Technique

Perfusion Strategies for Low-Dose and Heparin-Free Bypass

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ABSTRACT

An increasing number of clinical reports are being published regarding various uses of heparin-bonded extracorporeal bypass circuits with altered coagulation regimens. Although the reasons for lowered heparinization levels have been discussed, there has been a lack of information detailing perfusion strategies necessary to manage this emerging technology.

The decreased use or elimination of heparin during bypass procedures has been successfully achieved using heparin-bonded surfaces in carefully selected patients. However, if used inappropriately, the results may be catastrophic. Clotted circuits, thrombus formation and increased patient morbidity have resulted from poor circuit design and a poor understanding of the technology. Alterations in blood flow management, circuit design, cardiotomy suction, cardiac chamber venting, bypass weaning and anticoagulation management are essential for improved patient outcome.

It must be stressed that "heparin-bonded" does not imply heparin-free and that any blood damage is magnified under conditions of lowered heparin levels. The risks associated with low-dose or heparin-free bypass must be carefully weighed against the potential beneftis thought to be gained from this strategy.

This report summarizes our current experience, observations and perfusion techniques used in conjunction with low-dose or heparin-free extracorporeal bypass support for selected patients requiring cardiopulmonary bypass, extracorporeal cardiopulmonary support, ventricular assist devices, or extracorporeal membrane oxygenation.

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INTRODUCTION

The development of the heart-lung machine, followed by its successful use by Gibbon in 1953, demonstrated that patients could be kept alive using extracorporeal circulation and an artificial lung (1). This development led to a proliferation of heart surgery, which continues today. The ability to remove the patient's blood, circulate it through plastic tubes and return it to the body is possible only by inactivating the body's coagulation mechanism. This is accomplished by the use of heparin, which has widespread effects on the coagulation cascade, mediated through antithrombin III. However, a major drawback to the technology is the quantity of heparin necessary to reduce the probability of a thromboembolic event. The blood is also exposed to a "foreign surface," which causes damage to the blood and its components, especially platelets (2).

In most circumstances, patients tolerate cardiopulmonary bypass with minimal postoperative bleeding and do not require blood products. However, certain categories of patients present with conditions in which full systemic heparinization (300-400 IU/kg) is extremely undesirable or potentially lethal. Bleeding associated with blood component consumption, full systemic heparinization or incomplete heparin neutralization has been problematic in patients presenting with recent gastrointestinal bleeding, recent alcohol abuse, aortic dissection with associated coagulopathies, recent transurethral resection of the prostate (TURP) and difficult cardiac reoperations. Other patients have religious objections to the transfusion of blood products and must be managed carefully.

In an effort to make the extracorporeal bypass circuit "biocompatible," two heparin-bonding processes have been developed and are currently commercially available: Carmeda BioActive Surface[a] and Duraflo II[b]. The heparin-coated blood contact areas attempt to mimic the antithrombogenic properties of the natural endothelium. The goal of using heparin-bonded bypass circuits is the preservation of the blood components exposed to extracorporeal circulation.

The utilization of various heparin-bonded extracorporeal bypass circuits has been previously reported (3-6). Laboratory and clinical reports have demonstrated the beneficial effects of heparin-coated bypass equipment when compared to non-coated systems as shown by decreased complement activation and the preservation of the components of the coagulation system (7,8). Recent laboratory and clinical reports have demonstrated the potential for safely reducing the amount of anticoagulant administered when the blood contact surfaces of the extracorporeal circuit are heparin-bonded (9,10). Clinicians have also reported the successful use of heparin-free cardiopulmonary support in cases of trauma and profound hypothermia (11,12).

To date very little has been written that addresses the perfusion management necessary for conducting bypass using heparin-bonded circuits when the patient has received a lower than normal dose of heparin systemically, or received no heparin at all. To effectively use this technology and gain its full benefit for the patient, surgical and perfusion techniques must be modified to accommodate the altered coagulation state of the patient. Because the patient is not fully anticoagulated, the perfusionist must consider blood flow management, circuit design, cardiotomy suction, venting, blood stasis, air/blood interface reactions, and anticoagulation management (both levels of anticoagulation and the tests to determine adequacy).

a Medtronic Cardiopulmonary, Anaheim, CA 92807
b Baxter Healthcare Corp., Bentley Laboratories Division, Irvine, CA 92714

Table 1. Potential candidates for low-dose heparin CPB.

- Difficult reoperative patients
- Active gastrointestinal bleed
- Recent alcohol abuse
- Recent TURP
- Potential protamine reaction
- Patient who refuses all blood products
- Aortic dissection

MATERIALS AND METHODS

Different configurations of heparin-bonded perfusion circuits, in both adults and pediatric patient populations, were used clinically for a variety of patient conditions including aortocoronary bypass, cardiac valve replacement, replacement of the ascending aorta, hypothermia rewarming, trauma resuscitation and stabilization, cardiogenic shock, neurosurgery, pulmonary insufficiency, and ventricular assist (n=65).

CARDIOPULMONARY BYPASS (CPB) CIRCUIT

Adult patients undergoing aortocoronary bypass, valve replacement or replacement of the ascending aorta that met our selection criteria were systemically heparinized with 100 IU/kg bovine heparin and placed on heparin-coated CPB circuits (Table 1). The coated components included the cannulae, heat exchanger/oxygenator, arterial filter, suction/vent lines, cardiotomy reservoir, venous reservoir bag, tubing and connectors. The system was primed with 1000 ml 10% mannitol solution, 700 ml of an isotonic, isoelectric crystalloid, and 50 mEq sodium bicarbonate. No heparin was added to the prime.

EXTRACORPOREAL CARDIOPULMONARY SUPPORT (ECPS) CIRCUIT

The Medtronic Closed-Chest Support circuit[a] consists of the following heparin-coated components: centrifugal pump, heat exchanger/oxygenator, connectors and tubing. This circuit was used for adult patients undergoing emergency resuscitation and stabilization, hypothermia rewarming, neurosurgery, or other procedures in which femoral artery-femoral vein bypass was used. When a pediatric patient presented to the operating room requiring ECPS, a custom circuit was assembled at the bedside consisting of the following heparin-bonded components: connectors, tubing, centrifugal pump[a], and a hollow fiber oxygenator[a] (Figure 1).

Systemic heparinization of the patients was determined by the procedure to be performed and the presenting clinical picture. If the patient presented with a consumptive coagulopathy and trauma or was hypothermic, no systemic heparin was administered to the patient. If the patient requiring resuscitation presented with a normal coagulation profile and normothermic without trauma, or was an elective case, an initial bolus of heparin (2000-2500 IU) was administered to attain an activated clotting time (ACT) of > 200 seconds. Each circuit type was primed with an isotonic, isoelectric crystalloid solution. No heparin was added to the priming solution.

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

Patients meeting the criteria for ECMO were placed on either veno-venous or veno-arterial ECMO. When veno-venous ECMO was used, two oxygenators in parallel were set up (Figure 2). Whenever feasible, all circuit components (heat exchanger/ oxygenator, connectors, tubing, centrifugal pump and cannulae) were heparin-bonded. However, the cannulae were not always heparin-bonded. Heparin requirements were set on a case-by-case basis with a target activated partial thromboplastin time (aPTT) of 40-60 seconds or an ACT of 150-175 seconds during high flow perfusion.

VENTRICULAR ASSIST DEVICES (VAD)

When a post-cardiotomy patient was unable to be weaned from cardiopulmonary bypass and met the criteria for ventricular assistance, either left ventricular assist or biventricular assist was initiated using heparin-bonded centrifugal pumps and tubing. The circuits were primed with an isotonic, isoelectric crystalloid solution.

Figure 1. Pediatric ECPS circuit with heparin-bonded MiniMax hollow-fiber oxygenator.

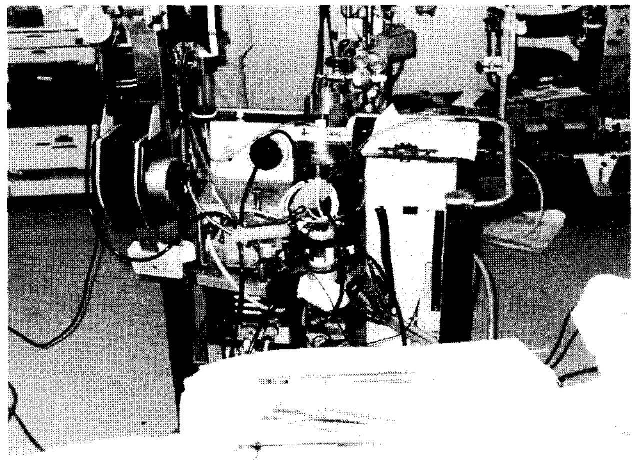


Figure 2. Veno-venous ECMO with parallel oxygenators.

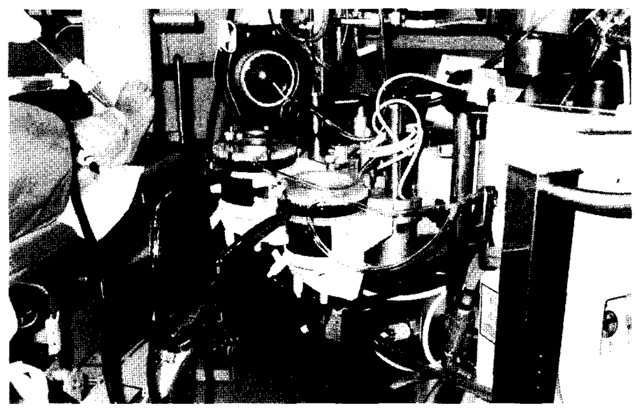
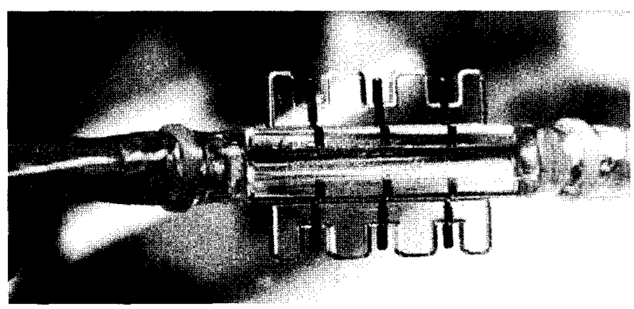


Figure 3. Fibrin ring at connector site.



TECHNIQUES

When the perfusionist is presented with a patient that requires the use of a heparin-bonded circuit, modifications in technique must be made to accommodate the change from normal anticoagulation management. The perfusionist must take into account the flow dynamics of the circuit, eliminating all possible low flow and blood stasis areas as well as minimizing zones of turbulence. Areas of low flow and stasis are areas of potential thrombus formation. The total surface area of the circuit should be minimized as much as is practical. Connectors should be kept to a minimum since they tend to harm the blood components, allowing fibrin rings to form (Figure 3). Non-bonded components should not be mixed with coated components during low-dose or heparin-free bypass because blood component damage as well as thrombus formation can occur (Figure 4).

During the bypass procedure, it is imperative that perfusion flow rates remain high (>3.5 L/min). If prolonged low flow rates are anticipated, the amount of heparinization needs to be increased to prevent clotting of the circuit. During ECMO and VAD procedures, it must be remembered that even though a lower dose of heparin may be used during maximal flows, the

Figure 4. A: Non-coated connector/cannula; B: Heparin-coated tubing.

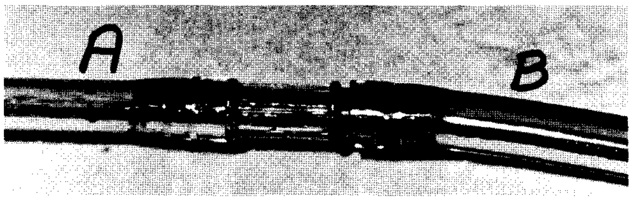


Table 2. Suggested tests for anticoagulation monitoring during low-dose or heparin-free bypass.

CPB	ECPS	ECMO	VAD
ACT	ACT	ACT	ACT
TT	aPTT	aPTT	aPTT
aPTT	PLT	PLT	PLT
PLT	FIB	FIB	FIB
FIB		PFH	d-Dimer
TEG		d-Dimer	
Heparin Assay		TEG	

CPB = cardiopulmonary bypass
ECPS = extracorporeal cardiopulmonary support
ECMO = extracorporeal membrane oxygenation
VAD = ventricular assist device
ACT = activated clotting time
aPTT = activated partial thromboplastin time
FIB = fibrinogen
PFH = plasma free hemoglobin
PLT = platelets
TEG = thrombelastograph

anticoagulation level of the patient should be increased as the weaning phase is begun since the blood will have an increased transit time through the circuit, potentially promoting thrombus formation (Figure 5). If a bridge is used during the ECMO procedure, it must be flushed regularly to prevent thrombus formation in the stasis area of the connector.

Cardiopulmonary bypass procedures provide a challenge for the perfusionist. The circuit must be free of all tubing loops, especially in the cardiotomy line. All tubing should be as short as possible, decreasing the amount of surface area exposed to the blood. The most problematic area of the circuit is the cardiotomy suction and cardiac vent provided by the heart-lung machine. Pump suction causes blood damage with normal anticoagulation levels, but during times of lowered heparinization (even with a slow pump speed) the damage is accentuated (Figure 6). The air/blood interface must be minimized or eliminated. It may be more advantageous to the patient to use an anticoagulated suction line attached to an autotransfusion device to salvage blood during the bypass procedure. A gravity vent line may be attached to the venous line to drain the cardiac chambers.

Figure 5. VAD circuit that was too long and heparin was not increased during weaning phase.

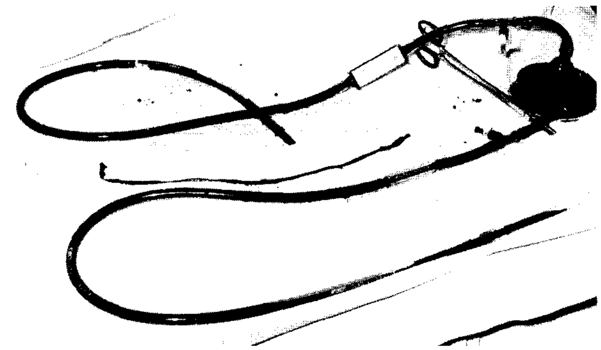
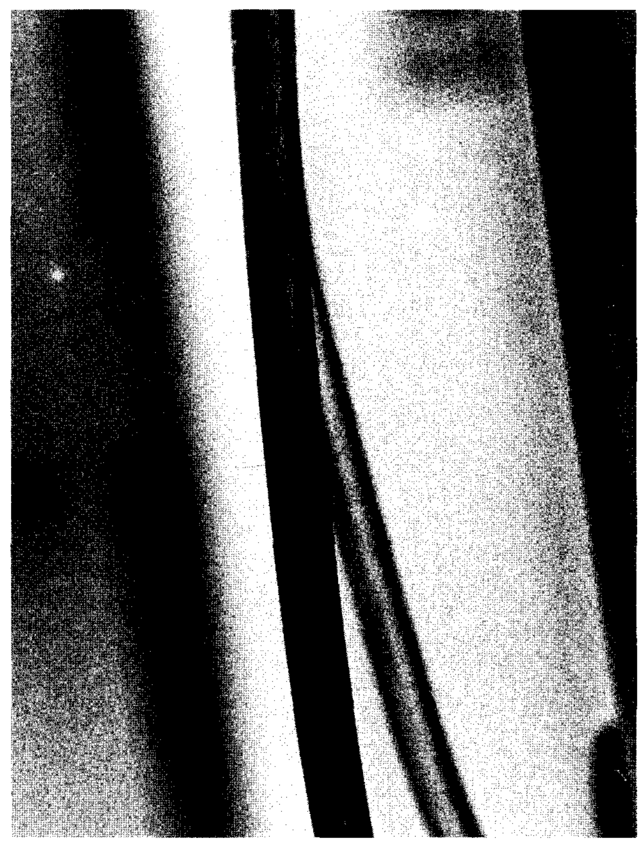


Figure 6. Cardiotomy suction line post-bypass, low-to-moderate pump speed with low-dose heparinization.



During the course of the various bypass modalities, it was noted that the ACT is not an adequate indicator of anticoagulation. It may be necessary to review a battery of tests to determine adequate anticoagulation and antithrombogenicity. Table 2 lists suggested testing for the various bypass modalities when using low-dose heparin.

DISCUSSION

Heparin-bonded circuits were developed to allow the extracorporeal circuit to be more "biocompatible." Under certain circumstances it was found that this new technology allowed the safe decrease, or even elimination, of heparin in specific groups of patients. It must be stressed that heparin-bonded does not imply heparin-free and that these circuits should be used for the property of biocompatibility rather than just as a way to decrease the amount of heparin administered. The risks of altering existing anticoagulation protocols must be weighed carefully against the perceived benefits to the patient. Since a test or battery of tests necessary to determine adequate anticoagulation/antithrombogenicity for the various bypass modalities has yet to be established, caution must be exercised at all times.

A team strategy must be developed to determine what surgical and perfusion technique will best benefit the patient. Thought must be given to the circuit design and flowrates necessary to protect the patient during the period of low-dose or heparin-free bypass.

Heparin-bonded circuits allow the flexibility to adjust the heparinization level to meet the patient's requirements. If used appropriately, heparin-bonded bypass circuits can greatly assist in the treatment of patients who would otherwise undergo detrimental (or even fatal) effects from the "normal" heparinization required to protect bypass circuits from clotting.

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