

B. Bierbach<sup>1</sup>  
W. Kasper-König<sup>1</sup>  
T. Haist<sup>1</sup>  
M. Meier<sup>2</sup>  
H. Pritzer<sup>2</sup>  
U. Hanenkamp<sup>2</sup>  
G. Horstick<sup>3</sup>  
O. Kempfski<sup>2</sup>  
H. Oelert<sup>1</sup>

## Effect of Different Operative Techniques for Myocardial Revascularisation on Hemodynamics and Myocardial Perfusion in a Porcine Model

### Abstract

**Background:** During surgical coronary revascularisation hemodynamics and myocardial contractility can be affected. This *in vivo* study aimed to determine the effects of different operative techniques on hemodynamics and regional myocardial perfusion. **Methods:** In 24 pigs IMA to LAD bypass was constructed using ECC (n = 8) and cardioplegic arrest, OPCAB techniques (n = 8), or the Impella® elect 100 support device (n = 8). 8 animals received a sham operation. Mean arterial pressure (MAP), cardiac output (CO), and left ventricular pressure (LVP, LVdp/dt) were recorded. Regional myocardial perfusion (RMP) of both ventricles was assessed by fluorescent microspheres. **Results:** MAP significantly decreased during revascularisation in all groups ( $p < 0.05$ ), staying below preoperative values thereafter ( $p < 0.05$ ). After ECC

norepinephrine was administered to maintain MAP. CO and LVdp/dt were impaired more distinctly during OPCAB than with Impella ( $p < 0.05$ ) during subsequent recovery. RMP showed global reactive hyperemia during early reperfusion after ECC, remained unchanged in OPCAB, and showed low flow during and after Impella pump run ( $p < 0.05$ ). **Conclusions:** ECC led to hemodynamic impairment with post-ischemic reactive hyperemia. OPCAB created hemodynamic depression but left RMP unchanged. Hemodynamic depression can be reduced by the Impella® pump, however regional myocardial blood flow is decreased.

### Key words

Coronary artery bypass grafting · hemodynamics · regional myocardial perfusion and microaxial blood pump

### Introduction

Hemodynamic impairment during and after coronary artery bypass grafting (CABG) performed with cardiopulmonary bypass and cardioplegic arrest as well as off-pump surgery is well described [1–3]. However, the effects of hemodynamic depression or microvascular obstruction due to endothelial dysfunction, cellular microaggregates, or microbubbles on regional myocardial

perfusion in the perioperative period caused by different surgical techniques has not yet been investigated.

Off-pump coronary artery bypass grafting (OPCABG) plays an increasingly important role in many surgical programs. The prerequisite for efficient long-term results after surgical treatment of coronary artery disease is the complete revascularization of the affected coronary vessels. In some cases conversion from an

### Affiliation

<sup>1</sup> Klinik und Poliklinik für Herz-, Thorax- und Gefäßchirurgie, Universitätsklinik Mainz, Mainz, Germany

<sup>2</sup> Institut für Neurochirurgische Pathophysiologie, Universitätsklinik Mainz, Mainz, Germany

<sup>3</sup> II. Medizinische Klinik und Poliklinik, Universitätsklinik Mainz, Mainz, Germany

### Dedication

Presented at the 33rd Annual Meeting of the German Society for Thoracic and Cardiovascular Surgery, Hamburg February 16–18, 2004

### Correspondence

Dr. Benjamin Bierbach · Department of Cardiothoracic and Vascular Surgery, Johannes Gutenberg University Mainz · Langenbeckstraße 1 · 55131 Mainz · Germany · Phone: + 49 61 31 17 29 35 · Fax: + 49 61 31 17 36 26 · E-mail: bier.bach@gmx.de

Received May 3, 2004

### Bibliography

Thorac Cardiovasc Surg 2005; 53: 103–109 © Georg Thieme Verlag KG · Stuttgart · New York · DOI 10.1055/s-2004-830442 · ISSN 0171-6425

off-pump to an on-pump bypass procedure with extracorporeal circulation is necessary. One reason for this is the impossibility of reaching target vessels on the rear or lateral wall of the heart affected by hemodynamic instability or severe arrhythmias [4]. To avoid these complications, strategies such as ischemic preconditioning, atrial pacing, pretreatment with adenosine and  $\beta$ -adrenergic antagonists to reduce myocardial oxygen demand have been introduced [5]. The insertion of a shunt into the arteriotomy additionally maintains distal perfusion and achieves hemostasis during anastomosis construction [6].

An on-pump beating heart procedure, first published by Sweeney and Frazier, presents an alternative concept for myocardial revascularisation [7]. On-pump beating heart myocardial revascularisation for ventricular augmentation was introduced into clinical practice to avoid hemodynamic deterioration [8].

A new device, the Impella<sup>®</sup> elect 100 microaxial blood pump (Impella Cardiosystems, Aachen, Germany) has been developed for clinical use to avoid hemodynamic instabilities while retracting the heart to expose lateral and back wall vessels and to allow prolonged stabilisation [9,10]. Technical details of the pump system are described elsewhere [9].

We used an experimental adult porcine model for coronary artery bypass grafting to evaluate the effect of these three different operative techniques on hemodynamic variables, global left ventricular contractility, and regional myocardial perfusion.

## Material and Methods

In 24 adult German Landrace pigs of either sex aged 6–7 months weighing 68–91 kg an internal mammarian artery (IMA) to the left anterior descending (LAD) coronary artery bypass was performed. The anastomosis was carried out just underneath the ramus diagonalis I. Group I received 60 minutes extracorporeal circulation during 40 minutes cardioplegic arrest ( $n=8$ ), group II underwent a 60-minute off-pump procedure ( $n=8$ ), and group III a 60-minute beating heart procedure assisted by a microaxial blood pump ( $n=8$ ). A fourth group without bypass surgery (sham operation,  $n=8$ ) served as control. The study protocol was approved by the Ethical Committee for Laboratory Animals Rheinland-Pfalz. All animals in this study received humane care in compliance with the "Principles of Laboratory Animals Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animal Resources" published by the National Institutes of Health (NIH publication 85–23, revised 1985).

## Surgical preparation

Animals were premedicated with Ketamin 15 mg/kg, Azaperon 3 mg/kg, and 2 mg atropin. General anesthesia was induced with Thiopental 2–3 mg/kg and Piritramid 15 mg. After oral intubation the animals were ventilated: ventilation was pressure controlled with a Servo 900 b (Siemens Elema-Schönander AB, Solna, Sweden). Anesthesia was maintained with Thiopental 3–6 mg/kg and Piritramid 7.5 mg/h. Arterial blood gases were maintained in physiological ranges. Sterofundin<sup>®</sup> 5 to 10 ml/kg

(Braun, Melsungen, Germany) was administered for constant volume replacement.

Both femoral arteries were cannulated with an 8-Fr cannula (Medex, Klein-Winternheim, Germany) for pressure recording, reference blood and blood gas sampling. A Swan-Ganz catheter (Edwards Lifesciences, Unterschleissheim, Germany) was placed in the main pulmonary artery for cardiac output monitoring via the femoral vein. A Foley catheter was inserted in the urine bladder through a median mini-laparotomy. After median sternotomy the internal mammarian artery was dissected and stored in a moistened towel. A fluid-filled plastic catheter was inserted into the left atrium for microspheres application and a further catheter was advanced into the left ventricle via the apex for pressure recording and for dp/dt-calculation, respectively.

## Experimental protocol

Baseline values were acquired one hour after finishing surgical manipulations during a pre-interventional period of 20 minutes. Following baseline measurements the animals were randomised to one of the three treatment groups or to the sham operated group. All animals received heparin 500 units/kg and an equivalent dose of protamine. Body temperature was held at normothermia in all groups throughout the whole experiment. The surgical intervention lasted 60 minutes followed by 4 hours' observation. Blood gases were maintained within physiological ranges throughout the experiment (Alpha stat method).

## Surgical set-up

In group ECC the coronary artery bypass was performed with 40 minutes' aortic cross-clamping and cardioplegic arrest using 4–8°C modified St. Thomas solution (potassium concentration: 35 mmol/l, 1000 ml initially and 500 ml after 30 minutes cross-clamping) via antegrade application and topic cooling during a total of 60 minutes extracorporeal circulation. A 36-/51-Fr dual stage venous return catheter (Jostra, Hirrlingen, Germany) was placed in the right atrium and inferior vena cava, respectively. The arterial 21-Fr cannula (Jostra, Hirrlingen, Germany) was inserted in the ascending aorta. A standard roller pump head, a Quadrox membrane oxygenator (Jostra, Hirrlingen, Germany), and a sterile tubing set containing a 40  $\mu$ m arterial filter (Edwards PAS, Wörrstadt, Germany) were used. The pump speed was adjusted to maintain a mean arterial pressure between 55 and 75 mm Hg; no vasopressor medication during extracorporeal circulation was used. A bulldog clamp occluded the completed bypass until cross-clamp opening.

In group II the IMA to LAD bypass was carried out on the beating heart. An Octopus suction stabilisator (Medtronic, Minnesota, USA) was placed in the anastomosis region. A 1.75- to 2.5-mm Axius (Guidant Corporation, Santa Clara, USA) coronary shunt was inserted after short coronary occlusion (15 to 40 seconds) by vessel loops. The stabilisator remained in position for 60 minutes. A bulldog clamp occluded the completed bypass until the 40th minute.

In group III the manubrium sterni's left side was removed to get access to the ascending aorta to insert the Impella<sup>®</sup> elect 100 microaxial blood pump (Impella Cardiosystems, Aachen, Germany) through a double purse-string suture. 500 to 1000 ml Voluven

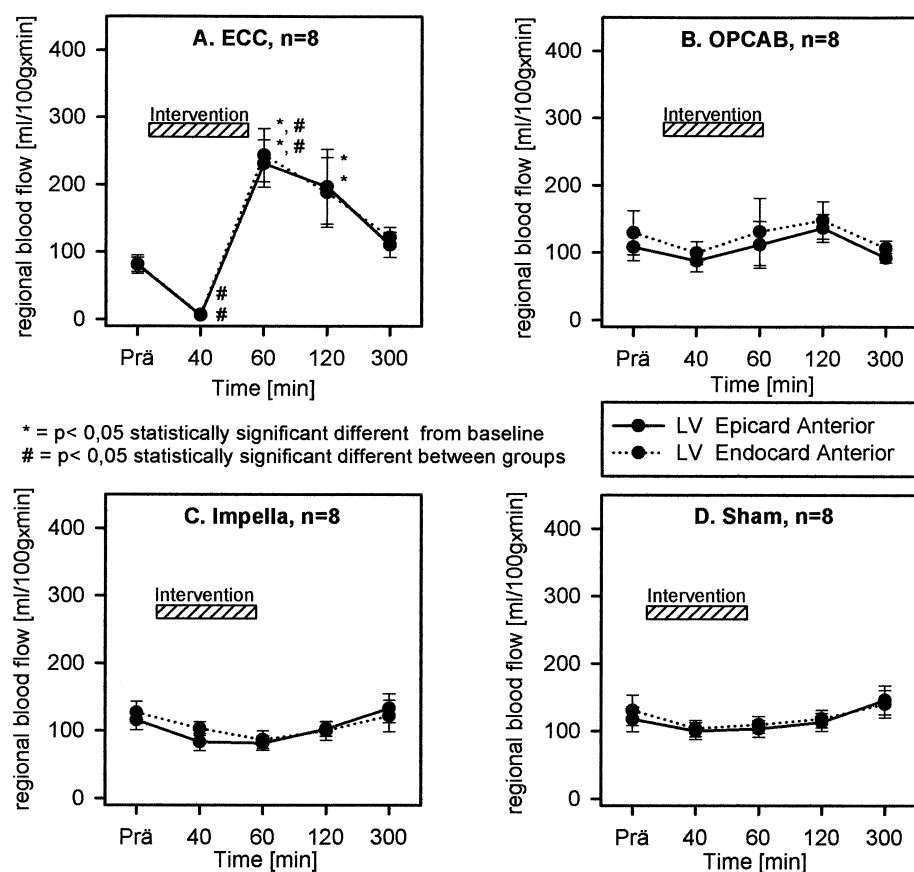


Fig. 1 A to D Anterior wall myocardial blood flow in pigs before, during 60 minutes surgery, one and four hours after operative myocardial revascularisation performed by (A) cardiopulmonary bypass with cardioplegic arrest (group ECC), (B) off-pump coronary artery bypass grafting (group OPCAB), (C) Impella® elect 100 supported beating heart surgery (group Impella), (D) sham operation (group Sham); —●— left ventricular anterior wall epicardial blood flow, "...●..." left ventricular anterior wall endocardial blood flow. Values are means  $\pm$  standard error of mean. N gives numbers of animals per group. \* Signifies  $p < 0.05$  versus pre surgery myocardial blood flow and # signifies  $p < 0.05$  between groups.

6% (Braun, Melsungen, Germany) were infused before pump insertion. The correct position was checked by diastolic pressure difference between the aortic and the left ventricular diastolic pressure [11]. Rotation speed was adjusted so that maximum ventricular unloading could be achieved. The Impella pump ran for 60 minutes and as in group II the stabilisator was in place for 60 minutes. The anastomosis was sutured in the same way as in group II and after completion the bulldog clamp also stayed on the graft until the 40th minute.

#### Hemodynamic parameters and myocardial contractility

Heart rate, left and right atrial pressure, left ventricular pressure, mean arterial and mean pulmonary arterial pressure were recorded on a Sirecust 1280 (Siemens, Nürnberg, Germany) at different time points (see Fig. 1). Cardiac output was continuously determined and displayed on a Vigilance Monitor (Edwards Lifesciences, Unterschleissheim, Germany). Left ventricular pressure first derivative over time was calculated and displayed on a System 6+ hemodynamic module (Triton Technology, San Diego, USA). Heart rate, left and right atrial pressure, left ventricular pressure, and mean pulmonary arterial pressure were not recorded during extracorporeal circulation.

#### Graft patency

Verification of graft patency was assessed by a CM 1005 transit time flow meter with a 3-mm probe (Cardio Med GmbH, Taufkirchen, Germany). The probe was placed 15 to 25 mm proximal to the anastomosis.

#### Myocardial perfusion measurement

Myocardial blood flow (MBF) was examined at baseline, twice during the surgical procedure (40 and 60 minutes) and 1 hour (120 minutes) and 4 hours (300 minutes) after bypass by fluorescence labelled microspheres (Molecular probes, Leiden, Netherlands) as previously described [12]. Two million spheres per colour were injected in a randomised manner into the left atrium over 30 seconds via the left atrial catheter. A reference blood sample of 10 ml was withdrawn from the abdominal aorta over a 3-minute period starting 30 seconds before microsphere's injection with a syringe pump (TSE model 540210, Bad Homburg, Germany). At the end of the experiment the heart was removed from the chest and rinsed with sterile saline and immersed in 4% paraformaldehyde. After 7 to 10 days immersion three 5- to 7-mm sections were cut at the height of the anastomosis, above, and underneath. Per section the left ventricular part was divided into 4 sectors (anterior, lateral, posterior, and septal) and every sector was separated into an endo- and an epicardial aspect. The right ventricular part was divided into an anterior and a posterior sector and both sectors were separated into an endo- and an epicardial aspect. Every specimen was finally divided in two parts. So, in total, 72 areas resulted. For digestion and dye extraction we used a previously published protocol [12]. Myocardial blood flow values below  $20 \text{ ml/min} \times 100 \text{ g}$  were assumed as critical low flow areas resulting in reduced myocardial function [13].

#### Statistics

Data are presented as mean  $\pm$  SEM. Statistical analysis was performed with Sigma Stat 3.0 (Jandel Scientific Corp., San Rafael, USA). The statistical significance of changes from baseline values

within each group was tested with repeated measures ANOVA. Differences between groups were statistically analysed by one-way ANOVA comparing several groups. If values did not show a normal distribution, ANOVA for nonparametric values (Kruskal Wallis test) with multiple comparison method (Student-Newman-Keul's test) was used. Statistical significance was accepted at an error probability of  $p \leq 0.05$ .

## Results

All animals survived surgery and the post interventional 4-hour period. All constructed anastomoses showed acceptable flow without significant differences between groups. The observed flow patterns revealed no signs of bypass obstruction. In group I norepinephrine had to be administered to maintain an adequate perfusion pressure. Maximum dose was  $18.75 \mu\text{g}/\text{kg} \times \text{h}$ .

### Hemodynamic parameters

The hemodynamic changes during and after myocardial revascularisation are summarized in Table 1. During surgery only the timepoint at 30 minutes is displayed. For immediate reactions after surgery the timepoint 70 minutes is shown, as is timepoint 300 minutes for early changes after surgery.

Hemodynamic impairment in response to extracorporeal circulation with cardioplegic arrest was observed regularly with decreased MAP, tachycardia, and the need for vasopressor application ( $91 \pm 3$  to  $68 \pm 3$  and  $71 \pm 3$  mmHg as well as  $63 \pm 4$  to  $120 \pm 7$  and  $104 \pm 8$  beats/min). Cardiac output was slightly elevated immediately after aortic cross-clamp opening and returned to baseline values at the end of the observation period. Left ventricular contractility was significantly increased early after separation from cardiopulmonary bypass, even before vasopressors were administered and normalised to starting point values ( $2359 \pm 157$ ,  $3574 \pm 409$ , and  $2296 \pm 105$  mmHg/s). Filling pressures, left ventricular and mean pulmonary artery pressure remained unchanged.

During off-pump bypass grafting hemodynamic deterioration occurred with statistically significant decreases in cardiac output, mean arterial pressure, left ventricular pressure, and left ventricular contractility ( $4.8 \pm 0.3$  to  $3.4 \pm 0.2$  l/min,  $92 \pm 5$  to  $79 \pm 4$  mmHg,  $126 \pm 6$  to  $100 \pm 5$  mmHg, and  $2519 \pm 296$  to  $1666 \pm 147$  mmHg/s, respectively). Cardiac output, mean arterial and left ventricular pressure as well as left ventricular contractility did not recover baseline values. In opposition filling and mean pulmonary artery pressure remained within physiological ranges. However, no conversion to bypass grafting with extracorporeal circulation due to the observed hemodynamic deterioration was necessary.

The Impella® elect 100 assisted bypass grafting showed milder hemodynamic impairment compared to the off-pump procedure. Pump flow ranged from 1.9 to 3.5 l/min. Initiation of mechanical unloading resulted in a decrease in left atrial pressure, a significant reduction of ventricular pressure, and LV pressure first derivative. Additionally, the left ventricular contractility recovered completely after four hours. Cardiac output and mean arterial pressure drop off could be reduced compared to OPCAB

( $4.7 \pm 0.4$  to  $4.0 \pm 0.2$  and  $91 \pm 3$  to  $84 \pm 3$  mmHg), but still remained statistically significant although it returned to control levels at the end of the experiment ( $4.3 \pm 0.2$  l/min and  $80 \pm 2$  mmHg). In contrast to off-pump bypass grafting tachycardia was noticed postoperatively ( $95 \pm 7$  beats/min). Mean pulmonary artery pressure was slightly elevated in this group throughout the whole experiment due to preoperative volume loading. All groups showed a mild increase in MPAP immediately after termination of surgery at the time of protamine administration.

### Regional myocardial perfusion

Left ventricular epi- and endocardial myocardial blood flow of the anterior wall at the level of the anastomosis is shown in Fig. 1. The other areas studied displayed similar flow courses.

All baseline values in the 72 specimens from both ventricles revealed no statistical difference between the studied groups (epicardial blood flow:  $107 \pm 8$ , range: 50 to 220 ml/min  $\times$  100 g; endocardial blood flow:  $118 \pm 11$ , range: 46 to 302 ml/min  $\times$  100 g).

As expected during aortic cross clamping and cardioplegic arrest no myocardial perfusion in any observed specimen could be found. Reactive hyperemia occurred during early reperfusion uniformly without regional hypoperfusion (epicardial blood flow:  $214 \pm 19$ , range: 81 to 402 ml/min  $\times$  100 g and endocardial blood flow:  $235 \pm 23$ , range: 104 to 454 ml/min  $\times$  100 g). 80 minutes ( $t = 120$  min) after cross-clamp opening increased myocardial blood flow was still present (Fig. 1A). Even at the end of the experiment myocardial blood flow exceeded baseline values. Low flow was detected only in four specimens in one animal out of a total of 576 specimens at the end (Fig. 2).

Off-pump surgery with shunt insertion created only a mild and not significant decrease in myocardial perfusion in both ventricles during stabilisator placement (epicardial blood flow:  $86 \pm 8$ , range: 19 to 158 ml/min  $\times$  100 g and endocardial blood flow:  $96 \pm 7$ , range: 25 to 146 ml/min  $\times$  100 g) (Fig. 1B). After surgery myocardial blood flow reached baseline values. Two animals presented with sporadic myocardial low flow during surgery ( $t = 40$  minutes 1 area and  $t = 60$  minutes 4 and 5 areas) (Fig. 2).

During microaxial blood pump support myocardial blood flow also decreased mildly in all areas (epicardial blood flow:  $84 \pm 8$ , range: 11 to 193 ml/min  $\times$  100 g and endocardial blood flow:  $91 \pm 7$ , range: 21 to 168 ml/min  $\times$  100 g) (Fig. 1C). After surgery myocardial blood flow returned to baseline values. Six animals had myocardial low flow during surgery in 1 to 18 areas. One specimen was hypoperfused immediately after surgery, while four hours after surgery in three animals 1 to 16 specimens again showed myocardial low perfusion (Fig. 2).

There were no significant changes in myocardial blood flow in the control group (Fig. 1D). Myocardial low flow occurred in eleven specimens in two animals at 60 minutes and in one animal in three areas at 120 and 300 minutes (Fig. 2).

**Table 1** Hemodynamic variables in pigs before, during, 10 minutes, and four hours after operative myocardial revascularisation performed by cardiopulmonary bypass with cardioplegic arrest (group 1 **ECC**), off-pump coronary artery bypass grafting (group 2 **OPCAB**), Impella® elect 100 supported beating heart surgery (group 3 **Impella**), sham operation (group 4 **Sham**); CVP: central venous pressure, dp/dt: left ventricular pressure first derivative over time, LAP: left atrial pressure, LVP: left ventricular pressure, MAP: mean arterial pressure and MPAP: mean pulmonary artery pressure. Values are means  $\pm$  standard error of mean. N gives numbers of animals per group

|                                      | Baseline       | Surgery          | 70 min          | 300 min         |
|--------------------------------------|----------------|------------------|-----------------|-----------------|
| <b>Heart rate (min<sup>-1</sup>)</b> |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 63 $\pm$ 4     | –                | 120 $\pm$ 7*#   | 104 $\pm$ 8*#   |
| Group 2 OPCAB (n = 8)                | 67 $\pm$ 3     | 71 $\pm$ 3       | 74 $\pm$ 5      | 80 $\pm$ 4      |
| Group 3 Impella (n = 8)              | 65 $\pm$ 2     | 78 $\pm$ 4#      | 87 $\pm$ 7*#    | 95 $\pm$ 7*#    |
| Group 4 Sham (n = 8)                 | 64 $\pm$ 2     | 66 $\pm$ 2       | 65 $\pm$ 3      | 70 $\pm$ 3      |
| <b>Cardiac output (l/min)</b>        |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 4.5 $\pm$ 0.2  | 4.5 $\pm$ 0.2    | 4.9 $\pm$ 0.4   | 4.6 $\pm$ 0.3   |
| Group 2 OPCAB (n = 8)                | 4.8 $\pm$ 0.3  | 3.4 $\pm$ 0.2*#  | 3.9 $\pm$ 0.3*  | 4.2 $\pm$ 0.3   |
| Group 3 Impella (n = 8)              | 4.7 $\pm$ 0.4  | 4.0 $\pm$ 0.2    | 4.2 $\pm$ 0.3   | 4.3 $\pm$ 0.2   |
| Group 4 Sham (n = 8)                 | 4.9 $\pm$ 0.2  | 4.6 $\pm$ 0.1    | 4.3 $\pm$ 0.2*  | 4.3 $\pm$ 0.2*  |
| <b>MAP (mm Hg)</b>                   |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 91 $\pm$ 3     | 67 $\pm$ 4*#     | 68 $\pm$ 3*#    | 71 $\pm$ 3*     |
| Group 2 OPCAB (n = 8)                | 92 $\pm$ 5     | 79 $\pm$ 4*#     | 80 $\pm$ 3*     | 70 $\pm$ 3*     |
| Group 3 Impella (n = 8)              | 91 $\pm$ 3     | 84 $\pm$ 3*      | 82 $\pm$ 2*     | 80 $\pm$ 2*     |
| Group 4 Sham (n = 8)                 | 88 $\pm$ 4     | 91 $\pm$ 3       | 88 $\pm$ 3      | 80 $\pm$ 2*     |
| <b>MPAP (mm Hg)</b>                  |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 17 $\pm$ 1     | –                | 21 $\pm$ 2      | 21 $\pm$ 2      |
| Group 2 OPCAB (n = 8)                | 17 $\pm$ 1     | 18 $\pm$ 1       | 19 $\pm$ 2      | 17 $\pm$ 1      |
| Group 3 Impella (n = 8)              | 23 $\pm$ 2#    | 23 $\pm$ 1#      | 24 $\pm$ 1      | 25 $\pm$ 1#     |
| Group 4 Sham (n = 8)                 | 18 $\pm$ 1     | 19 $\pm$ 1       | 21 $\pm$ 1      | 19 $\pm$ 1      |
| <b>LAP (mm Hg)</b>                   |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 7 $\pm$ 1      | –                | 5 $\pm$ 1       | 6 $\pm$ 1       |
| Group 2 OPCAB (n = 8)                | 7 $\pm$ 1      | 10 $\pm$ 1*      | 7 $\pm$ 1       | 7 $\pm$ 1       |
| Group 3 Impella (n = 8)              | 9 $\pm$ 1      | 8 $\pm$ 1        | 8 $\pm$ 1       | 9 $\pm$ 0.4     |
| Group 4 Sham (n = 8)                 | 8 $\pm$ 1      | 8 $\pm$ 1        | 8 $\pm$ 1       | 7 $\pm$ 1       |
| <b>CVP (mm Hg)</b>                   |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 6 $\pm$ 1      | –                | 5 $\pm$ 1       | 6 $\pm$ 1       |
| Group 2 OPCAB (n = 8)                | 7 $\pm$ 1      | 8 $\pm$ 1        | 7 $\pm$ 1       | 7 $\pm$ 1       |
| Group 3 Impella (n = 8)              | 10 $\pm$ 1     | 11 $\pm$ 1#      | 9 $\pm$ 1       | 10 $\pm$ 1      |
| Group 4 Sham (n = 8)                 | 7 $\pm$ 1      | 7 $\pm$ 1        | 7 $\pm$ 1       | 7 $\pm$ 1       |
| <b>LVP (mm Hg)</b>                   |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 119 $\pm$ 5    | –                | 120 $\pm$ 6     | 117 $\pm$ 5     |
| Group 2 OPCAB (n = 8)                | 126 $\pm$ 6    | 100 $\pm$ 5*#    | 102 $\pm$ 5*    | 105 $\pm$ 5*    |
| Group 3 Impella (n = 8)              | 113 $\pm$ 3    | 98 $\pm$ 4*#     | 104 $\pm$ 3*    | 107 $\pm$ 3*    |
| Group 4 Sham (n = 8)                 | 121 $\pm$ 4    | 118 $\pm$ 4      | 114 $\pm$ 3     | 115 $\pm$ 4     |
| <b>dp/dt (mmHg/s)</b>                |                |                  |                 |                 |
| Group 1 ECC (n = 8)                  | 2359 $\pm$ 157 | –                | 3574 $\pm$ 409* | 2296 $\pm$ 105  |
| Group 2 OPCAB (n = 8)                | 2519 $\pm$ 296 | 1666 $\pm$ 147*# | 1750 $\pm$ 174* | 2131 $\pm$ 185* |
| Group 3 Impella (n = 8)              | 2433 $\pm$ 117 | 1773 $\pm$ 75*#  | 2173 $\pm$ 154  | 2236 $\pm$ 162  |
| Group 4 Sham (n = 8)                 | 2677 $\pm$ 93  | 2341 $\pm$ 88*   | 2264 $\pm$ 105* | 1937 $\pm$ 69*  |

\*  $p < 0.05$  versus pre surgery myocardial blood flow; #  $p < 0.05$  between groups

## Discussion

In our study, we observed hemodynamic impairment in all treated groups. Most markedly it was seen in the ECC group with the need for vasopressor administration. Hypotension occurred

although increased cardiac output and global left ventricular contractility was present as already described [1]. This observation is related to the well-described inflammatory triggered post perfusion syndrome [14]. In addition, released NO, which is stimulated by the surgical inflammatory response, contributes to the

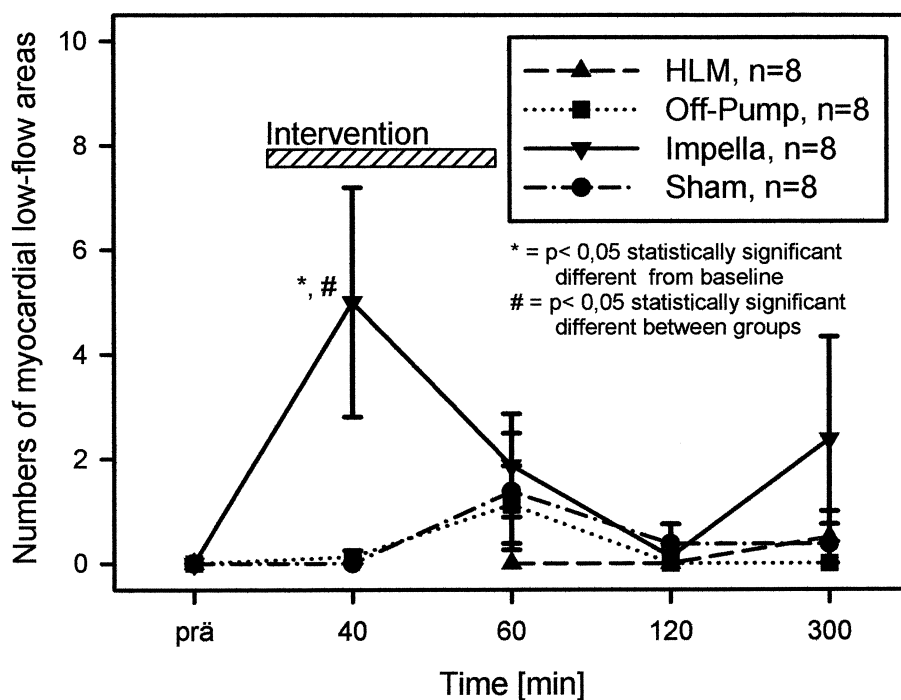


Fig. 2 Number of myocardial low flow areas in pigs before, during 60 minutes surgery, one and four hours after operative myocardial revascularisation performed by cardiopulmonary bypass with cardioplegic arrest (group **ECC** --▲--), off-pump coronary artery bypass grafting (group **OPCAB** ·■·), Impella® elect 100 supported beating heart surgery (group **Impella** —▼—), sham operation (group **Sham** -·●-); values are means  $\pm$  standard error of mean. N gives numbers of animals per group. \* Signifies  $p < 0.05$  versus pre surgery myocardial blood flow and # signifies  $p < 0.05$  between groups.

increase in cardiac output that accompanies the reduced systemic vascular resistance after cardiovascular surgery [15]. Furthermore, hypotension is caused by extracorporeal circulation through generation of serotonin from pump-activated platelets triggered by nitric oxide release [16]. One simple aspect of the negative influence on peripheral resistance could be the cardioplegic solution which is drained into systemic circulation using a two-stage venous cannula [17,18]. Normothermic body temperature during coronary bypass grafting with cardiopulmonary bypass and hypothermic crystalloid cardioplegia is one major factor reducing systemic vascular resistance [18]. In opposition to our findings reduced ventricular contractility was observed in a porcine model of cardiopulmonary bypass without cardioplegia and in a canine model with blood cardioplegia due to myocardial edema [19,20].

During off-pump bypass grafting hemodynamic instability was still tolerated in all animals without inotropic support. Cardiac output altered significantly during revascularisation more markedly than reported previously [3]. In contrast to earlier findings significant but not critical changes in MAP, LVP, LAP, and global left ventricular contractility occurred during surgery [3]. This might be related to the extended duration (60 minutes) of mechanical anterior wall stabilisation. Additionally approximately half of the left ventricle's free anterior was compressed by the stabilisator used. This could be the reason for incomplete and delayed hemodynamic recovery. Previous publications without hemodynamic impairment caused by OPCAB surgery employed much shorter interventions [21]. The idea of a 60-minute interventional period in our model was used to simulate a multivessel procedure and for the concordance of the surgical period in each experimental group.

The use of the Impella® microaxial blood pump for left ventricular support during beating heart myocardial revascularisation achieved ventricular unloading as indicated by the fall in LAP. Re-

cently similar findings were observed in an ovine model for microaxial pump support reducing infarct size [11].

In addition, augmented cardiac output and preserved global left ventricular contractility during and after surgery compared to the OPCAB group in our study were present.

The major finding in our study were the results of regional myocardial perfusion. ECC with cardioplegia in contrast to earlier studies revealed uniform reperfusion after 40 minutes' cardioplegic arrest without signs of microvascular obstruction [22]. As described by other groups transient microvascular obstruction as well as malperfusion after cold crystalloid cardioplegic arrest were not found [22,23].

There was no negative effect on regional myocardial perfusion although hemodynamic alteration occurred during OPCAB surgery. The major reason was the shunt insertion into the LAD's arteriotomy [6]. Reduced ventricular contractility during surgery due to hypoperfusion could therefore be excluded. Surgical trauma results in an inflammatory response contributing to mediator release and myocardial depression after cardiovascular surgery [15]. In support of this conclusion control animals showed decreases in MAP, cardiac output and global left ventricular contractility at the end of the observation period.

Although the microaxial blood pump mitigates hemodynamic alterations, no improvement in regional myocardial perfusion is observed. Even worse, sporadic myocardial low flow was seen. This might be due to microembolies generated by the intracardiac pump. A high pump speed might be able to produce gaseous microembolies by cavitation. In addition the pump caused suction to the ventricular wall during external ventricular compression, thereby also creating cavitation. Inflammatory response to intracardiac pump operation creating cellular microaggregates seems to be less probable, because a reduced inflammatory re-

sponse during and after pump run compared to cardiopulmonary bypass has been reported as indicated by a postoperative release of granulocyte elastase and complement C3a elevation [10]. Embolisation of plaque material can be excluded as an explanation, because no animal showed signs of atherosclerosis at organ removal. Further clinical examinations should be performed to test the hypothesis of the clinical relevance of heterogeneous microvascular obstruction [24]. One clinical limitation could be the lack of coronary artery disease in our model.

In conclusion, the intracardiac microaxial support device augments cardiac output during beating heart myocardial revascularisation in a porcine model but leads to microvascular low flow areas. In contrast, conventional techniques led to mild hemodynamic impairment but did not aggravate microvascular perfusion.

## Acknowledgments

This study was supported by the German Heart Foundation (project number F/13/01). The disposals for cardiopulmonary bypass were donated by Edwards PAS, Wörrstadt, Germany. The Impella elect 100<sup>®</sup> microaxial blood pumps were donated by Impella Cardiosystems, Aachen, Germany. We thank Mr. Mitch Malzahn, Mr. Laszlo Kopacz, and Mrs. Andrea Schollmaier for their excellent technical support.

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