Effects of Acute Pump Speed Changes on Cerebral Hemodynamics in Patients With an Implantable Continuous-Flow Left Ventricular Assist Devices

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Summary

Mechanical circulatory support (MCS) with an implantable left ventricular assist device (LVAD) is an established therapeutic option for advanced heart failure. Most of the currently used LVADs generate a continuous stream of blood that decreases arterial pulse pressure. This study investigated whether a change of the pulse pressure during different pump speed settings would affect cerebral autoregulation and thereby affect cerebral blood flow (CBF). The study included 21 haemodynamically stable outpatients with a continuous-flow LVAD (HeartMate II, Abbott, USA) implanted a median of 6 months before the study (interquartile range 3 to 14 months). Arterial blood pressure (measured by finger plethysmography) was recorded simultaneously with CBF (measured by transcranial Doppler ultrasound) during baseline pump speed (8900 rpm [IQR 8800; 9200]) and during minimum and maximum tolerated pump speeds (8000 rpm [IQR 8000; 8200] and 9800 rpm [IQR 9800; 10 000]). An increase in LVAD pump speed by 800 rpm [IQR 800; 1000] from the baseline lead to a significant decrease in arterial pulse pressure and cerebral blood flow pulsatility (relative change −24 % and −32 %, both $p < 0.01$), but it did not affect mean arterial pressure and mean CBF velocity (relative change 1 % and −1.7 %, p=0.1 and 0.7). In stable patients with a continuous-flow LVAD, changes of pump speed settings within a clinically used range did not impair static cerebral autoregulation and cerebral blood flow.

Key words

LVAD • Continuous flow • Plethysmography • Cerebral autoregulation

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Introduction

Heart failure is one of the major causes of morbidity and mortality, with an increasing prevalence of 1–2 %, burdened by an unfavorable 5-year mortality of 45–60 % (Pirk *et al.* 2019). Available therapeutic options for refractory heart failure are heart transplantation or mechanical circulatory support (MCS) implantation. MCSs have been broadly adopted as a treatment based on excellent survival rates and reasonable rates of adverse events, both of which are linked to the rapid evolution of these devices in recent years. Almost 95 % of todays'

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long-term MCS systems generate non-pulsatile, i.e., continuous flow (Kirklin *et al.* 2017), challenging the physiological paradigm of pulsatility being indispensable for proper end-organ function, including cerebral autoregulation.

Cerebral autoregulation is a crucial mechanism for managing the delivery of oxygenated blood to the brain in response to blood pressure variations. This complex regulatory mechanism consists of the following determinants of cerebral blood flow (CBF): (a) metabolic autoregulation, which is sensitive to changes in arterial PO2 and PCO2, (b) myogenic autoregulation, which alters arterial diameter, i.e., changes vascular resistance in response to blood pressure changes, (c) matches local blood flow to localized metabolic needs, and (d) facilitates the need to extract large amounts of the available oxygen (Kittnar *et al.* 2011, Willie *et al.* 2011).

Changes in cerebral circulation can occur perioperatively during left ventricular assist device (LVAD) implantation (e.g., ischemia or subsequent microembolisation) or shortly after LVAD implantation (e.g., cerebral hyperperfusion syndrome after long periods of tissue hypoperfusion). Later on, changes in cerebral circulation can be caused by disruption of the baroreflex or the failure of cerebrovascular regulatory mechanisms (Cornwell *et al.* 2015).

The arterial pulse pressure is thought to be an important determinant of cerebral autoregulation. The rate of pulsatility in continuous-flow left ventricular assist devices (CF-LVAD) closely correlates with pump speed settings, i.e., the higher the pump speed, the lower the observed pulsatility. Nevertheless, there is still a residual, although non-physiological, pulse pressure regardless of flow rate (Cornwell *et al.* 2015). Published data suggest that CF-LVAD patients are exposed to low-oscillatory blood flows, which negatively affects physiological hemodynamics. Thus, indicating that a modest increase in arterial pulsatility to preserve cerebral autoregulation, i.e., to maintain normal brain physiology, may be beneficial (Stöhr *et al.* 2019).

Therefore, our study aimed to investigate the effect of different LVAD pump speed settings on cerebral perfusion, especially high-speed settings, which are characterized by the greatest suppression of pulsatility.

Methods

The study was approved by the Institutional Ethics Committee, and all patients signed informed consent. The study population comprised 21 haemodynamically stable outpatients with an implanted continuous-flow LVAD (HeartMate II, Abbott, USA). All patients had international normalized ratios (INR) within the therapeutic range (1.8–3.0) maintained by warfarin.

The experiment was performed with patients in a supine position, in a quiet, darkened room, after a resting period of at least 10 minutes. Arterial blood pressure was measured continuously using finger plethysmography (Finometer™, Finapres Medical Systems, Amsterdam, The Netherlands). Cerebral blood flow in both middle cerebral arteries was measured

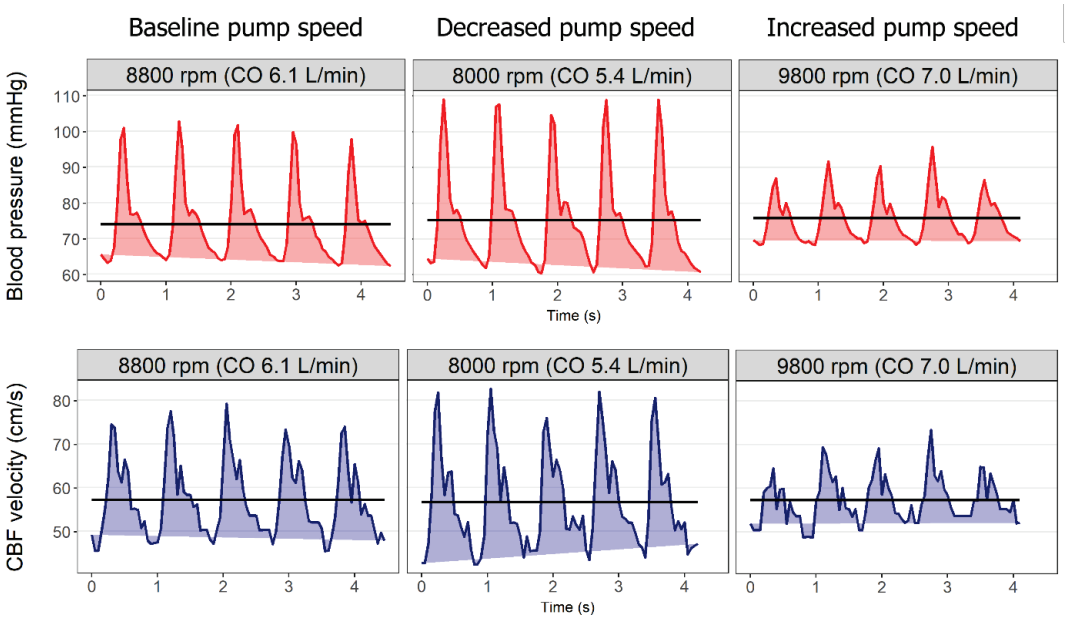

Fig. 1. An example of hemodynamic data measured during different pump speed. CBF=cerebral blood flow; CO=pump flow.

continuously using transcranial Doppler ultrasound fixed to the temples (Rimed Rigi-Lite ™ version 16, Rimed Ltd., Ra'anana, Israel). All signals were simultaneously recorded at 1 kHz by a data acquisition system (PowerLab 16/35, ADInstruments, Sydney, Australia). The first recording was obtained at the default pump speed (i.e., baseline; 8900 rpm [IQR 8800; 9200]). A second recording was obtained for pump speeds that were decreased by −800 rpm [IQR 800; 1000] from baseline (MIN; 8000 rpm [IQR 8000; 8200]), all while taking into consideration the patient's hemodynamic tolerance. A third recording was obtained for pump speeds increased by 800 rpm [IQR 800; 1000] above baseline (MAX; 9800 rpm [IQR 9800; 10 000]) while avoiding suction of the emptied left ventricle by the LVAD inflow cannula. Each recording was 2 minutes long. Each recording was preceded by a 2-minute stabilisation period. An example of the recorded blood pressure and CBF signals at different pump speed settings is shown in Figure 1.

The recorded signals were processed offline using a dedicated software package (LabChart 7, ADInstruments). Analyzed parameters included beat-by-beat mean arterial pressure (MAP), arterial pulse pressure, mean CBF velocity, CBF pulsatility (maximum–minimum CBF velocity), and heart rate. MAP and CBF were obtained from the electronic mean of the signal curves. Pump flow, expressed in l/min, was estimated by the LVAD control console (software algorithm based on actual electrical power consumption and pump speed). For each 2-minute segment, the beat-by-beat values were averaged to a single value. Values of CBF and CBF pulsatility from both cerebral arteries were averaged.

Statistical analyses were performed in R 3.4 (R-project.org, Vienna, Austria). Continuous normally distributed variables are expressed as mean ± standard deviation, non-normally distributed variables as median and interquartile range. The significance of hemodynamic changes for the three pump speed settings was analyzed using one-way ANOVA. Comparisons of hemodynamic parameters between any two different pump speed settings were analyzed using a paired t-test. Group comparisons were performed using the Student's t-test, chi-square test, and the Fisher's test, as appropriate. Correlations among continuous variables were analyzed using Pearson's test. A p-value < 0.05 was considered statistically significant. A non-significant change of mean CBF velocity after a significant change of the pump flow was considered a sign of preserved static cerebral autoregulation.

Results

The study protocol was completed in all 21 patients. The patients' clinical characteristics are summarised in Table 1; the measured hemodynamic parameters are summarised in Table 2. The average patient age was 47 ± 13 years, and 19 patients (91 %) were males. The median time on the LVAD support at the time of the study was 167 days [IQR 81; 411]. Although one-third of the patients had a history of atrial fibrillation, all of them were in sinus rhythm at the time of the study. Eight patients (38 %) had a previous history of a cerebrovascular accident (TIA, n=3; stroke, n=5). All patients were on chronic therapy with beta-blockers. At baseline, the pump speed was set to 8900 rpm [IQR 8800; 9200], which generated a pump flow of 4.1 ± 0.8 L/min (Table 2). A decrease in the pump speed from baseline by 800 rpm [IQR 800; 1000] led to a decrease in the pump flow by −15 % ([IQR −26; −15]; $p < 0.001$) and a decrease in MAP pressure by −3.4 % ([IQR −6.5; −1.2]; p=0.1).

Table 1. Baseline characteristics of the study population

Characteristic	21 (100)
Male gender	19 (91)
Mean Age (years)	47 ± 13
Ischemic cardiomyopathy	8 (38)
Non-ischemic cardiomyopathy	13 (62)
Duration of heart failure, days	599 [393; 2049]
History of atrial fibrillation	7 (33)
Transient ischemic attack or stroke	8 (38)
Stroke	5 (24)
Transient ischemic attack	3 (14)
Stenosis of carotid artery >70 %	0 (0 %)
Arterial hypertension	5 (24)
Diabetes mellitus	4 (19)
Smoking history	13 (62)
LVAD as a bridge to transplantation	20 (95)
LVAD as a destination therapy	1 (5)
Time on LVAD, days	167 [81; 411]
Beta-blockers	21 (100)
ACEI/ARB	17 (81)

The values are mean ± standard deviation, median [inter-quartile range] and frequency (percentage). ACEI/ARB=angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; LVAD=left ventricular assist device.

Table 2. Hemodynamics at the different pump speed settings

Variable	Baseline setting	Min (decreased pump speed)	Max (increased pump speed)	P-value		
				Baseline vs. Min	Max vs. baseline	Max vs. Min
Pump speed, revolutions/min	8929 ± 222	8048 ± 108	9819 ± 244	<0.001	<0.001	<0.001
Pump flow, l/min	5.1 ± 0.8	4.1 ± 0.8	6.0 ± 0.9	<0.001	<0.001	<0.001
Heart rate, beats/min	76 ± 15	78 ± 15	76 ± 16	0.3	0.2	0.5
Mean arterial pressure, mmHg	98 ± 15	94 ± 15	99 ± 16	<0.001	0.1	<0.001
Arterial pulse pressure, mmHg	18 ± 80	22 ± 10	13 ± 60	<0.001	<0.001	<0.001
Mean CBF, cm/s	71 ± 16	67 ± 16	74 ± 18	<0.01	0.7	<0.001
CBF pulsatility, cm/s	23 ± 11	32 ± 15	18 ± 9	<0.001	<0.001	<0.001

The p-values were obtained by paired t-test. CBF=cerebral blood flow

Table 3. Hemodynamics according to the history of a previous cerebrovascular accident

	No history of CVA (n=13)	History of CVA* (n=8)	P-value
Baseline pump speed (8900 rpm [IQR 8800; 9200])			
Heart rate, beats/min	82 ± 16	73 ± 13	0.2
Pump flow, l/min	5.1 ± 0.7	5.2 ± 0.9	0.8
Mean arterial pressure, mmHg	99 ± 18	95 ± 16	0.6
Arterial pulse pressure, mmHg	16 ± 9	21 ± 6	0.2
Mean CBF, cm/s	60 ± 10	69 ± 22	0.3
CBF pulsatility, cm/s	22 ± 10	27 ± 13	0.4
Minimal pump speed (8000 rpm [IQR 8000; 8200])			
Heart rate, beats/min	83 ± 16	72 ± 12	0.1
Pump flow, l/min	4.0 ± 0.9	4.3 ± 0.6	0.5
Mean arterial pressure, mmHg	96 ± 17	90 ± 14	0.4
Arterial pulse pressure, mmHg	21 ± 12	26 ± 5	0.2
Mean CBF, cm/s	57 ± 8	66 ± 20	0.3
CBF pulsatility, cm/s	30 ± 13	35 ± 15	0.5
Maximal pump speed (9800 rpm [IQR 9800; 10 000])			
Heart rate, beats/min	80 ± 17	70 ± 12	0.1
Pump flow, l/min	6.0 ± 0.9	5.9 ± 1.1	0.8
Mean arterial pressure, mmHg	101 ± 18	97 ± 16	0.7
Arterial pulse pressure, mmHg	11 ± 5	14 ± 4	0.09
Mean CBF, cm/s	62 ± 10	68 ± 20	0.5
CBF pulsatility, cm/s	14 ± 5	20 ± 12	0.2

CBF=cerebral blood flow; CVA=cerebrovascular accident; The table shows no significant differences in the systemic hemodynamics and cerebral blood flow in patients with a history of CVA (transient ischemic attack, n=3; stroke, n=5) compared to the rest of the study population.

As a result of the greater contribution of the native left ventricular contractions, the pump flow decrease was accompanied by a significant increase in arterial pulse pressure by 19 % ([IQR 10; 40]; $p < 0.001$) and CBF pulsatility by 31 % ([IQR 21; 50]; $p < 0.001$) (Table 2).

However, the decrease in MAP led to systemic

hypoperfusion with a decrease in the mean CBF velocity by −8 % ([IQR −11; −1.6]; p < 0.01) (Table 2).

An increase in pump speed by 800 rpm [IQR 800; 1000] above baseline caused an increase in pump flow by 15 % ([IQR 11; 22]; p < 0.001), a decrease in arterial pulse pressure by −24 % ([IQR −29; −13]; p < 0.001), and a decrease in CBF pulsatility by −18 % ([IQR –34; −6]; p < 0.001), but it did not affect the MAP or the mean CBF velocity (Table 2).

There was a strong correlation only between CBF pulsatility and pump flow and arterial pulse pressure but not between the mean CBF velocity and pump flow and arterial pulse pressure (Fig. 2).

Based on the analysis of variance, pump speed settings were only associated with changes in pump flow, arterial pulse pressure, and CBF pulsatility but were not associated with significant changes in HR, MAP, or mean CBF velocity (Fig. 3).

Discussion

This study investigated the acute effect of different LVAD pump speed settings on static cerebral autoregulation. An important finding was that even at the maximum tolerated pump speed, measurable arterial pulsatility, and CBF pulsatility remained. Additionally, the study found that CBF did not change significantly at the increased pump speeds. The latter finding suggests that within the clinically feasible range of pump speed settings, experimental changes in blood flow do not affect static cerebral autoregulation and CBF, despite significant changes in arterial pressure pulsatility.

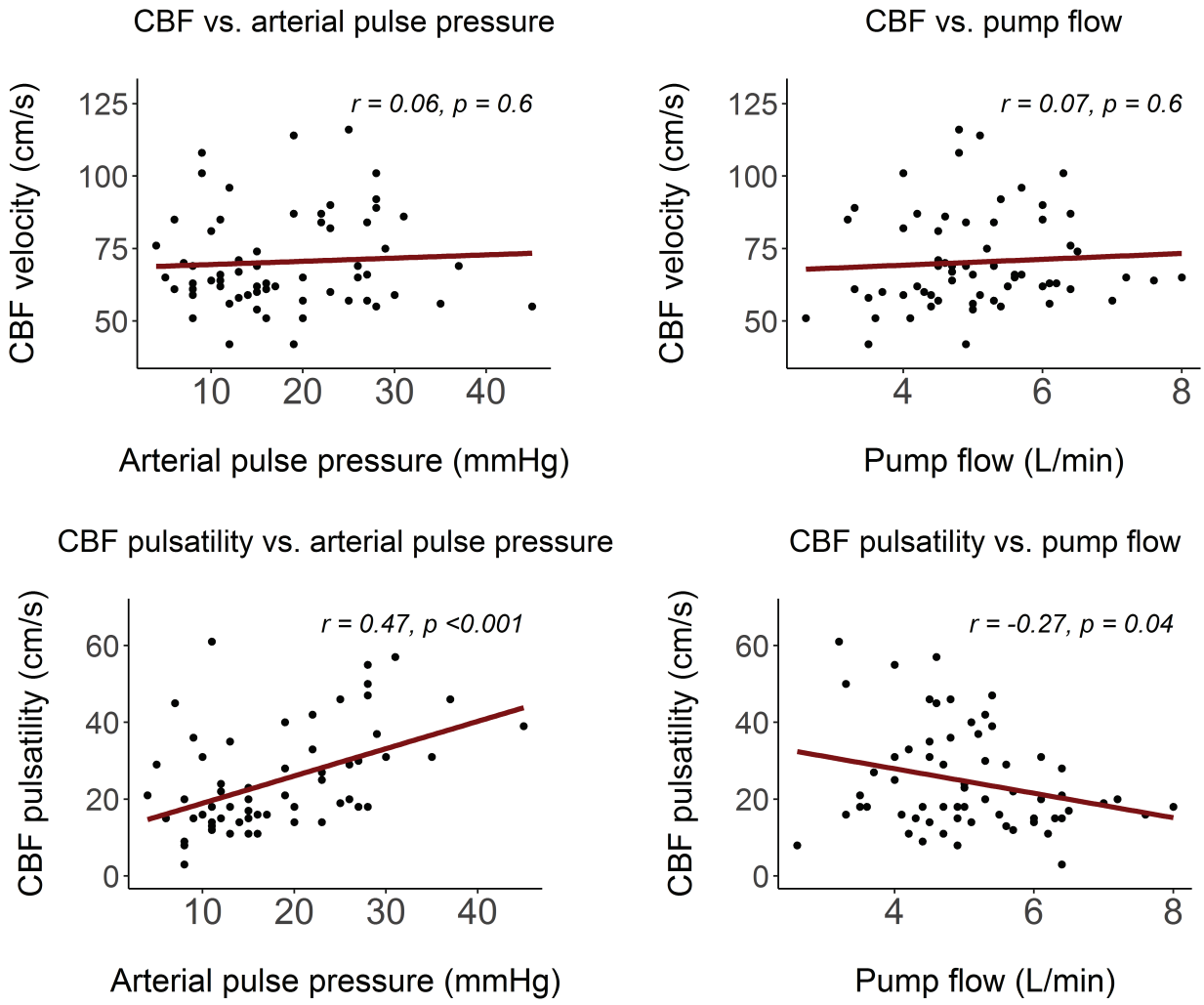

Fig. 2. Correlation between mean cerebral blood flow velocity and pulsatility relative to pump flow and arterial pulse pressure.
CBF=cerebral blood flow. The datapoints were pooled from all continuous-flow left ventricular assist device patients at the three different pump speeds (MIN=8000 rpm [IQR 8000; 8200]; baseline=8900 rpm [8800; 9200]; MAX=9800 rpm [9800; 10 000]). The graphs show constant mean cerebral blood flow velocity despite variable arterial pulse pressure and pump speed, pump flow respectively.

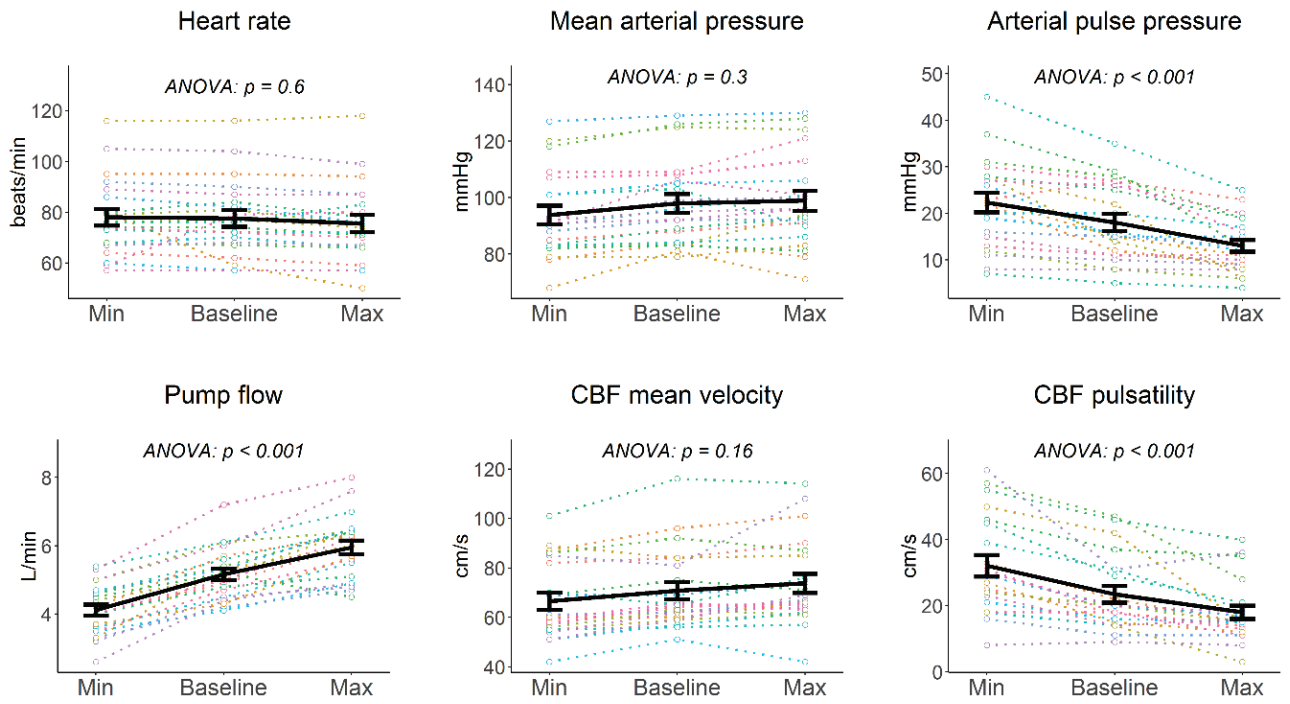

Fig. 3. Systemic Hemodynamics and cerebral blood flow at different pump speeds. CBF=cerebral blood flow. The graphs show the change in the hemodynamic parameters at different pump speeds. The colored dotted lines represent data from each patient. The thick black lines represent the average values with the standard error.

CF-LVADs represent the majority of long-term MCS implants in the current era (Kirklin *et al.* 2017). Although CF-LVADs have several advantages over pulsatile devices, controversy remains over the effects of CF-LVADs on end-organ function due to the reduction in pulsatility, particularly as it relates to cerebral perfusion and autoregulation (Ono *et al.* 2012). There are few published papers concerning cerebral autoregulation in CF-LVAD patients; however, unambiguous conclusions are missing. Katherine Lietz *et al.* described for the first time in 2009, the relationship between LVAD high speeds, i.e., high pump flow, and the increased occurrence of neurologic dysfunction in the early post-implant period. The reported prevalence reached 27 % of LVAD implanted patients in the first 30 days. In 87 % of affected patients, the neurologic deficit was transient and reversed after reducing LVAD flow. The authors of this article suggested that this was due to the sudden hyperperfusion, after LVAD implantation, of long-term hypoperfused cerebral tissue, which is typical with chronic heart failure. Cerebral autoregulatory mechanisms cannot adequately correct for a precipitous increase in cardiac output (Lietz *et al.* 2009).

Another study dealing with cerebrovascular dysregulation in LVAD patients was conducted by Judith Bellapart *et al.* However, a definite conclusion concerning the possible failure of cerebrovascular regulation was not reached even though the authors of the study were leaning towards some degree of dysregulation. The study's main limitations were the low number of study subjects (n=5) and the use of pulsatile devices (Bellapart *et al.* 2011). On the other hand, Masahiro Ono *et al.* reported preserved cerebrovascular regulation in a cohort of 15 patients implanted with CF-LVADs (Ono *et al.* 2012). However, the patients were only followed during the early post-implant period, which limits long-term conclusions. A recent study by Cornwell *et al.* investigated 14 LVAD patients (9 of whom had CF-LVADs) and compared them to ten healthy controls. The authors also assessed the dynamic part of cerebral autoregulation. They found that cerebral blood flow was comparable, suggesting that the reduction in pulsatility associated with CF-LVADs does not impair normal autoregulatory processes (Cornwell *et al.* 2014).

Impaired cerebral autoregulation goes hand in hand with adverse neurological outcomes (Bellapart *et al.* 2011, Bozkurt 2018, Caldas *et al.* 2018, Lietz *et al.* 2009, Pham *et al.* 2015). However, things other than malfunctions of the autoregulatory processes can be responsible for neurological deficits in CF-LVAD patients. There are several views on this topic, with most of them emphasizing, to some degree, the importance of

altered pulsatility. Impairment of microcirculation oxygen kinetics due to low pulsatile, diastolic-dominant Hemodynamics was postulated by Stöhr *et al.* (Stöhr *et al.* 2019). On the other hand, Cornwell *et al.* found adverse neurologic events to be a consequence of other LVAD-related complications, such as gastrointestinal bleeding, pump thrombosis, infection, and atrial fibrillation (Cornwell *et al.* 2019), which diminished the influence of lower pulse pressures.

Of note, eight patients (38 %) had a previous history of a cerebrovascular accident, but none of them had any apparent residual neurological symptoms at the time of the study. There was also no difference in the hemodynamics between the patients with previous cerebrovascular history and the rest of the patients (Table 3).

Since improvements in the morbidity and mortality of LVAD-implanted patients are always warranted, more studies on this topic need to be conducted. We focused on the possible effect of variable LVAD pump speed settings on neurological disturbances because of its potential to impair cerebral autoregulation. Our findings should be of great interest to clinicians since the optimization of LVAD pump speed settings is crucial for implanted patients. Adequate unloading of the failing ventricle accompanied by loss of native contractility results in a substantial loss of pulsatility in LVAD-implanted patients, potentially leading to cerebral autoregulation disturbances.

Optimal pump speed settings should lead to sufficient unloading of the ventricle and enable the intermittent opening of the aortic valve to prevent blood stasis and provide adequate cardiac output. Maintaining the patient's INR within the therapeutic range is a precondition for any change in pump speed. In our department, echocardiographic guidance is routinely used to optimize LVAD parameters so that patients are discharged in an optimized hemodynamic condition. The optimised LVAD settings described above represent the baseline condition of the patients in our study.

In our study, LVAD pump speeds were reduced to accentuate the residual contractility of the dysfunctional ventricle, thus increasing systolic-diastolic differences. Increasing the pulsatile element of blood pressure mimics physiological conditions, i.e., there is no cerebral autoregulation impairment, which is the expected finding. Conversely, increasing LVAD revolutions per minute (rpm) simulated total loss of pulsatility. This adjustment of LVAD settings led to a substantial increase in blood flow, while the mean arterial pressure and mean CBF velocity remained stable. In our opinion, the constancy of these particular parameters leads to the preservation of cerebral vascular resistance. In other words, stable mean CBF velocity maintains adequate tension variability in vascular smooth muscle cells in response to intraluminal pressure changes.

It is noteworthy that even at maximally tolerated pump speeds, the average pulse pressure was still around 13 mmHg. This phenomenon has been well-described in previously published papers and is often referred to as a non-physiological pulse (i.e., approx. 20 mmHg) (Cornwell *et al.* 2015). It results from the left ventricle ejecting blood through the LVAD pathway (Pagani 2008). It results from fluctuations in the intra-ventricular pressures during each cardiac cycle (Pham *et al.* 2015). Regardless of LVAD pump speeds, the permanent presence of residual pulsatility in CF-LVAD patients might be beneficial in the sense of a reduction in adverse events (Stöhr *et al.* 2019).

Our findings from a relatively large group of patients with continuous-flow LVAD suggest that static cerebral autoregulation is preserved when pulsatility is experimentally reduced. Additionally, LVAD pump speed optimization is a routine and safe procedure performed during the post-implant period and is not associated with neurological disturbances.

Limitations

Due to safety considerations, the study evaluated only the static component of cerebral autoregulation. Evaluation of dynamic autoregulation would require periodic manipulation of blood pressure using manoeuvres such as synchronized deep breathing. However, sudden changes in blood pressure in LVAD patients often lead to suction events with an increased risk of ventricular arrhythmias. Furthermore, it should be highlighted that the study evaluated only acute hemodynamic changes in otherwise stable LVAD patients. Long-term manipulation via pump speed settings would impose an unacceptable risk of hemodynamic decompensation or symptomatic suction events. The majority of patients were young males with non-ischemic etiologies of chronic heart failure and more likely to have intact reflexes such as cerebral autoregulation than elderly patients or patients with ischemic chronic heart failure. This study primarily reflects male physiology since women were only 9 % of the cohort. A major part of the patients in our study cohort were using

beta-blockers, angiotensin-converting enzyme inhibitors, or angiotensin-receptor blocker antagonists at the time of the study. The possible influence of these medications on study results cannot be ruled out.

Conflict of Interest

There is no conflict of interest.

References

BELLAPART J, CHAN GC, TZENG YC, AINSLIE P, BARNETT AG, DUNSTER KR, BOOTS R, FRASER JF: The effect of ventricular assist devices on cerebral autoregulation: a preliminary study. BMC Anesthesiol 11: 1-8, 2011. https://doi.org/10.1186/1471-2253-11-4

BOZKURT S: Effect of cerebral flow autoregulation function on cerebral flow rate under continuous flow left ventricular assist device support. Artif Organs 42: 800-813, 2018. https://doi.org/10.1111/aor.13148

CALDAS JR, HAUNTON VJ, PANERAI RB, HAJJAR LA, ROBINSON TG: Cerebral autoregulation in cardiopulmonary bypass surgery: a systematic review. Interact Cardiovasc Thorac Surg 26: 494-503, 2018. https://doi.org/10.1093/icvts/ivx357

CORNWELL WK 3rd, TARUMI T, AENGEVAEREN VL, AYERS C, DIVANJI P, FU Q, PALMER D, DRAZNER MH, MEYER DM, BETHEA BT, HASTINGS JL, FUJIMOTO N, SHIBATA S, ZHANG R, MARKHAM DW, LEVINE BD: Effect of pulsatile and nonpulsatile flow on cerebral perfusion in patients with left ventricular assist devices. J Heart Lung Transplant 33: 1295-1303, 2014. https://doi.org/10.1016/j.healun.2014.08.013

CORNWELL WK 3rd, TARUMI T, STICKFORD A, LAWLEY J, ROBERTS M, PARKER R., FITZSIMMONS C, KIBE J, AYERS C, MARKHAM D, DRAZNER MH, FU Q, LEVINE BD: Restoration of pulsatile flow reduces flow sympathetic nerve activity among individuals with continuous-flow left ventricular assist devices. Circulation 132: 2316-2322, 2015. https://doi.org/10.1161/CIRCULATIONAHA.115.017647

CORNWELL WK 3rd, TARUMI T, LAWLEY J, AMBARDEKAR AV: Crosstalk opposing view: Blood flow pulsatility in left ventricular assist device patients is not essential to maintain normal blood physiology. J Physiol 597: 357-359, 2019. https://doi.org/10.1113/JP276730

KIRKLIN JK, PAGANI FD, KORMOS RL, STEVENSON LW, BLUME ED, MYERS SL, MILLER MA, BALDWIN JT, YOUNG JB, NAFTEL DC: Eight annual INTERMACS report: Special focus on framing the impact of adverse events. J Heart Lung Transplant 36: 1080-1086, 2017. https://doi.org/10.1016/j.healun.2017.07.005

KITTNAR O: Medical Physiology. LOMICEK J, Grada, Prague, 2011, pp 241-242.

LIETZ K, BROWN K, ALI SS, COLVIN-ADAMS M, BOYLE AJ, ANDERSON D, WEINBERG AD, MILLER LW, PARK S, JOHN R, LAZAR RM: The role of cerebral hyperperfusion in postoperative neurologic dysfunction after left ventricular assist device implantation for end-stage heart failure. J Thorac Cardiovascular Surg 137: 1012-1019, 2009. https://doi.org/10.1016/j.jtcvs.2008.11.034

ONO M, JOSHI B, BRADY K, EASLEY RB, KIBLER K, CONTE J, SHAH A, RUSSELL SD, HOGUE CW: Cerebral blood flow autoregulation is preserved after continuous-flow left ventricular assist device implantation. J Cardiothorac Vasc Anesth 26:1022-1028, 2012. https://doi.org/10.1053/j.jvca.2012.07.014

PAGANI FD: Continuous-flow rotary left ventricular assist devices with "3rd generation" design. Semin Thorac Cardiovasc Surg 20: 255-263, 2008. https://doi.org/10.1053/j.semtcvs.2008.08.002

PHAM P, BINDRA J, CHUAN A, JAEGER M., ANEMAN A: Are changes in cerebrovascular autoregulation following cardiac arrest associated with neurological outcome? Results of a pilot study. Resuscitation 96: 192-198, 2015. https://doi.org/10.1016/j.resuscitation.2015.08.007

PIRK J: Cardiac surgery (in Czech). SPICKOVA M, KRATOCHVILOVA I, PATKOVA V (Eds.), Maxdorf, Prague, 2019, pp 192-193.

STÖHR EJ, McDONNELL BJ, COLOMBO PC, WILLEY JZ: Crosstalk proposal: Blood flow pulsatility in left ventricular assist device patients is essential to maintain normal brain physiology. J Physiol 597: 353-356, 2019. https://doi.org/10.1113/JP276729

WILLIE CK, COLINO FL, BAILEY DM, TZENG YC, BINSTED G, JONES LW, HAYKOWSKY MJ, BELLAPART J, OGOH S, SMITH KJ, SMIRL JD, DAY TA, LUCAS SJ, ELLER LK, AINSLIE PN: Utility of transcranial doppler ultrasound for the integrative assessment of cerebrovascular function. J Neurosci Methods 196: 221-237, 2011. https://doi.org/10.1016/j.jneumeth.2011.01.011