlined, while deeper dive into systolic index of contractility, the end systolic elastance is provided with references to older, while comparing it to novel approaches. Transient preload reduction using inferior vena cava occlusion (IVCO) is the current standardized maneuver used in hemodynamic protocols to provide an assessment of contractile responsiveness. In this article an example of standard measures from a single catheterization lab were depicted using tables and figures, giving background to transient preload reduction to assess the values of systolic cardiac contractility. Additionally, novel twists on other possible index(ices) coming from capturing ES point may well present future opportunities to collect systolic cardiac contractility. In this instance, both single beat systolic PPESPVR and IVCO using ES points present unique opportunities in this niche area of research. Final two sections of this article are dedicated to procedural steps and how to standardize execution of IVCO. Final section is reserved for analytical steps of how to visually compare systolic indices post-IVCO in case of linear and quadratic relationship.

Keywords: Hemodynamic modeling, inotropy, physiological concepts and modeling, PV loop (PVL), systolic index of cardiac contractility.

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F. Konecny*
Department of Surgery, Division of Plastic Surgery, McMaster University, Hamilton, ON, Canada.
(e-mail: konecny@mcmaster.ca)

****Corresponding Author***

I. Why modeling Cardiac Response to Transitory Hemodynamic Changes Is Important

In mammals heart muscle pumps operate within closed hemodynamic circuitry. Work of the mechanical pump is to displace blood to circulate it through the body. This hemodynamic load (blood) is to influence overall muscle function (mechanics) and its activity (hemodynamics). Mechanics could be assessed using e.g., isolated papillary muscle during isometric and isotonic contractions. Then the simple mechanical concept is translated into the heart as an organ by exploring external factors having an impact such as preload, afterload contractility/inotropy and HR. Changes influenced by load are guided by Frank Starling (F-S) law, the relationship of stroke volume (SV) and end-diastolic pressure (EDP), shifting the final curvilinear relationship up and down. On cellular level, cardiac muscle possesses contractile sarcomere apparatus with its contractile proteins that determine cardiac muscle activity. Excitation, the rapid spread of depolarization wave on the myocardial fiber, leads to excitation-contraction coupling by delivering calcium from the sarcoplasmic reticulum from outside of cell to troponin and releasing the troponin-tropomyosin inhibition of actin-myosin binding. Cyclic interaction between actin and myosin develops force of contraction and shortens the muscle while using energy released from ATP. When examining contractile function using derivatives of LV pressure dp/dt, it is limited as e.g., maximal values dP/dt are firmly dependent on LV preload. Dp/dt provides information about the rate of tension development during isovolumetric contraction phase. Index is preload-dependent, caused in part by length-dependent changes in myofilament calcium sensitivity [1], and somewhat less afterload (AL) independent as the dp/dt max occurs during isovolumic contraction before opening of the aortic valve [2]. In case the initial preload is greater in a given cardiac cycle, isovolumetric contraction starts at greater EDV, and final value of dp/dt is also greater [3]. For that reason, an empirical correction to adjust for LV preload (dp/dt max/EDV) was designed by Little [4]. Taken together, dp/dt max provides limited clinical evidence about isometric or isovolumetric phase of cardiac cycle within static F-S law [5]. Dp/dt provides information about static load-dependent contractility. Due to constant load presence in the closed mammalian circulation system, manipulation of preload or AL is essential to obtain further information about response of central or peripheral hemodynamics. During this modeling,

preload is usually stressed by temporary occlusion of major vein such as inferior vena cava (IVC), while the AL is kept constant [6]. When performing temporary preload reduction by inferior vena cava occlusion (IVCO) there will be always presence of AL impedance. When preload is acutely reduced by IVCO, the AL impedance or (ESP) of successive beats decreases along with preload (Fig. 2 and 3) Additionally, the instant impedance during pre-load maneuvers matters; moreover, the position of the pressure-volume loop (PVL) on the X-volume axis before the preload reduction maneuver is initiated is equally important (Fig. 1).

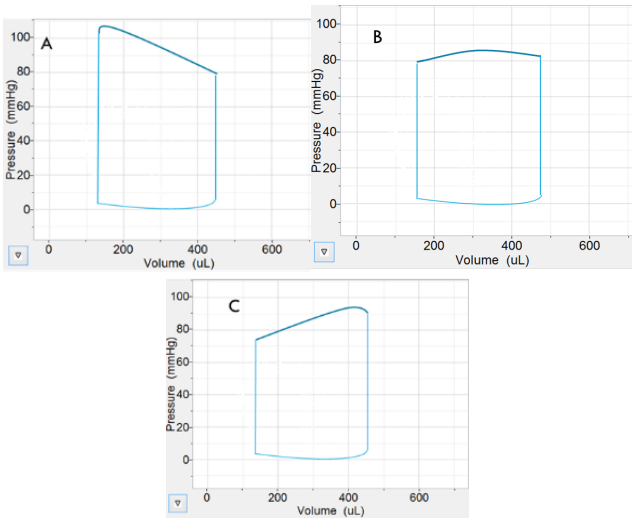

Fig. 1. Variability of ejection phase of cardiac cycle based on an immediate hemodynamic load, 3 possible conditions before performing transient preload reduction

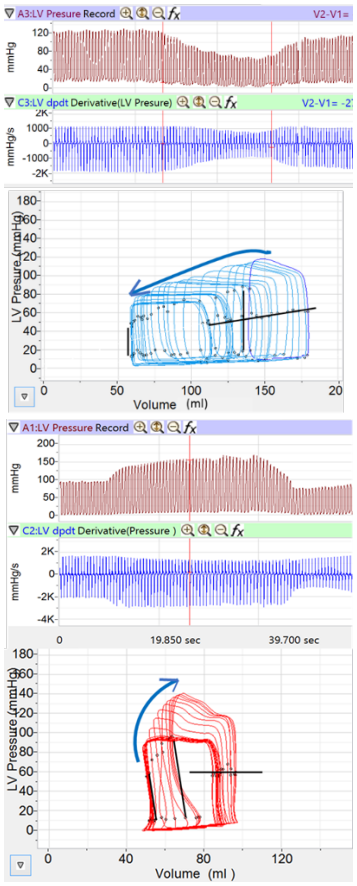

Fig. 2. Difference of dp/dt max and min during transient preload vs. afterload occlusion.

Fig. 1 is a graphical representation of planes of left ventricle pressure-volume loop (PVL) from 3 different steady-state hemodynamic conditions before preload reduction by IVCO. Ideally gathered systolic indices of load-independent contractile function should be obtained by reducing filling volume under a stable or constant AL impedance. However, in this case we could observe that in example A, the ejection phase of the cardiac cycle has to be adjusted to large AL impedance coming from systemic vasculature. In the example C, the situation is opposite. The idealized condition could be seen as condition B, where the systemic vascular impedance is close to being constant. This does not mean that the IVCO could not be performed in all conditions outlined in this figure, however attention has to be paid to account for the initial steady state condition when describing the outcomes.

Level of impedance would vary in course of a single experiment or be present in the course of different clinical conditions, attention has to be paid on how to account for the initial AL steady-state condition when describing the outcomes. Moreover, final AL impedance is intricately interconnected with properties of the aortic valve, aorta, and its distributing arteries (systemic vascular resistance). Remarkably, AL (or hindrance to eject against) is frequently adjusted during ejection periods of cardiac cycle. This adjustment could lead to change of valve timing, which needs to be well-captured during a variety of hemodynamic conditions [7].

Different patterns of left ventricle pressure and its LV pressure derivate during preload (image on top) and AL occlusion by aortic outflow (on bottom). Typical decrease of max and min dp/dt during load-independent maneuvers in case of transient preload (blue PVL) is contrasted with an increase of dp/dt min (isovolumic relaxation time) during transient AL occlusion (red PVL). Moreover, in case of aortic outflow occlusion the dp/dt max stays almost constant.

Consequently, there is possibility to complete AL occlusion by swift aortic constriction to complement data collected using preload reduction, if variation is excessive.

Lastly, another important concept when performing hemodynamic study is to adjust the total circulating volume (also known as non-stressed volume) in order to place animals at the same starting load-dependent or steady-state position on the Frank-Starling curve [8].

II. Major Systolic Index Gathered using Transient Preload Reduction

The time-varying elastance model of ventricular contraction is the present-day foundation of load-independent indices of inotropic state. In the PVL plane (XY plot), the maximal PV ratio of ventricular elastance occurs at the uppermost left hand corner of each loop. This point could be identified by using automatic corner identification described by Lankhaar [9].

The end systolic ventricular elastances Emax (max PV points for each loop), when connected, relationship ESPVR is generated; in this case a curve-linear slope called Ees (the end-systolic elastance). The ratio of max elastances is referred to as end systolic *chamber* elastance (to generalize it for LV and RV chamber). Curvilinear modeling was selected

based on earlier work of [10-13]; due to their observation that ESPVR was frequently curvilinear, and a significant correlation exists between the extent of nonlinearity and contractile state and also since in high-volume range, high pressures are required to increase volume to its maximum value, while in the low-volume range large negative pressures are required to reduce volume to negligible values [13], [14]. Moreover, observation of elastance has been paralleled with Hooke's Law of elasticity. The similarity of heart and spring were illustrated using force acting on spring as it can return to its original state when the force is removed (limit of proportionality). Both examples were similar until the force reached the limit of elasticity in modeling stress vs. strain, after which the material did not return to its original length, when the force acting on the material was removed. This force–length relationship is fairly linear however, at extreme muscle lengths, the relationship plateaus at a maximum tension, in part because, with increasing stretch, overlap between actin and myosin filaments reaches a maximum and then decreases [3]. Additionally, when one reflects on the force–length relations of cardiac muscle, LV chamber geometrical factors play crucial roles in modeling and assessment of end systolic elastance using isochrones. For more information, please refer to the work of [9].

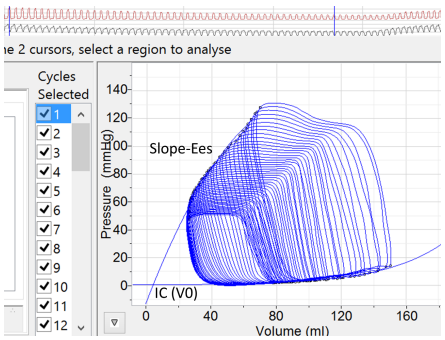

Fig. 3. Software modeling of End Systolic P-V relationship (ESPVR).

As discussed in previous paragraph, max PV points i.e., Emax at the left hand corner of PVL were observed to be the classical points of interest to describe the ventricular elastance, similar to elastic deformation of spring. However, max elastance points within each PVL do not coincide with the end of systole in the LV chamber, or end of individual systolic cycle (if we use precise ECG signal as a guide). Moreover, software programs using automatic corner point identification are currently used to detect the Max PV point as opposed to ES point that could be detected using cardiac cycle-based physiology. The difference between Max PV (Emax) and ES points are explored in 2 examples below, and by using the ES point, assessment of systolic contractility is provided.

In case of displaying differences of PV points, it is crucial to find proper ES points within PVL using LV dp/dt min or dicrotic notch area on aortic pressure wave trace (Fig. 4). Modeled by the software, direct comparison of max PV points as compared to ES points when creating Ees slope can be established, also capturing the volume axis intercept V_0. Fig. 5 discusses differences in capture of points while classical and new ESPVR relationships are summarized.

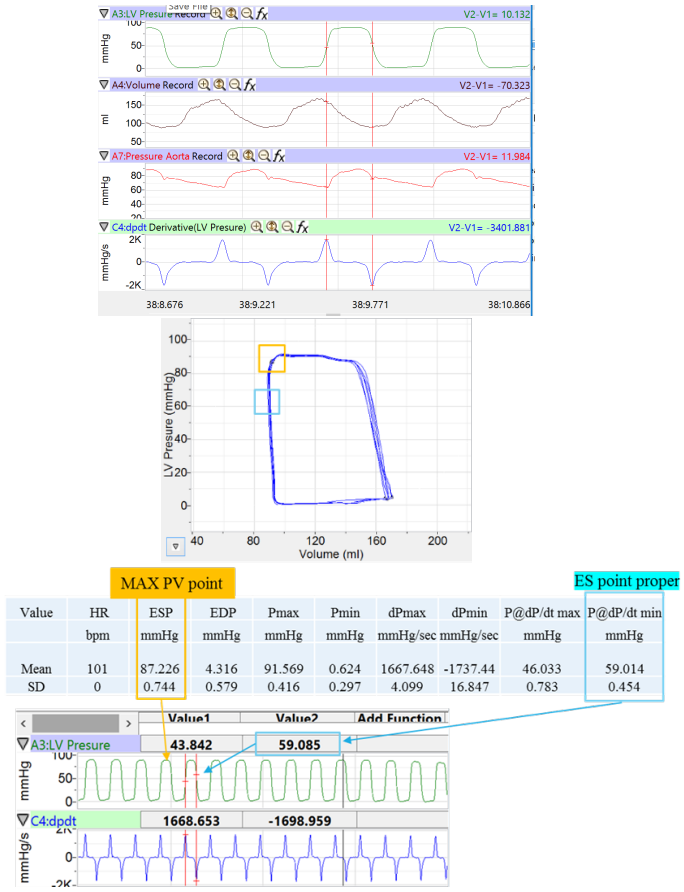

Fig. 4. Max PV point and ES point.

At the upper hand side of the figure, example from 3 full cardiac cycles using data collected from swine. Channels are as follows: LVP, LV volume (LVV), Ao P trace and calculated LV dp/dt channel. Red cursors indicate the ejection phase of cardiac cycle (from dp/dt max to min). AoP trace's dicrotic notch coincides with dp/dt min (both align well in this case). Dp/dt min is associated with closure of Ao valve (notch on the trace), which specifies the end of systole in LV. Pressure at this location is also known as P@dp/dt min using proprietary software nomenclature (as shown below on the waveform graph). In this case P@dp/dt min is associated with the ES proper (PV loop plane), while blue square indicates its location as compared to max PV point (orange).

Additional modeling of systolic PV relationship presented in this article, comes from the relationship of the LV Peak Pressure (PP) in combination with ES point. This relationship couples 2 distinct PVL cycle points within one cardiac cycle. Connecting the LV Peak Pressure (PP) with ES point relationship (PPESPVR) could be established, extending this linear relationship downward towards the volume axis, it also detects the volume axis intercept Vint. The association is linear and includes a non-fixed volume axis intercept V_{int}. Furthermore, PPESPVR could be captured during cyclical load dependent periods of PVL (without need of further stressing the hemodynamics using IVCO). This creates an opportunity to obtain slope and intercept values, such in case of other PVL methods such as e.g., the single beat elastance. Collected V_{int} could provide a similar assessment of dead volume during hypothetical P0, as in case of classical ESPVR modeling. Importance of V_{int}. is discussed in the next paragraphs.

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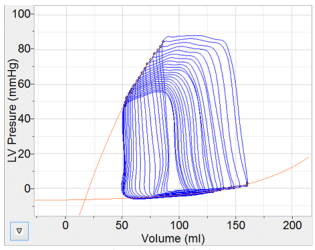
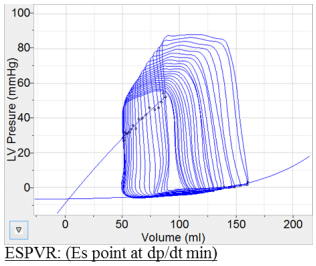


ESPVR: (Max PV point)
Selection Duration: 13.905 sec
Eq: P = -0.007967*V^2 + 2.114354*V + -39.138)
SSE Value = 9.845
Intercept(V0) = 20.021
ESPVR slope (sqrt(b2_4ac)) = 1.795



ESPVR: (Es point at dp/dt min)
Selection Duration: 13.905 sec
Eq: P = -0.001300*V^2 + 0.808009*V + -8.616)
SSE Value = 55.24
Intercept(V0) = 10.853
ESPVR slope (sqrt(b2_4ac)) = 0.78

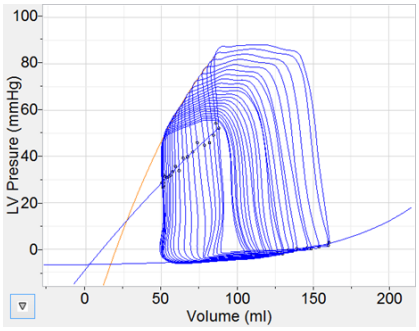


Fig. 5. ESPVR modeled using Max PV and ES points and compared.

Software program captures ESPVR by using max PV and ES points (above). Both relationships are compared below (orange vs. blue curvilinear relationship). Selection of the same number of loops yield different values characterizing classical vs. new Ees and V0 notch for modeled systolic relationships. Modeled by the software, direct comparison of max PV points with true ES points when creating Ees slope can be established, capturing the volume axis intercept V0. max PV points differ from Pmax or max pressure, that could be seen on Fig 1B and 1C.

In PPESPVR, the V_{int} is an imaginary volume of LV chamber at a given cardiac cycle, based on the direct relationship of V at PP and V during ES point, within a single cardiac cycle. This steady-state parameter might characterize 2 states: ending systole and (adjusted isovolumic relaxation phase) aIVR. This relationship could lead further to creation of the *end-systolic fraction* (ESF) in (%), i.e., fraction of imaginary volume of LV chamber during a given cardiac cycle, based on V at PP and V at ES point. Consequently, ESF could also be characterized inside one cardiac cycle's pre/afterload constraints (Fig. 6 and 7). Simple calculation could be mathematically defined as follows (1):

$$\text{ESF}\ (\%) = \frac{ESV - V\,(int)}{V\,(PP) - V(int)} \qquad (1)$$

To better understand this relationship, a quick example could be given based on Fig. 6 and 7. On the image Fig 6, the V_{int} is estimated to be about 50 ml (end of dotted line crossing the volume axis). Once again, the relationship is linear with a slope and an intercept and could be precisely calculated. Following Fig. 6 example, the straight line raised from PP intersects the area of ES point. By extending this linear relationship downward towards the volume axis, it crosses the volume axis intercept V_{int}. The intercept of volume axis $V_{int.}$ is regarded as a very important determinant of ESF.

To organize (2): The nominator comes from ESV and volume at V_{int} (yellow bracket in Fig. 7; as nominator) divided by volume at PP minus volume at V int. (red denominator). Further in numbers captured using the waveform graph in Fig. 6:

$$\text{ESF} = \frac{84.49-50}{101.68-50} = \frac{34.49}{51.68} = 66.7\% \qquad (2)$$

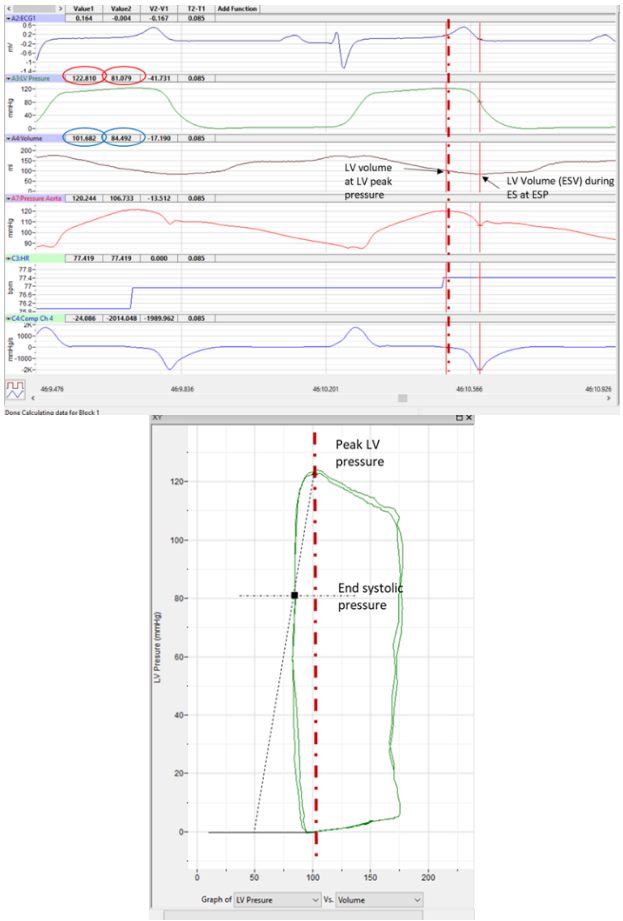


Fig. 6. Steady state single beat PV relationship of the LV Peak Pressure (PP) with ES point (PPESPVR).

Presented channels are as follows, ECG (in mV), LV pressure (in mmHg), Channel 3 LV volume (in ml), Aortic pressure (in mmHg), channel 5 is HR in (bpm) and last channel is LVP derivative of channel 2 (LV dp/dt in mmHg/sec). There are multiple time related events and relationships presented as for example: the end systole is captured by using aortic dicrotic notch; tracing seen on the aortic pressure trace using channel 4, which corresponds to LV dp/dt min (channel 6) and post-peak T wave at (channel 1). LV volume at PP is shown on channel 3 as a red dotted line. Likewise, LV volume at ESP (ESV) is captured during ES (by solid red line) and shown at channel 3 for comparison. The LV peak pressure (PP) is associated with LV volume that is still being ejected as LVP decreases from PP of 122.81 to ESP 81.1 mmHg to that is (41.73 mmHg difference) within 85 msec. Both exact volumes at PP (101.68 ml) and at ESV (84.49 ml) are shown at channels 3 and are blue color encircled. Difference of volumes is 17.19 ml.

To summarize, the systolic relationship is measured by stressing the load imposed on the heart by transiently occluding vena cava, an already well-known and currently used hemodynamic maneuver. Max PV points are calculated by software using automatic point detection.

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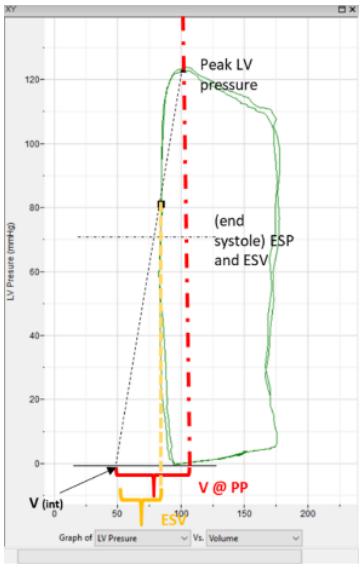

Fig. 7. End Systolic Fraction (ESF) relationship in (%)

Fig. 6. The figure above shows one complete cardiac cycle PVL relationship. From PP the straight line intersects the area of ES point. The intercept of volume axis Vint. is regarded as a very important determinant of ESF relationship. The nominator comes from ESV from PVL minus V int. (yellow as nominator) divided by volume at PP minus the V int. (red denominator). The bottom figure shows LV volume at PP and the LV volume at closed aortic valve (ESP).

Adding novel physiologically-focused-ES points into ESPVR, two novel systolic interactions could be generated, both working with ES points in the PVL cycle. The ES point in PVL plays a vital role in systolic contractility assessment as it could be easily discovered. Moreover, ES point could be easily compared during different phases of hemodynamic testing as it also indicates, in extension, true amount of AL impedance within a single cardiac cycle and indicates variability of ejection phase of multiple cardiac cycles, centered around hemodynamic load. The ES-based interactions could be considered an enhancement of the systolic contractility portfolio.

III. Timing and Composition of Transient Preload Reduction, Standard Procedure to Assess Systolic Contractile Indices

Timing and characterization of classical preload maneuver using IVCO plays an important role in its comparison in-between pre-clinical laboratories or clinical catheterization labs. It is not well characterized in current literature as it mostly resides in the form of standard operating procedures within clinical catheterization labs. In Table I, specific characteristics of such protocol are outlined. Before performing the IVCO maneuver to eliminate breathing artifacts in the recorded data, short breath-hold should be staged during mechanical ventilation. Breathing should be temporarily halted in the inspiration phase i.e., using (hanging bellow in ascend) in case of using common large animal ventilators. Also, attention has to be paid to the amount of time required to perform preload reduction e.g., closed chest swine and open chest sheep examples, or HR at the beginning and its change during IVCO (all in Table 1). To further verify the quality of IVCO, maximal LV pressure P(max) drop to pressure at the end of IVCO called P(end) needs to be standardized. In Table I, delta (ΔP), the change from P(max) to P(end) was at 43 and 44 mmHg, respectively. Furthermore, some software programs allow further characterization of the isochrone by Goodness-of-Fit statistics using sum of squares due to error (SSE). The value refers to the residual sum of squares (the sum of squared errors) of a regression line; the sum of the squares of the deviations of the actual values from the predicted values, within the sample used for estimation. SSE fit is calculated using software, and tightness of the fit enables it to judge the quality of IVCO, while also enabling it to select the 3 of the best occlusion samples for further analysis. In case of quadratic load-independent PV, the end systolic elastance curve (Ees), software fitting is using logarithmic relationship, which describes relationships between variables that are not as easy to interpret as e.g., in case of linear relationship. A small standard error of the regression indicates that the data points are closer to the fitted values. One of the disadvantages of non-linear fitting is a strong sensitivity to outliers, hence precise timing and repeatable IVC balloon occlusion maneuver plays a major role in capturing stable isochrones with low SSE.

The presence of few outliers in the data might potentially impact the results of a nonlinear analysis. This could be captured by a larger SSE number, and in this case IVCO should be repeated.

To further assess the IVCO, HR changes and concurrent ECG assessment could aid in determination whether the activation of sympathetic or parasympathetic systems has influenced the final Max PV point (Emax), V0 or Ees as in cases of modulation of autonomic nervous system described earlier using isolated canine heart [15]. Furthermore, an initial PVL position on the x-axis (volume axis) before executing transient preload reduction has to be also considered. In case of changes of key indicators of load or in case of an abrupt change of AL impedance during IVCO, adjustments of volume axis intercept, Ees slope or the entire ESPVR should be reviewed. To establish clear and well-positioned PVL before stressing hemodynamics is key to good practice and should be also written into the standard assessment of PVL catheterization protocol.

TABLE I: Measures to Be Captured during IVCO in Large Animals

Preclinical Hemodynamic (PV) model	Animal body weight (kg) (Mean ± SD)	Δ HR during IVCO (bpm) Start to end IVCO	IVCO SSE (Mean ± SD)	Time of Preload reduction by IVCO (sec) (Mean ± SEM)	Δ P (mmHg) P (max)- (P end) in mmHg (Mean ± SEM)
Swine LV (n=19) Closed chest balloon catheter	57.2±13.4	3 (min)	251.8±79.2	17.38±1.87	42.8±4.13
Sheep LV (n=7) Open chest torniquet	35-56	2-3 (min)	541±77.2	10.86±2.3 (open chest)	43.89±12.2

In conclusion, when performing temporary preload reduction by IVCO there will always be presence of an AL impedance. Level of impedance would vary during e.g., single experiment or in-between groups of control animals, which might be e.g., dependent on autonomic system activity, leading to different patterns of LV ejection phase of PVL as shown in Fig. 1. The quality of the preload reduction should be judged by e.g., IVCO SSE (sum of squared errors); time of preload reduction by IVCO (sec); Δ P (mmHg) P (max)-(P end) in mmHg (all in Table I.). Lastly, Max PV points might not always be determined suitably as compared to well-defined ES points. To appreciate specifics of max PV point detection, automatic corner point identification should be well-understood [3]. Current software programs are in many cases able to detect Max PV (Emax) points without any difficulties. Understanding of its value is crucial in determination of classical systolic contractile parameters.

IV. Analysis of Quadratic EeS and Linear PRSW Isochrone Fitting to Compare Group Systolic Contractile Indices

To compare 2 primary systolic indices i.e., ESPVR and preload-recruitable stroke work (PRSW), its slopes (Ees and Mw) and its respective intercepts, quadratic and linear formulae need to be copied from software into a spreadsheet. To make meaningful group comparison, a steady-state example from loading ranges, before putting stress on hemodynamics needs to be considered (bottom black brace under load dependent steady-state PVL in the Fig. 8 indicates loading ranges). Loading range values are used to create factorial volumes in order to help in load-independent data comparison. Example of calculation using factorial volumes is given in Table II.

TABLE II: Example of Spreadsheet to Calculate Values Based on Factorial Volumes (Linear Relationship)

Factorial Volumes (x)	100	125	150	200	250
GR A	Determine P (y)	Det. P (y)	Det. P (y)	Det. P (y)	Det. P (y)
GR B	Determine P (y)	Det. P (y)	Det. P (y)	Det. P (y)	Det. P (y)
GR C	Determine P (y)	Det. P (y)	Det. P (y)	Det. P (y)	Det. P (y)

Equation y=69.731x+/- 1057.766

In case of PRSW linear relationship of SW (J) vs. EDV (ml) is followed described by [16], using values from group calculations for A, B, and C (Fig. 8). In the spread sheet on Table II, factorial volume ranges of 100, 125, 150, 200 and 250ml were selected based on the steady-state loading ranges for all groups. Later, computation of mean data values from individual timepoints was made, allowing to construct linear slope and IC and to compare all animals in respective groups. Later, the PRSW linear relationship could be further visually compared using group's IC and Mw. Finally, correlation coefficients were calculated, and additional statistical tests performed. Analysis of variance and post-hoc statistical tests were performed on values obtained using the factorial comparison method.

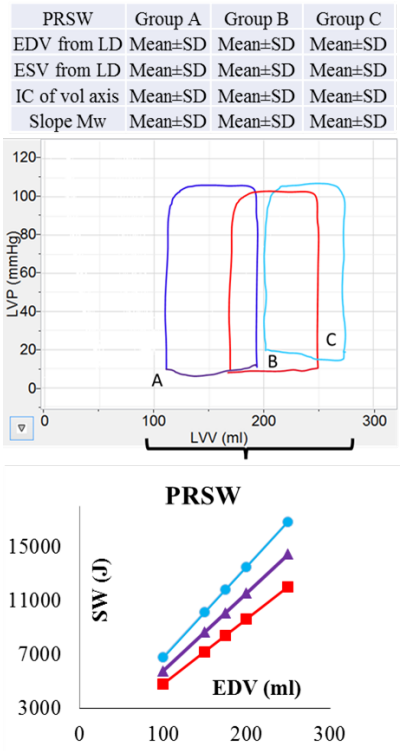

Fig. 8. PVL factorial values were used to construct group visual comparison of PRSW linear slopes and respective IC.

The linear PRSW formula is y=mx+b, where y= Pressure; m=PRSW slope Mw; b=PRSW IC. For loading factorial volume values: x=100, 125, 150, 200, 250ml to allow comparison of all animal's groups A, B and C and to erect representative linear relationships.

In the case of comparison of quadratic relationships, similar steps were taken. The quadratic-based formula is once more copied from software into the spreadsheet and all formulas are calculated for a given group using factorial volumes. Table II and Fig. 9 shows final comparison of multiple individual Ees evaluated as group A, B and C on one graph.

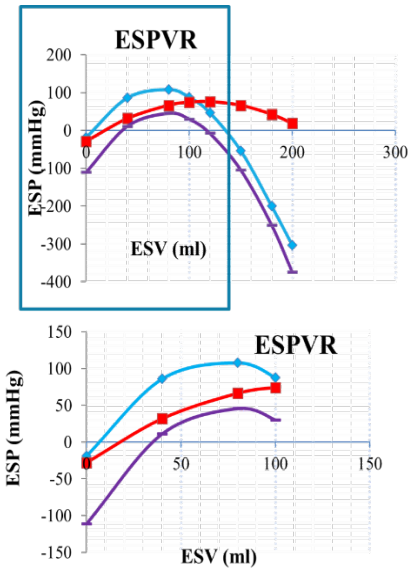

Fig. 9. Using PVL factorial values from previous figures to construct group visual comparison of ESPVR, quadratic Ees and IC visual assessment for A, B and C .

TABLE III: EXAMPLE OF SPREADSHEET TO CALCULATE VALUES BASED ON FACTORIAL VOLUMES (QUADRATIC RELATIONSHIP)

Factorial volumes (x)	100	125	150	200	250
GR A	Determine P (y)	Det. P (y)	Det. P (y)	Det. P (y)	Det. P (y)
GR B	Determine P (y)	Det. P (y)	Det. P (y)	Det. P (y)	Det. P (y)
GR C	Determine P (y)	Det. P (y)	Det. P (y)	Det. P (y)	Det. P (y)

Equation y=-0.003302*x^2+1.105112*x+19.895

In this case slope Ees and IC could be better visually compared using selected 0 to 100 ml volumes, instead of plotting a full factorial relationship.

In the case of quadratic ESPVR formula is y=ax2+bx+c, where y= Pressure; x=factorial volume. For loading factorial volume values: x=100, 125, 150, 200, 250ml to allow comparison of all animal groups A, B and C and to erect representative linear relationships.

Selection of important visual comparisons in case of ESPVR (x-axis IC and Ees) are shown in the bottom graph, after performing a general overview of the data upper graph blue rectangle.

V. LIMITATION OF FINDINGS

In this article an example of standard measures from single catheterization lab were described using Table I, giving background to transient preload reduction to assess the values of systolic cardiac contractility. This standardization is not very well described in current hemodynamic pressure-volume based literature. Lack of description of standard measures, equipment and its proper use during an experiment plays a critical role in the final assessment of hemodynamics and cardiac mechanics. In many instances, to refine the initial protocol, pilot experiment should be instituted to find correct IVCO balloon size, investigate adequacy of anesthesia, examine quality of breath hold maneuver, while anticipating technical and procedural challenges. In the current state, as written in this article, it might present an opportunity, if other labs are compelled to publish their standard measures and values, they collect during IVCO. In this short article, data have been collected using different vascular occlusion devices enabling the transient preload reduction. Data were only added after an initial quality assessment using Table I. Moreover, on the majority of occasions, IVCO was performed after a brief breath-hold during mechanical ventilation. ECG was used in many cases to properly assess cardiac cycle during steady state, and during IVCO. IVCO was in majority of cases completed under ECG gating to be able to reduce possible sympathetic or parasympathetic influence on LV inotropy. Additionally, the effects on central and peripheral hemodynamics (heart rate, pre, afterload) should be well-documented. After successful data collection, analysis of results plays a major role in comparison of contractile systolic responsiveness of a particular group. Article presents quadratic based ESPVR and linear based PRSW graphical comparisons to visualize and further investigate potential differences across experimental as opposed to control conditions. Data analysis was performed on samples without the presence of an arrhythmia. Both inotropy influencing effects i.e., Anrep and Bowditch in case of abrupt increase of AL or HR were limited to minimum in cases of intact healthy animals.

VI. DISCUSSION AND CONCLUSION

In this short article I have tried to summarize why modeling of cardiac response to transient hemodynamic (load) changes is important as compared to using only non-stressed dp/dt max. In a few examples "classical" preload-based hemodynamic "manipulation" with indexes of systolic contractile response using IVCO were outlined. Novel twist on other possible index(ices) coming from capturing ES point may well present future opportunities to collect systolic cardiac contractility data. In this instance, both single beat systolic PPESPVR and IVCO using ES points present unique opportunities in this niche area of research. Final two sections of this article are dedicated to the procedural steps and how to standardize execution of IVCO for others to compare their notes. The last section is reserved to analytical steps of how to visually compare systolic indices from classical IVCO in case of linear and quadratic relationship.

CONFLICT OF INTEREST

Author declares that he does not have any conflict of interest.

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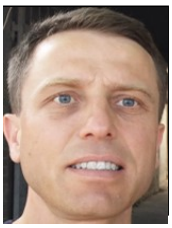

F. Konecny was born in the Czech Republic in 1976. He received his master's and D.V.M. degree in 2000, from the University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic. He finished his doctoral studies in 2011 and received Ph.D. from a combined program between McMaster University, Ontario, Canada, and the University of Veterinary and Pharmaceutical Sciences, Czech Republic. His extensive postgraduate research at the University of Toronto focused on experimental surgery, characterizing rodent protein therapy post-myocardial infarction, and creating mostly rodent cardiovascular models. Later, he concentrated on the assessment of ventricular function using both, invasive and non-invasive methods to evaluate ventricular pressure, pressure-volume, transthoracic echocardiography, CT, and other imaging methods.

He is currently Application Scientist and Surgical trainer at Transonic System Inc. with teaching duties at McMaster University, Hamilton, ON, where he focuses on lecturing surgery. His recent research efforts focus on heart failure modelling in large animals while combining acute ventricular catheterization with non-invasive imaging. Recently, his emphasis has been on left-ventricle-assisted devices (LVADs) helping with the characterization of biventricular (RV and LV) pressure-volume during mechanical cardiac support to characterize the influence of LVADs on beat-to-beat central and peripheral hemodynamic.

Dr. Konecny is a member of the European Heart Failure Association of ESC, a member of (EAPCI, EACVI, EAPC, and the Czech Cardiovascular Society).