Does Roller Pump–Induced Pulsatile CPB Perfusion Affect Microvascular Fluid Shifts and Tissue Perfusion?

Bjørg Elvevoll, MD, Steinar Lundemoen, MD, PhD, Øyvind S. Svendsen, MD, PhD, Arve Mongstad, CCP, Ketil Grong, MD, PhD, Venny L. Kvalheim, MD, PhD, and Paul Husby, MD, PhD

Department of Anesthesia and Surgical Services, Haukeland University Hospital, Bergen; Department of Heart Disease, Haukeland University Hospital, Bergen; Department of Clinical Science, Faculty of Medicine and Dentistry, University of Bergen, Bergen; and Department of Clinical Medicine, Faculty of Medicine and Dentistry, University of Bergen, Bergen, Norway

Background. **Pulsatile versus nonpulsatile cardiopulmonary bypass (CPB) perfusion remains debated. Beneficial effects on tissue perfusion, inflammation, and microvascular fluid exchange have been linked to pulsatile perfusion by some investigators and denied by others. This study evaluated fluid extravasation and tissue perfusion during nonpulsatile or pulsatile roller pump–induced CPB perfusion.**

Methods. **Fourteen pigs underwent roller pump–induced pulsatile (n = 7) or nonpulsatile CPB perfusion (n = 7) for 90 minutes. Fluid input/losses, colloid osmotic pressures (plasma/interstitium), hematocrit, serum electrolytes, serum proteins, tissue perfusion, and total tissue water content were measured, and plasma volume and fluid extravasation were calculated.**

Results. **Fluid additions/losses, plasma volume, and fluid extravasation changed similarly in both groups during CPB with no between-group differences. Neither was between-group differences observed for tissue perfusion and total tissue water content, with one exception. Total tissue water content of the right (3.92 ± 0.26 versus 4.32 ± 0.28 g/g dry weight) and left ventricle (4.02 ± 0.25 versus 4.33 ± 0.24 g/g dry weight) was lowered in the pulsatile group.**

Conclusions. **No important differences were found between pulsatile and nonpulsatile CPB perfusion for microvascular fluid balance and tissue perfusion.**

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The superiority of pulsatile cardiopulmonary bypass (CPB) perfusion has been related to delivery of a surplus of hemodynamic energy that affects tissue perfusion and inflammation beneficially [1]. Animal experiments have confirmed better cerebral, myocardial, and renal blood and lymph flow after pulsatile than nonpulsatile CPB perfusion [2, 3]. Similarly, studies on pulmonary microcirculation have found beneficial effects of pulsatile CPB perfusion, whereas nonpulsatile perfusion (NP) has uncovered more heterogeneous flow distribution [4] that could trigger microvascular dysfunction as observed in tissue samples from liver, kidneys, and lungs [5].

Waaben and colleagues [6], however, found differences to be absent when pulsatile CPB perfusion was compared with NP and judged by intracellular adenosine trlphosphate as an indicator of cellular damage. Similarly, Voss and colleagues [7] concluded that pulsatile flow pattern closely mimicking physiologic waveforms were of no advantage when related to tissue perfusion or systemic inflammatory response. Other prospective human studies on pulsatile perfusion (PP) versus NP have in the same way been conflicting related to mortality, myocardial infarction, stroke, or renal failure and were thus unable to recommend or reject PP [8].

Microvascular fluid exchange has been supposed to be beneficially influenced by pulsatile CPB perfusion as judged by reduced weight gain and edema formation. This could, however, equally be related to modulated inflammation after CPB [9] because opposite increased fluid shifts from circulation to the interstitial space after PP per se has been observed [10].

Recently, we evaluated microvascular fluid exchange [11] and tissue perfusion [12] when "real" pulsatility was achieved by combining a centrifugal pump and intraaortic counterpulsation (IABP) during bypass. Under these conditions benefits of pulsatility on microvascular fluid exchange were absent [11]. Note that pulsatility achieved with the use of IABP may interfere with microvascular fluid balance through IABP-induced intraaortic obstruction [12] that affects the central venous pressure and the capillary hydrostatic pressure that partly controls fluid exchange at the microvascular level. To the best of our knowledge no studies have so far focused explicitly on microvascular fluid exchange and organ perfusion with roller pump–induced pulsatile compared with nonpulsatile CPB. In a number of previous studies even nonphysiologic PP achieved with conventional roller pumps

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Address correspondence to Dr Husby, Department of Anesthesia and Intensive Care, Haukeland University Hospital, 5021 Bergen, Norway; email: paul.husby@k1.uib.no.

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Abbreviations and Acronyms

COP = colloid osmotic pressure
CPB = cardiopulmonary bypass
FER = fluid extravasation rate
IABP = intraaortic counterpulsation
NFB = net fluid balance
NP = nonpulsatile perfusion
PP = pulsatile perfusion
PV = plasma volume
SHE = surplus hemodynamic energy
TTW = total tissue water content

has been found superior to NP for end-organ recovery, as reported in animal studies [2] and clinical practice [13].

The current study was therefore undertaken with the aim to uncover possible differences in organ perfusion and microvascular fluid exchange during CPB with a roller pump operated in pulsatile or nonpulsatile mode.

Material and Methods

Animals, Anesthesia, and Surgical Preparation

Female pigs (n = 14; Norwegian Landrace; Norhybrid, Hordaland, Norway) were randomly assigned to the PP (n = 7) or the NP (n = 7) group, received human care, and were acclimatized for 1 week within the laboratory housing area before the experiments. One animal, allocated to the PP group went into cardiac arrest during instrumentation/preparation and was excluded. Consequently, only six PP animals were included for further analysis.

The anesthetic and experimental protocol was approved by the Institutional Animal Use and Care Committee under surveillance of the Norwegian Animal Research Authority, (Oslo, Norway) and was conducted in accordance with national and international guidelines. All animals were deprived of food overnight with continuous free access to water. Premedication and general anesthesia included midazolam, fentanyl, pancuronium, and isoflurane [14].

Instrumentation and CPB

A transit-time flow meter probe (3 mm; CM 4000; MediStim AS, Oslo, Norway) was placed on the right carotid artery. After median sternotomy, a catheter (Millar MPC-500; Millar Instruments Inc, Houston, TX) was introduced into the ascending aorta about 4 cm from the flow probe. Blood flow (carotid artery) and pressure signals (aorta) were sampled (Ponemah ACQ-7700; Data Sciences International, St. Paul, MN); ASCII files were exported for energy equivalent pressure and surplus hemodynamic energy (SHE) determination before and during CPB (LabVIEW; National Instruments, Austin, TX).

A catheter was placed in the left atrium for administration of baseline microspheres.

Cannulation for CPB was done with a 22F EOPA aortic arch cannula (Medtronic Inc, Minneapolis, MN) in the ascending aorta and 28F/36F two-stage venous return cannula (MC2X 91228C; Medtronic) in the right atrium, connected to Quadrox-I Adult hollow fiber membrane oxygenator system (VHK 4200; Jostra AG, Hirrlingen, Germany) after administration of heparin, 6 mg/kg, followed 1 hour later by 4 mg/kg body weight.

Right femoral artery and vein were used for blood sampling, fluid supplementation, and femoral venous pressure monitoring. A thermodilution catheter (5F; Edwards Lifesciences, Irvine, CA) was introduced to wedging position in the pulmonary artery. Cardiac output at baseline was calculated as the mean of three consecutive injections. A suprapubic urine catheter was placed into the urine bladder.

Operations were normally completed within 30 minutes, followed by 60-minute stabilization before start of normothermic CPB (38°C) for 90 minutes. Once on, calculated blood flow ventricular fibrillation was achieved with a 9-V DC battery held shortly onto the right ventricle before a left ventricular vent was introduced through the apex into the left ventricle.

Block randomization determined perfusion mode. Pulsatile roller pump settings were commenced 5 minutes after start of CPB with frequency of 60 per minute, runtime 35% and base flow 70% (Stöckert S3 roller pump; Sorin Group, Munich, Germany). One perfusionist contributed in all experiments.

Maintenance fluid was given as a continuous infusion of acetated Ringer's solution (5 mL $\cdot$ kg^{-1} $\cdot$ h^{-1}) throughout the experiments. Blood loss before heparin administration was substituted by Ringer's solution in volumes three times the blood loss volume. During CPB blood loss into the open chest was returned to circulation through the machine reservoir.

The CPB circuit was primed with 1030 mL of acetated Ringer's solution, resulting in filling of the machine reservoir to the 400-mL level. On CPB, this fluid level was followed closely and recorded at 5-minute intervals. Changes from the 400-mL level were used as a fluid gauge to indicate fluid loss (or gain) from the intravascular compartment or changes in vascular tone. Whenever the reservoir fluid level decreased, acetated Ringer's solution was added to restore the 400-mL level.

During the experiments there was a constant fixed height difference (73 $\pm$ 3 cm) between the level of the machine reservoir and the site of venous drainage (right atrium). Free venous drainage was controlled continuously by visual inspection and measured atrial pressure.

Blood Volume Determination With the Carbon Monoxide Method

Red cell blood volume and plasma volume (PV) determination before CPB was performed with carbon monoxide as label [15]. Subsequent red cell blood volume and PV values were calculated every 30 minutes from blood loss recordings and simultaneous hematocrit levels. PV of the CPB circuit was subtracted from the total calculated PV to obtain the actual PV within the animal at 30, 60, and 90 minutes on CPB.