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Evaluation of the Optimal Driving Mode During Left Ventricular Assist with Pulsatile Catheter Pump in Calves

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Abstract: The pulsatile catheter (PUCA) pump, a left ventricular assist device, was tested during acute experiments in calves using asynchronous and ECG-synchronous assist modes. The aim of the study is to compare ECG-synchronous and asynchronous assist and to find the optimal driving mode for the PUCA pump with respect to left ventricular myocardial oxygen consumption (LV MVO_2), pump flow, and coronary flow. LV MVO_2 decreased significantly during the asynchronous (from 7.77 to 6.46 ml/min/100 g) as well as during the ECG-synchronous mode (from 8.88 to 7.84 ml/min/100 g). The pump flow was highest during the ECG-synchronous assist (2.94 L/min), followed by the asynchronous assist (2.79 L/min). The peak coronary flow depended strongly on pump ejection timing and showed the best flow patterns during the ECG-synchronous assist. We concluded that for PUCA pump support both asynchronous and ECG-synchronous assists significantly reduce LV MVO_2 and that the pump flow generated is enough to maintain the systemic circulation. However, we find the ECG-synchronous mode preferable because this mode optimizes coronary flow patterns at the same time. **Key Words:** Left ventricular assist device—Catheter pump—Assist mode—Calf.

Left ventricular failure (LVF) is the most frequent cause of death in cardiac surgery (1). For patients with a severe heart condition, temporary cardiac assistance to overcome the stunning period of the myocardium presents the only chance of survival. Intraaortic balloon pumping (IABP) is the most commonly used cardiac assist procedure for temporary support of the acute failing left ventricle (2). Patients in severe cardiogenic shock, refractory to pharmacological support and IABP, are potential candidates for left ventricular assistance with a blood pump. When compared with continuous flow devices, such as the roller pump and the centrifugal pump, pulsatile left ventricular assist devices (LVAD) are more often used for long-term support (3). These can be used in an asynchronous full-to-empty or in an ECG synchronized mode. In the asynchronous mode, the device works independently of the cardiac cycle. In the synchronous mode, the LVAD is synchronized with the R-wave of the ECG to realize pump ejection during diastole, thus increasing diastolic aortic pressure and coronary perfusion pressure. Moreover, in the ECG-synchronous mode, the pump can be adjusted to eject during every first, second, or third cardiac cycle (respectively mode 1:1, 1:2, 1:3) with or without delay after the R-wave of the ECG.

Both asynchronous and synchronous modes have specific advantages and disadvantages. An LVAD working in an asynchronous mode works efficiently even during cardiac arrhythmia or fibrillation, but intermittently ejects blood during the cardiac systole, increasing the left ventricular afterload. An LVAD working in an ECG-synchronous mode increases coronary flow during diastole and has minimal effect on the afterload, but works properly only during absence of cardiac arrhythmias. The results reported in the literature about asynchronous and synchronous assist are inconsistent. Some authors report that synchronous left ventricular (LV) assist offers no advantage (3); others report that synchronous LV assist is

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the most effective method to maintain the systemic circulation and coronary blood flow (4). A third group recommended asynchronous assist during the first 12–48 h, followed by synchronous assist (5).

The pulsatile catheter (PUCA) pump is an intraventricular blood pump that can be used as an LVAD. The device consists of an extracorporeally placed pneumatically driven single-port membrane pump connected to a valved indwelling polyurethane catheter (6). The PUCA pump is ECG-triggered and aspirates blood from the left ventricle and ejects it into the ascending aorta during the diastolic phase (Fig. 1). Thus, the PUCA pump combines direct left ventricular unloading with counterpulsation, creating a pulsatile flow. In case of severe arrhythmia or ventricular fibrillation, the PUCA pump switches to an asynchronous mode. The aim of the present study is to compare ECG-synchronous and asynchronous assist and to find the optimal driving mode for the PUCA pump with respect to left ventricular myocardial oxygen consumption (LV MVO_2), pump flow, and coronary flow.

MATERIALS AND METHODS

All animal experiments were performed according to the rules of the Ethical Committee on Animal Research at the University of Groningen. Four clinically healthy calves with mean body weight 73 ± 10.7 kg were premedicated with 0.0044 mg/kg Robinul (Wyeth, Hoofddorp, Holland) i.m. Anesthesia was induced with 30 mg/kg Nesdonal (Rhône-Poulenc Rorer, Amstelveen, Holland) i.v. The animals were intubated and ventilated (Ohmeda 7000 Ventilator, Ohmeda, Madison, WI, U.S.A.) with oxygen, nitrogen dioxide, and Isoflurane (ABBOTT, Queenborough, Kent, U.K.). Perioperative analgesia was provided with 2–4 ml IV Finadyne (Schering-Plough, Brussels, Belgium). The left jugular vein was cannulated to administer drugs and fluids. Five needle-electrodes were positioned on the animal to monitor ECG as well as for PUCA-pump triggering during the ECG-synchronous driving modes. A left thoracotomy was performed in the fifth intercostal space and the pericardium was opened. Initial anticoagulation (2,500 IU/h Heparin IV, Leo, Weesp, Holland) was started immediately after the opening of the pericardium. Pressure catheters were inserted into the descending thoracic aorta and the left ventricle. A 20 gauge Hydrocath sample catheter (Hydrocath, Ohmeda, Madison, WI, U.S.A.) was positioned into the coronary sinus via the great cardiac vein to take blood samples for measuring oxygen content. A flow probe (Transonic Systems Inc., Ithaca, NY, U.S.A.) was placed around the pulmonary artery to monitor cardiac output; an additional flow probe (Transonic Systems Inc., Ithaca, NY, U.S.A.) was placed around the left common coronary artery (LCA). The left azygous vein, running over the proximal part of the descending thoracic aorta, was dissected and ligated. Under total heparinization (5,000 IU heparin/h), a 14 mm woven Dacron graft was sutured end-to-side to the descending thoracic aorta. The tip of the PUCA pump catheter was positioned into the left ventricle using a cardiac catheter both as a guide wire and for monitoring the pressure as described previously (7). The PUCA pump catheter (25 Fr, 40 cm length) was de-aired and connected to a 60 ml single-port membrane pump (Polymedica, Aachen, Germany). A flow probe (Transonic Systems Inc., Ithaca, NY, U.S.A.) was placed around the proximal part of the PUCA pump catheter to monitor the pump flow. After hemodynamic stabilization, the experimental protocol was started.

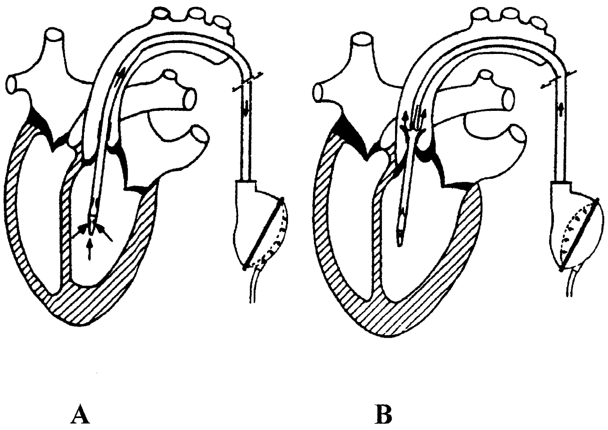

FIG. 1. The schema of the PUCA pump performance shows the PUCA pump during aspiration (**A**) and the PUCA pump during ejection (**B**).

The following parameters were monitored and recorded during the experiments: aortic pressure, LV pressure, ECG, cardiac output, PUCA pump flow, LCA flow, and oxygen content in the aorta and in the coronary sinus.

During ECG-synchronous assist, the PUCA pump was synchronized with the R-wave of the animal's ECG. The delay and percent systole for the PUCA pump in this mode were related to the duration of LV ejection time in such a way that the device ejects blood into the aorta between the onset and the end of the diastole. The duration of LV ejection time was calculated from the heart rate (8).

Experimental protocol

The experimental protocol consisted of the following: first, record baseline values followed by asynchronous LV assist for 40 min with a frequency of one half the heart rate and a rest period ±30 min (PUCA pump off), and second, record baseline values followed by ECG-synchronous LV assist for 40 min in Mode 1:2 (heart:pump).

The pumping and resting time was based on the time needed to measure the effect of short-term mechanical LV support on LV MVO_2 and coronary flow, and the time the heart needed to restore to baseline values after mechanical LV support.

Data analysis

LV MVO_2 (ml O_2/min/100 g LV) was calculated as the difference between aortic and coronary sinus blood oxygen content (vol %) multiplied by LCA flow (ml/min). The blood gas analysis was performed with ABL 330 (Radiometer, Copenhagen, Denmark) and OSM 3 (Radiometer, Copenhagen, Denmark).

Left ventricular weight (free wall + septum) was calculated from animal body weight (9) and was used to present LCA flow and LV MVO_2 per 100 g LV. The results were compared with paired Student's *t*-test. Differences were considered significant at $p < 0.05$. All data are presented in the text as mean ± standard deviation (SD).

RESULTS

Asynchronous assist

A fixed pump frequency one half of the animal heart rate (47 ± 2 beats/min) was used in order to compare the asynchronous assist and ECG-synchronous 1:2 assist. LV MVO_2 decreased significantly by 17% from the baseline value (from 7.77 ± 1.31 to 6.48 ± 1.42 ml O_2/min/100 g, $p < 0.01$, Table 1). The cardiac output ranged from 3.55 ± 0.07 to 3.85 ± 0.07 L/min ($p > 0.05$). The PUCA pump flow was 2.79 ± 0.13 L/min (full-to-empty mode, 50% systole). The coronary flow was dependent on pump ejection timing (Fig. 2).

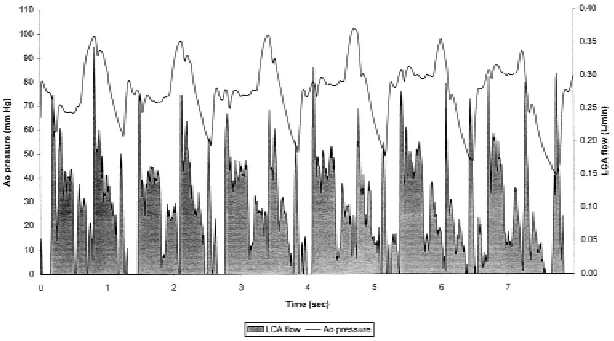

FIG. 2. Shown are aortic pressure (mm Hg) and coronary flow (L/min) during asynchronous LV assist with the PUCA pump. The peak coronary flow depended strongly on pump ejection timing.

ECG-synchronous assist

The pump frequency was 49 ± 9 beats/min. LV MVO_2 decreased significantly by 12% from the baseline value (from 8.88 ± 2.46 to 7.84 ± 2.18 ml O_2/min/100 g, $p < 0.01$, Table 1). The cardiac output ranged from 3.4 ± 0.6 to 3.48 ± 0.68 L/min ($p > 0.05$). The PUCA pump generated up to 2.94 ± 0.54 L/min flow. The coronary flow increased regularly during every second diastole (Fig. 3).

The pulse frequency monitored in the aorta was half that of the heart rate (Fig. 4). The aortic pressure remained high during 2 consecutive LV systolic periods plus the intervening LV diastolic period. The typical diastolic aortic pressure curve presented itself only during every second LV diastolic period.

DISCUSSION

ECG-synchronous 1:1 LV assist mode is considered the most effective assist mode for maintaining the systemic circulation and coronary blood flow (4). During this mode, the pump unloads the LV during every systole, ejects blood into the ascending aorta during every diastole increasing the coronary flow, and provides maximum pump flow. The pump flow

TABLE 1. *Results before and during LV assist with the PUCA pump*

	Baseline (PUCA pump off)	LV assist values (PUCA pump on)
LV MVO_2 (ml O_2/min/100 g)		
Asynchronous	7.77 ± 1.31	6.46 ± 1.42[a]
ECG-synchronous	8.88 ± 2.46	7.84 ± 2.18[a]
Cardiac output (L/min)		
Asynchronous	3.55 ± 0.07	3.85 ± 0.21
ECG-synchronous	3.40 ± 0.6	3.48 ± 0.68
PUCA pump flow (L/min)		
Asynchronous	0	2.79 ± 0.13 (72% from CO)
ECG-synchronous	0	2.94 ± 0.54 (84% from CO)

LV MVO_2: left ventricular myocardial oxygen consumption.

[a] $p < 0.05$.

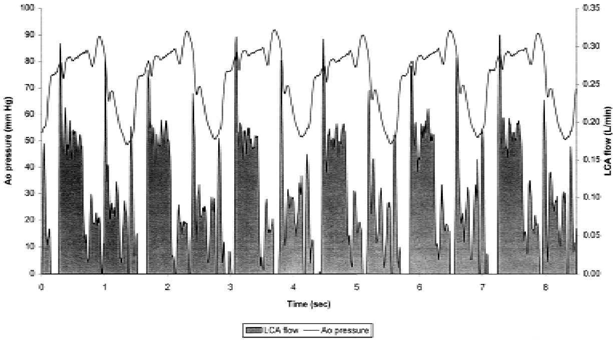

FIG. 3. Shown are aortic pressure (mm Hg) and coronary flow (L/min) during ECG-synchronous 1:2 assist with the PUCA pump. The peak coronary flow increased during every second diastole.

in this mode is closely related to the heart rate and pump driving pressure. A heart rate increase results in a reduction of both systolic and diastolic time. Because of this, beyond a certain heart rate, the pump filling and ejection time becomes too short to insure a proper pump performance, and therefore the pump flow decreases. High positive and/or negative driving pressures could create optimal pump filling and ejection but would lead to blood damage. In such a situation, the pump should be switched to ECG-synchronous 1:2 mode. The LV assist with the PUCA pump in ECG-synchronous 1:1 mode failed for the same reason. The heart rate exceeded 100 beats/min, leading to excessively short pump filling/ejection time to allow proper pump performance. Decreasing the heart rate during the experiment by ice cooling or drugs is inappropriate because this will affect the monitored myocardial oxygen consumption and will lead to incorrect results and conclusions. Therefore, the PUCA pump was switched to ECG-synchronous 1:2 mode, which led to optimal pump performance within the normal driving pressure range. This suggests that for the PUCA pump the choice of the optimal ECG-synchronous assist mode (1:1 or 1:2) depends chiefly on the heart rate: the 1:1 assist mode is the method of choice for a heart rate below 60 beats/min; the 1:2 assist mode should be used in cases of a higher heart rate.

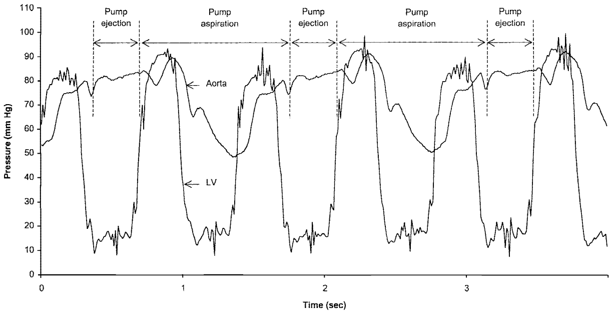

FIG. 4. Shown are aortic pressure (mm Hg), LV pressure (mm Hg), and PUCA pump action during ECG-synchronous 1:2 assist with the PUCA pump. The pulse monitored in the aorta is two times lower than this monitored in the LV.

LV MVO$_2$

In the present study, LV MVO$_2$ decreased significantly during the asynchronous assist as well as during the ECG-synchronous assist. These results led to the conclusion that both assist modes could be used for reducing LV MVO$_2$. This is in line with the results reported by others as well (4). Of course, ECG-synchronous assist is possible only if a good triggering signal can be achieved and if a severe cardiac arrhythmia is not present.

Cardiac output

The cardiac output looks small with respect to the body weight. However, it should be kept in mind that the cardiac output was monitored not in awake calves, but in calves under general anesthesia with isoflurane, which decreases the cardiac output.

Neither ECG-synchronous nor ECG-asynchronous assist led to a significant change of the cardiac output during the experiments. This is in line with the results found by others (10) during LV assist in healthy animals.

During the ECG-synchronous mode, the PUCA pump generated up to 2.94 L/min flow (84% from cardiac output, Table 1), which is enough to maintain the systemic circulation. The pump flow during the asynchronous mode (up to 2.79 ± 0.13 L/min, 72% from cardiac output) was large enough to maintain the systemic circulation as well. It should be kept in mind that a large LVAD flow increases the venous return to the right ventricle. If this flow is too large, right heart failure can result with a subsequent reduction in right ventricular output and reduction in LVAD filling (11,12).

Coronary flow

Coronary flow is closely related to the aortic blood pressure and particularly to the diastolic pressure. Normally, the flow increases rapidly after onset of LV diastole and follows closely the decrease of diastolic pressure. During the ECG-synchronous mode, the PUCA pump ejected during every second diastole (Fig. 4). Because of this, the systolic aortic pressure monitored was actually the result of a combination of the pressure generated from the PUCA pump ejection and the pressure generated from the previous and following LV systole. Therefore, the "systolic" aortic pressure was present not only during the LV systole, as in the normal case, but also during every second LV diastole. As a consequence, the coronary flow remained at a high level through every second diastolic period (Fig. 3). Paradoxically, the average LCA flow decreased. This effect was found also by others (10,13) during pulsatile as well as nonpulsatile LV support in healthy animals. The coronary blood flow at rest depends on the determinants of myocardial oxygen demand: heart rate, contractility, and ventricular load (14). Therefore, the observed decrease of the average LCA flow during the LV assist is an autoadaptation of the coronary blood flow to the LV MVO_2 reduction due to the LV unloading (coronary autoregulation). Despite the fact that during the asynchronous mode the coronary flow increase was irregular (Fig. 2) and was present only when the pump coincidentally ejected during LV diastole, the average LCA flow decreased also in this case presumably because of coronary autoregulation.

It should be kept in mind that these results were obtained during experiments with healthy animals. After maximum arteriolar vasodilatation (e.g., in case of ischemic heart failure), the coronary blood flow is no longer autoregulated and varies linearly with the perfusion pressure (15). During the ECG-synchronous mode, the diastolic aortic pressure was almost equal to the systolic aortic pressure during every second diastolic period. Therefore, we expect that the ECG-synchronous mode during ischemic heart failure will increase the average LCA flow. Because the synchronous mode increased the diastolic aortic pressure on a regular basis, we concluded that this should be the preferred assist mode for optimizing coronary flow patterns.

IABP is the most commonly used cardiac assist procedure for temporary support of the failing left ventricle (2). In cases of persistent low cardiac output despite pharmacological support and IABP use, the transthoracic Hemopump device could be chosen as an LVAD (16). However, the Hemopump generates nonpulsatile flow, which is less desirable than the pulsatile flow (17–19). The PUCA pump is the only transvalvular LVAD that combines direct LV unloading with pulsatile flow. Moreover, due to the presence of a unique valve system, the PUCA pump could be temporarily switched off and kept in place without backflow from aorta to LV. If the Hemopump is switched off, a backflow occurs (16).

Recent research has demonstrated that the combination of Hemopump with IABP is an excellent support system for the ischemic failing heart (16). The PUCA pump in fact combines the direct LV unloading effect of the Hemopump with the counterpulsation effect of IABP. Because of this, we expect a similar effect during PUCA pump assist in an acute LV failure condition.

The effect of LVAD could vary according to the condition of the heart (10). In order to obtain more information on these varying effects, further animal experiments with the PUCA pump during acute heart failure are in preparation in our laboratory.

CONCLUSIONS

The results obtained in the present study led to the conclusion that for PUCA pump support both asynchronous and ECG-synchronous assists significantly reduce LV MVO_2 and that the pump flow generated is enough to maintain the systemic circulation. However, we find the ECG-synchronous mode preferable because this mode optimizes coronary flow patterns at the same time.

The choice of the optimal ECG-synchronous assist mode (1:1 or 1:2) depends chiefly on the heart rate: the 1:1 assist mode is the method of choice for a heart rate below 60 beats/min, and the 1:2 assist mode should be used in cases of a higher heart rate.

The asynchronous assist should be used in case of severe cardiac arrhythmia or when a good triggering signal cannot be achieved.

REFERENCES

1. Edwards FH, Clark RE, Schwartz M. Coronary artery bypass grafting: The Society of Thoracic Surgeons National Database experience. *Ann Thorac Surg* 1994;57:12–9.
2. American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Coronary Artery Bypass Graft Surgery). Guidelines and indications for coronary artery bypass graft surgery. *J Am Coll Cardiol* 1991;17:543–89.
3. Cohen DJ, Clem MF, Luther M, Genecov DG, Hamel JD, Begia BC, Sangalli M, Evans K, Flores J, Bunegin M, Mihaylov D, Verkerke GJ, Blanksma P, Elstrodt J, de Jong ED, Rakhorst G. Effect of synchronous and asynchronous pulsatile flow during left, right, and biventricular bypass. *Artif Organs* 1992;16:614–22.
4. Nakamura T, Hayashi K, Seki J, Nakatani T, Noda H, Takano H, Akutsu T. Effect of drive mode of left ventricular assist device on the left ventricular mechanics. *Artif Organs* 1988;12:56–66.
5. Gutfinger DE, Ott RA, Eugene J, Gazzaniga AB. Concepts in the application of pneumatic ventricular assist devices for ischemic myocardial injury. *ASAIO J* 1995;41:162–8
6. Verkerke B, de Muinck ED, Rakhorst G, Blanksma PK. The PUCA pump: A left ventricular assist device. *Artif Organs* 1993;17:365–8.
7. Mihaylov D, Kik C, Elstrodt J, Verkerke GJ, Blanksma PK, Rakhorst G. Development of a new introduction technique for the pulsatile catheter pump. *Artif Organs* 1997;21:425–7.
8. Craige E. Phonocardiography, apexcardiography, recording of carotid, and jugular venous pulses. In: Willerson JT, Sanders CA, eds. *Clinical cardiology*. New York/San Francisco/London: Grune & Stratton, 1977:111–30.
9. Gross DR. *Animal models in cardiovascular research*. Dordrecht, The Netherlands: Kluwer Academic Publishers, 1994:341–402.
10. Shiiya N, Zelinsky R, Deleuze PH, Loisance DY. Changes in hemodynamics and coronary blood flow during left ventricu-

lar assistance with the Hemopump. *Ann Thorac Surg* 1992;53: 1074–9.

11. Pavie A, Leger P. Physiology of univentricular versus biventricular support. *Ann Thorac Surg* 1996;61:347–9.
12. Farrar DJ, Compton PG, Hershon JJ, Fonger JD, Hill JD. Right heart interaction with the mechanically assisted left heart. *World J Surg* 1985;9:89–102.
13. Noda H, Takano H, Taenaka Y, Kinoshita M, Tatsumi E, Yagura A, Sekii H, Sasaki E, Akutsu T. Regulation of coronary circulation during left ventricular assist. *ASAIO Trans* 1989;35:445–7.
14. Nitenberg A, Antony I. Coronary vascular reserve in humans: A critical review of methods of evaluation and of interpretation of the results. *Eur Heart J* 1995;16(Suppl. I):7–21.
15. Bourdarias JP. Coronary reserve: concept and physiological variations. *Eur Heart J* 1995;16(Suppl. I):2–6.
16. Meyns B, Nishimura Y, Racz R, Jashari R, Flameng W. Organ perfusion with Hemopump device assistance with and without intraaortic balloon pumping. *J Thorac Cardiovasc Surg* 1997; 114:243–53.
17. Fukae K, Tominaga R, Tokunaga S, Kawachi Y, Imaizumi T, Yasui H. The effects of pulsatile and nonpulsatile systemic perfusion on renal sympathetic nerve activity in anesthetized dogs. *J Thorac Cardiovasc Surg* 1996;111:478–84.
18. Lee JJ, Tyml K, Menkis AH, Novick RJ, Mckenzie FN. Evaluation of pulsatile and nonpulsatile flow in capillaries of goat skeletal muscle using intravital microscopy. *Microvasc Res* 1994;48:316–27.
19. Anstadt MP, Tedder M, Hegde SS, Perez TR, Crain BJ, Khian HV, Abdel AS, White WD, Lowe JE. Pulsatile versus nonpulsatile reperfusion improves cerebral blood flow after cardiac arrest. *Ann Thorac Surg* 1993;56:453–61.