Effects of Shed Mediastinal Blood on Cardiovascular and Pulmonary Function: A Randomized, Double-Blind Study

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Background. **Shed mediastinal blood during cardiopulmonary bypass (cardiotomy blood) contains fat, particulate matter, and vasoactive mediators that can adversely affect the pulmonary and systemic vasculature, as well as impair gas exchange. Our aim was to evaluate the effects of processing cardiotomy blood on cardiovascular and pulmonary function after cardiac surgery.**

Methods. **Patients undergoing coronary artery bypass or aortic valve surgery, or both, using cardiopulmonary bypass were randomly allocated to receiving processed (treated, n = 132) or unprocessed shed blood (control, n = 134) In the treated group, shed blood was processed by centrifugation, washing, and additional filtration. Pulmonary function, arterial and venous blood gases, and hemodynamics were measured before, immediately after, and 2 hours after cardiopulmonary bypass in a consecutive subset of patients (n = 154). Patients and treating physicians were blinded to treatment assignment.**

Results. **Preoperative characteristics were similar between groups. There were no significant differences between groups in indexes of pulmonary mechanical function at any of the measured time points. Patients in the treated group demonstrated reduced pulmonary and systemic vascular resistance (both $p < 0.01$) as well as increased cardiac index in the perioperative period (2.6 ± 0.07 versus 2.3 ± 0.06 L · min^{-1} · m^{-2} at 2 hours after CPB, $p = 0.004$). Larger volumes of cardiotomy blood were associated with greater changes in systemic and pulmonary vascular resistance. Indicators of pulmonary gas exchange were similar between groups at all measured time points. Treated patients demonstrated a trend toward reduced length of ventilation (11.0 ± 1.9 versus 13.9 ± 2.4 hours, $p = 0.12$).**

Conclusions. **Processing of shed mediastinal blood improves cardiopulmonary hemodynamics and may reduce ventilatory requirements after cardiac surgery.**

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Cardiopulmonary bypass (CPB) is a key technology for most cardiac surgical procedures. However, its use is associated with a number of adverse sequelae [1, 2]. It is now recognized that one of the major contributors to CPB-induced morbidity is the recirculation of shed pericardial and mediastinal blood, which is typically suctioned from the operative field back to the CPB circuit (cardiotomy blood). This blood has been shown to be a major contributor to thrombin generation during CPB [3], and it has been demonstrated to be a major source of fat [4], particulate matter [5, 6], and vasoactive mediators [7, 8].

Reinfusion of unprocessed cardiotomy blood can theoretically lead to increased bleeding [3, 9, 10], and it may adversely affect the pulmonary and systemic vasculature [11]. Processing of cardiotomy blood, through centrifugation and additional filtration, can potentially improve the quality of the transfused blood and reduce associated adverse effects [11–14]. Despite the theoretical advantages of this approach, no adequately powered, randomized controlled trials assessing clinically relevant endpoints have been reported to date. As a result, there continues to be considerable practice variation in the management of cardiotomy blood in cardiac surgical centers [15].

The Cardiotomy Trial [16] was a randomized, double-blind study undertaken to evaluate whether processing of cardiotomy blood with centrifugation and filtration affected postoperative neurocognitive outcomes as well as bleeding and transfusion rates after cardiac surgery. We found that processing of cardiotomy blood had no effect on postoperative neurocogni-

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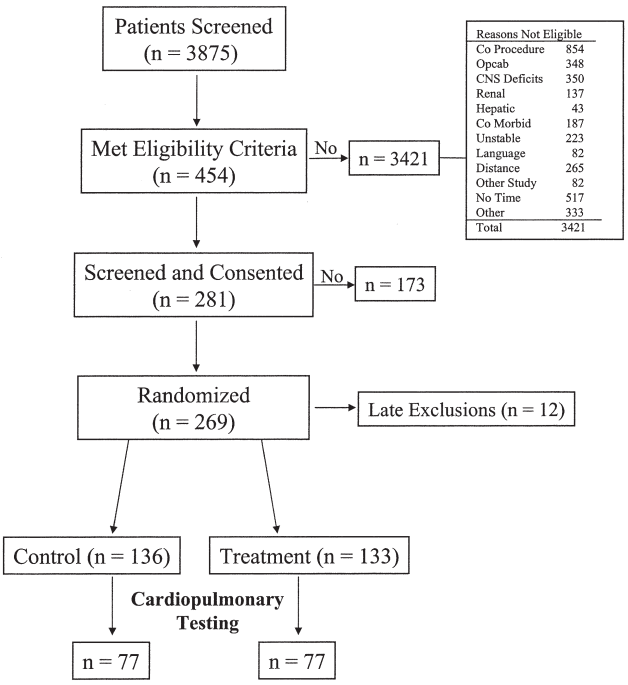

Fig 1. Patient screening and enrollment for the Cardiotomy Trial. (CNS = central nervous system; Opcab = off-pump coronary artery bypass graft surgery.)

tive deficits, but did result in increased postoperative bleeding and blood product use.

The aim of this substudy was to determine the effects of cardiotomy blood processing on prospectively identified endpoints evaluating cardiovascular function, pulmonary mechanics, and gas exchange in a subset of the total cohort. We hypothesized that processing of cardiotomy blood would result in improved cardiovascular hemodynamics as well as improved pulmonary gas exchange, without change in mechanical pulmonary function.

Material and Methods

Patient Population

The study protocol was approved by the Human Research Ethics Board of the University of Ottawa Heart Institute, and written informed consent was obtained from all patients. A total of 266 patients undergoing isolated, nonemergent coronary artery bypass surgery or aortic valve replacement, or both, using CPB at the Heart Institute were recruited. Patients with known neurologic deficits, preoperative coagulopathy, bleeding diathesis, or thrombocytopenia (<140,000/μL) as well as those with renal insufficiency (creatinine > twice normal) or hepatic insufficiency (elevated liver function tests, elevated baseline international normalized ratio) were excluded. A subset of 154 consecutive patients (n = 77 per group) underwent additional cardiovascular and pulmonary evaluation and serve as the cohort for this analysis.

Randomization and Blinding

Randomization, supervised by the data manager, was computer-generated in blocks of 8 (SAS version 8.2; SAS Institute, Cary, North Carolina) stratified for age (<75 years), and the assignment was concealed until the interventions were assigned. A sealed opaque envelope containing the treatment allocation was opened by the research coordinator just before the patient received heparin prior to the initiation of CPB. The perfusionist was informed of the treatment assignment. The patients and all clinical and research staff were blinded to treatment assignment. Intraoperative blinding of all members of the surgical team (except for the perfusionist) was accomplished by the positioning of an opaque drape over the CPB circuit and the cell-saving device. All intraoperative decisions to transfuse during CPB were made by the anesthetist, who was unaware of treatment assignment.

Intraoperative Protocol

A narcotic-based anesthetic was used. After sternotomy and conduit preparation, patients were administered heparin to achieve an activated clotting time greater than 400 s. Cardiopulmonary bypass was conducted using a roller pump, a membrane oxygenator (COBE CML Duo; COBE Cardiovascular, Arvada, Colorado), a 43-μm arte-

Table 1. Preoperative Data[a]

	Control (n = 77)	Treatment (n = 77)
Age (years)	56.7 ± 8.6	56.4 ± 9.0
Male sex	68 (88)	69 (90)
Left ventricular ejection fraction < 35%	31 (40)	30 (39)
CCS angina classification		
1	10 (13)	6 (8)
2	20 (26)	26 (34)
3	35 (45)	35 (45)
4	12 (16)	10 (13)
Left main disease	21 (27)	15 (19)
Number of diseased vessels		
0	2 (3)	2 (3)
1	2 (3)	3 (3)
2	16 (21)	19 (25)
3	57 (74)	54 (70)
Aortic stenosis	8 (10)	8 (10)
Hypertension	50 (65)	52 (68)
Previous myocardial infarction	34 (44)	37 (48)
Smoking history	46 (60)	46 (60)
Preoperative hemoglobin	143 ± 13	143 ± 13
Preoperative medications		
Aspirin	71 (92)	73 (95)
Clopidogrel	8 (10)	7 (9)
Diabetes mellitus	26 (34)	23 (30)

[a] Continuous values are presented as mean ± SD; categorical data are presented as number (%).

CCS = Canadian Cardiovascular Society.