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A New PRECiSe (Priming Reduced Extracorporeal Circulation Setup) Minimizes the Need for Blood Transfusions: First Clinical Results in Coronary Artery Bypass Grafting

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ABSTRACT

Hemodilution by the crystalloid priming volume of standard heart-lung machines in cardiac surgery is associated with impaired organ function and increased blood transfusion requirements. The aim of this study was to evaluate the effect of the use of the newly developed priming reduced extracorporeal circulation setup (PRECiSe) on perioperative hemodilution and transfusion requirements. In a matched prospective study, 40 patients who underwent operations with the PRECiSe in elective primary coronary artery bypass surgery were compared with 40 patients who underwent operations with the standard heart-lung machine. A significant reduction in final priming volume resulted in a significantly reduced degree of hemodilution and transfusion requirements during and after extracorporeal circulation. In the PRECiSe group, only 10% of the patients needed transfusions during their hospital stay, whereas 35% of the patients in the control group required any transfusion ($P < .05$). The average transfusion per patient was 0.16 units in the PRECiSe group and 1.25 units in the control group ($P < .05$). The PRECiSe was demonstrated to be safe and effective in coronary artery bypass surgery with respect to transfusion requirements and hemodilution, as well as with regard to patient safety, as represented by perioperative myocardial performance.

INTRODUCTION

Although off-pump coronary artery bypass grafting (OPCAB) was introduced into clinics several years ago [Benetti 1991], these procedures have not found general application in coronary artery bypass surgery because of cases of hemodynamic instability during revascularization of posterior wall vessels [Beholz 2002]. Furthermore, the long-term results compared with the gold standard of coronary revascularization, as represented by the use of extracorporeal circulation (ECC) and cardioplegic heart arrest, are yet unknown. Additionally, reimbursement strategies have limited their application in clinical practice. In Germany, the use of OPCAB strategies is limited to 5% to 7% of patients [Kalmar 2003].

Some of the adverse effects of ECC have been overcome through the introduction of several low-priming systems into clinical practice in the last 5 years. Most of these systems are configured as a closed loop consisting of a centrifugal pump, membrane oxygenator, and filter connected with tubing, with the drive unit positioned beside the patient as in regular cardiopulmonary bypass (CPB). These systems, originally designed for assisted circulation in beating-heart surgery, usually do not provide decompression of the heart to enable revascularization of the posterior wall in an appropriate fashion. The use of these systems is associated with substantial losses of blood because they do not provide suction or cardiac-decompression systems. Hence, their use is limited to closed heart surgery as isolated coronary artery bypass grafting (CABG).

With the priming reduced extracorporeal circulation setup (PRECiSe), we developed a new low-priming system incorporating the new DeltaStream diagonal pump (Medos AG, Stolberg, Germany) [Beholz 2003b]. This system provides all of the features of regular CPB and enables full revascularization as well as open heart procedures in a safe and simple fashion [Beholz 2003a]. The purpose of this prospective matched study was to investigate the effect of using the PRECiSe system in isolated elective CABG surgery on perioperative hemodilution and the need for the transfusion of blood products.

MATERIALS AND METHODS

Eighty patients with coronary artery disease who were designated for isolated CABG surgery were included in the study (Table 1). Forty patients underwent operations with the PRECiSe system (PRECiSe group), and 40 patients under-

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Table 1. Inclusion and Exclusion Criteria

Inclusion criteria
- Elective primary isolated coronary artery bypass grafting surgery
- Age >18 y

Exclusion criteria
- Prior cardiac operations with opening of the pericardium or other diseases with suspected pericardial adhesions
- Preoperative circulatory instability or a need for inotropics or mechanical circulatory assistance
- Myocardial infarction within 14 d
- Patent foramen ovale
- Blood disorders

went operations with standard CPB (control group). The patients were matched to the 2 groups with respect to age, sex, and left ventricular ejection fraction. All patients gave written informed consent to participate in the study according to our protocol for clinical studies and to the principles of good clinical practice [Beholz 2003c].

The system used in the PRECiSe group has been described in detail [Beholz 2003b]. This system basically consists of a closed loop of extremely short lengths of tubing connected with standard cannulae and the following CE-labeled components:

- Diagonal pump (DeltaStream; Medos AG),
- Membrane oxygenator (Hilite 7000; Medos AG),
- Arterial filter (Quart; Jostra AG, Hirrlingen, Germany).

Parallel to this closed loop, a hard-shelled reservoir is connected to the inlet and outlet of the diagonal pump to maintain quick cardiac decompression and to enable the use of suction and vents to reduce blood loss during surgery. The system is primed and deaired with crystalloid solution, and autologous priming is maintained, depending on the hemodynamics. Only the amount of priming delivered to the patient is registered as the final priming volume.

In the control group, the standard ECC setup consisted of the same components except for the pump. In these patients, the Jostra Rotaflow was used. Priming consisted of 1500 mL of modified crystalloid priming, and an additional 2.5 million units of aprotinin were added. No autologous priming was used in this group because such priming is not part of our routine perfusion protocol.

Activated clotting times in both groups were held in the range between 450 and 500 seconds during ECC. After termination of ECC and the removal of the cannula, full reversal with protamine was performed. In both groups, perfusion was maintained with a mean flow rate of 2.4 to 2.8 L/min per m^2 with a temperature range of 35°C to 36°C. During ECC, volume management was performed in cases of standard CPB by flow control and, if necessary, by small amounts of vasopressors (noradrenaline). To achieve adequate flow in the PRECiSe group, we added small amounts of fluid to the circulation from the reservoir to prevent the inferior vena cava from collapsing around the venous return cannula and to avoid the danger of air entrapment.

Warm antegrade blood cardioplegia was intermittently applied to the aortic root [Calafiore 1995] in both groups.

Table 2. Patient Characteristics in the Control and PRECiSe Groups*

	PRECiSe (n = 40)	Control (n = 40)	*P*
Age, y	64.9 ± 7.9	63.6 ± 7.8	NS
Male/female sex, n	28/12	28/12	NS
Left ventricular ejection fraction, %	60.4 ± 13.1	60.2 ± 13.9	NS
Body surface area, m^2	1.92 ± 0.20	1.94 ± 0.21	NS
Extracorporeal circulation time, min	64.2 ± 17.3	69.4 ± 15.8	NS
Cross-clamping time, min	37.3 ± 12.1	42.6 ± 16.4	NS
No. of distal anastomoses	3.1 ± 0.8	3.2 ± 1.1	NS
Use of left internal thoracic artery, %	100	100	NS
Q-wave myocardial infarction, n	0	0	NS
Predicted mortality, %	1.57	1.53	NS
Observed mortality, %	0	0	NS

*Data are presented as the mean ± SD where appropriate. PRECiSe indicates priming reduced extracorporeal circulation setup; NS, not statistically significant.

Preoperative, intraoperative, and postoperative substitution of volume was performed with crystalloid solution or 6% hydroxyethyl starch. One unit of packed red blood cells was given if the patient's hematocrit dropped below the following levels:

- 25% after institution of anesthesia,
- 20% during ECC,
- 25% in the first 24 hours,
- 28% before discharge from the hospital.

Before additional units of packed red blood cells were administered, a new investigation of the red blood cell count was performed, and the same transfusion criteria were applied.

Fluid management during the institution of anesthesia, CPB, and the first 2 postoperative days included monitoring fluid balances, crystalloid and colloidal substitution, and transfusions of blood components, as well as the final priming as described above.

Hematocrits and creatine kinase (CK) and CK MB isoenzyme (CK-MB) levels were obtained preoperatively, after the institution of anesthesia, after the beginning and the end of ECC, at the end of the operation, at 6, 24, and 48 hours after the end of operation, and at discharge. Predicted mortality was calculated by the use of the logistic EuroSCORE [Roques 1999].

Data are expressed as the mean ± SD. The Mann-Whitney *U* test was used for statistical analysis. A *P* value less than .05 was considered statistically significant.

RESULTS

The course of perfusion was uneventful in all patients in both groups. In addition to the matching criteria of age, sex, and left ventricular ejection fraction, both groups were comparable with respect to body surface area, time of perfusion and ischemia, completeness of revascularization, and the frequency of use of the left internal thoracic artery for the left anterior descending artery (Table 2). There were no myocardial infarctions or major adverse events, and the observed mortality in the 2 groups was below the mortality predicted according to the logistic EuroSCORE.

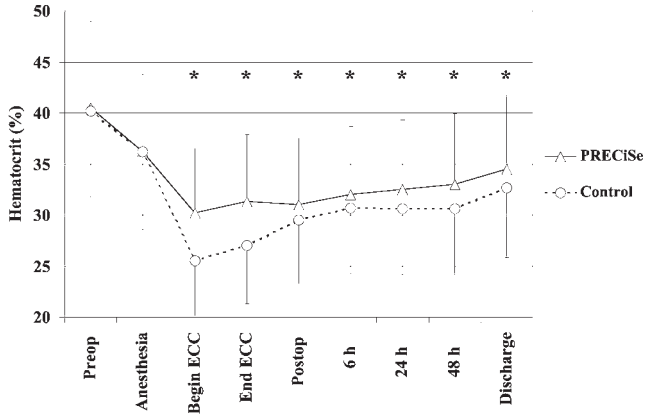

Figure 1. Perioperative course of hematocrit (mean ± SD; *P < .05). PRECiSe indicates priming reduced extracorporeal circulation setup; Preop, preoperative; ECC, extracorporeal circulation; Postop, postoperative.

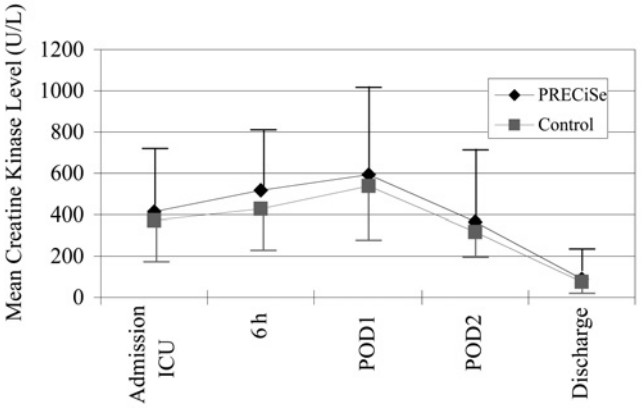

Figure 3. Course of perioperative creatine kinase level (mean ± SD). PRECiSe indicates priming reduced extracorporeal circulation setup; ICU, intensive care unit; POD1, postoperative day 1.

The final priming volume applied per patient was 1506.3 ± 58.5 mL in the control group and 257.1 ± 146.5 mL in the PRECiSe group (P < .05). Similar preoperative hematocrits in the PRECiSe group (40.5% ± 3.5%) and the control group (40.2% ± 2.8%) were followed by drops in both groups at the beginning of ECC (Figure 1). The hematocrits in the control group were significantly lower than in the PRECiSe group during ECC and remained significantly reduced until patient discharge.

The frequency of freedom from red blood cell transfusion during the hospital stay was 65% in the control group and 90% in the PRECiSe group. In the PRECiSe group, 1 patient received 1 unit intraoperatively, and 3 patients received 1 to 2 units postoperatively. In contrast, 8 patients in the control group received 1 to 3 units of red blood cells intraoperatively (P < .05), and 7 patients received 2 to 6 units postoperatively (P < .05) (Figure 2). There were no transfusions of fresh frozen plasma or platelets in the 2 groups. The mean volume lost through the chest tube was 373 ± 119 mL in the PRECiSe group and 501 ± 272 mL in the control group (P < .01).

There was no significant difference in the perioperative courses of CK or CK-MB levels (Figures 3 and 4).

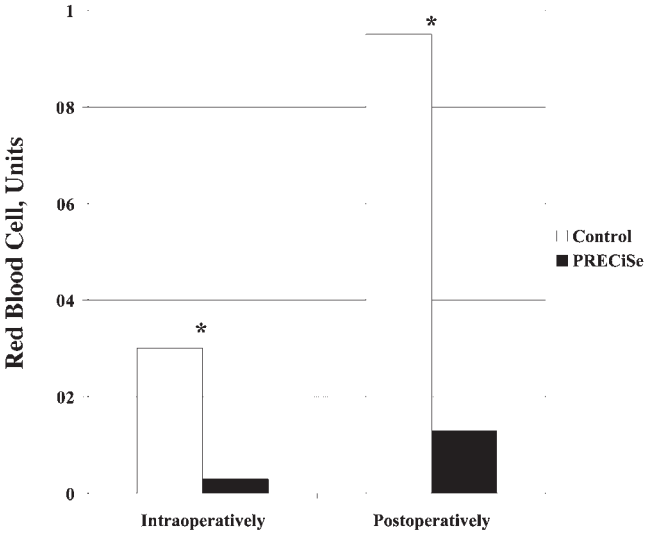

Figure 2. Units of red blood cells transfused intraoperatively and postoperatively (mean ± SD; *P < .05). PRECiSe indicates priming reduced extracorporeal circulation setup.

DISCUSSION

After the introduction of CPB into clinics by Gibbon in the early 1950s [Gibbon 1954], ECC became rapidly available for open heart procedures. The need for foreign blood for the priming volume was reduced when crystalloid priming became the standard in adult cardiac surgery [Gravlee 2000]. Because crystalloid priming of 1.5 to 2.5 L is delivered to the patient at the beginning of ECC, CPB nowadays is associated with significant hemodilution. In normothermic as well as hypothermic settings, this hemodilution may be associated with adverse effects, such as the impairment of liver metabolic function [Nollert 2001] and renal function [Swaminathan 2003]. Low hematocrit levels during ECC

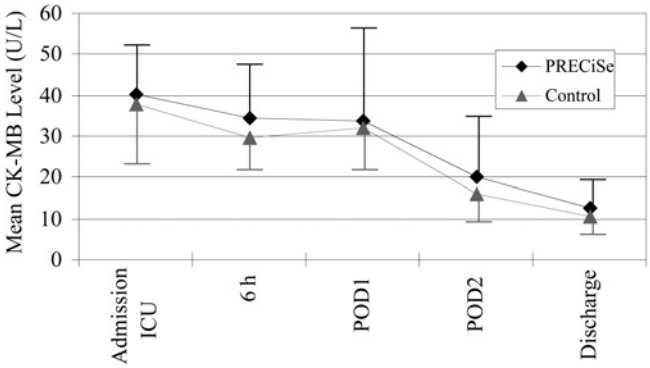

Figure 4. Course of perioperative creatine kinase MB isoenzyme (CK-MB) level (mean ± SD). PRECiSe indicates priming reduced extracorporeal circulation setup; ICU, intensive care unit; POD1, postoperative day 1.

may additionally lead to postoperative myocardial depression, resulting in an increased need for inotropic drugs [Fang 1997]. Finally, extreme hemodilution may lead to coagulation disorders, resulting in increased blood loss postoperatively and thus increased postoperative transfusion requirements [Hardy 1998]. Therefore, extreme hemodilution is avoided by the transfusion of 0.5 to 1.4 units of red blood cells, depending on the type of operation, and this strategy remains routine in German cardiac centers [Dietrich 1999]. A recent review [Mack 2003] described the frequency of patient transfusions during hospital stays, even in OPCAB surgery, to be 18% to 28%, compared with 29% to 49% in control groups in which the standard heart-lung machine was used.

Priming reduced CPB setups, originally designed for assisted circulation in beating-heart CABG surgery, have been proved to reduce the inflammatory response [Fromes 2002] through their used of a closed loop that avoids blood-air contact. However, these setups have failed to reduce the need for perioperative transfusions [Folliguet 2003] because they do not provide the possibility to return shed mediastinal blood directly into the patient's circulation. Additionally, the closed loop limits the ability for a rapid and effective decompression of the heart via returning blood to a reservoir. This design results in an increase in the central venous pressure in cases of tilting up of the full heart. Revascularization of posterior wall vessels may be limited in these situations.

The PRECiSe was designed to overcome these adverse effects of conventional priming reduced systems, and its safe and effective use in elective CABG surgery was demonstrated in a recent study [Beholz 2003a]. In this first matched clinical trial, the substantial reduction in transfusion frequency and amount compared with standard ECC setups was the result of a significant decrease in the priming volume delivered to the patient. Additionally, we demonstrated safe perfusion and complete revascularization in comparison with a matched control group. In cases involving the use of the PRECiSe system, the patients could be operated on with the same myocardial performance, as demonstrated by the comparable courses of CK and CK-MB levels. Further studies will have to investigate the safe and effective use of the PRECiSe system in valvular and combined surgery procedures.

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