Evaluation of the HeartWare ventricular assist device Lavare cycle in a particle image velocimetry model and in clinical practice

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Abstract

OBJECTIVES: Ventricular blood stasis is a concern for continuous flow mechanical support devices and might contribute to the formation of thromboembolic events. The HeartWare® Ventricular Assist System (HVAD®) is equipped with the Lavare™ cycle that is a periodic speed modulation feature designed to alter flow patterns within the left ventricle and reduce areas of potential blood stasis. Here, we report in vitro and clinical findings on the effects of the Lavare cycle.

METHODS: The effect of pump speed changes on the intraventricular flow field was examined with an in vitro particle image velocimetry model. The clinical impact of the Lavare cycle was evaluated through a retrospective review of the ReVOLVE study which includes 248 patients implanted with the HVAD following Conformité Européenne Mark in nine centres in Europe and Australia. Baseline characteristics, adverse event profiles and Kaplan–Meier survival estimates were stratified by patients using/not using the Lavare cycle.

RESULTS: Particle image velocimetry showed increased ventricular washout with an active Lavare cycle as measured by the fluid velocities and angular dispersion parameters. With the Lavare cycle on, there was also a 22% decrease in the stagnation index compared with when the Lavare cycle was off. In the ReVOLVE registry, patients with the Lavare cycle turned on (n = 215) were supported for 497 patient-years, whereas patients who did not use the speed modulation (n = 33) were supported for 39.3 patient-years. The Lavare cycle did not significantly affect patient survival as both groups had approximately an 80% survival after 1 year. Patients using the Lavare cycle had significantly fewer rates of stroke (0.06 vs 0.20 events per patient-year (EPPY), P = 0.0008), sepsis (0.03 vs 0.15 EPPY, P = 0.0003) and right heart failure (0.03 vs 0.18 EPPY, P < 0.0001) with no difference in the transplant or recovery rates among the two cohorts.

CONCLUSIONS: The Lavare cycle effectively generates ventricular washout and the adverse event profiles of ReVOLVE patients with the Lavare cycle on were better than those with the Lavare cycle off. Larger studies are warranted to verify the positive effect of the Lavare cycle and to optimize speed modulation settings, so additional clinically relevant improvements can be realized.

Keywords: Left ventricular assist device • Lavare cycle • Particle image velocimetry • HVAD

INTRODUCTION

End-stage heart failure patients often face repeated hospitalization and a severely reduced quality of life even with optimal medical management [1]. Despite the clear benefits of left ventricular assist devices (LVADs), mechanical circulatory support imposes changes to the natural circulatory flow and is associated with serious adverse events. In a healthy left ventricle, the blood moves in a vortex pattern to most efficiently enter and exit through the mitral and aortic valves, respectively [2, 3]. The implantation of a continuous flow LVAD alters the ventricular flow, 

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potentially creating areas of blood stasis that may develop into adverse events.

Recirculation of the blood can create a hypercoagulable state resulting in thrombosis or stroke [4-7]. The activation of blood coagulation can also lead to sepsis and right heart failure [8-10]. In Conformité Européenne (CE) Mark countries, the HeartWare® Ventricular Assist System (HVAD®, HeartWare Inc., Framingham, MA, USA) includes a Lavare™ cycle feature. This speed modulation feature is designed to promote ventricular mixing and minimize potential regions of blood stasis [11]. The HVAD System significantly improved patient’s quality of life and had a 1-year survival rate greater than 84% in the CE Mark trial [12]. The post-market European ReVOLVE experience was very similar and reported survival rates of 85, 79 and 73% after 1, 2 and 3 years, respectively [13].

Traditional methods of directly measuring intraventricular fluid flow and potential regions of blood stasis with contrast echocardiography or echocardiographic particle image velocimetry (PIV) are not possible with LVAD patients due to the metal components of the device [2, 3]. A previous study did investigate the flow patterns in a mock loop with the HeartMate II (Thoratec Corp., Pleasanton, CA, USA) and found a region of fluid stasis near the left ventricle outflow tract [14]. Here, an in vitro examination of the changes in intraventricular flows due to HVAD Pump speed modulation will be paired with a retrospective analysis of ReVOLVE registry patients to determine the effectiveness of the Lavare cycle on (LON) reducing blood stasis in the left ventricle in both laboratory and clinical settings.

![Figure 1](image_url)
METHODS

Particle image velocimetry set-up

To visualize the flow with PIV, the titanium inflow cannula was replaced with a transparent cannula of the same dimensions. The ventricle of a patient suffering from dilated cardiomyopathy was scanned with CT (Fig. 1A) and a simplified polyethylene reservoir was created based on the active contour segmentation of the CT data [15] (Fig. 1B and C). Although the left ventricle volume was determined by a single patient, the volume was within the range suggested for chamber quantification studies [16] and the simplified geometry provides more generalized information. The ventricular model and modified HVAD system were then connected to the mock circulation loop with a 40%/60% glycerol–water mixture as blood analogue fluid (Fig. 1C). The fluid was seeded with fluorescent particles [poly(methyl methacrylate)–Rhodamine B particles 1–20 µm, microparticles GmbH, Berlin, Germany] and the patterns were recorded and analysed with Dynamics Studio 3.20 (Dantec Measurement Technology A/S, Skovlunde, Denmark).

A custom user interface developed within a Simulink (R2012a, MathWorks Inc., Natick, MA, USA) and a dSPACE environment (DS1103 PPC Controller Board, dSPACE GmbH, Paderborn, Germany) was used for real-time control of the HVAD Pump as well as data acquisition of flow and pressure measurements. Pump speed settings were transferred to the pump using the HVAD System monitor cable and RS232-serial interface, whereas a parallel trigger signal was transferred to the PIV-timing box. The pressure at the outflow of the HVAD Pump was measured with disposable clinical pressure transducers (TruWave pressure transducer, Edwards Lifesciences LLC, Irvine, CA, USA) and a clinical pressure monitor (M1166A Model 68S, Hewlett Packard, Böblingen, DE, USA). Ventricular flows were measured by an ultrasonic flow probe and meters (H9XL and HT110R, Transonic Systems Inc., Ithaca, NY, USA). Velocity vectors were calculated using an adaptive correlation algorithm with an interrogation area size of 32 × 32 pixels and 50% overlap in horizontal and vertical direction. Peak, moving average and range validation methods were used to identify wrongly calculated vectors and vector masking was applied to filter vectors outside of the ventricle.

Quantitative assessment of flow fields with the Lavare cycle

The Lavare cycle consists in lowering the pump speed by 200 r.p.m. for 2 s, increasing it by 400 r.p.m. for 1 s and then lowering the

![Figure 2: Mean velocity and standard deviation of the velocity in the ventricle when the Lavare cycle is on (panels C, D) and off (panels A, B).](https://academic.oup.com/ejcts/article-abstract/50/5/839/2444540)
speed back to baseline. This speed modulation occurs every 60 s. To determine the changes in the ventricular flow patterns during the Lavare cycle, first a baseline setting of 2800 r.p.m. was input to the pump. This resulted in a flow rate of 3.5 l/min with a pressure in the mock aorta of 85 mmHg. After determining the ventricular flows for a constant speed, the Lavare cycle was activated and the resulting changes in flow patterns were visualized with the PIV. In addition to testing the Lavare cycle, step changes in the speed of ±100, ±200, ±300, ±400 and ±500 r.p.m. lasting for 2 s were also examined.

For the quantitative analysis of the flow field data, three sets of parameters were calculated with the LON or with the Lavare cycle off (LOFF). First, the local mean velocities in the ventricle over the whole measurement time of 4.5 s and their standard deviation due to the fluctuations at a constant speed, respectively, due to the Lavare cycle were determined (see appendix for equations). The local directions of these mean velocities and their angular dispersion for the same conditions were also quantified. The third calculated parameter included the local stagnation indices as well as an overall stagnation index as mean of the local indices which has been previously described by Wong et al. [14]. It should be noted that a high standard deviation of velocities or angles describes a large change of flow conditions during the cycle, whereas the angular dispersion ranges from 0 for high variability to 1 for stable conditions, and a high stagnation index indicates low washout of an area.

**Clinical assessment of Lavare cycle**

The study design of the ReVOLVE registry was previously described in full detail [13]. Briefly, 254 patients were implanted with the HVAD following CE Mark approval between February 2009 and March 2012 at seven centres in Europe and two from Australia. Patients were followed to device explant, heart transplantation or death. Six patients were lost to additional follow-up and all analyses are performed using a denominator of 248 patients [17]. The majority of participating sites utilize the Lavare cycle and 215 patients had the Lavare cycle active, whereas 33 patients did not use the Lavare cycle feature. Major adverse events were defined using Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) adverse event definitions [18].

![Figure 3: Mean vector angles and the standard deviation in vector angles in the ventricle when the Lavare cycle is on (panels C, D) and off (panels A, B).](https://academic.oup.com/ejcts/article-abstract/50/5/839/2444540)
Statistical analysis

Baseline clinical characteristics were reported as mean ± standard deviation for continuous variables and as number of events (percent) for binary variables. Comparisons between the groups with and without the Lavare cycle were made with a two-sample t-test for continuous variables and Fisher’s exact test for categorical variables. Survival estimates were generated using Kaplan–Meier methodology and between-group comparisons were made by the log-rank test. Adverse events are reported as number of patients, number of events and events per patient-year (EPPY) and the EPPY were compared by Poisson regression. All statistical analyses were performed with the SAS v. 9.2 software (SAS Institute, Cary, NC, USA).

RESULTS

Mock loop ventricular flow changes

The PIV testing showed that flow field parameters changed with the LON and LOFF. Representative figures are presented with colour-coded contour plots and the arrows provide emphasis on the mean velocities and directions. The mean velocities and standard deviations during LON and LOFF settings are shown in Fig. 2. The flow patterns are highly similar for both conditions, but the mean standard deviations are much higher when the Lavare cycle is on (LON: $\sigma_v = 0.027 \pm 0.019$ m/s versus LOFF: $\sigma_v = 0.015 \pm 0.007$ m/s). The larger standard deviations indicate there were more variations in the flow patterns not only in the inflow jet but also in other regions with lower velocities. The mean angles and angular deviations during LON and LOFF operation are presented in Fig. 3. The mean angular dispersion $r$ is higher with the LOFF ($r = 0.70 \pm 0.19$) versus LON ($r = 0.84 \pm 0.18$), indicating a more aligned and consistent orientation of flow during a constant pump speed setting. A large rotational vortex can also be seen in Fig. 3C and D as a result of the speed change from having the Lavare cycle activated. The stagnation index is a parameter used to identify regions with low washout and the fluid stagnation during LON and LOFF is presented in Fig. 4. The stagnation index is lowest in the main flow jet and increases in regions closer to the ventricle walls. With the Lavare cycle turned on, the stagnation index becomes lower (LON, $SI = 3.05 \pm 2.14$ s) with an $\approx 22\%$ improvement in ventricle washout compared with static conditions (LOFF, $SI = 3.92 \pm 4.98$ s).

The speed step change protocol showed pump flow is directly related to pump speed as expected. The ventricular flow patterns were also similar to what was seen during the Lavare cycle testing as changes in pump speed resulted in increased angular dispersion of the velocity vectors and a lower stagnation index indicating increased washout. These changes in ventricular flow patterns were more pronounced for greater step sizes in the speed. The velocity of the fluid at the inflow and cannula positions was also recorded during the speed step protocol. A large drop in speed (step sizes of 400 and 500 r.p.m.) resulted in a short period of time where there were zero or even reverse flows at the ventricular inflow and inflow cannula positions (Fig. 5).

ReVOLVE patients with and without the Lavare cycle

The 248 patients in the long-term ReVOLVE study had an average time on device of 789.9 days (range: 1–2108 days) with a total of 497.0 patient-years of support. The ReVOLVE patient population represented a bridge to transplant population; therefore, the time on support was highly variable. Baseline characteristics showed no significant differences between patients who had the Lavare cycle turned on ($n = 215$) and off ($n = 33$) (Table 1). Similarly, the survival of patients with and without the Lavare cycle was not significantly different (Fig. 6). The adverse event profiles were largely similar for both patient groups and
Figure 5: Velocity extracts at ventricle inflow and cannula positions show the potential for reversed flow for the larger 400 and 500 r.p.m. speed drops.

Table 1: Baseline characteristics of ReVOLVE patients with and without the Lavare cycle

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ReVOLVE (n = 248)</th>
<th>Lavare on (n = 215)</th>
<th>Lavare off (n = 33)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>187 (75.4%)</td>
<td>163 (75.8%)</td>
<td>24 (72.7%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Female</td>
<td>61 (24.6%)</td>
<td>52 (24.2%)</td>
<td>9 (27.3%)</td>
<td>0.67</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.1 ± 12.1</td>
<td>52.4 ± 12.1</td>
<td>50.2 ± 11.9</td>
<td>0.33</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.93 ± 0.23</td>
<td>1.95 ± 0.21</td>
<td>1.85 ± 0.29</td>
<td>0.08</td>
</tr>
<tr>
<td>Type of cardiomyopathy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic</td>
<td>161 (64.9%)</td>
<td>139 (64.7%)</td>
<td>22 (66.7%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Ischaemic</td>
<td>68 (27.4%)</td>
<td>59 (27.4%)</td>
<td>9 (27.3%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Hypertrophic</td>
<td>6 (2.4%)</td>
<td>4 (1.9%)</td>
<td>2 (6.1%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Familial</td>
<td>4 (1.6%)</td>
<td>4 (1.9%)</td>
<td>0 (0%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Valvular</td>
<td>2 (0.8%)</td>
<td>2 (0.9%)</td>
<td>0 (0%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>1 (0.4%)</td>
<td>1 (0.5%)</td>
<td>0 (0%)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Other</td>
<td>5 (2.0%)</td>
<td>5 (2.3%)</td>
<td>0 (0%)</td>
<td>&gt;0.99</td>
</tr>
</tbody>
</table>

*P-values compare patients with and without the Lavare cycle using a two-sample t-test for continuous variables and Fisher's exact test for categorical variables.
the rates of pump thrombus and pump exchange were not significantly different. However, there did appear to be potential benefits for utilizing the speed modulation feature as patients with the Lavare cycle enabled had significantly lower rates of stroke (P = 0.0008), sepsis (P = 0.0003) and right heart failure (P < 0.0001) (Table 2). The mortality and recovery rates of the two groups were similar. Of the LON patients, 29.3% died and 3.3% recovered, compared with 27.3% died and 3.0% recovered for the LOF patients. Transplant occurred in 33.0% of LON patients compared with 63.6% of LOF patients.

DISCUSSION

The laboratory PIV investigation of the Lavare cycle revealed changes in the fluid velocities, angular dispersion and stagnation index within the ventricle. With the Lavare cycle activated, there was a 22% decrease in the stagnation index compared with the LOF setting. This change is still below the 63% reduction that has been previously measured for a fully ejecting heart [14], but the decrease in fluid stagnation is still a significant improvement. Other measures of ventricular fluid movement included the standard deviation in fluid velocities as well as the degree of angular dispersion. A large rotational vortex is common for the ventricular fluid movement of non-LVAD patients [3], whereas patients with abnormal LV function have a diminished strength of vortex [2]. Although the results of the in vitro PIV set-up cannot be directly correlated to clinical results, the deviation in fluid velocity and mean angular dispersion indicate there was increased washout when the HVAD has the Lavare cycle activated.

With the mock loop PIV testing, the direct relationship between pump speed and flow concurs with previously published reports as expected [11]. Interestingly, there were short periods of zero or negative flows at the inflow and cannula when the drop in speed exceeded 400 r.p.m. It is possible that a large drop in speed or a longer duration of low pump speed could promote the opening of the aortic valve which is associated with reduced gastrointestinal (GI) bleeding in previous studies [19, 20]. Larger variations in the flow velocity or longer periods of lowered respectively increased speed could, of course, promote further increased washout of the left ventricle. Such improvements to the speed modulation protocol deserve consideration in future studies.

Despite multiple indications of increased washout with LON, there are clear differences between the simplified PIV ventricle model and a natural heart that limit extending these results to the clinical setting. However, the clinical complications that can result from having blood stasis in the ventricle are well documented. Blood stasis can create a concentration of activation factors, hypercoaguable state and thromboembolism [5, 21] and has been correlated with a higher ischaemic stroke risk [7]. Sepsis is another adverse event that may develop after the activation of blood coagulation due to stasis [8, 9] and right ventricular dysfunction is commonly associated with sepsis and septic shock [10]. The reduction of stasis has been reported to lower the risk of thrombus formation both in the heart and in the pump [4, 6]. Overall, there is a general consensus on the importance of reducing stasis for LVAD patients.

In the retrospective analysis of the ReVOLVE patients, those with LON had an excellent 85% 1-year survival which is comparable with the 80% 1-year survival for continuous flow LVADs [13, 17, 22]. The 1-year Kaplan–Meier survival estimates for LON and LOFF cohorts were not significantly different. Even in longer periods of support, patients continued to maintain such outcomes.

![Figure 6: Kaplan–Meier estimate of survival for patients with and without the Lavare cycle.](https://example.com/fig6)

### Table 2: Adverse events of ReVOLVE patients with and without the Lavare cycle

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Lavare on (n = 215) (PY = 497.0)</th>
<th>Lavare off (n = 33) (PY = 39.3)</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>bleeding</td>
<td>71 (33)</td>
<td>101</td>
<td>0.20</td>
</tr>
<tr>
<td>stroke</td>
<td>28 (13)</td>
<td>29</td>
<td>0.06</td>
</tr>
<tr>
<td>GI bleed</td>
<td>13 (6)</td>
<td>18</td>
<td>0.04</td>
</tr>
<tr>
<td>Driveline infection</td>
<td>37 (17)</td>
<td>41</td>
<td>0.08</td>
</tr>
<tr>
<td>Renal failure</td>
<td>11 (5)</td>
<td>11</td>
<td>0.02</td>
</tr>
<tr>
<td>Sepsis</td>
<td>16 (7)</td>
<td>16</td>
<td>0.03</td>
</tr>
<tr>
<td>Pump thrombus</td>
<td>28 (13)</td>
<td>35</td>
<td>0.07</td>
</tr>
<tr>
<td>Pump exchange</td>
<td>16 (7)</td>
<td>19</td>
<td>0.04</td>
</tr>
<tr>
<td>Respiratory</td>
<td>3 (1)</td>
<td>3</td>
<td>0.01</td>
</tr>
<tr>
<td>Right heart failure</td>
<td>16 (7)</td>
<td>16</td>
<td>0.03</td>
</tr>
</tbody>
</table>

PY: patient-years; EPPY: events per patient-year; GI: gastrointestinal.

<sup>a</sup>P-value is for the comparison of EPPY and calculated with Poisson regression and Fisher’s exact tests.
with a 79% survival after 2 years [13]. There was no significant difference in the rates of pump thrombus or GI bleeding for the ReVOLVE patients. However, the LON patients had a significantly lower rate of stroke, reduced occurrence of sepsis and less right heart failure. This might possibly be due to the improved ventricular washing that may limit sluggish areas and consequently lower the risk of adverse events related to coagulopathies and blood stasis. From this analysis, there was no difference in the outcomes of HVAD patients with the LON or LOFF, although having the Lavare cycle activated possibly could have played some role in the improved adverse event profiles.

**Limitations**

Although the PIV model was capable of quantifying several changes in the flow patterns with LON and LOF, the occurrence of those ventricular flows in the clinical patients is not shown in this study. The PIV model mock loop in this study could be improved by creating a more realistic ventricle model and using a pulsatil setting to investigate the interaction between heart pulse and Lavare cycle. While PIV was effective at determining changes in ventricular vortices, computational fluid dynamics could be incorporated to gain additional insights into secondary flow patterns in parts of the ventricle such as the apical region. One important limitation of the retrospective analysis of the ReVOLVE registry is that patients without the Lavare cycle had a mean follow-up of 1.2 years, whereas the follow-up for patients with the Lavare cycle enabled exceeded 2 years. As adverse events are more likely to occur within the first-year post VAD implantation [23], the event rates of the patients without the Lavare cycle enabled may be higher than expected. In addition, the group of patients not using the Lavare cycle is relatively small and most are from a single institution which chooses not to use the Lavare cycle and this could have imparted a site-specific bias.

**Conclusions**

The Lavare cycle effectively generates ventricular washout as determined by the PIV that showed increases in deviation in fluid velocities and angular dispersion and decrease in stagnation index. Improvements to the speed modulation settings could further allow for increased washout or potentially aortic valve opening. There was no impact on survival in those patients with the Lavare cycle enabled, as it was comparable with the survival rates in previously published reports. However, patients with the LON had better adverse event profiles, with significantly lower rates of stroke, sepsis and right heart failure. However, the small numbers of patients without the LON makes these comparisons thought-provoking at best, and larger studies are warranted to verify the clinical implications of the HVAD Lavare cycle as well as modifications to further optimize this speed modulation feature.

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**Conflict of interest:** Daniel Zimpfer, Martin Strueber, Jan D. Schmitto, Arnt E. Fiane, Steven Tsui, Paul Jansz and Stephan Schueler are consultants for HeartWare Inc. Andre Simon is a consultant for HeartWare Inc. and TransMedics Inc. Daniel Zimpfer received research grant support from Thoratec Corp. Jan D. Schmitto received research grant support from Thoratec Corp. Heinrich Schima received research support from HeartWare Inc.

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APPENDIX. CONFERENCE DISCUSSION

Dr G. Wieseltaler (San Francisco, CA, USA): Overall, I think it’s a very valuable study because it’s providing us some theoretical, as well as clinical data on the use of the Lavare cycle. Also as Dr Zimpfer pointed out, for whatever reason, the Lavare cycle is not available in the United States and I think it doesn’t make sense. But, nevertheless, I think this might even help the colleagues in the U.S. to advance in this field as well.

Overall, I think it’s an interesting finding. It gives the results that you obviously expected in a way, that you see the stroke rate with a better washout within the ventricle is getting lower, and this is something we expect and we actually want to have and want to see.

The question is at least to me by reading your manuscript and also listening to you right over here, can you allude a little bit on the impact of reducing the rate of sepsis and the rate of right heart failure, because I think it’s not quite clear how a better washout should impact on sepsis and on right heart failure.

Dr Zimpfer: Actually, I cannot give you a definite answer. What we did, this particular imaging only shows you flow in the ventricle. Also, as far as hypothesis generation is concerned, this only can explain why you would see a lower incidence of thromboembolic events. So what we did basically, cannot explain the lower incidence in right heart failure and also the lower incidence in infections. What has to be mentioned is that the patients without the Lavare cycle were from a limited number of centers, and that might reflect some bias of this study. But I cannot answer you how the Lavare cycle should reduce the incidence of right heart failure or sepsis.

Dr Wieseltaler: The second question is, as we heard, you can turn on and turn off the Lavare cycle. So, usually the company recommends that whenever you start implanting, you turn it off for the first couple of days, and then if the patient is hemodynamically stable, you turn it on.

So my question is do you have any idea when in your patient cohort the Lavare cycle was turned on? In addition to that, a concomitant question that comes along with that, when did the strokes that appeared in these patients occur? Is there any correlation between that? Did you look at that?

Dr Zimpfer: At our department, and you probably know that, because you are from the department, and you were the first one to implant this pump in Vienna, we always turn it on when we leave the operation room nowadays. We keep it turned on, and that’s basically the policy of the departments in Europe; that it simply is turned on. What I cannot tell you is if any strokes in the group that ultimately had the Lavare cycle turned on, occurred in the time frame between implanting the ventricular assist device and turning on the Lavare cycle.

Dr Wieseltaler: Overall, I think it’s very favorable to have this data, and hopefully the Food and Drug Administration is looking at this data appropriately, and we are going to have it in the United States as well, pretty soon.

Dr S. Klotz (Luebeck, Germany): Interesting study. What do you think the Lavare cycle is used for, for the pump, for washout and preventing thrombosis, or for the left ventricle to wash out and prevent thrombosis? Because in your study, there is a little bit more nonsignificant left ventricular assist device thrombosis in the patients with the Lavare cycle on.

Dr Zimpfer: So, I think it’s designed basically to protect the pump and also to create those flow changes in the ventricle. From the model we did, the particular velocity imaging can only give you hints as to what happens in the ventricle and there we could really show, that these disruptions of flow induced by speed changes of the pump lead to a washout of the apex and also the region around the inflow cannula. What happens in the pump cannot be clarified by that model.

Dr D. Saeed (Dusseldorf, Germany): I have two questions. The first one, regarding these two groups, I don’t know if I’ve missed it in your slides. Were these two groups comparable? I mean, is that the reason why we see more strokes in these patients in these patients they had more right heart failure, they had more sepsis, they were more sicker patients than this other group that they didn’t get these complications? Is that the reason? Are they comparable?

Dr Zimpfer: No, they are comparable, and that’s going to be part of the manuscript.

Dr Saeed: All right. And the second question is, did you look at the opening status of the aortic valve in this group of patients? Because, theoretically what we hypothesize is, if we keep the Lavare cycle on, and I’m big fan of Lavare cycle, then you will have intermittent opening of the aortic valve, and you may not have that status. That may end up in stroke at some point.

Dr Zimpfer: So at least in our experience, and we have a very dedicated echo guy nowadays, the Lavare cycle does not result in opening of the aortic valve. So you have patients with internal Lavare cycle with an aortic valve that stays closed throughout the entire cardiac cycle and throughout the entire support. What I cannot tell you, because it was not part of the design of the RevOLVE registry, is how many patients had aortic valve opening in this cohort. It was not prospectively assessed.

Appendix – Equations

Mean values and the standard deviation of variables were calculated according to the generalized Equation 1 and Equation 2.

\[
x = \frac{1}{n} \sum_{i=1}^{n} x_i \quad \text{Equation 1: General definition of the arithmetic Mean}
\]

\[
x \quad \text{Mean value of variable}
\]

\[
x_i \quad \text{Variable of interest}
\]

\[
n \quad \text{Number of elements}
\]

\[
i \quad \text{index}
\]

\[
\sigma_x = \sqrt{\frac{1}{n-1} \sum_{i=1}^{n} (x_i - \bar{x})^2} \quad \text{Equation 2: Standard Deviation}
\]

\[
\sigma \quad \text{Standard Deviation of parameter}
\]

The angle of the single flow vectors \( \theta \) was calculated according to Equation 3 out of the velocity components in \( x \) and \( y \) direction. To assign the angles to the correct quadrants the angle \( \theta \) was corrected to \( \theta_{\text{MOD}} \) according to the quadrants.

\[
\theta(x, y) = \tan^{-1}\left(\frac{\bar{v}_y}{\bar{v}_x}\right) \quad \text{Equation 3: Vector angle}
\]

\[
\theta_{\text{MOD}} = \begin{cases} 
\theta, & \text{for } \bar{v}_x > 0, \bar{v}_y > 0 \quad (\text{quadrant I}) \\
180 + \theta, & \text{for } \bar{v}_x < 0, \bar{v}_y > 0 \quad (\text{quadrant II + III}) \\
360 - \theta, & \text{for } \bar{v}_x > 0, \bar{v}_y < 0 \quad (\text{quadrant IV}) \\
\end{cases}
\]

\[
\text{Angle correction for quadrants}
\]

\( \bar{v}_x, \bar{v}_y \) Velocities in \( x \) and \( y \) direction

The fact that \( 0^\circ \) and \( 360^\circ \) are identical angles requires that the mean angle over time \( \theta \) cannot simply be the sum of the angles divided by the sample size, because the mean angle of \( 359^\circ \) and \( 1^\circ \) would be \( 180^\circ \) Therefore Equation 4 was used:

\[
\theta(x, y) = \tan^{-1}\left(\frac{\sum_{i=1}^{n} \sin \theta}{\sum_{i=1}^{n} \cos \theta}\right) \quad \text{Equation 4: Mean Vector direction}
\]

The angular dispersion \( r \) (see Equation 5) was calculated to get a parameter that is similar to the standard deviation but ranges from zero (largest possible variation) to one (no variation in direction).

\[
r(x, y) = \sqrt{\left(\frac{\sum_{i=1}^{n} \sin \theta}{n}\right)^2 + \left(\frac{\sum_{i=1}^{n} \cos \theta}{n}\right)^2} \quad \text{Equation 5: Angular dispersion}
\]

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A stagnation index as defined by [1] (see Equation 6) was used to identify areas of flow stagnation that might result in thrombus formation. The index has dimensions of time and is inversely proportional to the time averaged kinetic energy in each point. It can be used to compare situations with similar flow conditions. High values describe areas where low blood velocities are sustained for long time fluid stagnation is likely there.

\[
SI(x, y) = \sqrt{\frac{A_U \cdot T}{\int |v(x, y)|^2 \, dt}}
\]

Equation 6: Stagnation Index

- \(A_U\) Average area of the left ventricle
- \(T\) Period of interest
- \(v(x, y)\) velocity