

**Original Article**

***Technique for Routine Use of Heparin Bonded Circuits with a Reduced Anticoagulation Protocol***

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**ABSTRACT**

The use of heparin-bonded cardiopulmonary bypass circuits (HBCs) with reduced anticoagulation protocol during cardiac surgery attenuates some of the adverse pathophysiologic responses to cardiopulmonary bypass (CPB). The strategies of how to maximize improvements in clinical outcomes using this technique are still debated. This article describes in detail a comprehensive approach to strategies developed at Boston Medical Center and the West Roxbury Veteran Affairs Medical Center in over 4000 cases in which HBC with a reduced anticoagulation protocol is used routinely. Important elements of this technique include elimination of cardiotomy reservoir during coronary artery bypass graft surgery (CABG), autologous blood priming, normothermic CPB, and precise heparin and protamine titration. Adaptation and variation in this technique to specific clinical situations is also highlighted.

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## INTRODUCTION

The development of heparin-bonded cardiopulmonary bypass circuits (HBC) during cardiac surgery has been shown to attenuate some of the adverse pathophysiological responses associated with conventional cardiopulmonary bypass (CPB) (1–4). The debate continues how to best use this technology with appropriate techniques to enhance clinical outcomes while ensuring patient safety. We offer a strategy that incorporates the use of HBC with a reduced anticoagulation protocol, elimination of cardiomy suction during coronary artery bypass grafting surgery (CABG), maximal cell saving, autologous blood priming, normothermic CPB, and precise heparin and protamine management.

The techniques presented in this article are the cumulative case clinical experience of over 4000 patients accrued over 5 years at Boston Medical Center and the West Roxbury Veteran Affairs Medical Center. At these institutions, HBC with a reduced anticoagulation protocol is used routinely as an important but integral part of a comprehensive blood conservation and perfusion strategy in all cardiac surgery procedures. An overview of this strategy is represented in Table 1. This article outlines the general principles of HBC use and the proposed techniques and to delineate specific modifications to match varied clinical circumstances.

## CIRCUIT DESIGN

The specific components of the HBC are an important feature in optimizing the outcomes with this technique. A schematic of the circuit used during CABG surgery is represented in Figure 1. A large (>1500 mL closed collapsible (soft-shell) venous reservoir is used to minimize air to blood interface and avoid stagnant blood storage in the cardiomy reservoir. Centrifugal pumps are used exclusively to minimize hemolysis during cardiopulmonary bypass (CPB). An arterial to venous shunt line distal to the arterial filter allows for blood recirculation and crystalloid siphoning after CPB. Cardiomy suction is avoided as a further step to create a true closed system and to prevent the introduction of anti-foam agents from the reservoir into the circuit, as well as hemolytic pericardial blood, fluid, and debris from the surgical field. All field suction is directed to the cell-saving device, and the heart is vented by gravity through the aortic root or left ventricle. Pressure monitoring capability at the inlet and outlet of the membrane oxygenator is available for early clot detection during CPB. A large bore venous cannula is used to optimize drainage, and directional flow arterial cannula is used to minimize shear rates. The lines of the HBC are kept as short as possible to minimize blood exposure and prime volume but long enough to ensure safety and sterility. All components of the HBC should

**Table 1: Boston Medical Center and West Roxbury Veteran Affairs Medical Center Integrated Blood Conservation-Strategy**

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- Use of heparin bonded circuits
  - Reduced anticoagulation protocol
  - Exclusive use of centrifugal pumps
  - Precise (individual) heparin and protamine titration
  - Closed collapsible soft shell venous reservoir
  - No active systemic cooling
  - Directional arterial cannula and large bore venous cannula
  - Autologous blood priming
  - Amicar during bypass
  - Maximal cell saving
  - Soaking and rinsing of surgical sponges
  - Strict transfusion thresholds
  - Collaborative effort on the part of surgeons, perfusionists, anesthesiologists, and nurses to minimize allogeneic transfusion
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be coated from venous cannula to arterial cannula. Any segments uncoated (particularly in areas of stagnation and turbulence) warrant increasing the level of anticoagulation during CPB.

## CIRCUIT SELECTION

The decision to incorporate a cardiomy reservoir into the CPB circuit is based on the expected amount of blood loss during the surgical procedure. During closed heart surgery (primary CABG or low-risk reoperation), blood loss is minimal and the aortic root or left ventricle can be effectively vented by gravity drainage alone. In these circumstances, the perfusion circuit does not include a cardiomy reservoir and a pump suction line. The quick prime line connects where the cardiomy reservoir would otherwise fit, and the aortic root vent is connected to drain into the venous reservoir. A cardiomy reservoir is readily available and can be added to the system in the case of unanticipated bleeding that would require pump suction.

During open heart procedures such as valve replacement, aortic surgery, or any reoperative procedure where large amounts of intraoperative blood loss could be expected, a reservoir is added to create a standard CPB circuit with both pump suction and vent lines that can aspirate via roller pumps.

## LEVEL OF ANTICOAGULATION

When HBC is used with the specific techniques described, maintaining the activated coagulation time (ACT) at 250 sec or greater has been demonstrated to blunt thrombin generation to a similar degree as full anticoagulation (ACT > 450 sec) in CABG patients without increasing thromboembolic complications (5). We theorize that when using a reduced anticoagula-

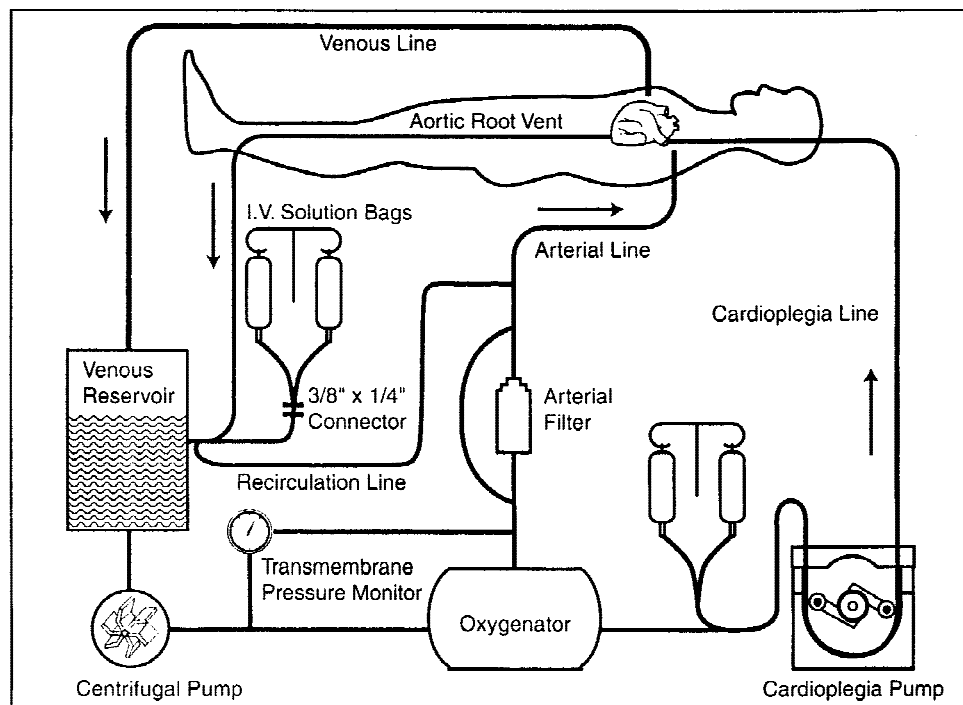


Figure 1: Scheme of CPB circuit used during CABG surgery.

tion protocol, potential thrombogenicity is increased with extensive air to blood interface experienced during CPB. In our early experience using HBC, large amounts of cardiomy suction return with low heparin levels would result in some clot formation in the sock of the cardiomy reservoir.

Because CABG surgery can be performed as a closed heart procedure with minimal blood loss, cardiomy suction is not routinely required, and ACTs can be safely reduced. Open-heart procedures, however (such as valve repair/replacement, left ventricular aneurysm resection, or aortic surgery), with increased field blood loss and vent return to the cardiomy reservoir result in more air-to-blood exposure, and therefore increased platelet activation, thrombin generation, and fibrinolysis. Maintaining the ACT at 350 sec or greater is warranted in these situations.

Cases in which aprotinin is used excludes patients from a reduced anticoagulation protocol since the resulting hypercoagulable state risks clot formation. Full heparinization (ACT > 480 sec) is mandated in these cases.

Because no artificial perfusion system is non-thrombogenic, heparin-free CPB is never advocated even in clinical situations where any systemic heparin is potentially deleterious (i.e., history of protamine allergy or a recent bleed). Though HBC is less thrombogenic, blood contact with non-endothelialized surfaces without systemic heparinization may pose a risk of clot formation, particularly in turbulent and stagnant areas. The overall decision making process of circuit selection and anticoagulation management is represented in Figure 2.

## ANTICOAGULATION MANAGEMENT

Precise heparin management is essential for safe implementation of HBC and a reduced anticoagulation protocol. Lowering the target ACT is safe and clinically effective when used with appropriate perfusion techniques and does not compromise patient safety. It does however, require an attentive and diligent clinician. To allow for differences in individual response to heparinization (and reversal), the Hemostasis Management System (HMS)<sup>a</sup> routinely is used. An automated system minimizes human sampling error and measures circulating whole blood heparin levels as well as a two-channel kaolin-activated ACT. Anticoagulation management decisions with this strategy, however, are based on ACT.

Rather than using empiric (per kg) values, the HMS performs a heparin dose response curve (HDR) using heparin titration and calculating a more accurate individualized dose for that specific patient. This facilitates the identification of heparin-resistant states, (such as anti thrombin III deficiency). A target ACT is chosen based on the operative procedure being performed. Typical heparin doses range from 80–100 USP units/kg is needed to achieve an ACT greater than of 250 sec.

<sup>a</sup> Medtronic Hemotec, Englewood, CO

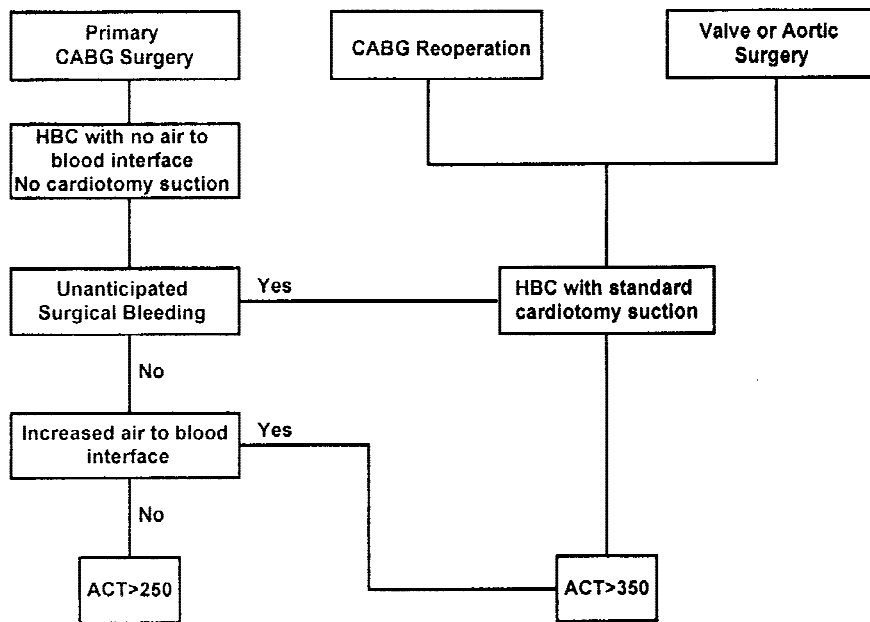


Figure 2: Anticoagulation level decision making process with HBC. (Note: Patients receiving aprotinin are excluded from this protocol and mandate keeping ACT > 480 sec.)

Once CPB is initiated, frequent monitoring (every 20 min) of ACT is advised. If additional heparin is required during CPB, it is given in 500- to 2000-unit increments.

With the incorporation of normothermic CPB and autologous blood priming techniques, a more accurate ACT should be realized since the confounding effects of hypothermia and hemodilution are minimized.

## CONDUCTION OF PERFUSION

### ASSEMBLY OF CIRCUIT

The heparin coating on the surface of the HBC tends to be more lubricious than non-coated circuits and can become disconnected between the connector and the tubing if not securely applied. All connections in the HBC must be checked and tightly fitted. Tubing clamps should be placed close to connectors to minimize blood stagnation and “streamline” the circuit.

### INITIATION OF CPB

After an adequate level of anticoagulation is reached, CPB is initiated slowly. Once on CPB, active cooling is avoided in all cases and the patient’s core temperature is maintained at 34°C or greater unless clinical circumstances dictate otherwise. Pressure drop across the membrane oxygenator is routinely monitored. Though HBC with reduced anticoagulation has yet to be associated with any oxygenator or circuit mishaps at this institution, we suggest adopting this technique in the early clinical practice to highlight the need for careful monitoring of early clot detection and ensure patient safety.

### AUTOLOGOUS BLOOD PRIMING

Minimizing hemodilution during CPB is an important component of this blood conservation strategy. The prime volume can be decreased by replacing the prime in the circuit with the patient’s own blood as CPB is initiated. As the prime is removed from the circuit, it is replaced slowly by the patient’s own blood. CPB is not initiated until either the prime volume is removed or hemodynamic instability requires immediate initiation of CPB. Use of vasopressors is discouraged to facilitate additional prime removal during this technique. To minimize hemodilution, a reduction of the pump prime to 800 mL or less before initiation of CPB is attempted whenever clinically possible. Albumin is not used as a prime component since protein contact with the coated surface prior to blood exposure to the HBC surface may limit its biocompatible properties.

### PRIMING THE AORTIC ROOT OR LEFT VENTRICULAR VENT

In CABG surgery, the aortic root or left ventricle is vented by gravity to the venous reservoir to help clear blood from the surgical field during construction of the distal coronary anastomosis. To achieve the necessary siphoning effect, the vent must be primed either through retrograde filling prior to CPB or gravity filling before cardioplegia is delivered.

### CARDIOPLEGIA DELIVERY

Antegrade and retrograde cold blood cardioplegia is typically delivered with a terminal hot shot at the conclusion of the aortic clamp period. Interrupted cardioplegia delivery and periodic stagnation in the system has not produced clot formation. This is thought to be due to the low temperature of the cardioplegia solution. Nonetheless, the initial 30–50 cc of stag-

nant blood is discarded into the field (and directed to the cell saving device) prior to delivering blood into the aortic root, grafts, or coronary sinus.

### **TERMINATION OF CPB**

At the end of CPB, an HMS heparin protamine titration assay is used to assess a circulating heparin level to determine the corresponding protamine reversal dose. Slow wean from CPB with continuous TEE monitoring is performed once patient is warmed to 37°C. Once off CPB and the patient is hemodynamically stable, the venous cannula is removed. A test dose of protamine is then administered and hemodynamics are monitored for any adverse reaction. With stability confirmed, protamine reversal is continued until 70%–80% of the total protamine dose is given at which time the aorta is decannulated. With reduced anticoagulation protocol and normothermic CPB increasing heparin metabolism, average protamine doses range from 30–70 mg. Once the cannula is removed, reversal is completed and confirmed by performing a heparin-protamine titration assay for detectable circulating heparin. During this postoperative period, all components of the HBC are observed for active clot formation.

### **RECIRCULATION OFF CPB**

After CPB, blood in the HBC is kept in constant motion through the recirculation line distal to the arterial filter and through a purge line on the arterial filter to avoid stagnation and potential clot formation.

### **SIPHONING ARTERIAL AND VENOUS LINE**

After the venous cannula is removed, the blood in the tubing is siphoned with crystalloid solution. With the protamine administered and the arterial cannula removed, the blood in the arterial line is also replaced with crystalloid solution. The siphon is directed in a retrograde fashion through the recirculation line so that the arterial filter is isolated, and in the event air is introduced while flushing, it is shunted to the venous side of the circuit. The siphoning of the venous and arterial lines prevents blood stagnation in the lines and allows for rapid processing of the residual circuit blood to the cell saving device.

### **AUTOLOGOUS BLOOD RECOVERY**

All remaining blood from the HBC is directed to the cell saving device and replaced with crystalloid to keep it primed and debubbled in case of emergent reinstatement of CPB. With the HBC now refilled with crystalloid, a careful visual inspection is made to insure that no clot has formed within the system. Any area of the HBC suspected of having clot formation must be replaced immediately.

All patients are treated intraoperatively with the compulsive care afforded to Jehovah's Witnesses. Surgical sponges are soaked in saline, wrung out into a basin, and directed into the cell saving device. No discard suction is used in CABG procedures.

### **AFTER CPB**

An important aspect of a blood conservation strategy is a firm transfusion threshold and clinical pathways leading to a standardized transfusion strategy. Regardless of initial hematocrit (HCT), packed (allogeneic) red blood cells are not transfused unless HCT during CPB falls below 20% or below 25% in the intensive care unit after cell saver blood administration. Postoperative bleeding is assessed after heparin reversal is confirmed by HMS assay. No platelets, cryoprecipitate, or fresh frozen plasma is transfused regardless of pre-, intra-, or post-operative counts or international normalized ratio unless associated with clinical post-op bleeding (defined as 300 cc 1 h post-operation, > 500 cc 2 h post-operation). Specific blood components are administered based on hematological and laboratory evaluations following CPB. Amicaproic acid (Amicar) is used routinely. A bolus intravenous infusion of 10 g is given over 30 min after heparin administration (and before initiation of CPB) A 10-g infusion is continued over the next 5 h.

## **DISCUSSION**

Blood exposure to non-endothelialized surfaces of any CPB circuit stimulates adverse pathophysiological responses. These include stimulation of the inflammatory response, complement, leukocyte, and platelet activation as well as disturbances in the hemostatic system (6). Commonly practiced techniques of systemic cooling (7) and hemodilution during CPB may also contribute to impaired postoperative hemostasis and homologous transfusion requirement (8). Heparinization alone has been shown to cause platelet dysfunction and fibrinolysis (9), which can be further exacerbated by heparin-protamine complexes after reversal. It is the intense inflammatory response responsible for post CPB organ dysfunction that includes pulmonary injury, myocardial dysfunction, and excessive bleeding (6). This morbidity and dysfunction can be either transient or permanent and can impact on high-risk patients with limited reserve in particular. HBC have been demonstrated to attenuate these responses by reducing whole body inflammatory response, complement activation, as well as platelet, granulocyte and neutrophil activation (1–4). The less thrombogenic nature of HBC allows for safe reduction of systemic heparinization during CPB without an increase in thrombin generation. Reduction of heparin dosing during CPB may further attenuate granulocyte activation and improve post-operative hemostasis (10).

In several prospective trials, we have demonstrated that the application of HBC with a reduced anticoagulation protocol during CABG in conjunction with an integrated blood conservation strategy results in reduction of homologous transfusion requirements, intra- and post-operative complications (such as myocardial infarction and inotropic requirement) and decreased ventilatory time, resulting in reduced intensive care



and hospital stay and, therefore, costs (11). In retrospective analysis, improved outcomes have also been noted in emergency CABG (12) and valve surgery as well (13).

Recently, we have shown that patients treated with HBC and reduced anticoagulation protocol can be used without any increase of thrombin generation when compared to full anticoagulation. In fact, fewer clinical thromboembolic complications (defined as CVA/TIA, myocardial infarction and vascular complications) were found in the reduced anticoagulation group. These patients also required less homologous transfusion (5).

Concerns over the thrombogenic potential and higher cost of the circuit have limited the routine use HBC with reduced anticoagulation protocol. In most institutions, this equipment is only used in selected high-risk cases in which full heparinization needs to be avoided, such as in patients with protamine allergy or recent bleeds. Evidence of attenuation of thromboembolic complications without increased thrombin generation noted in our studies indicates that patients are not put at any additional thrombogenic risk and that these techniques should be adopted for routine procedures as well. The clinical benefits and resultant cost savings were noted in both routine and high-risk cases, suggesting that the routine use of HBC is cost justified. The additional cost of the HBC is less than the cost of administering a single homologous blood unit (5).

Our perfusion strategy is designed to address specific aspects of the perfusion circuit and techniques that contribute to post operative coagulopathy and homologous transfusion requirement. Use of CPB circuits with an open hard shell venous reservoir results in extensive air to blood exposure. This has been shown to stimulate complement activation when compared with a closed soft-shell venous reservoir (14). We believe that optimal results with this technique are obtained with the exclusive use of a closed venous bag.

The elimination of cardiomy suction in CABG surgery creates a true closed system. It avoids tainting of the circuit perfusate with pericardial field blood, which triggers the extrinsic clotting cascade (15) as well as complement activation and platelet degranulation (16). Absence of cardiomy suction further limits contamination of perfusate with debris, such as silicon or lipid emboli, which may pass through the depth filter in the cardiomy reservoir sock. Their introduction into the patient's circulation adversely influences neurologic outcome (17). Centrifugal blood pumps are used exclusively because they have shown to be less hemolytic than roller blood pumps (18, 19). Large-bore arterial cannulas are used to reduce shear rates during CPB. The commonly practiced perfusion techniques of systemic cooling (7) and hemodilution (8) during CPB contribute significantly to post operative platelet dysfunction. Near normothermic CPB minimizes the platelet dysfunction associated with systemic cooling. Autologous blood priming of the HBC further reduces hemodilution that independently reduces homologous blood product usage (20).

Our extensive experience involves two of the available heparin coated products, the ionically bonded Duraflo II process<sup>b</sup> and the covalently bonded Carmeda<sup>c</sup> coating. We have found both circuits to perform equally well in the clinical setting, significantly improving outcomes compared with identical non bonded circuits. A small amount of heparin wash off from the surface of the Duraflo II circuit (1400 units based on our circuit specifications) with the initiation of CPB, but does not influence clinical management. Concerns have been raised as to the degradation of the Duraflo II coating over time. Both circuits have been used in prolonged CPB (8 h) albeit rarely, with no manifestation of thrombin generation, clot formation, or adverse clinical outcomes suggesting that HBC with reduced anticoagulation protocol are clinically stable for both standard and prolonged CPB.

Other manufacturers of CPB circuits have realized the importance of making the CPB more "biocompatible" and are responding by developing new coating processes or surface modification additives (SMA). It is not known whether these new, coated products will safely allow a reduction in heparin dosing or result in comparably improved patient outcomes described here. Basic research and large randomized clinical trials are needed to confirm that newer biocompatible circuits share the properties of the ionic and covalent bound circuits currently available.

## CONCLUSION

Our extensive clinical experience, laboratory studies, and improved clinical outcomes demonstrate that use of HBC with a reduced anticoagulation protocol is safe and effective. Significantly improved results translate into considerable cost savings which justify the use of HBC in all cardiac procedures.

In this era of "off-pump" and "minimally invasive" surgery, it is important to remind ourselves that the most invasive aspect of cardiac surgery are the effects of the CPB circuit. The use of biocompatible circuits is truly a significant step towards less invasive surgery by blunting some of the pathophysiological responses to surgery. In our opinion this represents a breakthrough toward improving clinical outcomes that highlights important role of the perfusionist and should be widely adopted for routine use.

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<sup>c</sup> Medtronic, Minneapolis, MN

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