

Cardiopulmonary Bypass: It's Not the Size, It's How You Use It! Review of a Comprehensive Blood-Conservation Strategy

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Presented at the 2002 Outcomes Meeting in Key West Florida, Perfusion Innovations in Cardiac Surgery
(PICS) Section

Abstract: Several of the manufacturers of cardiopulmonary bypass equipment have recently introduced new miniature cardiopulmonary bypass systems. New advancements in cardiopulmonary bypass technology are almost always of interest to the perfusion community. However, the question arises, *what advantages do these systems offer over our present technology?* The manufacturers claim that these new systems will add to our perfusion armamentarium by offering us an opportunity to further reduce priming volume and the surface area to which the blood is exposed. Our group, in the Department of Cardiac Sur-

gery at Boston Medical Center has been involved in the development of a comprehensive blood conservation strategy since 1994. Our published data clearly demonstrates improved clinical outcomes using coated circuit technology as part of a comprehensive blood conservation strategy. In an effort to clearly evaluate this new technology, in this article we review our current technique at Boston Medical Center. **Keywords:** blood-conservation strategy, heparin-bonded circuits, cardiotomy suction. *JECT. 2004;36:263–268*

Several of the manufacturers of equipment for cardiopulmonary bypass (CPB) have recently introduced new miniaturized CPB systems. Although it is encouraging to see new research and development of such systems, the question arises; *do these systems offer any advantage over our present technology when our present technology is optimally used?* For many years our perfusion group at Boston Medical Center has used heparin bonded CPB circuits as part of a comprehensive blood conservation strategy (Table 1). This strategy has evolved to incorporate all aspects of CPB, including heparin-protamine management, minimal priming volume, normothermic bypass, large-bore direction cannulas, and the exclusion of shed mediastinal blood from the systemic circulation. Our published data clearly show improved clinical outcomes, decreased length of stay, and decreased cost (1–10). Will miniatur-

ization of the CPB achieve the same? In an effort to make clear comparisons, we review our current clinical practice as well as the scientific rationale for those practices.

HEPARIN-BONDED CIRCUITS (HBCs)

HBCs for CPB have been commercially available for some time. In fact, almost every manufacturer of perfusion equipment now offers some form of a coated circuit. Since 1993, our group at Boston Medical Center has worked exclusively with the Duraflo II (Jostra-Bentley Irvine, CA) coated circuit as well as the Carmeda (Medtronic Inc., Anaheim, CA) coated circuit. In 1994, we embarked on a clinical study designed to answer the question, "Do HBCs with a lowered anticoagulation protocol (LAP) improve blood conservation and further improve clinical outcomes?" The results of that study indicate that patients treated with a HBC and LAP as part of a comprehensive blood conservation strategy had a decrease in both the

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Table 1. Comprehensive blood-conservation strategy at Boston Medical Center.

- Use of heparin-bonded cardiopulmonary bypass circuits
- Reduced anticoagulation protocol
- Exclusive use of centrifugal pumps
- Closed collapsible soft-shell venous reservoir bag
- No active systemic cooling
- Large-bore directional arterial and venous cannulars
- Autologous blood priming
- Maximal cell saving
- Soaking and rinsing of surgical sponges
- Collaborative effort on the part of the *all* team members to minimize allogeneic transfusions

incidence (31.6% vs. 47.9%; $p = 0.01$) and magnitude (1.98 ± 4.8 vs. 4.29 ± 10.1 ; $p = 0.029$) of homologous transfusion (1). They required fewer hours of ventilatory support (13.2 ± 16.9 vs. 23.4 ± 50.0 ; $p = 0.04$), they spent less time in the intensive care unit (20.7 ± 17.4 vs. 35.5 ± 61.7 hours; $p = 0.01$), and had a reduced length of hospital stay (6.0 ± 2.5 vs. 7.3 ± 5.2 days; $p = 0.02$) and reduced cost. Total hospital charges were substantially lower in patients treated with a HBCs ($\$39,332 \pm \$10,998$ vs. $\$44,777 \pm \$20,209$; $p < 0.05$) (1). Overall postoperative complications were significantly reduced (25.6 vs. 39.3%; $p = 0.03$; Table 2). These improved clinical outcomes were repeated and verified in subsequent studies at our institution and were also observed in the high-risk populations as well (2–7).

In an effort to ensure that patients treated with a HBC and LAP were not at any additional risk of thromboembolic event, a follow-up study was undertaken (2). This study was designed to answer the question, “Is it the HBC or the LAP that accounts for the demonstrated improvement in clinical outcomes and are we placing these patients at any higher risk?”

A prospective randomized study was conducted in which 244 patients undergoing primary coronary artery bypass grafting (CABG) with a HBC were randomized to either a full anticoagulation protocol (FAP; activated clot-

ting time [ACT] >480 s) or a LAP (activated clotting time >280 s). This study demonstrated a decrease in the incidence (24.2% vs. 35.8%, $p = 0.047$) and magnitude (0.50 ± 0.92 vs. 1.08 ± 2.10 Units; $p = 0.005$) of homologous transfusion when a HBC was used in conjunction with a LAP. Clinical outcomes were similar in both treatment groups with a modest reduction in LOS (5.26 ± 1.23 vs. 5.63 ± 1.73 days) in the LAP group.

In an effort to determine whether the LAP treatment group was at any higher risk of a thromboembolic event, a subset of 30 patients (LAP = 19, FAP = 11) were selected to undergo neurologic and neuropsychologic examination. These patients were evaluated before CABG (preoperative day 1.93 ± 3.06 ; session 1), just before discharge (postoperative day 3.77 ± 0.73 ; session 2) and approximately three weeks after discharge (postoperative day 23.25 ± 7.34 ; session 3). This subset of patients was examined using the National Institute of Health stroke scale and a broad spectrum of neuropsychological tests. The results showed that 86.6% of all patients exhibited post CABG deficits in session 2. However, this subset as a whole showed evidence of return to baseline or higher as early as 3 weeks after the operation.

CLOSED VENOUS RESERVOIR/NO CARDIOTOMY SUCTION/MAXIMAL CELL SAVING TECHNIQUE

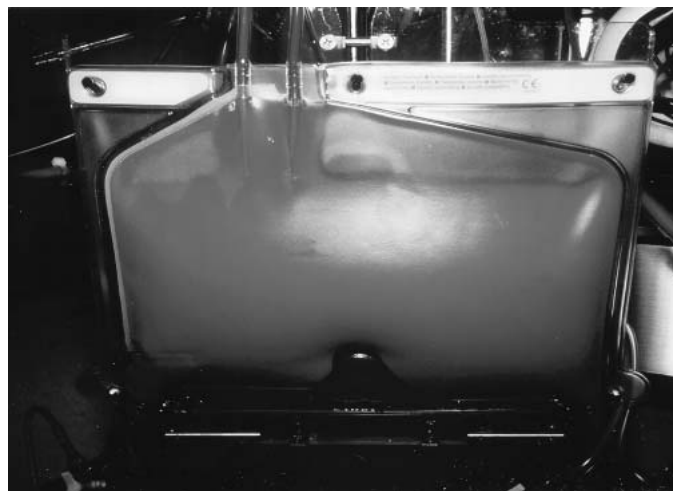
One of the more important considerations of using a HBC with LAP is the avoidance of procoagulant triggers and areas of blood stagnation in the CPB circuit (22,25,26). In our practice, we use a large-capacity venous reservoir bag, the Duraflo II coated Jostra-Bentley BMR 1900 (Jostra-Bentley, Irvine, CA; Figure 1). This “closed system” in conjunction with our minimal priming volume strategy has helped to facilitate the removal of the car-

Table 2. Comparison of morbidity and mortality in the NHBC/FAP and HBC/LAP treatment groups.

Variable	NHBC N = 117 (%)	HBC N = 117 (%)	<i>p</i> Value
Mortality rate	2.56	0.85	0.31
Reop bleeding	2.56	0.85	0.31
Perioperative MI	4.27	0.00*	0.024
Postop Inotropic agents	10.3	2.6*	0.016
Postop CVA/TIA	2.56	0.85	0.31
Ventilator >3 days	6.84	0.85 ^a	0.017
Pneumonia	5.13	2.56	0.31
Tracheostomy	4.27	0.85	0.09
Atrial fibrillation	34.2	23.9	0.08
Postop complications	39.3	25.6*	0.026

CVA, cerebrovascular accident; MI, myocardial infarction; TIA, transient ischemic attack.

* $p < 0.05$.

**Figure 1.** Jostra-Bentley BMR 1900 Closed Venous Reservoir.

diotomy (Figure 2) and the cardiotomy suction in most of our primary CABGs. The removal of the cardiotomy and cardiotomy suction helps to avoid or minimize the blood to gas interface. The aspiration of blood with a cardiotomy suction results in the mixing of room air, mostly nitrogen, with the blood. These nitrogen bubbles or foam in the blood can act as a foreign surface (15,16), which can result in platelet and neutrophil activation, as well as the denaturation of plasma proteins (16). Blood aspirated with cardiotomy suction must then pass through a defoaming soak before its reintroduction into the systemic circulation, further activating the formed elements of blood.

In 1982 Orenstein and his colleagues demonstrated the embolization of Anti-Foam A (Dow Corning Corp. Midland, MI; dimethylpolysiloxane and particulate silica) during cardiopulmonary bypass (17). This particle-droplet complex was detected in the brain as well as every major organ system. It was believed that the fate of these emboli was to remain in the patient's circulation potentially causing delayed and long-term postoperative sequelae.

Recent evidence suggests that a pathological process similar to that described by Orenstein continues to adversely impact neurologic outcomes in cardiac surgery today (17–19). Moody and his colleagues have established that adverse neurologic outcomes can be detected in at least 24% to 50% of patients requiring CPB (18,19). Another report suggests that the incidence of subtle cognitive dysfunction may be as high as 79% (20).

Small capillary and arteriolar dilations can be detected in all patients exposed to CPB (19–21). Evidence suggests that small capillary and arteriolar dilations probably result from the aspiration of shed blood from the surgical field and reinfusion into the cardiopulmonary bypass circuit. Another advantage to a “closed system” with no cardiotomy suction is avoidance of blood tainted by the

pericardial wound. The adverse effects of suctioning blood from the pericardium and pleural spaces and its reintroduction into the systemic circulation has been well recognized for many years. In repeated studies de Haan, Boonstra, and others have demonstrated that blood suctioned from these damaged tissues has great capacity to impair homeostasis (15,22–25). Hemolysis, platelet degranulation, complement activation, and an increase in thrombin-antithrombin (TAT III) formation all occur as a result of exposing blood to the pericardial wound (22,23). Tissue factor, a strong stimulus of the extrinsic clotting pathway, and tissue-type plasminogen activator, a potent activator of the fibrinolytic system, are present in suctioned blood in substantial quantity. Removal of the cardiotomy from the bypass circuit avoids these clinical issues. Blood suctioned from the pericardial wound is directed towards the cell saver. All surgical sponges are rinsed in saline (Figure 3) and also directed to the cell saver. As a general guideline if more than two units have been processed while on CPB, the perfusionist will ask the surgeon whether they would like to add a cardiotomy suction to the circuit.

MINIMAL PRIMING VOLUME STRATEGIES/ AUTOLOGOUS BLOOD-PRIMING TECHNIQUE

In the early years of open-heart surgery, prior to 1961, CPB circuits were routinely primed with fresh whole blood. This technique not only placed the hospital blood bank under significant strain but also contributed to the perioperative morbidity and mortality of cardiac surgery. Postoperative hepatitis and intra-operative blood transfusion reactions were common (27). Hemodilution and autologous blood priming techniques, as an alternative to fresh homologous blood priming, were first introduced by Panico and Neptune in 1959 and later by Zuhdi in 1961 (28,29). Hemodilution and crystalloid priming of the oxy-

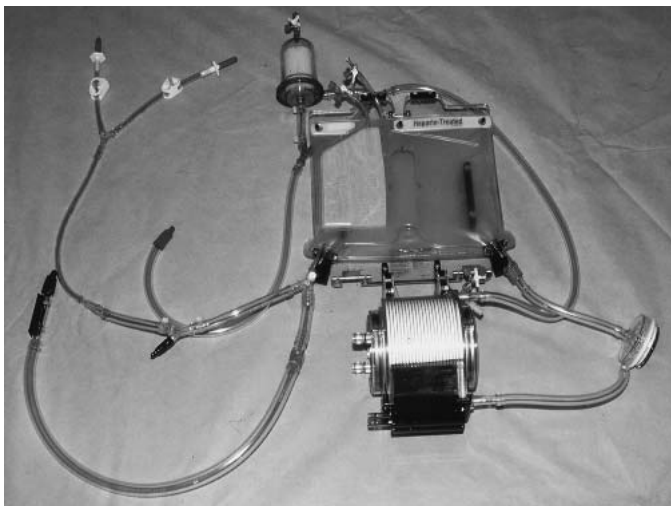


Figure 2. Boston Medical Centers' heparin-bonded CPB circuit without a cardiotomy.



Figure 3. Surgical sponges rinsed in saline and directed to the cell saver.

generator became a standard perfusion practice by the early 1970s.

The adverse effects of excessive hemodilution on CPB have also been extensively studied. Excessive hemodilution can result in diminished oxygen carrying capacity, tissue acidosis, decrease colloid osmotic pressure, and extravascular fluid shifts (30–33). These untoward effects can also adversely impact perioperative morbidity and mortality. The recent increased use of normothermic CPB by many centers has resulted in renewed interest in preserving hematocrit on bypass.

The autologous priming technique has been shown to be a safe and effective method of preserving hematocrit on CPB (34–36). Our group at Boston Medical Center uses the autologous blood priming method as part of our aggressive blood conservation strategy (8). This technique is deployed with the use of a 3M-Terumo Duraflo II coated centrifugal pump (Terumo Cardiovascular Systems, Somerset, NJ). After a tubing clamp is applied on the arterial line and a 1000-mL transfer pack attached to the arterial filter, blood is allowed to slowly move down the venous line (partial bite 5/8 with a tubing clamp) displacing the crystalloid in the circuit. The crystalloid prime is pumped into the 1000-mL transfer bag and discarded.

In a prospective randomized study of 114 patients undergoing open-heart operations at our center, we confirmed the findings of other investigators that lowering the priming volume reduce the need for homologous transfusion (34–36). The lowest hematocrit on CPB was higher in the reduced prime group $29.3\% \pm 4\%$ vs. $26.3\% \pm 5.3\%$ ($p = 0.009$). Total donor exposure in the reduced prime group was significantly less 1.0 ± 2.4 vs. 3.8 ± 10.1 units ($p = 0.044$). The autologous priming technique requires no additional expenditure on capital equipment and can significantly reduce the total cost of cardiac surgery (35).

Thermal Management

One of the more controversial issues in perfusion today is the debate over temperature management on CPB. For many years different levels of hypothermia (mild 32–37°C, moderate 28–32°C, deep 18–28°C, profound 0–18°C) have been used on CPB for the purpose of protection of the brain and other vital organs (31). In 1991 Dr. Litchenstein advocated the warm heart surgery technique as an advancement in myocardial protection (38). Other investigators reported a threefold increase in the incidence of stroke with this technique (39). Still, Engelman and colleagues noted no difference in adverse neurological outcomes (40).

A review of this literature illustrates the complexity of this subject. Conflicting definitions of hypothermia and normothermia between studies, differences in co-morbid risk factors, as well as differences in the type and extent of neurologic testing performed, are just some of the issues that need to be reconciled. One author correctly points

out that the period of CPB where the patient is at highest risk of an adverse event, during aortic manipulation, the patient's temperature is "normothermic" (41). The most efficacious strategy regarding the clinical use of hypothermia may be debated for some time.

Our group at Boston Medical Center has adopted what some call a "temperate approach" to systemic cooling (42). Patients undergoing primary CABG are allowed to drift down to 33–34°C. After the initiation of CPB, the heater-cooler is set at 38°C and the patient is slowly rewarmed to 37°C by the conclusion of surgery. This technique generally avoids the hypothermic temperatures associated with coagulopathy as well as any need to rapidly or excessively rewarm.

ANTICOAGULATION MANAGEMENT

An important component to our perfusion strategy is precise and accurate anticoagulation management. We believe in the importance of minimizing heparin and protamine dosing while still maintaining safe conduction of perfusion. It has been demonstrated that the effects of administering heparin alone have been shown to cause platelet dysfunction and fibrinolysis (43). Protamine administered to neutralize the effects of heparin can cause complement activation, hemodynamic instability, and leukocyte activation (44). Because these drugs are essential for conducting CPB, safely reducing their usage is an important component of minimizing the deleterious effects of CPB.

To achieve accurate and safe heparin and protamine dosing we use the Medtronic Hemostasis Management System (Medtronic Inc, Anaheim, CA). Instead of empiric dosing, a heparin dose–response curve is used to calculate the appropriate amount of heparin to reach a target ACT. The system is automated to minimize the risk of user error. Heparin–protamine titration assays are used to accurately monitor circulating heparin levels and calculate a corresponding protamine dose.

For procedures such as CABG, where air to blood interface are minimal, (no cardiotomy), a target ACT of 250 s is selected. Cases in which cardiac chambers will be open (valve and aortic procedures) and significantly more air will be introduced into the CPB circuit via the cardiotomy suction, a target of 480 s should be chosen. Procedures where the serine protease inhibitor aprotinin is used, full anticoagulation is required. In all cases ACTs are monitored frequently (every 20 min) and subsequent doses of heparin are given in 2000 to 3000 USP unit increments.

CONCLUSION

Our group at Boston Medical Center has clearly demonstrated that the use of a HBC with a lower anticoagu-

lation protocol as part of a comprehensive blood conservation strategy can reduce the incidence and magnitude of homologous transfusion.

This strategy has resulted in decrease ventilatory time, decrease time spent in the intensive care unit, decrease hospital stay, and decrease costs. We have used this technique since 1994 on thousands of cases and have demonstrated the safety and efficacy of this technique. The question that remains to be answered is, "Will the new miniaturized CPB systems offer any advantage over our current technology when our current technology is optimally employed?" In light of the controversy that now exists between the on-pump and off-pump CABG techniques, it is incumbent on all clinical perfusionists to help resolve this issue.

ACKNOWLEDGMENTS

The authors would like to acknowledge their colleagues in the following programs for their contribution to this work: The Departments of Perfusion at the West Roxbury VA Medical Center, Rhode Island Hospital, and Bay State Medical Center.

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