Arterial Compliance and Continuous-Flow Left Ventricular Assist Device Pump Function

Audrey Adji,*,†,‡,§ Sajad Shehab,† Pankaj Jain,* Desiree Robson,* Paul Jansz,*,†,‡,¶ and Christopher S. Hayward*,†,‡

Durable continuous-flow left ventricular assist devices (cfLVADs) demonstrate superior survival, cardiac functional status, and overall quality of life compared to medical therapy alone in advanced heart failure. Previous studies have not considered the impact arterial compliance may have on pump performance or developed arterial pressure. This study assessed the impact of alterations in arterial compliance, preload, and afterload on continuous-flow pump function and measured hemodynamics using an in-vitro pulsatile mock circulatory loop. Decreased arterial compliance was associated with a significant increase in arterial pressure pulsatility which was not evident in the flow pulsatility, as displayed in pump flow waveforms. There were marked changes in the pump flow waveforms due to the significant alteration in the aortoventricular gradient during diastole according to the changes in compliance. This study demonstrates that changes in systemic blood pressure, afterload, and left ventricular contractility each significantly affects the flow waveform. The association of hypertension with lower aortic compliance results in markedly decreased diastolic flow rates which may be important in contributing to a greater risk of adverse events under cfLVAD support. *ASAIO Journal* 2022; 68;925–931

Key Words: continuous flow, left ventricular assist device, arterial compliance, arterial pulsatility

The use of continuous-flow left ventricular assist devices (cfLVADs) in the treatment of advanced heart failure is well established.[1,2] Their success can the attributed to better patient selection, time of intervention, and technological advancements which has resulted in significant improvements in patient outcomes. According to the Eighth Annual Interagency Registry for Mechanical Assisted Circulatory Support report, patients receiving cfLVADs have a one- and two-year survival rate of 82% and 73%, respectively.[3] Although originally proposed as a bridge to cardiac transplantation (BTT), nearly three-quarters of cases are now implanted as the destination or long-term therapy (permanent implantation).[3] With the aging population resulting in a rise in the prevalence of heart failure, lack of donor hearts, and stringent eligibility criteria, the use of cfLVADs for long-term BTT and destination therapy is expected to increase.

Existing cfLVADs operate at pump speeds set by specialist clinicians according to the patient's activity level or medical condition and often remain constant despite changes to patients' circulatory demand. Overpumping has been associated with suction events, left ventricular (LV) collapse, right ventricular dysfunction, and hemolysis, whereas underpumping can result in persistent congestive symptoms, inadequate cardiac output, and thrombus formation.[4] Physiologic control algorithms have been suggested as a solution to reduce or even eliminate overpumping and underpumping events.[5–7] These ex-vivo control strategies are based on various mechanical and hemodynamic parameters, including pump flow, pump power, pump pressure head, mean aortic pressure, preload, afterload, heart rate, and LV pressure/contractility. There have not been any previous studies assessing the impact of varying arterial properties, such as compliance on pump performance and measured arterial pressure under cfLVAD support. The aim of this study was to assess the impact of arterial compliance, preload, and afterload on continuous flow pump function and measured hemodynamics using an in-vitro pulsatile mock circulatory loop (MCL).

Methods

Experimental Model

The pulsatile MCL using dual HeartWare Ventricular Assist Device (HeartWare Inc, Framingham, MA) has been previously described[8] (see Figure 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830). In brief, the pneumatic pulsatile MCL simulates various physiologic and pathologic conditions with and without mechanical support.[8] Pressure waveforms are recorded (Datex-Ohmeda, Inc. Madison, WI) for mean arterial pressure (MAP), left atrial pressure (LAP), right atrial pressure (RAP), and mean pulmonary artery pressure (MPAP), whereas LV pressure (LVP) is captured using a micro-transducer (Millar, Inc. Houston, TX) inserted within the LV cavity. Flow throughout the circuit is recorded using TS410 transit-time tubing flow meter (Transonic System, Inc. NY) positioned between the pulmonary compliance and the left atrial compliance chamber. Left and right pump flow data are

From the *Heart Failure and Transplant Unit, Cardiology Department, St Vincent's Hospital, Sydney, Australia; †Mechanical Circulatory Support Laboratory, Victor Chang Cardiac Research Institute, Sydney, Australia; ‡St Vincent's Clinical School, UNSW Medicine and Health, Sydney, Australia; §Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, Australia; and ¶School of Medicine, University of Notre Dame, Sydney, Australia

Submitted for consideration July 2021; accepted for publication in revised form April 2022.

Disclosure: C.H.: Medtronic - Speakers' Bureau, Consultancy to individual, Research grant to Hospital, Patent Holder (owned by hospital, Licenced by Medtronic). Other authors have no conflicts of interest to disclosure.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML and PDF versions of this article on the journal's Web site (www.asaiojournal.com).

Correspondence: Prof Christopher Hayward, Heart Failure and Transplant Unit, Cardiology Department, St Vincent's Hospital, Level 4, Xavier building, Darlinghurst NSW 2010, Australia. Email: cshayward@stvincents.com.au; Twitter: @Audrey_Adji.

DOI: 10.1097/MAT.0000000000001768

recorded directly from the pump controller at a 50 Hz sample rate using proprietary software.

In the current study, blood viscosity was replicated using a 40% glycerol solution at a constant temperature of 37°C to simulate a hematocrit (Hct) of 34%. The ventricular contraction was provided using a pneumatic SynCardia Companion 2 Driver with heart rate set at 80 beats per min, and minimum LV and right ventricular (RV) pneumatic pressures of 120 mmHg and 40 mmHg, respectively, as previously described.[8] Syncardia driver ejection duration was set at 280 msec for both left and right ventricles, and suction was set to 0 mmHg for all experiments. The aortic valve outflow was occluded to ensure complete emptying of the mock LV through the LVAD.

A constant RAP of 15 mmHg was selected for all experiments. Left atrial pressure varied from 5 to 20 mmHg in 5 mmHg increments. Mean pulmonary artery pressure and flows (flowmeter, LVAD, and right ventricular assist device [RVAD]) were not set with initial values and were dependent on baseline MAP, RAP, and LAP settings. Compliance was calculated using validated formula[9] (see Online Appendix, Supplemental Digital Content, http://links.lww.com/ASAIO/A830) and regulated by controlling the proportion of fluid and air in the aortic compliance chamber (Figure 1). A total of six different compliance levels were replicated throughout all experiments including maximum compliance (C1—fluid levels at the lowest storing capacity of the aortic chamber, maximum air), mid compliance (C2—fluid levels half full), and low compliance (C6—fluid levels at the maximum storing capacity, minimum air). To further assess the impact of compliance on waveform characteristics, three additional compliance levels were added between C2 and C6 in equidistant intervals. Finally, systemic vascular resistance (SVR) was regulated using tuning clamps and calculated using standardized hemodynamic calculations *e.g.* MAP-RAP ×79.9/cardiac output. Due to aortic valve occlusion, cardiac output equaled LVAD flow estimates.

Experimental Procedure

Three different experiments were performed: protocol 1 examined the effect of afterload variability on flow and pressure outcomes; protocol 2 examined the effect of differing arterial compliances; and protocol 3 assessed the impact of preload variability. A summary of the experimental methodology is outlined in Figure 2. The experiments began with a baseline setting of MAP80, LAP5, RAP15, LVAD pump speed of 2600RPM, RVAD speed of 2800 RPM, LVP of 120 mmHg, RVP of 40 mmHg, heart rate (HR) of 80, and maximal compliance (C1). Protocol 1 involved increasing MAP from 80 to 110 mmHg at increments of 10 mmHg by increasing SVR using tuning clamps downstream to the aortic compliance chamber. At each interval, hemodynamic measurements were recorded 2 minutes after a steady state was achieved. No other variables, such as pump speed, HR, LVP, RVP, HCT, and compliance were altered. After MAP of 110 mmHg was recorded, the SVR was reduced to restore baseline settings. Compliance was then reduced by increasing the fluid level in the aortic chamber from C1 to C2 (Protocol 2). Following the change to compliance, baseline hemodynamics were restored and Protocol 1 was repeated (MAP80 to 110 mmHg). Again, at the end of C2 (MAP110), compliance was decreased in the aortic chamber from C2 to C3. This shift between Protocol 1 and 2 was repeated until C6 (near full fluid in the chamber and low arterial compliance), at which point baseline hemodynamics and compliance levels were restored (from C6 to C1) and LAP was increased from 5 to 10 (Protocol 3). Using the new LAP10 as baseline (all other variables remained constant), protocols 1 and 2 were repeated. Upon completion, LAP was increased again from 10 to 15 mmHg and then from 15 to 20 mmHg. A baseline RA pressure of 15 mmHg was used to maintain MCL stability across the wide range of pressures, compliances and LVAD preloads.

Results

The outcomes of the experimental study have been summarized according to the experimental methodology used (Protocols 1–3).

The Effect of Varying Afterload (Protocol 1)

In protocol 1, afterload was regulated by controlling the level of SVR restriction. The greater the restriction, the higher

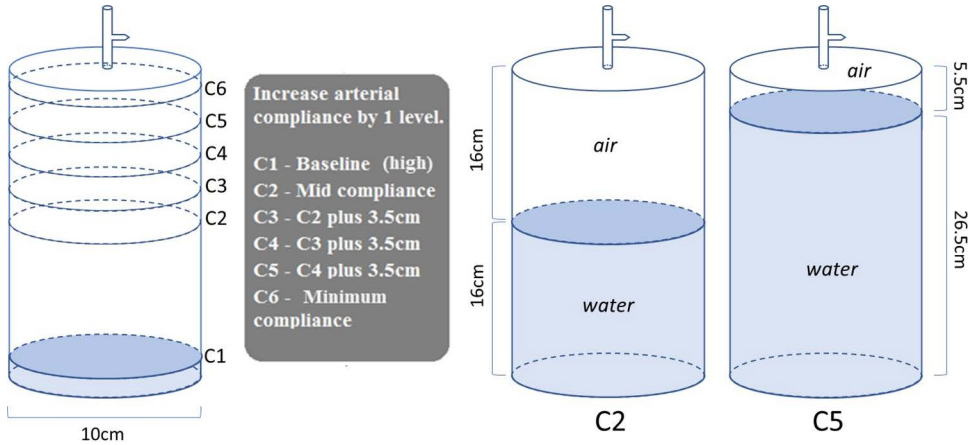

Figure 1. A total of six different compliance levels were replicated throughout all experiments including maximum compliance (C1—fluid levels at the lowest storing capacity of the aortic chamber, maximum air), mid compliance or high arterial compliance (High arterial compliance (HAC), C2—fluid levels half full), and low arterial compliance (Low arterial compliance (LAC), C6—fluid levels at the maximum storing capacity, minimum air). full color online

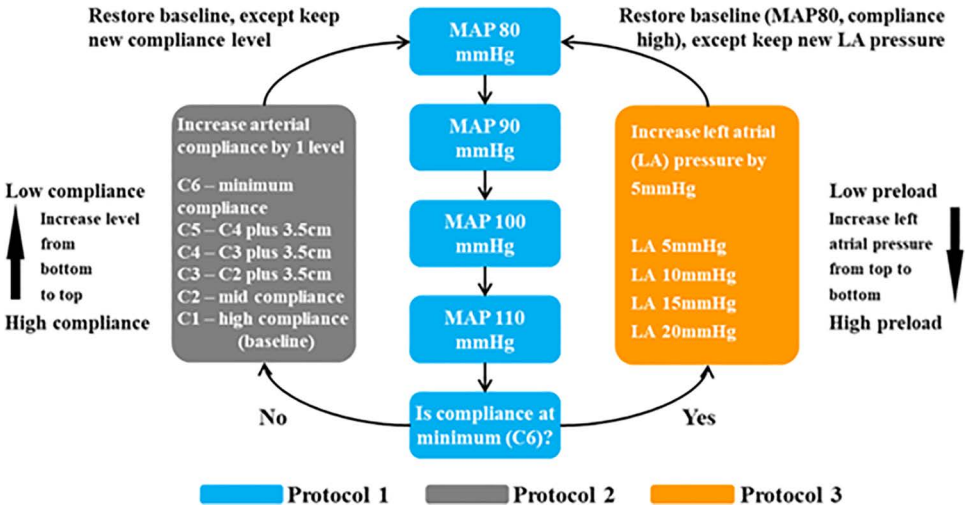

Figure 2. Experimental methodology. Baseline starting parameters include mean arterial pressure (MAP) 80 mmHg, high arterial compliance (LAC) (C6), left atrial pressure (LAP) 5 mmHg (unless changed during protocol 3). full color online

the afterload. As shown in **Figure 3A–D**, increasing SVR from MAP80 (solid line) to 110 mmHg (dotted line), which represented elevated systolic pressure, resulted in decreased LVAD flow (**Figure 4**, Table 1 and Table 2, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830). Although there was a slight elevation to maximum LVP pressure, the biggest change with increased SVR was the marked increase in the diastolic segment of the LVP pressure (See Figure 2, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830). This change in the LVP diastolic segment may be attributed to the rise in the LAP pressure during high SVR stages (Figure 3B,D). High LAP and LVP pressures may also be the cause of the change in morphology noted in the upslope of LVAD waveforms during diastole. Elevated MAP was associated with a decrease in mean flow (**Figure 4**), and was especially evident in the diastolic trough flow, regardless of filling pressures (**Figure 3A–3D**). Mean pump flows were only marginally greater with low arterial compliance for both the normal and hypertensive state (See Table 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830). With high preload (LAP 20 mmHg) the mean pump flows were marginally lower in both blood pressure states. The most significant difference is in the degree of flow pulsatility which is much higher in the high arterial compliance state for all blood pressures and preloads.

The Effect of Varying Compliance (Protocol 2)

In protocol 2, compliance was regulated by controlling the level of fluid/air in the aortic compliance chamber. **Figure 3** summarizes the impact of varying aortic compliance on pressure and flow waveform characteristics. When MAP was kept constant, a reduction in aortic compliance increases pressure pulsatility (**Figure 3B,D**). LVAD flow contour was altered with an increased slope of the diastolic segment. Mean LVAD flow fell as MAP increased (**Figure 4**), whereas the diastolic segment of the LVAD becomes shorter to the point that the upstroke of the cycle is initiated earlier as the tube became less compliant (**Figure 3B,D**). There was a trivial change in peak (maximum) flows whereas minimum (trough) flows were relatively unchanged (**Figure 4**), yet the flow pulsatility index decreased.

Impedance curves were derived from the ratio of pressure and flow harmonics, expressed as impedance modulus and phase. Characteristic impedance (Zc) was calculated from the average of the first five harmonics (See Table 2, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830). Examination of the compliance curves showed that impedance was significantly lower when compliance was higher, as expected (**Figure 5**). As seen by the pressure pulsatility generated by the least compliant state (C6, Table 2, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830), it is likely that the mock loop exceeds human arterial stiffness at that setting. Results are shown to demonstrate the extent of variation in parameters across the range of compliance (C2-C6).

The Impact of Preload Variability (Protocol 3)

Preload was manually assigned at the start of each experiment and was not manipulated once the experiment commenced. **Figure 3** summarizes the effect preload has on pressure and flow waveforms characteristics. Mean MAP values and pressure waveform morphology remained constant despite increased LAP. In contrast, peak LVAD flows slightly decreased whereas troughs appeared to slightly increase with increased LAP. The most notable change observed with LAP was the gradual rise in the diastolic flow waveform slope with increased pressure, as previously observed.[10,11] High LAP also resulted in an increase in the slope of the diastolic segment of LVP pressure (see Figure 2, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830). Increasing LAP has a trivial impact on MAP, however, it does produce a slightly reduced pulsatility and higher mean flow in LVAD flow parameters (**Figure 4**).

Discussion

Although durable cfLVADs have shown superiority to larger pulsatile pumps with enhanced durability, the risk of serious adverse events remains, including bleeding and stroke. Previous studies have shown to meet patients' cardiac output requirements; there are potential hemodynamic markers to

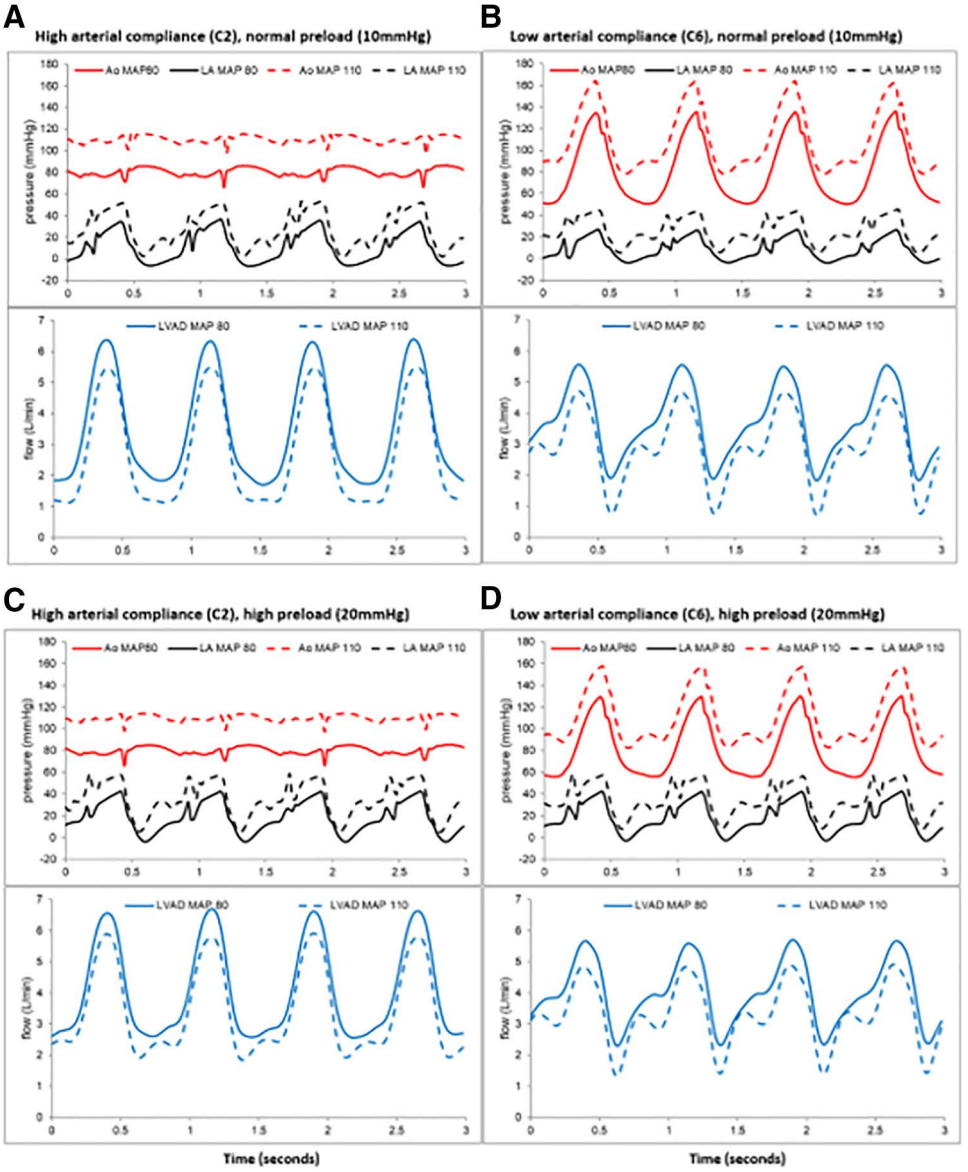

Figure 3. (**A**) High arterial compliance (HAC or C2)—normal preload (left atrial pressure [LAP10]), (**B**) Low arterial compliance (LAC or C6)—normal preload (LAP10). (**C**) HAC or C2—high preload (LAP20), (**D**) LAC or C6—high preload (LAP20). It can be seen that compliance markedly changes arterial pulsatility, with more marked changes in pump flow waveforms at the lower arterial compliance, largely independent of ventricular preload. Solid lines—mean arterial pressure (MAP) = 80 mmHg, dotted lines—MAP = 110 mmHg. full color online

adjust pump flow output. However, these markers generally measured under low pulsatile conditions without consideration of the effect of varying arterial compliance which may affect arterial pulsatility and pump performance. Our MCL study demonstrates for the first time that LVAD flow is significantly altered by changes in arterial compliance, independent of changes in either preload or afterload. Our study further highlighted the finding that arterial compliance is reduced in the setting of cfLVADs compared to pulsatile pumps,[12] and the fact that the LVAD population itself is aging, due to the higher rate of destination implants.[13,14] Furthermore, with improved LVAD outcomes, patients are expected to remain on mechanical support for increased periods of time. These factors may be expected to increase aortic stiffness,[15,16] as well as dilation and remodeling of proximal thoracic aorta,[17] due to continuous flow into the aortic root. In addition to these structural changes, it is recognized that most LVAD patients require multiple antihypertensive agents to control systemic blood pressure,[18] with elevated blood pressure itself also associated with significantly increased arterial stiffness.[19,20] This study is the first dedicated assessment of this physiologic trait in the era of continuous flow LVAD pumps.

Hypertension has been established as a long-term risk for cardiovascular disease, and likewise related to poor outcomes in cfLVAD patients.[21] A mean pressure of 90 mmHg or higher has been shown to be associated with a higher risk of stroke in this cohort,[18] and active mitigation of this has been shown to decrease rates of intracranial hemorrhage.[22] Loss of pulsatile flow may lead to endothelial dysfunction within the brain vessel wall, with loss of the protective blood-brain barrier and cerebral autoregulation.[23–25] Further, due to loss of pulsatility stretching the baroreceptors regulating blood pressure,

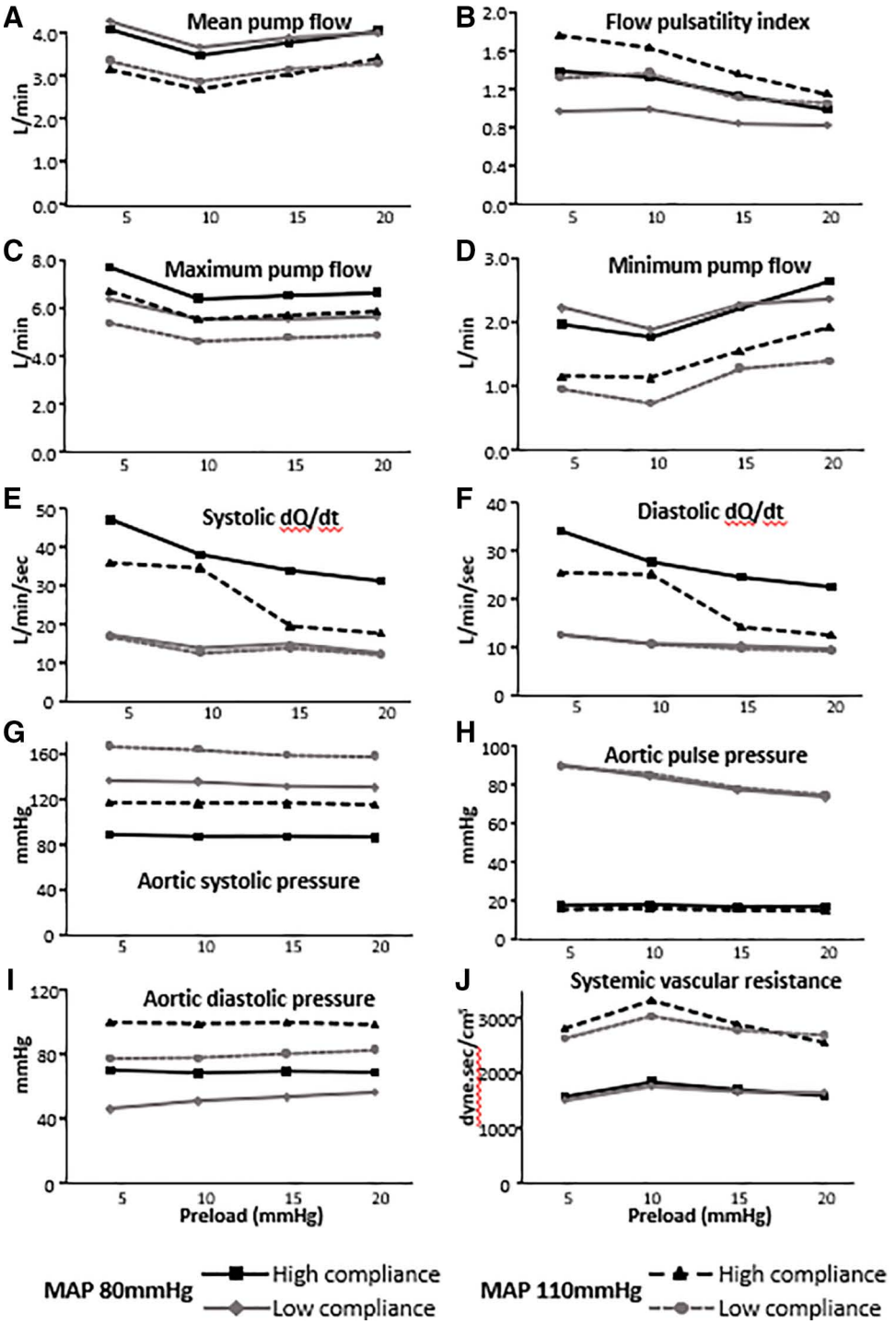

Figure 4. (**A–J**). Top panels (**A–F**) show changes in pump flow parameters (mean, maximum and minimum speed, flow pulsatility index, systolic and late diastolic dQ/dt), while lower panels (**G–J**) show changes in aortic pressure (systolic, pulse and diastolic), as well as systemic vascular resistance. It can be seen that higher mean arterial pressure (MAP) decreased pump flow (**A,C,D**), yet increased left atrial pressure (LAP) resulted in reduced flow pulsatility (**B**) and higher mean flow in left ventricular assist devices (LVAD) flow parameters (**A**). Higher arterial compliance results in a significant reduction in aortic pulse pressure (**H**) (pressure pulsatility), which is not seen as markedly in the flow pulsatility (**B**). Aortic systolic pressure is significantly affected by low compliance (**G**, gray lines), and diastolic pressure is more dependent on mean pressure (**I**, solid lines). Measures of flow upstroke (**E,F**) tend to be more dependent on compliance than pressure. High compliance = C2, low compliance = C6. X-axes denote increasing preload from 5 to 20 mmHg, with solid lines indicating MAP 80 mmHg (normal) and dashed lines indicating MAP 110 mmHg (hypertension). Error bars are omitted for clarity, and are reported in Table 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A830. full color online

elevated sympathetic nerve activity level has been postulated to drive blood pressure higher.[26] The interaction between increased arterial pressure pulsatility seen here in the setting of increased arterial stiffness and baroceptor function is not able to be examined in an MCL setting and remains an area for further investigation.

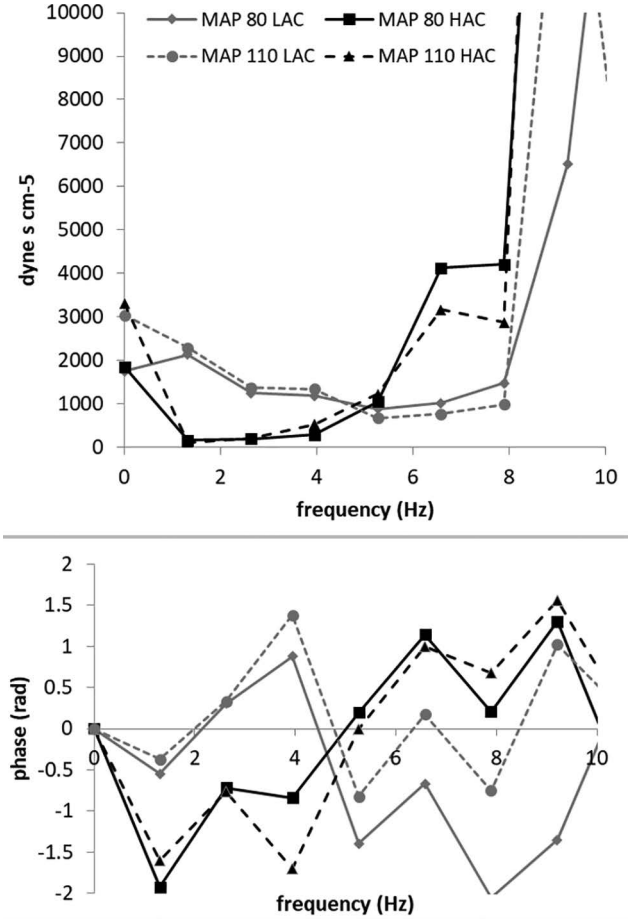

Figure 5. Impedance spectrum for normal preload (left atrial pressure 10 mmHg); HAC, high arterial compliance (C2 level), LAC, low arterial compliance (C6 level). The impedance spectra are much more affected by arterial compliance than by the mean arterial pressure. full color online

In our study, an increase in afterload through step increase in SVR (protocol 1) resulted in lower LVAD flow and higher flow pulsatility index. Elevation of blood pressure to a level of hypertension reduces pump flow, decreasing cardiac output, and resulting in less effective ventricular unloading. This can be seen as a reduction in peak flow, as well as a decrease in both minimum and mean flow, and an increase in LAP. Lower pump flow rates (particularly seen in the diastolic flow period) may increase the risk of thrombus formation and subsequent stroke. Elevated blood pressure has been shown to impact thromboembolic events,[27] and reduction in LVAD flow through increased afterload due to elevated blood pressure,[21,28] represents an important modifiable risk factor.

An important result from this study is the contribution of arterial compliance—*via* aortic pressure pulsatility and pump pressure head—on pump flow waveform morphology. It has been classically reported that the continuous flow results in low arterial pulsatility.[29] This assumption is implicit in algorithms that we and others have used in an attempt to derive LV preload from characteristics in the diastolic portion of the LVAD flow waveform.[10,11] Here we show that reduced arterial compliance has an even more marked impact on diastolic LVAD flow characteristics, independent of both afterload and, importantly, preload. Thus the relationship between preload and diastolic LVAD flow may be prone to significant variability depending on an individual patient's aortic compliance, which itself may change over time due to the effects of continuous flow on the vasculature. This finding may be significant in the creation of closed-loop control algorithms that may alter pump settings based on changes in the diastolic portion of the controller-estimated flow waveform in the future.

A further important result from the current study is the demonstration of marked pressure pulsatility—even in the setting of a closed aortic valve (as mandated in this experimental protocol) in the setting of low arterial compliance (stiff arteries). It may be expected therefore in clinical studies that the concept of lack of a palpable pulse will also be dependent on the intrinsic arterial stiffness for that individual. Although pressure pulsatility is markedly affected by changes in arterial compliance, LVAD flow pulsatility is much less so. This highlights the separation of pressure pulsatility from flow pulsatility, and no doubt contributes to the confusion within the literature over the true definition of pulsatility.[30]

Limitations

Limitations of the MCL include lack of interventricular interaction due to separate LV and RV pumping chambers. This separation is not likely to significantly impact the assessment of arterial on LVAD pump performance and is pragmatically used to ensure a stable mock circuit across the wide range of preloads, afterloads, and systemic arterial compliance. With respect to modeling of the arterial tree, the Windkessel chambers do not replicate arterial wave reflection in a pulsatile system. The impact of this is likely to be less significant than in the normal circulation as LVAD flow is continuous both in systole and diastole, rather than just during cardiac ejection, which occurs for a minority (~30%) of the cardiac cycle in the unsupported circulation. Finally, the lowest compliance (C6) setting is likely to be lower than an *in vivo* estimate of arterial compliance. Results between C2 and C6 are a continuum and the extremes are reported to demonstrate the maximum impact expected.

Conclusions

Changes in arterial compliance significantly affect cfLVAD pump performance independent of either preload or afterload in a mock circulatory loop. This needs to be considered in the management of an aging LVAD cohort and in the interpretation of waveforms in clinical practice and in the setting of future closed-loop control algorithms.

References

1. Gustafsson F, Rogers JG: Left ventricular assist device therapy in advanced heart failure: Patient selection and outcomes. *Eur J Heart Fail* 19: 595–602, 2017.
2. Schumer EM, Black MC, Monreal G, Slaughter MS: Left ventricular assist devices: Current controversies and future directions. *Eur Heart J* 37: 3434–3439, 2016.
3. Molina EJ, Shah P, Kiernan MS, *et al*: The Society of Thoracic Surgeons Intermacs 2020 annual report. *Ann Thorac Surg* 111: 778-792, 2021.
4. Tchantchaleishvili V, Luc JGY, Cohan CM, *et al*: Clinical implications of physiologic flow adjustment in continuous-flow left ventricular assist devices. *ASAIO J* 63: 241–250, 2017.
5. Asgari SS, Bonde P: Implantable physiologic controller for left ventricular assist devices with telemetry capability. *J Thorac Cardiovasc Surg* 147: 192–202, 2014.

6. Gohean JR, Larson ER, Longoria RG, Kurusz M, Smalling RW: Preload sensitivity with TORVAD counterpulse support prevents suction and overpumping. *Cardiovasc Eng Technol* 10: 520–530, 2019.
7. Mansouri M, Gregory SD, Salamonsen RF, *et al*: Preload-based Starling-like control of rotary blood pumps: An in-vitro evaluation. *PLoS One* 12: e0172393, 2017.
8. Shehab S, Allida SM, Davidson PM, *et al*: Right ventricular failure post LVAD implantation corrected with biventricular support: An in vitro model. *ASAIO J* 63: 41–47, 2017.
9. Liu Y, Allaire P, Wood H, Olsen D: Design and initial testing of a mock human circulatory loop for left ventricular assist device performance testing. *Artif Organs* 29: 341–345, 2005.
10. Grinstein J, Rodgers D, Kalantari S, *et al*: HVAD waveform analysis as a noninvasive marker of pulmonary capillary wedge pressure: a first step toward the development of a smart left ventricular assist device pump. *ASAIO J* 64: 10–15, 2018.
11. Lai JV, Muthiah K, Macdonald PS, Jansz P, Hayward CS: Estimation of left ventricular assist device pre-load using pump flow waveform analysis. *J Heart Lung Transplant* 36: 240–242, 2017.
12. Ambardekar AV, Hunter KS, Babu AN, Tuder RM, Dodson RB, Lindenfeld J: Changes in aortic wall structure, composition, and stiffness with continuous-flow left ventricular assist devices: A pilot study. *Circ Heart Fail* 8: 944–952, 2015.
13. Kirklin JK, Naftel DC, Pagani FD, *et al*: Seventh INTERMACS annual report: 15,000 patients and counting. *J Heart Lung Transplant* 34: 1495-1504, 2015.
14. Agrawal S, Garg L, Shah M, *et al*: Thirty-day readmissions after left ventricular assist device implantation in the United States: Insights from the Nationwide Readmissions Database. *Circ Heart Fail* 11: e004628, 2018.
15. Patel AC, Dodson RB, Cornwell WK 3rd, *et al*: Dynamic changes in aortic vascular stiffness in patients bridged to transplant with continuous-flow left ventricular assist devices. *JACC Heart Fail* 5: 449–459, 2017.
16. Rosenblum H, Pinsino A, Zuver A, *et al*: Increased aortic stiffness is associated with higher rates of stroke, gastrointestinal bleeding and pump thrombosis in patients with a continuous flow left ventricular assist device. *J Card Fail* 27: 696–699, 2021.
17. Fine NM, Park SJ, Stulak JM, *et al*: Proximal thoracic aorta dimensions after continuous-flow left ventricular assist device implantation: Longitudinal changes and relation to aortic valve insufficiency. *J Heart Lung Transplant* 35: 423–432, 2016.
18. Teuteberg JJ, Slaughter MS, Rogers JG, *et al*; ADVANCE Trial Investigators: The HVAD left ventricular assist device: Risk factors for neurological events and risk mitigation strategies. *JACC Heart Fail* 3: 818–828, 2015.
19. Elmously A, de Biasi AR, Risucci DA, Worku B, Horn EM, Salemi A: Systemic blood pressure trends and antihypertensive utilization following continuous-flow left ventricular assist device implantation: An analysis of the interagency registry for mechanically assisted circulatory support. *J Thorac Dis* 10: 2866–2875, 2018.
20. Lampert BC, Eckert C, Weaver S, *et al*: Blood pressure control in continuous flow left ventricular assist devices: Efficacy and impact on adverse events. *Ann Thorac Surg* 97: 139–146, 2014.
21. Wasson LT, Yuzefpolskaya M, Wakabayashi M, *et al*: Hypertension: An unstudied potential risk factor for adverse outcomes during continuous flow ventricular assist device support. *Heart Fail Rev* 20: 317–322, 2015.
22. Milano CA, Rogers JG, Tatooles AJ, *et al*; ENDURANCE Investigators: HVAD: The ENDURANCE supplemental trial. *JACC Heart Fail* 6: 792–802, 2018.
23. Willey JZ, Gavalas MV, Trinh PN, *et al*: Outcomes after stroke complicating left ventricular assist device. *J Heart Lung Transplant* 35: 1003–1009, 2016.
24. Cornwell WK 3rd, Ambardekar AV, Tran T, *et al*: Stroke incidence and impact of continuous-flow left ventricular assist devices on cerebrovascular physiology. *Stroke* 50: 542–548, 2019.
25. Cornwell WK 3rd, Tarumi T, Aengevaeren VL, *et al*: Effect of pulsatile and nonpulsatile flow on cerebral perfusion in patients with left ventricular assist devices. *J Heart Lung Transplant* 33: 1295–1303, 2014.
26. Markham DW, Fu Q, Palmer MD, *et al*: Sympathetic neural and hemodynamic responses to upright tilt in patients with pulsatile and nonpulsatile left ventricular assist devices. *Circ Heart Fail* 6: 293-299, 2013.
27. Saeed O, Jermyn R, Kargoli F, *et al*: Blood pressure and adverse events during continuous flow left ventricular assist device support. *Circ Heart Fail* 8: 551–556, 2015.
28. Najjar SS, Slaughter MS, Pagani FD, *et al*; HVAD Bridge to Transplant ADVANCE Trial Investigators: An analysis of pump thrombus events in patients in the HeartWare ADVANCE bridge to transplant and continued access protocol trial. *J Heart Lung Transplant* 33: 23–34, 2014.
29. Moazami N, Fukamachi K, Kobayashi M, *et al*: Axial and centrifugal continuous-flow rotary pumps: A translation from pump mechanics to clinical practice. *J Heart Lung Transplant* 32: 1–11, 2013.
30. Emmanuel S, Jansz P, Hayward C: How well do we understand pulsatility in the context of modern ventricular assist devices? *Int J Artif Organs* 44: 923-929, 2021.