A Review of Cardiac Contractility Indices during LVAD Support

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***Abstract*— Left ventricular assist devices (LVADs) are increasingly used as a mechanical circulatory support in heart failure patients. The diagnostic of cardiac contractility is important to monitor the state of heart failure in the course of reverse remodeling and right heart protection during LVADs. Several cardiac contractility indices were developed to determine contractility using left ventricular pressure (LVP) and/or left ventricular volume (LVV). Most of them are required an invasive measurement that is not suitable for frequently monitoring in long-term support. The new indices that can derive from non-invasive measurement had been proposed by using ultrasound measurement and pump flow. The benefits and limitations of cardiac contractility indices during LVAD support were discussed.**

Keywords— **Cardiac contractility index, Left Ventricular Assist Devices, Rotary Blood pump, E_{max}.**

I. INTRODUCTION

The clinical treatment of end-stage of heart failure patients is the left ventricular assist devices (LVADs) that mainly used the technology of rotary blood pumps (RBPs). These devices are mainly used as a bridge –to-transplantation (BTT), destination therapy (DT) and bridge-to-recovery (BTR). For all three applications of RBPs, cardiac contractility indices are used to monitor the state of heart failure and to diagnose the cardiac function in heart failure patients. In additional, the cardiac contractility index is used for right heart protection in RBP patients [1,2]. For the therapeutic approach of BTR [3-7], cardiac contractility must be assesses frequently. A useful cardiac contractility index must be sensitive to changes in contractility (muscular properties of the myocardium), insensitive to the changes in ventricular preload and after-load and be easy to use for assessment in a clinical environment.

II. CARDIAC CONTRACTILITY INDICES

In the past, all established cardiac contractility indices were investigated within the unassisted heart (normal heart, failure heart and pharmacological treated heart). Several cardiac contractility indices were developed to determine contractility using left ventricular pressure (LVP) and/or left ventricular volume (LVV). Some indices were derived from LVP alone such as end-diastolic LVP (EDP), the maximal derivative of LVP (dP/dt_{max}) and the maximal derivative of LVP divided by the instantaneous developed isovolumic pressure (dP/dt_{max} /IP). Some indices were derived from LVV alone such as end-diastolic LVV (EDV), the stroke volume (SV) and the ejection fraction (EF). Additionally, indices were derived based on pressure-volume analysis such as the end-systolic pressure volume relationship (ESPVR), the external work (EW), the maximal derivative of LVP vs. end-diastolic volume relationship (dP/dt_{max} vs. EDV) and the stroke work vs. end-diastolic volume relationship (preload-recuitable stroke work: PRSW). However, the determination of cardiac contractility with these indices is difficult to apply to RBP patients. The alternative indices were derived from pump information such as the pump flow.

A. Pressure derived cardiac contractility indices

Pressure derived cardiac contractility indices have been proposed using the dP/dt_{max} alone or the dP/dt_{max} divided by some ratio of LVP to prevent the effect of preload. The dP/dt_{max} alone has been reported to be preload-dependent. To correct the preload dependency of dP/dt_{max}, the normalized value has been used. dP/dt_{max} (a preload dependent index) divided by another preload dependent parameter can reduce the effect of preload. The dP/dt_{max} divided by an instantaneous developed isovolumic pressure (dP/dt_{max}/IP) and the dP/dt_{max} divided by a peak isovolumic pressure (dP/dt_{max}/PIP) have been reported to be a slightly load dependent index [8-10]. IP is the LVP at the time of dP/dt_{max} minus the LV-EDP. PIP is the aortic pressure at the time of EDV. However, both dP/dt_{max}/IP and dP/dt_{max}/PIP were investigated using the unassisted heart.

McConnell *et al.*[11] proposed the LV triple-product (TP = LVSP·dP/dt·HR) vs. LV EDP relationship (TP vs. EDP; $mmHg \cdot bpm \cdot s^{-1}$), which is the slope of the relationship, to estimate the changes in cardiac contractility during RBP support. The slope and intercept (d_0) of the TP vs. EDP relationship are estimated by least squares linear regression using a dataset of LVP including speed variation. However, an outline clustering of points was observed at the highest EDP. Below the flex point, TP vs. EDP showed the linear relationship and was independent to changes of afterload.

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The cause of this outline clustering of points remains unclear.

Naiyanetr *et al*. proposed the slope of the relationship (I_{pp}) between the dP/dt_{max} and the instantaneous LVP at dP/dt_{max} (dP/dt_{max} vs. IP) including a speed variation as a potential pressure-derived cardiac contractility index [12]. The slope of the relationship (I_{PP}) between dP/dt_{max} and IP was sensitive to contractility changes similar to other load independent contractility indices. I_{pp} is estimated by least squares linear regression (generate the slope and intercept (p_0)) using a dataset of LVP including speed variation

Additionally, pressure derived indices require the invasive measurement of LVP and a high quality of LVP signal is needed for an index determination (in case of the time derivative calculation). Therefore, pressure derived cardiac contractility indices are not practical parameters for continuous monitoring of cardiac contractility in clinical patients.

B. Volume derived cardiac contractility indices

Contractility indices which are derived from the LVV such as ejection fraction (EF) and fractional shortening (FS) shown the load dependent that depend on after-load (EF and FS would become zero at infinite afterload) [13]. This is confirmed by increasing the after-load in an animal experiment significantly affected EF [14]. According to the analysis of LVV and myocardial volume, Zhong *et al*. proposed a maximum rate of change of pressure-normalized stress ($d\sigma^*/dt_{max}$) by analysis of the myocardial chamber as a thick-walled sphere using ultrasound measurement (non-invasive index) in normal patients (without LVAD) [15]. However, Black et al. could show that the $d\sigma^*/dt_{max}$ is load dependent in the canine heart when preload is altered by an occlusion of the vena cava [16].

The LVV can be frequently measured by non-invasive methods using the ultrasound or the cardiac magnetic resonance imaging (cardiac MRI). However, during continuous left ventricular unloading by RBPs, the volume components, such as ESV, and EDV, are subjected to changes depending on the RBP drainage site (atrium or ventricle) and the support ratio [17]. Therefore, volume derived indices are not suitable in RBP recipients.

C. Pressure-volume derived cardiac contractility indices

Pressure–volume derived contractility indices, such as the dP/dt_{max} vs. EDV relationship, the preload-recruitable stroke work (PRSW: stroke work vs. EDV) and, the maximal elastance (E_{max}) or the slope of the end-systolic pressure-volume relationship (ESPVR) have been accepted as load-independent indices and used in many studies of contractility measurement [14,18,19]. According to other studies, both dP/dt_{max} vs. EDV and PRSW often display greater sensitivity to changes in cardiac contractility than E_{max}[10].

The dP/dt_{max} vs. EDV index is the slope of dP/dt_{max} vs. EDV relationship. The dP/dt_{max} vs. EDV relationship was found to be linear during load variation. The slope of dP/dt_{max} vs. EDV was increased in response to dobutamine intervention (increased contractility) similar to the increased slope of ESPVR. Note that the extrapolated volume-axis intercepts of dP/dt_{max} vs. EDV increased with dobutamine[20]. At an isovolumic contraction (constant left ventricular volume, LVV_{const}), the dP/dt_{max} vs. EDV index can be stated in the term of the left ventricular elastance ($E(t)=LVP(t)/(LVV(t)-V_0)$) as a maximal derivative of elastance ($dE/dt_{max}= dP/dt_{max}/(LVV_{const}-V_0)$)[19]. Furthermore, the dP/dt_{max} vs. EDV index was reported to be most sensitive for changes in contractility and slightly dependent on preload and afterload (aortic pressure)[20-21]. Using the dP/dt_{max} vs. EDV index, we should be aware that the determination of time-derivative of LVP and the volume estimation are also sensitive to noise caused by sensor artifacts.

The PRSW is the slope of the relationship between stroke work (SW) and EDV. SW is the area inside the pressure-volume loop. The value of PRSW and intercept (c_0) are estimated by using the small load variation. A linear relationship between SW and EDV would support the conviction of the Starling mechanism about the length-dependent phenomenon that reflects a basic property of cardiac muscle at the cellular level [18]. In the study of Little WC et al [20], the SW vs. EDV relationship was found to be linear during load variation. The slope of SW vs. EDV relationship was increased in a similar manner to the slope of ESPVR after the dobutamine intervention (increased contractility). The extrapolated volume-axis intercepts of the PRSW only marginally changed. Moreover, PRSW was reported as a robust parameter against changes in preload and afterload in the unassisted heart[10,20,21]; however, its sensitivity to changes in contractility was rather small in comparison with other indices.

The E_{max} is the slope of the end-systolic pressure-volume relationship (ESPVR) that is determined by least squares linear regression using several cardiac cycles during load variation (Assume to be linear relationship). However, the identification of the ESV, which is essential, is becoming ambiguous for the determination of E_{max} during RBP support. In a animal study of McConnell PI, Sun BC[22], the slope of ESPVR was determined from both an inferior vena cava (IVC) occlusion with the LVAD at 6,000 rpm (lowest support) and also when the LVAD was operated at 6,000 to 11,000 rpm to induce LV unloading [22]. E_{max} determination showed different values between IVC occlusion with minimal support and LV unloading until full support. The different values of E_{max} must relate to the nonlinear curve of ESPVR during a wide volume range of the left ventricle. A similar nonlinear relation was observed in another *in vivo* study by van der Velde *et al.*[23] Additionally, over a wide range of left ventricular volumes, ESPVR appeared to become nonlinear curve which increases the complexity of E_{max} estimation.[23] This nonlinear relationship has been demonstrated both in animal and clinical studies[17,22,24,25]. Thus, the original theory of the linear line of ESPVR (E_{max}) is not always obtainable in all animals. For example, E_{max} fails to provide a sufficiently robust model to account for changes in pressure and volume in the mouse ventricle [26].

Vandenberghe *et al.*[25] concluded that the original time-varying elastance theory insufficiently modeled the complex hemodynamic behavior of the left ventricle during assisted device support because V_0 depended on the pump flow level (as shown in the animal experiments using a displacement-type pump and a rotary blood pump). Therefore, E_{max} might not be a suitable index for RBP support.

D. Pump flow derived indices

Pump flow derived indices have been proposed for monitoring the cardiac contractility in rotary blood pump recipients because the necessary pump information is usually available in all pumps.

According to the studies of RBPs, the contraction of the native heart affects the patterns of pump flow, pump current and pump power. In the previous studies of cardiac contractility in RBP recipients [27,28], the pump-flow pulsatility (Q_{P2P}: peak-to-peak of pump flow), the pump-flow pulsatility index (Q_{P2P} divided by mean flow), and the maximal derivative of pump-flow (dQ/dt_{max}) were proposed to determine the cardiac contractility because pump flow was available, either measured or estimated.

Similar to the pulsatility of the arterial flow, the pump flow pulsatility and the pump flow pulsatility index depend on the pump speed. dQ/dt_{max} is also a speed dependent parameter. Moreover, dQ/dt_{max} seems to closely reflect the classical cardiac contractility index (dP/dt_{max}) because dQ/dt_{max} had an excellent correlation with the dP/dt_{max} during RBP support in animal experiments[29]. Similarly, the pattern of dQ/dt showed a strong correlation with the pattern of dP/dt during RBP support [27]. Naiyanetr *et al.* proposed the slope of the relationship between dQ/dt_{max} and-peak-to-peck of pump flow (dQ/dt_{max} vs.Q_{P2P}: I_Q) that was sensitive to change of cardiac contractility as shown in the animal experiment [29].

Discussion

All clinically established cardiac contractility indices remain rather theoretical or problematical for the assessment in RBP recipients because, first, the methods require invasive assessment and, second, there are large variations in ventricular preload and after-load due to changes in pump speed. Moreover, it becomes difficult to accurately define the EDV during continuous unloading as both ESV and EDV depend on the level of the pump support.

During clinical treatment, massive pump control interventions, such as off-pump or speed reduction, have been proposed for the evaluation of cardiac contractility, with both pulsatile and continuous devices. In clinical applications, echocardiography is the first choice to assess the cardiac contractility [2]. The Harefield group and the Berlin group proposed such protocols to assess the chance for pump weaning by using EF or walking a distance in 6 minutes after off-pump [30-31]. For pulsatile devices, the condition of the unassisted heart can be achieved by switching off the pump or reducing the pump frequency (contractions per minute) for a limited period of time - yet with a considerable risk of thrombus formation. For continuous-flow devices, a simple pump stop would generate a condition with additional load to the LV of the patient (back flow) [32]. The Berlin group proposed a speed reduction down to a zero net flow for the assessment protocol, which, however, would still mean additional load to the heart during back flow[32].

In general, ultrasound evaluation can only be performed infrequently, so the detailed time course of contractility in clinical practice would remain unknown. With present diagnostic and therapeutic, the probability of finding the right time for pump weaning is relatively low [1,33]. On the other hand, invasive methods are only practicable during a short post-operative period and eventually for a final decision about weaning.

Unfortunately so far all known load independent indices need an invasive measurement that is hardly possible in RBP recipients. Therefore, the novel cardiac contractility index that is derived from available signals, such as the pump flow, should be a practical tool to determine cardiac improvement during reverse remodeling in both the clinical and the ambulatory setting.

REFERENCES

1. Maybaum S, Mancini D, Xydas S, et al. (2007) Cardiac improvement during mechanical circulatory support a prospective multicenter study of the LVAD working group. Circulation. 115: 2497-505.
2. Mueller J, Wallukat G. (2007) Patients who have dilated cardiomyopathy must have a trial of bridge to recovery (Pro). Heart Fail Clin. 3:299-315
3. Long JW, Healy AH, Rasmusson BY, et al. (2008) Improving outcomes with long-term “destination” therapy using left ventricular assist devices. J Thorac Cardiovasc Surg. 135:1353-61

4. Lietz K, Long JW, Kfoury AG, et al. (2007) Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. Circulation. 116:497-505
5. Birks EJ, Tansley PD, Hardy J, et al. (2006) Left ventricular assist device and drug therapy for the reversal of heart failure. N Engl J Med. 355:1873-84.
6. Burkhoff D, Klotz S, Mancini DM. (2006) LVAD-induced reverse remodeling: basic and clinical implications for myocardial recovery. J Card Fail. 12:227-38.
7. Moscato F, Arabia M, Colacino FM, Naiyanetr P, Danieli GA, Schima H. (2010)"Left ventricle afterload impedance control by an axial flow ventricular assist device: a potential tool for ventricular recovery" *Artificial Organs*. 34(9):736-44
8. Pak PH, Kass DA. (1995) Assessment of ventricular function in dilated cardiomyopathies. Curr Opin Cardiol. 10:339–44
9. Mason DT. (1969) Usefulness and limitations of the rate of rise of the intraventricular pressure (dp/dt) in the evaluation of myocardial contractility in man. Am J Cardiol. 23:516-27
10. Kass DA, Maughan WL, Guo ZM, Kono A, Sunagawa K, Sagawa K. (1987) Comparative influence of load versus inotropic states on indexes of ventricular contractility: experimental and theoretical analysis based on pressure–volume relationships. Circulation. 76:1422–36
11. McConnell PI, Del Rio CL, Kwiatkowski P, Farrar DJ, Sun BC. (2007) Assessment of cardiac function during Axial-flow left ventricular assist device support using a left ventricular pressure-derived relationship: comparison with preload recruitable stroke work. J Heart Lung Transplant. 26:159-66
12. Naiyanetr P, Moscato F, Vollkron M, Zimpfer D, Wieselthaler G, Schima H. (2008) Estimation of cardiac contractility during rotary blood pump support using an index derived from left ventricular pressure. IFMBE Proceeding EMBEC08 "4th European Medical & Biological Engineering Conference, IFMBE European Conference on Biomedical Engineering" Antwerp, Belgium, 1885-87.
13. Borow KM, Neumann A, Marcus RH, Sareli P, Lang RM (1992) Effects of simultaneous alterations in preload and afterload on measurements of left ventricular contractility in patients with dilated cardiomyopathy: comparisons of ejection phase, isovolumetric and end-systolic force–velocity indexes. J Am Coll Cardiol. 20:787–95
14. Little WC. (1985) The left ventricular dP/dt_{max}-end-diastolic volume relation in closed-chest dog. Cir Res. 56: 808-15.
15. Zhong L, Tan RS, Ghista DN, Ng EY, Chua LP, Kassab GS. (2007) Validation of a novel noninvasive cardiac index of left ventricular contractility in patients. Am J Physiol Heart Circ Physiol. 292: H2764-72.
16. Black A, Grenz N, Niccole S, et al. (209) Assessment of $d\sigma^{*}/dt_{max}$, a load independent index of cardiac contractility, in the canine. Cardiovasc Eng. 9: 49-55IFMBE at http://www.ifmbe.org
17. Sakamoto T. (2002) Evaluation of native left ventricular function during mechanical circulatory support: theoretical basis and clinical limitations. Ann Thorac Cardiovasc Surg. 8:1-6.
18. Suga H. (2003) Cardiac energetics: from E(max) to pressure-volume area. Clin Exp Pharmacol Physiol. 30: 580-5.
19. Glower DD, Spratt JA, Snow ND, et al. (1985) Linearity of the Frank-Starling relationship in the intact heart: the concept of preload recruitable stroke work. Circulation. 71: 994-1009
20. Little WC, Cheng CP, Mumma M, Igarashi Y, Vinten-Johansen J, Johnston WE. (1989) Comparison of measures of left ventricular contractile performance derived from pressure-volume loops in conscious dogs. Circulation. 80(5):1378-87
21. Van den Bergh A, Flameng W, Herijgers P. (2008) Parameters of ventricular contractility in mice: influence of load and sensitivity to changes in inotropic state. Pflugers Arch. 455(6):987-94.
22. McConnell PI, Sun BC.(2006) Pressure-volume analysis during axial flow ventricular assist device support. J Heart Lung Transplant. 25(2):256-7.
23. van der Velde ET, Burkhoff D, Steendijk P, Karsdon J, Sagawa K, Baan J (1991) Nonlinearity and load sensitivity of end-systolic pressure–volume relation of canine left ventricle in vivo. Circulation. 83:315–27
24. McConnell PI, Del Rio CL, Kwiatkowski P, Farrar DJ, Sun BC. (2007) Assessment of cardiac function during Axial-flow left ventricular assist device support using a left ventricular pressure-derived relationship: comparison with preload recruitable stroke work. J Heart Lung Transplant. 26:159-66
25. Vandenberghe S, Segers P, Steendijk P, Meyns B, Dion RA, Antaki JF, Verdonck P. (2006) Modeling ventricular function during cardiac assist: does time-varying elastance work? ASAIO J. 52(1):4-8.
26. Claessens TE, Georgakopoulos D, Afanasyeva M, et al. (2006) Nonlinear isochrones in murine left ventricular pressure-volume loops: how well does the time-varying elastance concept hold? Am J Physiol Heart Circ Physiol. 290(4):H1474-83.
27. Nakata K, Akiyama K, Sankai Y et al. (2007) Estimation of cardiac function with rotary blood pump, Ann Thorac Cardiovasc Surg 13: 240–46
28. Wieselthaler GM, Schima H, Hiesmayr M, et al. (2000) First clinical experience with the DeBakey VAD continuous axial-flow pump for bridge to transplantation. Circulation. 101:356–9.
29. Naiyanetr P, Moscato F, Vollkron M, Zimpfer D, Wieselthaler G, Schima H. (2010) Continuous assessment of cardiac function during rotary blood pump support: A contractility index derived from pump flow. J Heart Lung Transplant. 29 (1): 37-44
30. Dandel M, Weng Y, Siniawski H, et al.(2008) Prediction of cardiac stability after weaning from left ventricular assist devices in patients with idiopathic dilated cardiomyopathy. Circulation. 118 (14 Suppl):S94-105.
31. George RS, Yacoub MH, Tasca G,et al.(2007) Hemodynamics and echocardiographic responses to acute interruption of left ventricular assist device support: relevance to assessment of myocardial recovery. J Heart Lung Transplant. 26(10):967-73.
32. Schima H, Vollkron M, Boehm H, et al. (2004) Weaning of rotary blood pump recipients after myocardial recovery: a computer study of changes in cardiac energetics. J Thorac Cardiovasc Surg. 127(6):1743-50.
33. O.H. Franzier and J.K. Kirklin. (2006) Mechanical Circulatory Support ISHLT Monograph Series 1; page 20

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