

## Original Articles

# Comparison of Warm Blood Cardioplegia Delivery With or Without the Use of a Roller Pump

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**Abstract:** Various techniques for administration of blood cardioplegia are used worldwide. In this study, the effect of warm blood cardioplegia administration with or without the use of a roller pump on perioperative myocardial injury was studied in patients undergoing coronary artery bypass grafting using minimal extracorporeal circuits (MECCs). Sixty-eight patients undergoing elective coronary bypass surgery with an MECC system were consecutively enrolled and randomized into a pumpless group (PL group: blood cardioplegia administration without roller pump) or roller pump group (RP group: blood cardioplegia administration with roller pump). No statistically significant differences were found between the PL group and RP group regarding release of cardiac biomarkers. Maximum postoperative biomarker values reached at T1 (after arrival intensive care unit) for heart-

type fatty acid binding protein (2.7 [1.5; 6.0] ng/mL PL group vs. 3.2 [1.6; 6.3] ng/mL RP group,  $p = .63$ ) and at T3 (first postoperative day) for troponin T high-sensitive (22.0 [14.5; 29.3] ng/L PL group vs. 21.1 [15.3; 31.6] ng/L RP group,  $p = .91$ ), N-terminal pro-brain natriuretic peptide (2.1 [1.7; 2.9] ng/mL PL group vs. 2.6 [1.6; 3.6] ng/mL RP group,  $p = .48$ ), and C-reactive protein (138 [106; 175]  $\mu\text{g/mL}$  PL group vs. 129 [105; 161]  $\mu\text{g/mL}$  RP group,  $p = .65$ ). Besides this, blood cardioplegia flow, blood cardioplegia line pressure, and aortic root pressure during blood cardioplegia administration were similar between the two groups. Administration of warm blood cardioplegia with or without the use of a roller pump results in similar clinically acceptable myocardial protection. **Keywords:** myocardial protection, coronary artery bypass grafting, warm blood cardioplegia, myocardial injury. *JECT. 2015;47:209–216*

Myocardial protection during on-pump cardiac surgery is used to reduce the negative effect of myocardial ischemia during aortic cross-clamping. Chemical protection of the myocardium can be rapidly achieved by the administration of a potassium-based blood cardioplegia solution into the coronary arteries. High potassium concentration in the myocardium prevents initiation of action potentials and results in diastolic cardiac arrest (1). Cardiac arrest leads to a reduction in myocardial oxygen consumption of approximately 90% and minimizes cellular use of high-energy phosphates (2,3).

In 1992, Calafiore et al. (4) introduced the method of administering warm blood cardioplegia with the use of a roller pump. This method has been used worldwide ever since. However, blood cardioplegia can also be administered without using a roller pump. When no roller pump is used, blood cardioplegia flow is generated by the arterial line pressure, which is created by the arterial centrifugal pump of the cardiopulmonary bypass (CPB) system. This technique is currently applied at some clinical sites. An advantage of this method may be that blood cardioplegia flow is dynamic and there is no risk of aortic root overpressurization. Besides this, the elimination of a roller pump can be a step toward reducing heart–lung machine hardware. As a result, the use of a mini heart–lung machine may become available for future use in cardiac surgery.

Received for publication August 12, 2015; accepted December 9, 2015. Address correspondence to: Mizja M. Faber, Department of Extracorporeal Circulation, St. Antonius Hospital, Koekoekslaan 1, 3435 CM Nieuwegein, The Netherlands. E-mail: mizjafaber@heartbeat5.nl The analysis of biomarkers was funded by Maquet AG.

The aim of this study is to compare the effect of warm blood cardioplegia administration with and without roller pump on perioperative myocardial injury, as reflected by postoperative biomarker release, in patients undergoing coronary artery bypass grafting (CABG) with a minimal extracorporeal circuit (MECC).

## MATERIALS AND METHODS

### Patients

Sixty-eight patients undergoing elective coronary bypass surgery with an MECC system were consecutively enrolled and randomized into a pumpless group (PL group: blood cardioplegia administration without roller pump) or roller pump group (RP group: blood cardioplegia administration with roller pump). Exclusion criteria were the following: previous cardiac surgery, any combined surgical procedures, scheduled surgery with less than three distal anastomoses, left ventricular ejection fraction <45%, chronic renal failure (defined by preoperative creatinine level > 177  $\mu\text{mol/L}$ ), and aortic insufficiency more than or equal to grade 1. The medical ethics committee of the St. Antonius Hospital approved this study and written informed consent was obtained for each patient prior to the surgical procedure.

### Administration of Blood Cardioplegia

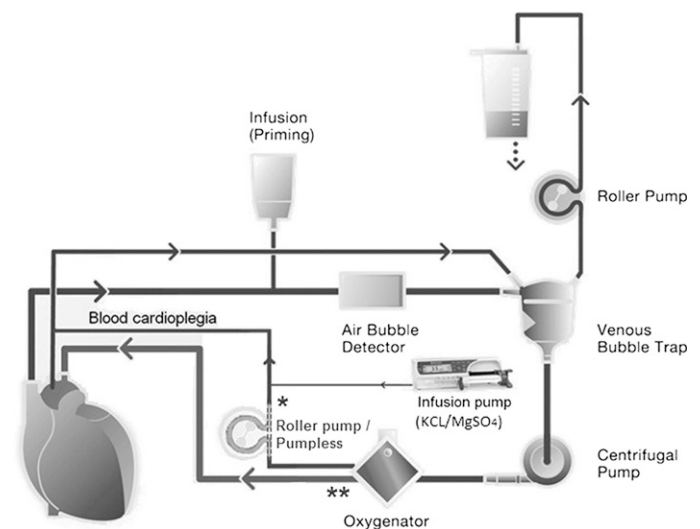
In all patients warm blood cardioplegia (34°C) was administered via the aortic root immediately after aortic cross-clamping. Warm blood cardioplegia consisted of oxygenated blood with added potassium chloride/magnesium sulfate (KCl/MgSO<sub>4</sub>; K<sup>+</sup> 1.7 mmol/mL, Cl<sup>-</sup> 1.7 mmol/mL, Mg<sup>2+</sup> .17 mmol/mL, and SO<sub>4</sub><sup>-</sup> .17 mmol/mL; Pharmacy Catharina Hospital, Eindhoven, The Netherlands). An infusion pump (Alaris® TIVA Syringe Pump, CareFusion, Rolle, Switzerland) was used for the addition of KCl/MgSO<sub>4</sub> in the blood cardioplegia line. Dosage was based on a blood cardioplegia flow of 200 mL/min and adjusted according to the following protocol: the initial dose of KCl/MgSO<sub>4</sub> was 11.4 mmol, the second dose was 6.8 mmol, and subsequent doses were 5.2 mmol. Each dose was given over a period of 2 minutes. Approximately, every 15 minutes the administration of blood cardioplegia was repeated. In case of recurring electrocardiography (ECG) activity, blood cardioplegia was given with aberrant intervals. In both groups, blood cardioplegia flow was measured with an ultrasonic flowmeter (SonoTT Flowmeter, Em-Tec, Finning/Munich, Germany) and aortic root pressure was measured with an 11 Fr. aortic root cannulae with a pressure monitoring tip (DLP®, Medtronic, Minneapolis, MN). Blood cardioplegia line pressure and arterial line pressure during blood cardioplegia delivery were measured in the same way and at the same locations in both groups.

In the PL group blood cardioplegia was delivered using the arterial line pressure, created by the arterial centrifu-

gal pump of the CPB system. Blood cardioplegia flow depended on the difference between arterial line pressure and aortic root pressure. In some cases, it was difficult to achieve an adequate blood cardioplegia flow if the arterial line pressure of the CPB system was not high enough and even negative flow could occur in the cardioplegia line. For instance, at the start of the initial dose, the heart is not yet in electromechanical arrest. As soon as the aortic clamp is placed on the aorta, the heart is still able to create output if not emptied properly. In that case, a partial clamp was temporarily placed on the arterial line. In exceptional cases, the use of a partial clamp caused a decreased patients' systemic arterial pressure and the revolutions per minute of the arterial centrifugal pump needed to be increased. In the RP group, blood cardioplegia was delivered using a roller pump. The blood cardioplegia flow was given at 200 mL/min. Figure 1 shows an overview of the used MECC system and the two blood cardioplegia administration techniques.

### CPB, Anesthesia, and Intensive Care Unit (ICU) Protocol

The closed loop MECC system, controlled by a HL30 heart-lung machine (Maquet, Hirrlingen, Germany) consisted of a tip-to-tip heparin-coated tubing system (Bioline; Maquet). A venous bubble trap (VBT; Maquet) was integrated in the venous line. Blood flow was created with a centrifugal pump (Rotaflow, Maquet) and blood was oxygenated by an oxygenator (Quadrox-i, Maquet). The MECC system was primed with approximately 650 mL priming solution in both groups. Priming solution was prepared by adding 500 mL of Haes 6% (Voluven, Fresenius Kabi, 's-Hertogenbosch, The Netherlands) into 1 L of priming solution for artificial heart (acetate: 34 mmol/L; Na<sup>+</sup>:



**Figure 1.** Overview of a minimal extracorporeal circuit system. RP group: blood cardioplegia administration with roller pump. PL group: blood cardioplegia administration without roller pump. \*Blood cardioplegia line pressure measurement. \*\*Arterial line pressure measurement.

137 mmol/L;  $K^+$ : 4.0 mmol/L;  $Mg^{2+}$ : 1.5 mmol/L; and  $Cl^-$ : 110.0 mmol/L; Pharmacy Catharina Hospital).

Anesthesia was induced by intravenous injection of midazolam (.05–.1 mg/kg) in combination with fentanyl (10–20  $\mu$ g/kg), propofol (1–2 mg/kg), and pancuronium (.1 mg/kg). Anesthesia was maintained by continuous infusion with propofol (2–4 mg/kg/h) and remifentanyl (5–10  $\mu$ g/kg/h). Heparin was administered at 150 IU/kg.

During CPB the nasopharyngeal temperature was kept at 34°C. During CPB the cardiac index was maintained at 2.4 L/min/m<sup>2</sup>. Mean blood pressure was maintained between 40 and 80 mmHg. Heparin was neutralized with protamine sulfate at a 1:1 ratio.

All patients received standardized postoperative care. Propofol was stopped and tracheal extubation was accomplished when a patient met the following conditions: stable hemodynamics (mean arterial pressure 65–80 mmHg), responsive and cooperative,  $F_iO_2 < 40\%$ ,  $p_aO_2 > 80$  mmHg,  $p_aCO_2$  35–45 mmHg, pH 7.35–7.45, core temperature  $> 36.5^\circ C$ , chest tube drainage  $< 50$  mL/h. Postoperative pain relief was achieved by administration of acetaminophen and morphine.

### Blood Sample Collection and Analyses

Blood was collected in EDTA (ethylenediaminetetraacetic acid) tubes (6 mL) at baseline after induction of anesthesia (T0), after arrival at the ICU (T1), 4 hours in ICU (T2), and at the first postoperative day (T3). Blood samples were fractionated by centrifuging 1500–2000  $\times g$  for 15 minutes. Plasma was collected and stored at  $-80^\circ C$  until analysis. The following biomarkers were analyzed: Troponin T high sensitive (TnT-hs), heart-type fatty acid binding protein (hFABP), N-terminal pro-brain natriuretic peptide (NT-pro-BNP), and C-reactive protein (CRP).

TnT-hs was determined by means of a solid-phase enzyme-linked immunosorbent assay (ELISA), with capture and biotin labeled tracer antibody (Hytest, Turku, Finland). Substrate consisted of luminol in Tris buffer containing 4-iodophenol and sodium perborate. Luminescence in a white maxisorp plate (Nunc) was measured with a 96 wells plate luminometer (Tecan Mannedorf, Switzerland). The TnT-hs standard (Hytest) ranged from 200 to 0 pg/mL. The assay detection limit was 10 pg/mL.

hFABP was determined by means of a solid-phase ELISA, with capture and peroxidase labeled tracer antibody (Hytest). The oxidase converts phenyldiamine dihydrochloride to a yellow color, which is proportional to the concentration of hFABP. The color was measured at 490 nm by a microtiter plate reader (Powerwave 200, Bio-Tek Instruments, Winoosky, VT). The assay detection limit was 49 pg/mL.

NT-pro-BNP was determined by means of a solid-phase ELISA, with capture and peroxidase labeled tracer antibody (Hytest). The oxidase converts phenyldiamine

dihydrochloride to a yellow color, which is proportional to the concentration of NT-pro-BNP. The color was measured at 490 nm by a microtiter plate reader (Powerwave 200, Bio-Tek Instruments). The assay detection limit was .6 ng/mL.

A high sensitive CRP ELISA (Dakopatts, Glostrup, Denmark) and coating antibody rabbit antihuman CRP (DAKO A0073, horseradish peroxidase-labeled anti-CRP detection antibody DAKO P0227) was used. The assay detection limit was 1.6  $\mu$ g/mL.

### Statistical Analysis

As proxy for myocardial cell injury, the maximum value of TnT-hs at T1, T2, or T3 was used as the primary end point, assuming the primary end point to be nearly normally distributed in this population (as to not violate the Student's *t* test conditions) and assuming the standard deviation to be half the size of the mean. Setting the alpha at 5% and the power at 90%, 34 patients in each group would have a minimal detectable difference of 80% of the standard deviation.

Post hoc we decided to analyze the data using nonparametric statistical hypothesis testing using the Mann–Whitney test due to the right skewness of the data. Consequently, we report medians and interquartile ranges (IQRs) for the biomarker data. Of note, we also performed Student's *t* tests and Cox proportional hazards method to calculate the *p* values and found no qualitative discrepancies with the reported *p* values (data not shown).

Standard statistical hypothesis testing was performed on the baseline characteristics for the sole purpose of a measure of precision, not as a hypothesis test.

## RESULTS

### Patient Characteristics

Between September 2012 and March 2013, 68 patients were included in this study and randomized to the RP group or PL group. Table 1 presents the demographic, intraoperative and surgical characteristics of the study population. Patient groups were similar with respect to gender, age, body surface area, body mass index, and comorbidities (hypertension, angina pectoris, chronic obstructive pulmonary disease, arrhythmias, and left ventricular function). In both groups more men than women participated in the study (94.1% males in PL group and 76.5% males in RP group,  $p = .09$ ). Regarding intraoperative and surgical characteristics, no differences were present between the two groups for number of distal anastomoses, CPB time, and aortic occlusion time.

### Blood Cardioplegia Characteristics

Blood cardioplegia characteristics are summarized in Table 2. Administration of blood cardioplegia in the RP

**Table 1.** Demographic, intraoperative and surgical data.

	PL Group (n = 34)	RP Group (n = 34)	p Value
Gender (number of male)	32 (94.1%)	26 (76.5%)	.0869
Age (years)	65.9 (11.0)	66.2 (11.3)	.9138
BSA (kg/m <sup>2</sup> )	2.03 (.18)	2.00 (.20)	.4675
BMI (m <sup>2</sup> )	27.9 (3.1)	28.1 (3.8)	.8122
Comorbidities			
Hypertension	20 (58.8%)	26 (76.5%)	.1949
Angina pectoris	31 (91.2%)	30 (88.2%)	1.0000
Chronic obstructive pulmonary disease	6 (17.6%)	4 (11.8%)	.7320
Arrhythmias	7 (20.6%)	2 (5.9%)	.1497
Left ventricular function (fair)	6 (17.6%)	3 (8.8%)	.4763
Cardiopulmonary bypass time (minutes)	92 (22)	95 (23)	.5763
Aortic occlusion time (minutes)	63 (17)	63 (18)	.9118
Number of distal anastomoses			.8948
3	11 (32.4%)	9 (26.5%)	
4	15 (44.1%)	14 (41.1%)	
5	6 (17.6%)	9 (26.5%)	
6	2 (5.9%)	2 (5.9%)	

Data represents mean (SD) or *n* (%).

BSA, body surface area; BMI, body mass index.

**Table 2.** Blood cardioplegia characteristics.

	PL Group (n = 34)	RP Group (n = 34)	p Value (t Test)
Mean blood cardioplegia flow (mL/min)	202 (37)	200 (10)	.7181
Initial dose blood cardioplegia flow (mL/min)	187 (55)	199 (3)	.1994
Mean blood cardioplegia line pressure (mmHg)	125 (19)	134 (21)	.0690
Initial dose blood cardioplegia line pressure (mmHg)	127 (33)	141 (25)	.0530
Mean aortic root pressure (mmHg)	52 (13)	59 (15)	.0685
Initial dose aortic root pressure (mmHg)	57 (17)	64 (23)	.1194
Mean arterial line pressure (mmHg)	127 (16)	116 (16)	.0056*
Initial dose arterial line pressure (mmHg)	130 (31)	113 (16)	.0085*
Number of blood cardioplegia doses			.8822
2	7 (20.6%)	4 (11.8%)	
3	16 (47.1%)	18 (52.9%)	
4	6 (17.6%)	8 (23.6%)	
5	4 (11.8%)	3 (8.8%)	
6	1 (2.9%)	1 (2.9%)	
Total dose of KCl/MgSO <sub>4</sub> (mL)	16.4 (4.2)	15.7 (3.1)	.4560

Data represents mean (SD) or *n* (%).

\*Significantly different between both groups (*p* < .05).

**Table 3.** Peroperative ECG activity, ECG deviations and defibrillations.

	PL Group (n = 34)	RP Group (n = 34)	p Value (t Test)
ECG activity during aortic occlusion period	10 (29%)	5 (15%)	.2421
ECG deviations after aortic clamp removal	6 (18%)	3 (9%)	.4763
Number of defibrillations after aortic clamp removal			.5101
0	27 (79%)	30 (88%)	
1	7 (21%)	4 (12%)	

Data represents *n* (%).

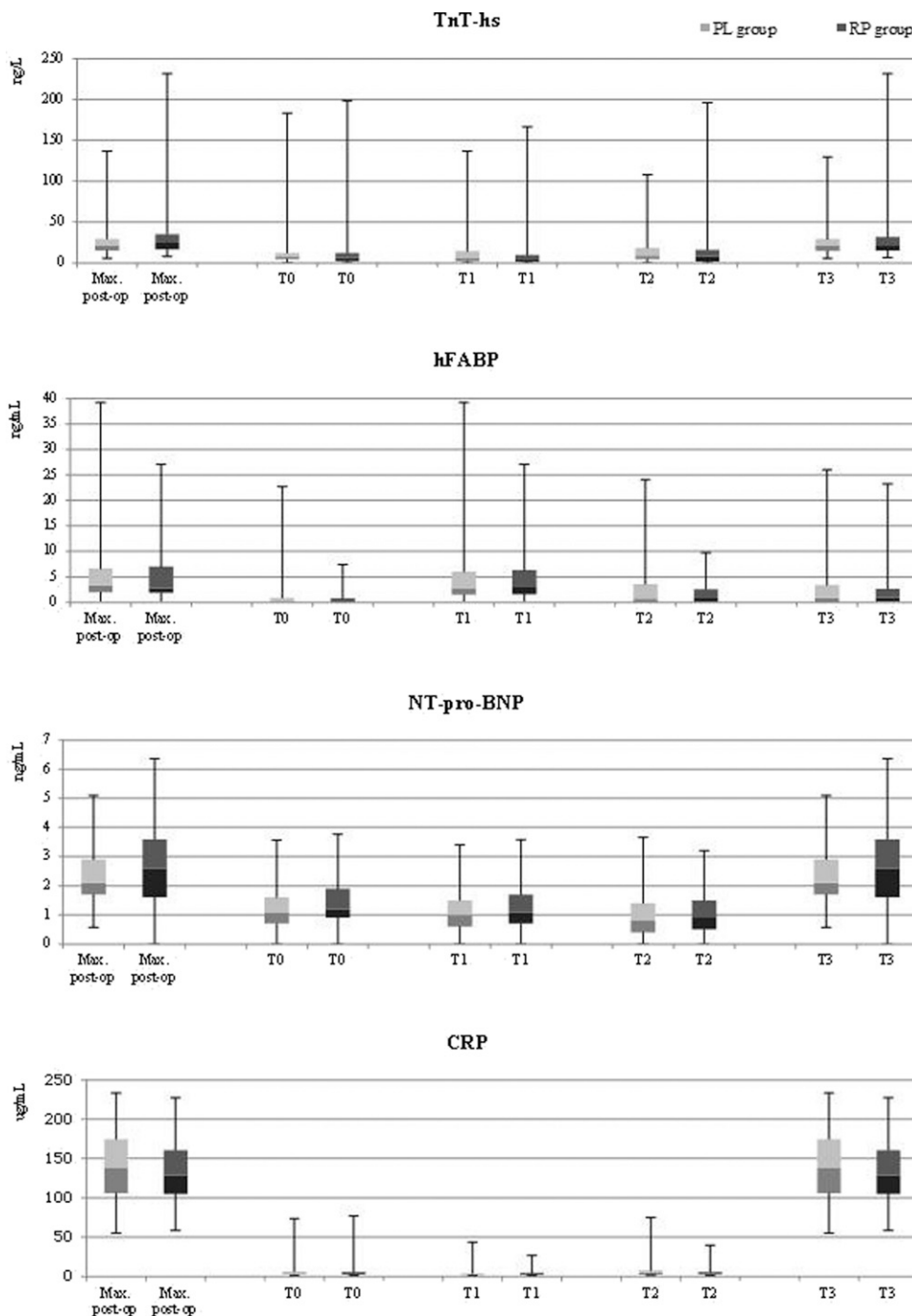
ECG, electrocardiography.

group resulted in a mean blood cardioplegia flow of 202 ± 37 mL/min, which was equal to the blood cardioplegia flow in the RP group 200 ± 10 mL/min (*p* = .72). However, a large variation was shown in the PL group with regard to

blood cardioplegia flow during the initial blood cardioplegia dose compared to the RP group (initial dose blood cardioplegia flow 187 mL/min ± 55 vs. 199 mL/min ± 3, *p* = .20). Patients in the PL group had a significantly

higher arterial line pressure during blood cardioplegia delivery compared to the RP group ( $127 \pm 16$  mmHg vs.  $116 \pm 16$  mmHg,  $p < .01$ ). No differences were found in blood cardioplegia line pressure (mmHg) and aortic root pressure (mmHg) between both groups. ECG activity during aortic occlusion period, ECG deviations after aortic clamp removal and the necessity of defibrillation after aortic clamp removal were more common in the PL group

than in the RP group (29% vs. 15%, 18% vs. 9%, and 21% vs. 12%, respectively) but this was not significantly different (Table 3). After the initial dose of blood cardioplegia, hemoglobin in the PL group was  $10.0 \pm 1.5$  g/dL and in RP group  $10.1 \pm 1.5$  g/dL ( $p = .57$ ). Right before the aortic clamp was removed, hemoglobin was  $9.8 \pm 1.5$  g/dL in the PL group and  $9.7 \pm 1.3$  g/dL in the RP group ( $p = .48$ ), potassium blood concentrations were



**Figure 2.** Plasma levels of cardiac biomarker release: preoperative and postoperative. Minimum, 25th percentile, medium, 75th percentile, and maximum are shown as T0 (baseline), T1 (after arrival intensive care unit [ICU]), T2 (4 hours in ICU), and T3 (first day postoperative), respectively.



5.1 ± .5 mmol/L in PL group and 5.0 ± .4 mmol/L in RP group ( $p = .82$ ).

### Biomarkers

Perioperative plasma levels of cardiac biomarkers are shown in Figure 1. Baseline median (IQR) plasma levels of TnT-hs and hFABP were not elevated in patients in the PL group and RP group (TnT: 8.2 [4.7; 12.5] ng/L vs. 6.6 [2.3; 12.5] ng/L,  $p = .45$ , hFABP: .0 [.0; .9] ng/mL vs. .0 [.0; .8] ng/mL,  $p = .77$ ). Maximum postoperative cardiac biomarker values were equal in both groups and were reached at T1 (after arrival ICU) for hFABP (2.7 [1.5; 6.0] ng/mL PL group vs. 3.2 [1.6; 6.3] ng/mL RP group,  $p = .63$ ) and at T3 (first postoperative day) for TnT-hs (22.0 [14.5; 29.3] ng/L PL group vs. 21.1 [15.3; 31.6] ng/L RP group,  $p = .91$ ). Similarly, no differences were found for NT-pro-BNP and CRP levels. Postoperative NT-pro-BNP and CRP levels were highest on the first postoperative day (NT-pro-BNP: PL group 2.1 [1.7; 2.9] ng/mL and RP group 2.6 [1.6; 3.6] ng/mL,  $p = .48$ ; CRP: PL group 138 [106; 175] µg/mL and RP group 129 [105; 161] µg/mL,  $p = .65$ ). At all time points, no differences were found between the two groups concerning release of TnT-hs, hFABP, NT-pro-BNP, and CRP (Figure 2).

### Postoperative Data

Clinical outcomes demonstrated no statistically significant differences between the two groups regarding use of inotropic support, postoperative myocardial infarction, and postoperative complications (transient ischemic attack/cerebrovascular accident [TIA/CVA], pneumonia, renal failure, rethoracotomy, and atrial fibrillation) (Table 4). One patient in the PL group had a postoperative myocardial infarction, which was caused by graft failure. Atrial fibrillation occurred equally in both groups, 35.3% in the PL group and 20.6% in the RP group ( $p = .28$ ). Length of ICU stay and hospital stay were similar between the PL group and RP group (19.5 [16.1; 20.5] hours vs. 19.8 [16.1; 20.0] hours and 7.0 [7.0; 10.0] days vs. 8.0 [7.0; 9.8] days, respectively).

### DISCUSSION

The results of this randomized controlled trial showed that the administration of blood cardioplegia with or without roller pump had no effect on the release of TnT-hs, hFABP, NT-pro-BNP, and CRP in patients undergoing CABG with an MECC. Moreover, no differences were found between the two groups regarding blood cardioplegia flow, blood cardioplegia line pressure, and aortic root pressure during blood cardioplegia administration. So, both blood cardioplegia methods, with and without roller pump, safely protects against perioperative myocardial injury in patients undergoing CABG with MECC.

A variety of techniques to administer cardioplegia are available. For example, cardioplegia may be administered by using a medical infusion bag with or without aid of a pressure chamber. However, cardioplegia flow induced with the use of a roller pump is considered standard care in hospitals all over the world. Used to a much lesser extent is the induction of cardioplegia flow using the arterial line pressure of the CPB system as the driving force. Grover et al. (5) investigated the difference between administration of cardioplegia by pressurized bag and roller pump technique in 14 dogs. In their study, cold cardioplegia was used every 20 minutes for a 2-hour period. No significant differences were found in myocardial blood flow, metabolism, and left ventricular function between both groups. Yao et al. (6) performed a randomized controlled trial of 35 patients to investigate optimal blood cardioplegia flow rates and hemoglobin concentrations on myocardial metabolic and functional recovery. They concluded that continuous normothermic cardioplegia must be delivered at a minimum of 80 mL/min, with a hemoglobin concentration of at least 8.0 g/dL. Roa et al. (7) reported in a human clinical trial that a total flow rate of 200 mL/min is required when using retrograde cardioplegia with simultaneous antegrade infusion into the vein graft. No consensus concerning required blood cardioplegia flow exists in current literature. Several studies on the optimal infusion pressure

**Table 4.** Postoperative data.

	PL Group (n = 34)	RP Group (n = 34)	p Value
Inotropic support (hours)	.0 (.0; .0)	.0 (.0; .0)	.2977
Postoperative myocardial infarction	1 (2.9%)	0 (.0%)	1.0000
Postoperative complications			
TIA/CVA	1 (2.9%)	0 (.0%)	1.0000
Pneumonia	3 (8.8%)	2 (5.9%)	1.0000
Renal failure (creatinine level > 177 µmol/L)	0 (.0%)	0 (.0%)	NA
Rethoracotomy	1 (2.9%)	1 (2.9%)	1.0000
Atrial fibrillation	12 (35.3%)	7 (20.6%)	.2797
Length of ICU stay (hours)	19.5 (16.1; 20.5)	19.8 (16.1; 20.0)	.7386
Length of hospital stay (days)	7.0 (7.0; 10.0)	8.0 (7.0; 9.8)	.4018

Data represents median (25th percentile; 75th percentile) or n (%).  
NA, nonavailable; ICU, intensive care unit.

of cardioplegia showed that high cardioplegia infusion pressures result in more rapid cooling, faster cardiac arrest, and increased flow distal to coronary stenosis (5,8,9). An aortic root pressure during cardioplegia delivery within the autoregulation range of blood pressure (60–100 mmHg) would be the most optimal pressure to stay within physiological ranges (10). In our study, blood cardioplegia flow and blood cardioplegia pressure have been studied in and between the two groups. Mean blood cardioplegia flow was  $202 \pm 37$  mL/min in the PL group and  $200 \pm 10$  mL/min in the RP group resulting in a mean aortic root pressure of  $52 \pm 13$  mmHg and  $59 \pm 15$  mmHg, respectively. These aortic root pressures were just below the autoregulation range.

In our study, no difference was found in biomarker release between patients with and without use of a roller pump for cardioplegia administration. Median plasma levels of TnT-hs, a traditional myocardial necrosis marker, were normal preoperatively. Myocardial infarction related to CABG is defined by the elevation of cardiac biomarker values ( $>10 \times 99$ th percentile) in patients with normal baseline TnT-hs values ( $<14$  ng/L) (11). In both groups median plasma levels of TnT-hs were slightly increased postoperatively. These results lead to the conclusion that perioperative myocardial protection was equally effective in both groups. Another marker for perioperative myocardial damage is hFABP. This biomarker is a rapid marker of myocardial damage and peaks earlier than CK-MB or TnT-hs. Normal ranges reported for hFABP in plasma and serum depend on the used assay and method. Values between .0 and 5 ng/mL are considered normal (12). The hFABP data support the results we obtained with the TnT-hs and also demonstrate that both groups were equally protected for myocardial injury. On the first postoperative day, both NT-pro-BNP and CRP showed increased values compared with previous time points. This increase corresponds to values obtained in other studies performed in CABG patients (13–20). NT-pro-BNP is a marker for heart failure. CRP is an acute phase protein, and an increased CRP level is an independent predictor of adverse outcomes in patients with acute or chronic heart failure. The normal value considered for NT-pro-BNP is .01–.3 ng/mL and for CRP is  $<10$   $\mu$ g/mL (21).

No differences were demonstrated for blood cardioplegia flow, blood cardioplegia line pressure, aortic root pressure, and administered KCl/MgSO<sub>4</sub> concentrations between both groups. Also, no differences were found in postoperative biomarker release. Therefore, both blood cardioplegia administration techniques can be considered equally effective in perioperative myocardial protection during CABG with MECC. Although blood cardioplegia characteristics were similar in both groups, the implementation of blood cardioplegia administration without using a roller pump has practical consequences. Blood cardio-

plegia administration with roller pump seems easier to handle compared to administration without roller pump. A roller pump can easily be regulated to a desired level of flow. Although one has to be careful to avoid exceedingly high aortic root pressures, because of possible mechanical damage, rupture of plaques and calcifications in the aorta and the risk of tissue edema. With the technique without roller pump, there is no risk of developing excessive aortic root pressures. This is a major advantage of the pumpless technique.

Blood cardioplegia flow created without a roller pump may be influenced by several static and dynamic factors. Static factors consist of CPB circuit hardware (tubing diameter, luer locks, aortic cannula, and aortic root cannula). In our study, we found larger variations in blood cardioplegia flow in the PL group compared to the RP group. This may be explained by the expected dynamic flow of the technique without roller pump. Besides the static factors, dynamic factors consist of the driving force of blood cardioplegia flow, which is dependent on the pressure difference between the arterial line and the aortic root. In some cases, a partial clamp was temporarily placed on the arterial line, as described in the method section. This intervention may explain the significantly higher arterial line pressure during the initial dose of blood cardioplegia delivery in the PL group compared with the RP group ( $130 \pm 31$  mmHg vs.  $113 \pm 16$  mmHg). During blood cardioplegia administration without roller pump, the manual adjustment of the KCl/MgSO<sub>4</sub> concentration to the resulting blood cardioplegia flow was not convenient due to the complexity of applying initial administration. This may be considered a disadvantage of the pumpless technique.

Delivering blood cardioplegia without using a roller pump is feasible and safe. The heart is arrested with adequate myocardial protection. Optimization of this technique is one of the directions for future research. Exclusion of a roller pump could be a step forward toward the development of a mini heart–lung machine. An important condition for using the technique without roller pump is that the heart is as empty as possible, to minimize output before the aortic clamp is placed. The addition of adenosine to the first blood cardioplegia dose may induce a quick myocardial arrest avoiding output (22). This can make the technique without roller pump more convenient and should be investigated further.

Our study was limited by the fact that the perfusionist was not blinded, which could not be avoided since the perfusionist applied the cardioplegia technique. A second limitation is that the blood cardioplegia flow and blood cardioplegia pressures during blood cardioplegia delivery are measured at fixed moments instead of continuously. This was due to practical reasons and may have had influence on the outcome measurements.

## CONCLUSION

This randomized controlled trial demonstrated that administration of warm blood cardioplegia with and without roller pump resulted in equal blood cardioplegia delivery flows and pressures, which led to similar myocardial protection. Blood cardioplegia delivery with and without the use of a roller pump safely protects against perioperative myocardial injury in patients undergoing CABG with an MECC.

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