i-cor - benefits of pulsatility

Better coronary perfusion

Jung et al.[34] (2007) randomly allocated 13 Yorkshire pigs to two groups for pulsatile (twin pulse pump, n=7) versus non-pulsatile (biopump, n=6) VAD treatment after electrically induced ventricular fibrillation and investigated the flow in the left coronary artery. After 20, 40, 60, 80, 100 and 120 min, they measured mean coronary flows of 0.77±0.3, 0.76±0.19, 0.95±0.23, 0.86±0.23, 1.00±0.24 and 0.95±0.17 ml/kg/min for pulsatile (50 bpm) support with 2 l/min (equating to 67±8 ml/kg/min). The flow measurements were always lower for the equivalent non-pulsatile support (equating to 70±9 ml/kg/min). Support at 20, 40 and 60 min had to be increased to 84±17, 87±24 and 85±18 ml/kg/min ($p<0.05$) and to 79±17, 75±13 and 73±13 ml/min/kg (not significant) at 80, 100 and 120 min to achieve the same coronary flow. During non-pulsatile perfusion, a flow that was 25%–28% higher was required to achieve the same coronary perfusion as for pulsatile perfusion.

Jung JS, Son HS, Lim CH, and Sun K. Pulsatile Versus Nonpulsatile Flow to Maintain the Equivalent Coronary Blood Flow in the Fibrillating Heart. ASAIO J 2007; 53:785–90.

Son et al.[36] (2005) established a centrally cannulated extracorporeal circulation system in 14 pigs that they operated for two hours under electrically induced ventricular fibrillation at a flow of 2 l/min, either in nonpulsatile mode with a centrifugal pump or in pulsatile mode with a T-PLS. In order to determine the effects on the myocardium, they measured vascular diameter, flow and flow velocity in the middle segment of the left coronary artery before ECC was started, and then subsequently every 20 minutes. At the same diameter, they found a trend towards a reduction in coronary resistance in the pulsatile group and a trend towards an increase in resistance in the non-pulsatile group. The flow in the pulsatile group was 19±6 ml/min before ECC and increased to 28±5 ml/min by the end of perfusion, while it remained constant in the non-pulsatile group at 18±3 ml/min and 18±5 ml/min. While flow velocity before ECC was 9.7±4.7 vs. 8.2±2.4 cm/s (pulsatile vs. non-pulsatile), it was significantly higher in the pulsatile group than in the non-pulsatile group at all points later on and was 22.1±3.7 in the pulsatile group vs. 11.7±3.6 cm/s in the non-pulsatile group after 120 minutes. There were no differences in the cardiac enzymes, CK, CK-MB, troponin I and myoglobin, determined after 60 and 120 minutes in arterial blood and sometimes also in blood from the coronary sinus, and nor were there any differences in lactate and free haemoglobin. The myocardial biopsies taken at the end revealed neutrophil infiltration, with intact cell nuclei, mitochondria and cell membranes in both groups.

Son HS, Sun K, Fang YH, Park SY, Hwang CM, Park SM, Lee SH, Kim KT, and Lee IS. The effects of pulsatile versus non-pulsatile extracorporeal circulation on the pattern of coronary artery blood flow during cardiac arrest. Int J Artif Organs 2005; 28:609–16.

Improved renal perfusion

Sezai et al.[38] (1997) cannulated the left atrium and the ascending aorta in six pigs, induced a myocardial infarction through occlusion of the LAD, supported the shock circulation produced by this for six hours either in pulsatile mode (using a pneumatic VAD) or in nonpulsatile mode (using a centrifugal pump) and investigated a number of parameters, including the blood flow in the renal artery, the regional perfusion in the renal cortex and medulla. In both groups, aortic pressure dropped from 140 auf 80 mmHg at induction of the cardiogenic shock and was stabilized at values of around 110–120 mmHg once the left heart bypass was started. Flow in the renal artery dropped to 34% of the

initial value in both groups. In the pulsatile group, flow increased again to 50%, 75% and 70% after 1, 3 and 6 hours of support. In contrast, for non-pulsatile support, it reached its maximum after 1 hour, at around 50% of the initial value, and then dropped off continuously until it had even fallen below the value that had established itself after induction of the cardiogenic shock. Microcirculation in the renal cortex, measured at a tissue depth of 5 mm using a laser probe, dropped to around 17% in both groups and then rose constantly to 54.4±25% after six hours under pulsatile support, while it dropped further to 11.2±4.3% under non-pulsatile support. However, tissue perfusion in the renal medulla increased by about half in both groups during the shock. It dropped to 65% after six hours under pulsatile perfusion – significantly less than under non-pulsatile perfusion, where it dropped to 20%. The authors sum up, stating that intrarenal distribution of perfusion is better under pulsatile perfusion.

Sezai A, Shiono M, Orime Y, Nakata K, Hata M, Yamada H, Iida M, Kashiwazaki S, Kinishita J, Nemoto M, Koujima T, Sezai Y, and Saitoh T. Renal Circulation and Cellular Metabolism During Left Ventricular Assisted Circulation: Comparison Study of Pulsatile and Nonpulsatile Assists. Artif Organs 1997; 21:830–5

Nakata et al.[39] (1996), belonging to the same research group, had previously published the results of an investigation using the same model with 18 animals, where they studied the effects of pulsatile vs. nonpulsatile support on the perfusion of heart and kidneys, using third group without mechanical circulatory support as a control group. After induction of the infarction, there was a drop in the flow in the LAD, as well as in perfusion of the endocardiac and epicardiac tissue, and the baseline value prior to the infarction was achieved again both under pulsatile and nonpulsatile perfusion. Microcirculation in the renal cortex and medulla also dropped during the shock. Although starting perfusion did not lead to a recovery to the initial values in this case, there was an increase in perfusion in the cortex in the pulsatile group. According to the authors, this implies that pulsatile circulatory support is better suited to protecting target organs from the consequences of a cardiogenic shock than non-pulsatile support.

Nakata K, Shiono M, Orime Y, Hata M, Sezai A, Saitoh T, and Sezai Y. Effect of pulsatile and nonpulsatile assist on heart and kidney microcirculation with cardiogenic shock. Artif Organs 1996;
20:681–4.

Improved cerebral perfusion

McCotter et al.[25] (2000) investigated the effects of pulsatile vs. nonpulsatile circulation on cerebral perfusion in a canine model (n=9). To this end, in addition to the roller pump, they placed a pulse wave generator with a capacity of 60 cm3, that generates a pulse frequency of 60–65 bpm and a pulse pressure of 45±5 mmHg using a lever arm compressor and piston, in the arterial tubing distal to the arterial filter in five circulatory systems. All animals were perfused for two hours at normothermia, without cardiac arrest and at an MAP of 60–75 mmHg. Before ECC was recorded
and 5, 60 and 120 minutes afterwards, radioactive microspheres, of 15µm in dimension, were injected and used to determine the coronary blood flow. In the pulsatile group, the flow increased to 119.3±30.5%, 161.5±49.8% and 133.1±22.3% of the baseline value before ECC after 5, 60 and 120 minutes. In contrast, in the non-pulsatile group, flow remained at the initial level, at 102.1±65.4%, 97.92±19.1% and 98.81±10.3% after 5, 60 and 120 minutes. At the time points of 60 and 120 minutes, these results were equally statistically significant as the O_2 supply, that was additionally determined by calculation.

McCotter CJ, Sun Y, Philpott J, Chitwood WR. Benefits of Pulsatile Cardiopulmonary Bypass on Cerebral Perfusion. ASAIO J 2000; 46:163.

Positive influence on the vascular system

Lanzarone et al.[45] (2009) investigated the effects of pulsatile perfusion on nitric oxide (NO) release from the endothelium and, to this end, allocated 18 patients aged between 49–78 years and undergoing surgical coronary intervention for the first time to two groups. During the ischaemic period, these patients were protected by an HLM and, using a Stockert S3 roller pump, received either pulsatile perfusion at a frequency of 70 bpm and at a systole-diastole ratio of 65:35 and a basic flow of 30% of the calculated target flow, or non-pulsatile perfusion with a nominal target flow of 2.4 l/min per m2 BSA. Blood samples were taken the day before surgery and after induction of anaesthesia (PRE), every 30 minutes during ECC (INTRA), and 1 and 2 hours afterwards (POST). The NO synthase, measured via the citrulline concentration, increased to 128±75 percent in the pulsatile group during ECC and then returned to the initial level, at 101±60 percent; in the non-pulsatile group, this increased to 150±138 during ECC and then dropped to 122±16 percent. The mean nitrite concentration increased to 108±18 percent of the PRE value in the pulsatile group during ECC and only dropped off slightly to 105±11 percent afterwards; in the non-pulsatile group, this value already decreased significantly to 88±11 percent during ECC and then remained unchanged at 92±15 percent. The differences during ECC were also significant when the two groups were compared (p=0.012). Mean nitrite concentration in the pulsatile group dropped to 95±20 and 88±16 percent during and after ECC; however, this drop was significantly greater in the non-pulsatile group, to 78±22 and 82±20 percent. This was reflected clinically in the MAP, which was lower under pulsatile perfusion, at 59.4±6.5 mmHg, than under non-pulsatile perfusion (68.8±7.4 mmHg, p=0.016) – a sign of the preservation of the vasodilating effect of endothelial NO release.

Lanzarone E, Gelmini F, Tessari M, Menon T, Suzuki H, Carini M, Costantino ML, Fumero R, Luciani GB, and Faggian G. Preservation of Endothelium Nitric Oxide Release by Pulsatile Flow Cardiopulmonary Bypass When Compared With Continuous Flow. Artif Organs 2009; 33:926–34.

Yu et al.[33] (2008) treated 13 dogs for one hour with an ECLS, 6 of which using a non-pulsatile centrifugal pump and 7 of which using a nonsynchronized twin pulse pump, and determined heart frequency and mean aortic pressure, coronary artery flow, lactate in the coronary sinus, left ventricular pressure, tension time index (TTI) and myocardial oxygen consumption at the time points 0, 30 and 60 minutes. Mean aortic pressure dropped significantly in both groups under ECLS. Coronary flow remained the same in the non-pulsatile group and increased in the pulsatile group. Myocardial oxygen consumption increased with increasing duration of perfusion in both groups, but the increase was not significant. Lactate increased from 21.3 through 114.0 to 126.0 mg/dl under non-pulsatile ECLS and from 22.6 through 89.1 to 102.0 mg/dl under pulsatile ECLS. This was significant both within groups as well as between groups. LV pressure and TTI decreased substantially during pulsatile perfusion, but remained unchanged in the other group.

Yu JJ, Son HS, Lim CH, Lee JJ, Park YW, Her K, Won YS, Sun K, and Choi JY. Comparison of Myocardial Loading Between Asynchronous Pulsatile and Nonpulsatile Percutaneous Extracorporeal Life Support. ASAIO J 2008; 54:177–80.

Improvements in microcirculation

O'Neil et al.[46] (2012) randomly allocated twenty adult high risk, cardiac surgery patients at 1:1 to pulsatile vs. non-pulsatile, mild hypothermic ECC with intermittent cold blood cardioplegia and determined sublingual microcirculation using orthogonal polarization spectral imaging (OPS) preoperatively, at 30 and 90 minutes during ECC and 1, 24 and 48 hours postoperatively. A pulse pressure of 36.8±6.5 mmHg was generated at a frequency of 70 bpm using the roller pump in the pulsatile group during 89% of the aortic clamping period lasting 116±11 min. Microcirculatory flow that corresponded to that prior to ECC was measured at all points during this procedure. When compared with the non-pulsatile circulation system, 66% more capillary vessels were perfused. At the same time,

the number of vessels with pathological hyperdynamic perfusion was lower (6.0±3.4% vs. 19.6±8.8%; $p<0.05$). Compared with non-pulsatile perfusion, leukocyte adherence was also statistically significantly lower for pulsatile perfusion. In addition, lower postoperative peak lactate values were measured in this group. The authors discussed a lower inflammatory response as the reason for this superiority of pulsatile perfusion.

O'Neil MP, Fleming JC, Badhwar A, and Guo LR. Pulsatile Versus Nonpulsatile Flow During Cardiopulmonary Bypass: Microcirculatory and Systemic Effects. Ann Thorac Surg 2012; 94:2046–53.

Sezai et al. (1999)[37] allocated 10 pigs 1:1 to pulsatile vs. non-pulsatile biventricular cardiac support lasting three hours after an induced cardiogenic shock, whereby cannulation was carried out on the pulmonary artery on the right and the right ventricle and transmitrally on the left ventricle and on the ascending aorta on the left. They measured microcirculation in the white and grey matter in the brain, in the renal cortex and medulla and in the liver using laser probes. In both groups, MAP dropped from approx. 106 mmHg before the shock to approx. 33 mmHg during the shock and, with support, reached approx. 96 mmHg after one hour and approx. 98 mmHg after three hours. PP dropped from approx. 32 mmHg to approx. 5 mmHg and was fully restored in the pulsatile group, whereby it remained at the shock value in the non-pulsatile group. At 2.9– 3.2 l/min・m2, the BVAD support provided 80–85% of the C.O. measured prior to the shock. In the carotid artery, flow was reduced to an approx. basal value of 20% during the shock and reached values of around 90% again in both groups with support. Regional perfusion in the brain exhibited a similar course. Flow in the left renal artery reached approx. 60% with pulsatile support and a maximum of 40% of basal flow with non-pulsatile support. Microcirculation in the renal cortex that had collapsed to 10% during the shock improved to 90% in the pulsatile group vs. 60% in the nonpulsatile group. Flow dropped to 25% in the renal medulla during the shock and recovered to an approx. basal value of 60–65% in both groups. In the hepatic artery, 100% of the basal flow was measured after three hours of BVAD, both in the pulsatile and the non-pulsatile groups, while this was only the case in the pulsatile group for the portal vein, where only approx. 80% was achieved in the non-pulsatile group. These results were statistically significant and were confirmed by measurements on the regional perfusion in the liver.

Sezai A, Shiono M, Orime Y, Nakata K, Hata M, Iida M, Kashiwazaki S, Kinoshita J, Nemoto M, Koujima T, Furuichi M, Eda K, Hirose H, Yoshino T, Saitoh A, Taniguchi Y, and Sezai Y. Major Organ Function Under Mechanical Support: Comparative Studies of Pulsatile and Nonpulsatile Circulation. Artif Organs 1999; 23:280–5.