Fellowship Award Recipient, 1992 AmSECT International Conference

Biocompatible Circuits: An Adjunct to Non-Cardiac Extracorporeal Cardiopulmonary Support

John Bennett, BS, CCP, Jonathan Hill, MD, FACS, William Long, MD, FACS, James Parsons, PA, Pamela Bruhn, BSN, RN, Albert Starr, MD, FACS[1], Hagop Hovaguimian, MD, FACCP[1], J. Edward Okies, MD, FACS[2]
Emanuel Hospital & Health Center, 1-St. Vincent Medical Center, 2-Good Samaritan Hospital, Portland, Oregon

Key Words: biocompatibility, cardiopulmonary support, anticoagulation, non-cardiac cardiopulmonary support

Abstract

The utilization of cardiopulmonary bypass systems, for circulatory and/or pulmonary support of patients undergoing non-cardiac procedures, has been previously reported. There is, however, a sub-group of patients for whom total systemic anticoagulation for cardiopulmonary support is extremely undesirable or contraindicated altogether, due to the presenting pathology or procedure to be performed.

Clinical and experimental reports have suggested that with the use of heparin-bonded bypass circuits, the amount of heparin required for anticoagulation of the patient may be substantially reduced, or eliminated, safely. This allows the resuscitation and/or support of patients in whom bypass would otherwise be contraindicated.

We present our clinical experience with heparin-bonded, biocompatible circuits, for support of patients undergoing non-cardiac procedures. In each case, low-dose or no heparin was administered. The group includes patients with trauma related pulmonary insufficiency, pulmonary embolism, hypothermia, neurosurgery, aortic aneurysm, aortic transection, respiratory distress syndrome, pericardiectomy, and cardiogenic shock.

Introduction

The utilization of cardiopulmonary bypass systems for circulatory and/or pulmonary support of patients undergoing non-cardiac procedures has been previously described (1-3). However, a major drawback to this technology is the level of heparinization required to prevent an embolic event. Due to the problems in maintaining hemostasis after full systemic heparinization, the use of cardiopulmonary bypass became limited for such procedures as trauma resuscitation (4) and neurosurgery (5).

Larm et al. (6) have developed a thromboresistant coating in which heparin is end-point attached and covalently bonded to the blood-contact surfaces. Recent clinical reports have shown the potential for safely reducing the amount of anticoagulant administered, when the blood-contacting surfaces of the extracorporeal circuit are covered with a heparin-bonded, thrombus resistant surface (7-9). Clinicians have also reported the successful use of heparin-free cardiopulmonary support with heparin-bonded circuits (10-11).

The experience at Emanuel Hospital and Health Center, a Level I Trauma Center, has been broad-based in the utilization of full or partial extracorporeal bypass to resuscitate or support patients presenting with a variety of injuries or cardiorespiratory failure. To date, 16 patients have been supported by full or partial bypass utilizing heparin-bonded circuits (Table 1). Full cardiopulmonary bypass was used in 13 of these patients and left atrial/left femoral artery bypass was used in three patients. Because of the injuries or presenting condition, each patient received low-dose or no systemic heparin prior to bypass initiation (Table 2). Bypass times ranged from 35 minutes to

Address correspondence to:
John Bennett, BS, CCP
Emanuel Hospital & Health Center
2801 N. Gantenbein Avenue
Portland, OR 97227

Table 1. Case summaries

Patient	Age (yrs)/Sex	Etiology	Circuit Type	Procedures On Bypass
TRAUMA				
1	26M	pulmonary contusion, hemorrhage	ECPS/CBAS veno-arterial	pelvic angiography, CT scan, DIC reversal, bronchoscopy, retroperitoneal clot removal
2	20M	pulmonary hemorrhage, insufficiency	ECPS/CBAS veno-arterial	thoracotomy, bronchoscopy
3	16M	pulmonary contusion , DIC, hypothermia, hyperemia	ECPS/CBAS veno-arterial	resuscitation, rewarming, bronchoscopy
4	32M	brain contusion, transection descending thoracic aorta	LA-FA/ Gott Shunt; venous cannula/CBAS	graft interposition in descending thoracic aorta
5	38F	pulmonary contusion, transsection descending thoracic aorta, rib fractures	LA-FA/CBAS	graft interposition in descending thoracic aorta
HYPOTHEPMIA				
6	40F	diabetic ketoacidosis, profound hypothermia	ECPS/CBAS veno-arterial	ground transport from referral hospital, core rewarming, transfer to ICU (decannulation)
7	31M	profound hypothermia, salt water drowning, cardiac arrest	ECPS/CBAS veno-arterial	core rewarming , laparotomy at referral hospital, air transport, thoracotomy, bronchoscopy, long-term ECMO support
PROLONGED EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)				
8	65M	pulmonary insufficiency, failure	ECPS/CBAS veno-arterial	lung biopsy, long-term ECMO support
9	16 months M	pulmonary insufficiency, carbon dioxide retention (s/p palliative shunts-TGA)	Mini-Max (parallel lungs)/CBAS veno-venous	carbon dioxide removal, thoracotomy, dialysis
10	26F	Varicella/Staphylococcal pneumonia, pulmonary insufficiency, CO2 retention	ECPS (parallel lungs)/CBAS veno-venous	carbon dioxide removal, instillation of intra-tracheal surfactant, V-V to V-A bypass
PULMONARY EMBOLUS				
11	20M	pulmonary insufficiency, pulmonary embolism, hemodynamic instability	ECPS/CBAS veno-arterial	pulmonary/hemodynamic stabilization, air transport, pulmonary angiography, pulmonary embolectomy
NEUROSURGICAL EMERGENCIES				
12	36F	cerebral aneurysm	ECPS/CBAS veno-arterial	circulatory arrest (20" @ 19 C), aneurysm clipping
MISCELLANEOUS				
13	42M	distal perfusion	ECPS/CBAS veno-arterial	repair thoraco-abdominal aneurysm
14	60M	cardiac decompression	ECPS/CBAS veno-arterial	pericardiectomy
15	65F	descending thoracic aortic aneurysm	LA-FA/CBAS with heat exchanger	graft replacement of descending thoracic aorta
16	65F	cardiogenic shock	ECPS/CBAS veno-arterial	resuscitation, aorto-coronary bypass grafts

Initiation etiology, circuit utilized, and procedures performed while the patient was on extracorporeal cardiopulmonary support. CBAS=Carmeda Bio-Active Surface; ECPS=Closed-Chest Cardiopulmonary Support Circuit; LA-FA=Left Atrial-Femoral Artery Bypass; V-A=veno-arterial; V-V=veno-venous

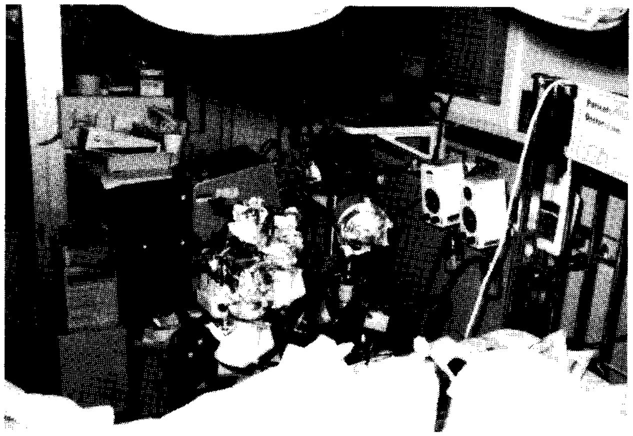

Figure 1.
Veno-venous ECMO with CBAS Mini-Max artificial lungs and circuit.

Figure 2.
Trauma patient with pulmonary hemorrhage, multiple fractures, disseminated intravascular coagulopathy and severe internal injuries. CBAS circuit, no heparinization administered. Outcome: survivor > 1 year.

138 hours and 44 minutes. Two of the patients were transported via aircraft from distant community hospitals while on full cardiopulmonary support. Ten of the 16 patients have survived greater than 60 days after support termination (Table 3).

Materials and Methods

Sixteen patients required some form of pulmonary or circulatory support for resuscitation or for the procedure that was to be performed. Of the sixteen patients, nine patients required extracorporeal cardiopulmonary support [ECPS] via veno-arterial access (<8 hours), four patients required prolonged extracorporeal membrane oxygenation [ECMO] either via veno-arterial or veno-venous access (>8 hours), and three patients required left atrial/femoral artery bypass (Table 1).

All extracorporeal blood contact areas had Carmeda BioActive Surface (CBAS)[a], except the Gott Shunt[b] (patient 4), the Sci-Med heat exchanger[c] (patient 14) and the Bio-Medicus pumpheads[d] (patients 4,5,9 and 15). Twelve patients were placed on the Medtronic CBAS Closed-Chest Support Circuit[a], three patients required left atrial/left femoral artery bypass and one patient required a CBAS Mini-Max[a] artificial lung with CBAS extracorporeal tubing (Figure 1).

An isotonic, isoelectric solution was used to prime all circuits. The amount of heparin used to systemically anticoagulate each patient was dependent upon the extent of injury to the patient or the procedure the patient was about to undergo. Initial systemic heparinization dosage ranged from 0 to 5000 IU bovine heparin (Table 2). Activated clotting times (ACT) and activated partial thromboplastin times (aPTT) were measured to determine the level of anticoagulation.

Patients presenting with pulmonary insufficiency as a result of traumatic injury, with an associated disseminated intravascular coagulopathy (DIC) and overt bleeding, were placed on bypass without systemic heparinization while the coagulopathy was treated with blood products and definitive treatments performed. Patients requiring prolonged bypass support (ECMO) received heparin via peripheral IV to attain an activated clotting time (ACT) of 150-175 seconds or an activated prothrombin time (aPTT) of 40-50 seconds. All other patients were given an IV bolus of heparin to attain a target ACT of 200-250 seconds. Additional heparin was administered in 1000 IU boluses if the ACT fell below 200 seconds.

Results

From October 1990 through January 1992, 16 patients required pulmonary and/or circulatory support. Due to the nature of the pathology involved or the procedure to be performed, it was determined a heparin-bonded bypass circuit should be utilized in conjunction with systemic heparinization which was substantially altered from our normal protocols. (Table 2) Technical problems arose in three of the 16 cases (Table 3), although none were the result of the altered anticoagulation levels. Ten of the patients (63%) have survived greater than 60 days post-bypass termination. (Table 3) A majority of the survivors have returned to their pre-bypass activities.

a Medtronic Cardiopulmonary, Anaheim, CA 92807
b Sherwood Medical, St. Louis, MO 63103
c Avecor Cardiovascular, Inc., Plymouth, MN 55441
d Bio-Medicus, Eden Prairie, MN 55340

Table 2. Anticoagulation Summary

	Heparin Dosage			Activated Clotting Time			
Patient	Initial	Maintenance	Total	Initial	High	Low	Pump Time
TRAUMA							
1.	0	0	0	142s ec	176 sec	68 sec	5' 22"
2.	0	0	0	219 sec	233 sec	177 sec	1' 48"
3.	0	0	0	155 sec	211 sec	127 sec	7' 46"
4.	0	0	0	127 sec	127 sec	127 sec	35"
5.	3000IU	0	3000IU	319 sec	319 sec	206 sec	64"
HYPOTHERMIA							
6.	0	0	0	139 sec	139 sec	139 sec	4' 30"
7..	0	500-1000IU/hr	15000IU	176 sec	232 sec	92 sec	52' 49"
PROLONGED EXTRACORPOREAL MEMBRANE OXYGENATION							
8.	2500IU	1000-2500IU/hr	31500IU	191 sec	304 sec	133 sec	23' 53"
9.	1000IU	150-360IU/hr		323 sec	443 sec	119 sec	138' 44"
10.	1000IU	250-5000IU/hr		119 sec	167 sec	104 sec	93' 09"
PULMONARY EMBOLUS							
11.	1000IU/hr	1000IU/hr	9000IU	184 sec	184 sec	138 sec	5' 42"
NEUROSURGICAL EMERGENCIES							
12.	2500IU	2000IU	4500IU	121 sec	262 sec	121 sec	3' 17"
MISCELLANEOUS							
13.	2500IU	3000IU	5500IU	190 sec	221 sec	157 sec	2' 25"
14.	2500IU	500IU	3000IU	168 sec	202 sec	164 sec	48"
15.	2500IU	1000IU	3500IU	171 sec	242 sec	135 sec	4' 14"
16.	5000IU	1000IU	6000IU	211 sec	328 sec	154 sec	2' 35"

Discussion

Traditionally, cardiopulmonary bypass required large doses of heparin to adequately anticoagulate the patient, however there are groups of patients (trauma, neurosurgical) for whom heparinization could be lethal (Figure 2). The thromboresistant property of heparin-coated circuits allows the flexibility to vary heparin dosage according to the clinical picture presented or the procedures to be performed (Figure 3).

Trauma/Hypothermia

Patients presenting with traumatic injuries or coagulopathies require special consideration when being evaluated as candidates for cardiopulmonary support. Clinicians have reported the successful use of biocompatible extracorporeal circuits, heparin-free, to support a severely injured, hemorrhaging patient in pulmonary failure (10), and a hypothermic patient with head injuries in cardiorespiratory arrest. (11) In each of these cases, the use of an anticoagulant would have exacerbated the injury, with increased risk of mortality. The ability

Figure 3.
Air transport of a patient who sustained a traumatic C-5/C-6 fracture with resultant quadriplegia and spinal cord hematoma, utilizing CBAS Closed-Chest Support Circuit. The patient developed massive pulmonary embolism. Low dose heparin administered. Outcome: survivor > 1 year.

to place selected injured patients on extracorporeal cardiopulmonary support, without the need to fully anticoagulate the patient, is of tremendous benefit. The hemodynamic, as well as pulmonary requirements of the patient can be maintained while a less hurried approach to a definitive diagnosis and treatment is sought. If a coagulopathy is present, aggressive blood component therapy (fresh frozen plasma, platelets, cryoprecipitate) to maintain hemostasis while on cardiopulmonary support, can be pursued without being counteracted by full heparinization, which would be required for non-coated systems.

Prolonged Extracorporeal Membrane Oxygenation (ECMO)

Bleeding, due to anticoagulation and blood contact with foreign surfaces, is the most common problem encountered in patients on ECMO. (12,13) Other side effects include the consumption of coagulation factors and thrombocytopenia. Because of these side effects, bleeding has been reported from the operative sites, mucous membranes, stomach, distal gastrointestinal tract as well as the head, pleura, pericardium or retroperitoneum. (12,13)

Table 3.
Technical Problems Encountered During Bypass, Patient Survival Greater Than 60 Days

Patient	Technical Problems Encountered	Survival Surv. > 60 Days
1.	None	Yes
2.	None	No
3.	None	Yes
4.	None	Yes
5.	None	Yes
6.	None	No
7.	None	No
8.	venous cannula dislodgement	No
9.	frequent oxygenator change-out:protein leakage	Yes
10.	loss of V-V access, changed to V-A bypass	No
11.	None	Yes
12.	None	Yes
13.	None	Yes
14.	None	Yes
15.	None	Yes
16.	None	No

With the use of biocompatible circuits, the prospect of decreased bleeding, due to minimized heparinization and the potential for the preservation of the blood and its formed elements, is promising.

Neurosurgery/Secondary Neurological Problems

The use of cardiopulmonary bypass (CPB) during neurosurgical procedures to provide deep hypothermia and cerebral vascular decompression was popularized in the early 1960's by Guiot and Le Poire. (14) However, between 1970 and 1980, due to improved surgical techniques and the problem of maintaining hemostasis, CPB as an adjunct to neurosurgery had fallen into disuse. (5,14) In the 1980's there was a resurgence of the use of CPB for complex neurovascular lesions not easily repaired by standard neurosurgical techniques. (14) The problems of post-operative hemorrhage (15), a disrupted coagulation system (16) and capillary ooze (17) continued to plague the neurosurgical community.

When a neurological impairment, such as quadriplegia, is due to a traumatic event, the patient is usually bedridden for a period of time. For these patients, the incidence of pulmonary embolism is increased, due to the patient's inability to be mobilized normally. Should the embolic event occur, compromising the patient's pulmonary status, cardiopulmonary bypass may be necessary to support the patient until a pulmonary embolectomy can be performed. There may be a potential for a cerebral hemorrhage, greater neurological deficit, or even death, if full anticoagulation for bypass is used.

Conclusion

The Division of Cardiothoracic Surgery and the Circulatory Assist Team at Emanuel Hospital has utilized biocompatible circuits for 16 patients, with varied etiologies for initiation. It has been our experience that heparin-free bypass can be successful, in specific circumstances, such as trauma and hypothermia, when heparinization is contraindicated and potentially fatal.

Utilization of biocompatible circuits during procedures such as neurosurgery, ECMO and thoracic aorta surgery may allow clinicians the flexibility to customize the anticoagulation level to the patient being treated, or to the specific procedure being performed. The preservation of the coagulation factors, along with minimal heparinization, has the potential for decreased blood and blood product exposure for the patient requiring the use of cardiopulmonary bypass, extracorporeal cardiopulmonary support, prolonged ECMO or left atrial/left femoral artery bypass. The use of biocompatible bypass circuits, when used appropriately, may result in the successful salvage of moribund patients previously categorized as untreatable.

References

1. Cooley DA, Beall AC. Surgical treatment of acute massive pulmonary embolism using temporary cardiopulmonary bypass. Dis Chest. 1962; 41:102-104.
2. Swain JA. Cardiopulmonary bypass in noncardiac disease. In: Utley JR ed. Pathophysiology and Techniques of Cardiopulmonary Bypass. Baltimore: Williams & Wilkins; 1983; 61-69.
3. Williams MD, Rainer WG, Fieger HG, Murray IP, Sanchez ML. Cardiopulmonary bypass, profound hypothermia, and circulatory arrest for neurosurgery. Ann Thorac Surg. 1991; 52:1069-1075.
4. Phillips SJ, Zeff RH, Kongtahworn C, et al. Percutaneous cardiopulmonary bypass: application and indication for use. Ann Thorac Surg. 1989; 47:121-123.
5. Drake CG, Barr HW, Coles JC, Gergely NF. The use of extracorporeal circulation and profound hypothermia in the treatment of ruptured intracranial aneurysm. J Neurosurg. 1964; 21:575-581.
6. Larm O, Larsson R, Olsson P A. new non-thrombogenic surface prepared by selective covalent bonding of heparin via modified reducing terminal residue. Biomater Med Dev Artif Organs. 1983; 2:161-173.
7. Bindslev L, Eklund J, Norlander O. Treatment of acute respiratory failure by extracorporeal carbon dioxide elimination performed with a surface heparinized artificial lung. Anesthesiology. 1987; 67:117-120.
8. Bindslev L. Adult ECMO performed with surface-heparinized equipment. Trans Am Soc Artif Intern Organs. 1988; 34:1009-1013.
9. von Segesser LK, Weiss BM, Garcia E, Turina MI. Clinical application of heparin-coated perfusion equipment with special emphasis on patients refusing homologous transfusions. Perfusion. 1991; 6:227-233.
10. Bennett JB, Hill J, Bruhn P, Long W, Parsons J. Heparin-free cardiopulmonary support, utilizing a Carmeda coated circuit, for a patient with pulmonary hemorrhage and multiple trauma. Proc 29th AmSECT Int Conf. 1991; p.89-91.
11. von Segesser LK, Garcia BA, Turina MI. Perfusion without systemic heparinization for rewarming in accidental hypothermia. Ann Thorac Surg. 1991; 52:560-561.
12. Bartlett RH, Gazzaniga AB, Toomasian JM, et al. Extracorporeal membrane oxygenation (ECMO) in neonatal respiratory failure: 100 cases. Ann Surg. 1986; 204:236-45.
13. Sinard JM, Bartlett RH. Extracorporeal membrane oxygenation: prolonged bedside cardiopulmonary bypass. Perfusion. 1990; 5:239-249.
14. Guegan Y, Scarabin JM, Le Guilcher C, Guillou L, Logeais Y, Pecker J. Extracorporeal circulation with deep hypothermia and circulatory arrest in the treatment of intracranial arterial aneurysms. Surg Neurol. 1985; 24:441-448.
15. Spetzler RF, Hadley MN, Rigamonti D, et al. Aneurysms of the basilar artery treated with circulatory arrest, hypothermia, and barbiturate cerebral protection. J Neurosurg. 1988; 68:868-879.
16. Thelin S, Almgren B, Hasson HE, Tyden H. Surgery of extracranial carotid artery aneurysm using cardiopulmonary bypass, hypothermia and circulatory arrest. J Cardiovasc Surg. 1988; 29:332-334.
17. Houston CS. Hypothermia and cardiac arrest in the treatment of giant aneurysms. J Neurosurg Nurs. 1984; 16:15-22.
18. Mottaghy K, Oedekoven B, Poppel K, et al. Heparin free long term extracorporeal circulation using bioactive surfaces. ASAIO. 1989; 35:635-637.
19. Toomasian JM, Hsu L, Hirschl RB, Heiss KF, Hultquist KA, Bartlett RH. Evaluation of Duraflo II heparin coating in prolonged extracorporeal membrane oxygenation. Trans Am Soc Artif Intern Organs. 1988; 34:410-414.