# Absence of Beneficial Effect of Acute Normovolemic Hemodilution Combined with Aprotinin on Allogeneic Blood Transfusion Requirements in Cardiac Surgery

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*Background:* The efficacy of acute normovolemic hemodilution (ANH) in decreasing allogeneic blood requirements remains controversial during cardiac surgery.

*Methods:* In a prospective, randomized study, 80 adult cardiac surgical patients with normal cardiac function and no high risk of ischemic complications were subjected either to ANH, from a mean hematocrit of 43% to 28%, or to a control group. Aprotinin and intraoperative blood cell salvage were used in both groups. Blood (autologous or allogeneic) was transfused when the hematocrit was less than 17% during cardiopulmonary bypass, less than 25% after cardiopulmonary bypass, or whenever clinically indicated.

*Results:* The amount of whole blood collected during ANH ranged from 10 to 40% of the patients' estimated blood volume. Intraoperative and postoperative blood losses were not different between control and ANH patients (total blood loss, control: 1,411 ± 570 ml, n = 41; ANH: 1,326 ± 509 ml, n = 36). Allogeneic blood was given in 29% of control patients (median, 2; range, 1–3 units of packed erythrocytes) and in 33% of ANH patients (median, 2; range, 1–5 units of packed erythrocytes; P = 0.219). Preoperative and postoperative platelet count, prothrombin time, and partial thromboplastin time were similar between groups. Perioperative morbidity and mortality were not different in both groups, and similar hematocrit values were observed at hospital discharge (33.7 ± 3.9% in the control group and 32.6 ± 3.7% in the ANH group; nonsignificant)

*Conclusions:* Hemodilution is not an effective means to lower the risk of allogeneic blood transfusion in elective cardiac surgical patients with normal cardiac function and in the absence of high risk for coronary ischemia, provided standard intraoperative cell saving and high-dose aprotinin are used.

IN the United States, 27–92% of cardiac surgical patients receive allogeneic packed erythrocytes,[1,2] representing an average of two to four donor exposures per patient.[3] Allogeneic transfusions expose patients to added risks of allergic reactions, transmission of infectious agents (bacteriae, viruses, parasites, or prions), and immunosuppression.[4] On the other hand, stricter criteria for blood donor selection have decreased the source of allogeneic blood for transfusion and have increased its cost of delivery.[3]

In the last decade, clinical investigators have therefore focused attention on interventions to decrease the use of allogeneic blood products in surgical patients. The serine protease inhibitor aprotinin has recently been demonstrated to decrease allogeneic blood transfusion requirements in patients undergoing repeat coronary artery surgery.[5] In cardiac surgery, intraoperative blood salvage is widely used, but there is still controversy on the efficacy of acute normovolemic hemodilution (ANH) in decreasing allogeneic blood needs. Whereas several studies demonstrated that the use of ANH reduces the transfusion rate of allogeneic erythrocytes, fresh frozen plasma, and platelet concentrates,[6–8] others did not.[9–11]

We conducted a prospective randomized study with strict transfusion criteria to test the efficacy of ANH in our institution. We hypothesized that introducing ANH in elective cardiac surgical patients would reduce by 30% the number of patients requiring allogeneic blood transfusion under pre-established transfusion criteria.

## Materials and Methods

### Patients

After obtaining institutional review board approval (Comité d'Ethique du Département d'Anesthésiologie, de Pharmacologie et de Soins Intensifs de Chirurgie, Hôpital Cantonal, Geneva, Switzerland) and written informed patient consent, 80 adult patients of both sexes scheduled for elective cardiac surgery with use of moderate (29–31°C) hypothermic cardiopulmonary bypass (CPB) were enrolled. Exclusion criteria consisted of recent (< 6 weeks) myocardial infarction, unstable angina, severe (> 70%) left main coronary artery stenosis, severe aortic valvular stenosis (area < 0.7 cm$^2$), severe alteration of left ventricular function (ejection fraction < 30%, inotropic support or mechanical assistance), significant carotid artery stenosis (> 70% or symptomatic), combined carotid and coronary surgery, combined coronary and valvular surgery, severe respiratory insufficiency (arterial oxygen tension < 60 mmHg when breathing room air), renal insufficiency (creatinin clearance < 40 ml/min), and anemia (hemoglobin < 12 g/dl or hematocrit < 36%). Preoperative autologous blood predonation in cardiac surgical patients is not practiced in our institution and was thus not an exclusion criterion.

### Study Design and Procedures

Patients were randomized to one of two groups according to a computer-generated random number sequence. The control group patients underwent cardiac surgery with means of blood-saving procedures usually used at our institution: filling of extracorporeal circuit with saline isotonic fluid only, intraoperative blood salvage (Cell-Saver IV®; Hemonetics Corp., GmbH, Braintree, MA), and reinfusion of shed mediastinal blood, integral reinfusion of blood contained in the extracorporeal circuit at the end of surgery, administration of intravenous aprotinin ($2 \times 10^6$ IU before CPB, $2 \times 10^6$ IU in the extracorporeal circuit, and $2 \times 10^5$ IU/h as continuous perfusion during surgery), and external heating at the end of CPB. In the treatment group, ANH was added to these procedures.

Complete leukocyte count with differential cell count, coagulation profile (prothrombin time, partial thromboplastin time), serum creatinine, and hepatic enzyme values were obtained before study entry on the day before surgery (baseline). Hematocrit, thrombocyte count, prothrombin time, and partial thromboplastin time were repeated the day of surgery, i.e., just before CPB; during CPB; after surgery; on postoperative days 1, 2, and 5; and at patient discharge from the hospital.

All patients were premedicated with morphine (0.1 mg/kg administered subcutaneously) and diazepam (0.1 mg/kg administered orally). If they were taking nitrate derivatives or β blockers, they received them on the morning of surgery. General anesthesia was induced with intravenous midazolam (3–10 mg) and fentanyl (5–10 µg/kg) and was maintained with continuous intravenous midazolam (0.1 mg · kg$^{-1}$ · h$^{-1}$) and intravenous boluses of fentanyl as needed (up to a total dose of 30–50 µg/kg). After muscle relaxation with pancuronium, the trachea was intubated, and the patient was ventilated with oxygen (50–100%) in air. Patients were heparinized with porcine heparin (initial dose of 300 IU/kg; additional heparin [5,000 IU] boluses were administered during CPB to maintain an activated cephalin time > 500 s). The extracorporeal circuit was primed with 2 l of Ringer lactate solution. Intermittent anterograde cold blood cardioplegia with moderate systemic cooling (29–31°C) was used for all cases. At the end of CPB, heparin was neutralized with protamine sulfate to achieve a postprotamine activated cephalin time value within 10% of the preheparin activated cephalin time value (initial protamine sulfate dose of 1 IU for 1 IU of heparin, and additional doses of 5,000 IU if needed). The whole blood contained in the CPB circuit was always restituted to the patient before decannulation with the help of intravenous nitroglycerin if it was necessary to dilate the venous pooling compartment. During surgery, crystalloids were perfused at a rate of 3 ml · kg$^{-1}$ · h$^{-1}$. Additional crystalloids were infused if the intravascular volume was insufficient during CPB. Before separation from CPB, all patients were warmed to a rectal temperature of at least 35.5°C by means of internal heating (during CPB) and external heating (convecting warming air device, Bair Hugger®; Augustine Medical Inc., Courtelary, Switzerland).

Intraoperative monitoring included continuous monitoring of leads II and $V_5$ of the electrocardiogram and automated ST-segment analysis. Blood pressure monitoring was obtained with a radial artery catheter, and central venous pressure with a catheter placed in the internal jugular vein. Oxygen saturation was continuously monitored with a pulsoxymeter. A transesophageal echocardiography monitored continuously the movement of ventricular walls (ischemic wall movement monitoring) and the filling of cardiac cavities.

The ANH group underwent moderate hemodilution after induction of general anesthesia. The approximate blood volume to be removed was calculated according to a standard formula,[12] to reach a hematocrit of 28% (a level that was reported to remain safe in patients with coronary artery disease[13]). Blood was withdrawn by gravity from an introducer of Swan-Ganz catheter (part of usual equipment of our patients) into standard citrate-phosphate-dextrose collection bags. It was simultaneously replaced with an equal volume of poly-(0–2-hydroxy-ethyl)-amidon (mean molecular weight, 200,000; 50% substitution degree; C2/C6 ratio = 5) (HAES 6; Fresenius Kabi, Stans, Switzerland). Collected blood was kept on a rocking platform shaker in the operating room at ambient temperature.

### Transfusion Criteria

Transfusion criteria were the same in both groups: before CPB if hematocrit was less than 28%, during CPB if hematocrit was less than 17% (< 20% in at increased mortality risk patients, i.e., in patients with previous cardiac surgery, age older than 74 yr, with preoperative ventricular arrhythmias, or diabetes),[14] and after CPB if hematocrit was less than 25%. We used central venous pressure and pulmonary capillary wedge pressure readings combined with the transesophageal echocardiography monitoring to determine the need for intravascular volume. When needed, both patient groups received first the autologous blood salvaged intraoperatively (Cell-Saver). ANH patients then received their blood removed by ANH, and when this was consumed, if necessary, additional allogeneic packed erythrocytes. All autologous blood was retransfused in any case at last before leaving the operating room. The anesthesiologist in charge of the patient during surgery was aware of the patient's group, but the medical staff caring for the patient in the intensive care unit after the operation was blinded to group assignment.

*Statistical Analysis*

With a sample size of 40 patients per group, the analysis was expected to have at least a 90% power to detect a 30% diminution of the number of patients who received any banked allogeneic blood, compared with transfusion practices at our institution (43% of cardiac surgical patients transfused).[15] A *P* value < 0.05 was used for statistical significance. Categorical data were analyzed with a two-tailed chi-square test, the number of units of blood with the Mann–Whitney U test, and parametric data with the Student unpaired two-tailed *t* test. Parametric data are expressed as mean ± SD.

## Results

Between May 1998 and May 1999, 80 patients were enrolled in the current protocol. Three ANH patients (8%) were withdrawn because of postoperative surgical lesion bleeding that needed reoperation for hemostasis (*P* = 0.098 compared with the control group). Forty-three percent of routine elective cardiac surgical patients were excluded before randomization according to our preestablished exclusion criteria (see Materials and Methods).

Patients' clinical characteristics are shown in table 1. The only significant difference between both groups at baseline was that more patients were taking diuretics in the ANH group than in the control group (*P* = 0.001). The various operating time parameters were comparable between groups (table 2). Length of stay in the intensive care unit and total in-hospital postoperative length of stay were also similar. Mean anesthesia time between induction and institution of CPB was not prolonged by the hemodilution procedure (137 ± 32 min [ANH group] and 138 ± 39 min [control group]).

Overall, chest tube drainage during stay in the intensive care unit was similar in both groups (fig. 1). Total amount of crystalloids received was comparable in both groups, whereas the amount of colloids was higher in ANH patients because of the pre-CPB replacement of autologous blood withdrawn for hemodilution (table 2).

The mean blood volume collected during ANH was 1,099 ± 333 ml (range, 430–1900 ml) with a mean hematocrit of 33 ± 5%. This represents 21 ± 6% (range, 10–40%) of the patients' estimated preoperative circulating blood volume. The total number of patients transfused with allogeneic blood and the median number of allogeneic blood units per transfused patient in both groups were not statistically different. Allogeneic transfusion was approximately evenly distributed between the operating room and the intensive care unit in both groups (table 3).

Because of a low hematocrit value during CPB, the collected autologous blood had already to be restituted completely during CPB in 33% of ANH patients. In eight other ANH patients (22%), restitution was initiated but

**Table 1. Preoperative Demographics**

| | Control Group n = 41 | ANH Group n = 36 | *P* Value |
|---|---|---|---|
| Age (yr) | 62 ± 12 | 65 ± 10 | 0.227 |
| Male | 32 (78%) | 28 (78%) | 0.977 |
| Female | 9 (22%) | 8 (22%) | 0.977 |
| Weight (kg) | 76 ± 13 | 77 ± 16 | 0.718 |
| Body surface area (m²) | 1.88 ± 0.18 | 1.86 ± 0.22 | 0.774 |
| Medical history | | | |
|   Hypertension | 25 (61%) | 18 (50%) | 0.333 |
|   Diabetes | 6 (15%) | 7 (19%) | 0.574 |
|   History of myocardial infarction | 12 (29%) | 13 (36%) | 0.522 |
|   Repeat cardiac surgery | 1 (2%) | 3 (8%) | 0.245 |
| Cardiac status | | | |
|   Coronary disease | 29 (71%) | 24 (67%) | 0.701 |
|   Valvular disease | 15 (37%) | 15 (42%) | 0.648 |
|   Ejection fraction (%) | 61 ± 13 | 61 ± 13 | 0.891 |
| Preoperative laboratory findings | | | |
|   Creatinine clearance (ml/min) | 54 ± 16 | 51 ± 14 | 0.361 |
| Preoperative medications | | | |
|   Beta-blockers | 21 (51%) | 20 (51%) | 0.704 |
|   Nitrates | 20 (49%) | 15 (38%) | 0.532 |
|   Calcium channel blockers | 7 (17%) | 4 (10%) | 0.456 |
|   ACE inhibitors | 17 (41%) | 15 (38%) | 0.986 |
|   Diuretics | 2 (5%) | 12 (31%) | 0.001 |
|   Aspirin | 23 (56%) | 22 (56%) | 0.656 |
|   Heparin | 1 (2%) | 5 (13%) | 0.062 |
|   Vitamin K antagonists | 3 (7%) | 4 (10%) | 0.563 |
| At increased mortality risk patient* | 12 (29%) | 14 (36%) | 0.373 |

Values are means ± SD, or number of patients with percentages in parenthesis.

* Age > 75 years, previous cardiac operation, diabetes, or ventricular arrythmias.[14]

ANH = acute normovolemic hemodilution; ACE = angiotensin converting enzyme.

not fully restituted during this period. In the remainder of ANH patients (45%), the collected blood was restituted after heparin neutralization, according to the protocol.

Perioperative patient hemoglobin and coagulation variables are shown in figure 2. Baseline hematocrit values (control, 43.2 ± 2.4%; ANH, 43.3 ± 3.9%; *P* = 0.814) and immediate postoperative hematocrit values (control, 25.7 ± 3.3%; ANH, 25 ± 3.5%; *P* = 0.382) were similar in both groups. Hematocrit was significantly lower in the ANH group (27.9 ± 2.7% *vs.* 36.9 ± 3.6% in the control group) only after hemodilution and during CPB. ANH did not affect coagulation tests during the entire study, except for prothrombin time, which was significantly prolonged immediately before CPB (fig. 2). Prothrombin time was not measured during CPB. In the control group, one patient received 1 unit and another patient 2 units of fresh frozen plasma. In the ANH group, one patient received 3 units of fresh frozen plasma. In each group, one patient received 1 unit of platelet concentrates.

There was no significant relation between starting he-

**Table 2. Intra- and Postoperative Data**

| | Control Group n = 41 | ANH Group n = 36 | P Value |
|---|---|---|---|
| Cross-clamp time (min) | 88 ± 31 | 74 ± 31 | 0.059 |
| Bypass time (min) | 126 ± 37 | 117 ± 37 | 0.279 |
| Surgical time (min) | 271 ± 80 | 245 ± 65 | 0.109 |
| Reoperation for bleeding | 0 (0%) | 3 (8%) | 0.059 |
| Blood recovered from the Cell-Saver (ml) | 367 ± 257 | 392 ± 400 | 0.745 |
| Chest tube drainage (ml) | 1035 ± 459 | 944 ± 454 | 0.384 |
| Total amount of IV fluids received | | | |
| Crystalloids (ml) | 7163 ± 2636 | 6840 ± 2175 | 0.562 |
| Colloids (ml) | 1258 ± 749 | 2016 ± 772 | <0.001 |
| Number of patients receiving allogeneic blood | 12 (29%) | 12 (33%) | 0.701 |
| Median number of allogeneic blood units per transfused patient | 2 (1–3) | 2 (1–5) | 0.219 |
| ICU length of stay (days) | 3.0 ± 1.3 | 3.1 ± 1.3 | 0.665 |
| Postoperative length of stay (days) | 13.4 ± 8.3 | 13.1 ± 3.7 | 0.849 |
| In-hospital mortality | 2 (5%) | 0 (0%) | 0.532 |

Values are means ± SD, or number of patients with percentages in parenthesis; median number of blood units are indicated with ranges.

ANH = acute normovolemic hemodilution; ICU = intensive care unit.
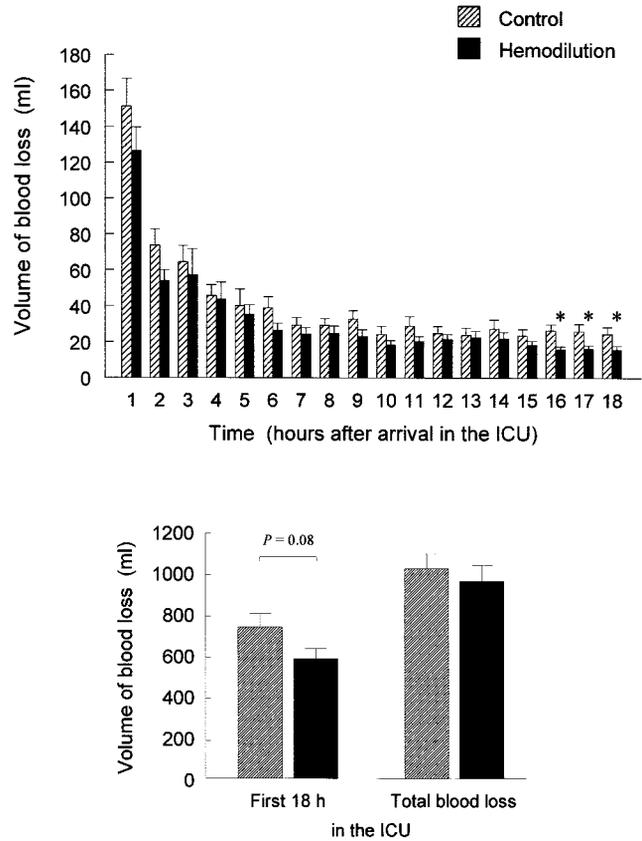




**Fig. 1. Time course of blood loss (chest tube drainage) during the first 18 h and during the whole stay in the intensive care unit (ICU). Data are mean ± SD. *P < 0.05 *versus* control group.**

matocrit and the number of erythrocyte transfusion units ($r = 0.36$ and $P = 0.25$ in ANH patients; $r = 0.02$ and $P = 0.96$ in control patients), nor was there a relation between the amount of blood withdrawn during hemodilution and the number of blood transfusion ($r = 0.07$; $P = 0.82$). Finally, we evaluated the impact of the patient's weight on transfusion requirements. Whereas in the ANH group, body weight was not associated with the number of blood units transfused, there was a significant inverse relation between patient weight and number of blood units transfused in the control group (slope = $-0.032$ units/kg body weight; $r = 0.59$; $P = 0.04$).

There were no differences in perioperative hemodynamics between both groups. There were no ST segment changes, but one patient in the control group showed ischemic changes on transesophageal echocardiography after CPB. Hepatic and renal function parameters as well as leukocyte counts showed no statistical differences at any time between groups. Postoperative complications were not statistically different between groups. The main complication was atrial fibrillation observed in 42% of control patients and in 36% of ANH patients. In-hospital mortality was 0% in the ANH group and 5% in the control group ($P = 0.532$) because of cardiac arrest on the ward (at the seventh and tenth postoperative days, respectively).

## Discussion

The results of this controlled, randomized study performed in cardiac surgical patients meeting preestab-

lished inclusion criteria, and by applying predefined transfusion criteria, demonstrate no benefits of a preoperative ANH to attenuate perioperative blood loss or to reduce allogeneic blood transfusion in those patients. The study was undertaken as transfusion of blood products remains still very frequent during and after cardiac surgery,[1,2] possibly inducing complications and supplemental hospital costs. We wanted to evaluate whether

**Table 3. Site and Reason for Allogeneic Transfusion**

| | Control Group n = 12 | ANH Group n = 12 | P Value |
|---|---|---|---|
| Site of transfusion | | | |
| Operating room, before CPB | 0 (0%) | 0 (0%) | 1.000 |
| Operating room, during CPB | 2 (17%) | 2 (17%) | 1.000 |
| Operating room, after CPB | 6 (50%) | 3 (25%) | 0.206 |
| Operating room, during and after CPB | 0 (0%) | 2 (17%) | 0.140 |
| Intensive care unit | 4 (33%) | 5 (42%) | 0.673 |
| Ward | 3 (25%) | 1 (8%) | 0.273 |
| Reason for transfusion | | | |
| Low hematocrit | 8 (67%) | 9 (75%) | 0.653 |
| Unstable hemodynamics and low hematocrit | 6 (50%) | 2 (17%) | 0.083 |
| Myocardial ischemia | 1 (8%) | 0 (0%) | 0.307 |

Values are number of patients with percentages in parenthesis.

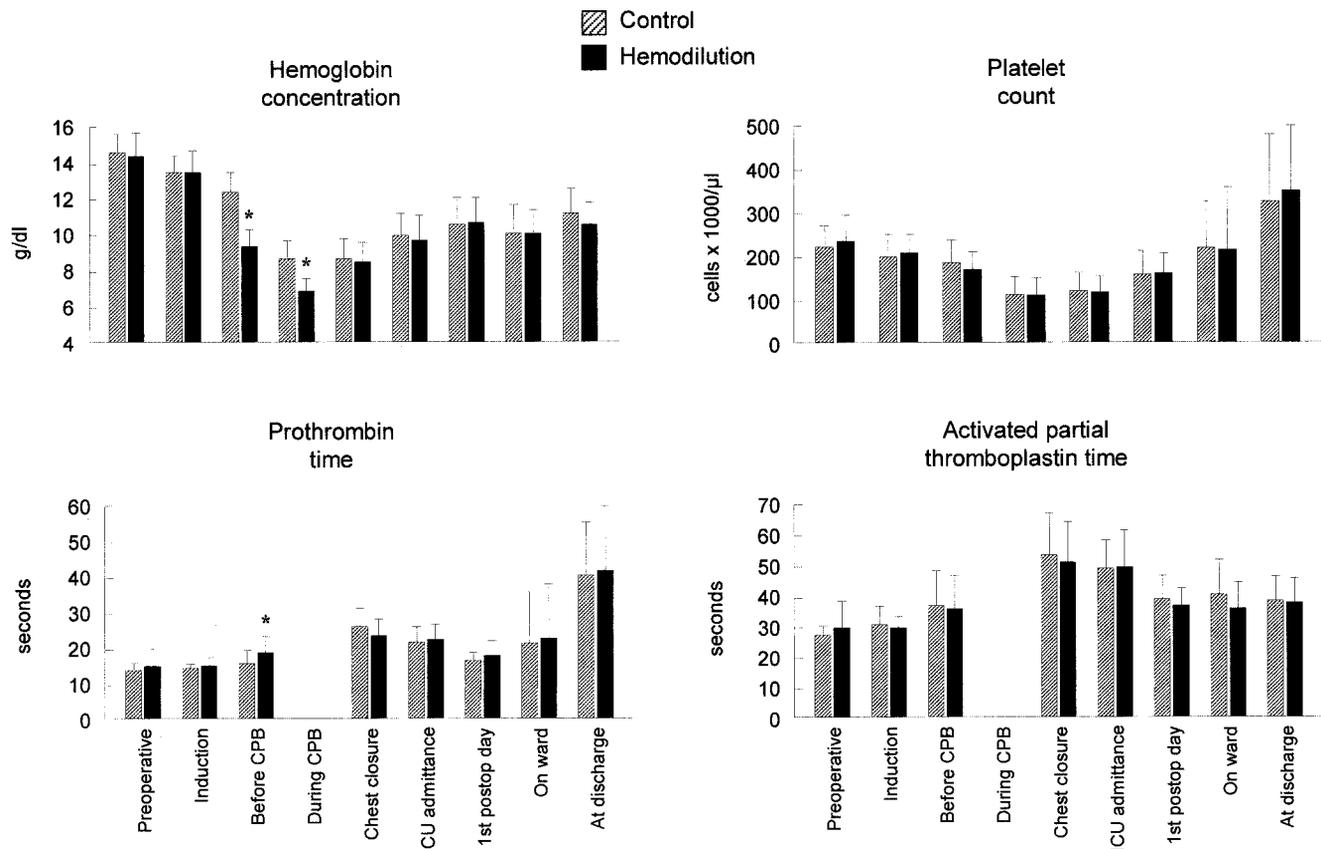ANH = acute normovolemic hemodilution; CPB = cardiopulmonary bypass.

Fig. 2. Time course of coagulation variables in control (hatched bars; n = 41) and hemodiluted patients (filled bars; n = 36). CPB = cardiopulmonary bypass; ICU = intensive care unit. Data are mean ± SD. *$P < 0.05$ *versus* control group.

adding ANH to intraoperative cell saving, aprotinin, and patient's external heating at the end of CPB could allow reduction of allogeneic blood transfusion. Previous studies on the efficacy of ANH in cardiac surgery have resulted in conflicting reports.[16] Sherman *et al.*,[10] in a controlled but nonrandomized study of 50 patients, showed no difference in blood loss with ANH, the requirement for allogeneic blood being actually greater in their ANH group than in a group of patients serving as controls. In a randomized controlled study including 122 patients, Pliam *et al.*[9] showed that the requirements of allogeneic blood tended even to be greater after ANH (although the difference did not reach statistical significance), but there were no strict transfusion criteria. In contrast, Scott *et al.*[6] showed that fewer blood products were transfused to patients who had been subjected to ANH before coronary surgery. However, that study was retrospective, with their control group being historical and the ANH group receiving significantly less aspirin than control patients. The reason for the discrepancy in the results of these and other studies is probably related to the fact that most of the reports on this topic actually included only small numbers of patients, were not randomized, or had no *a priori* defined criteria or too elevated hematocrit triggers for transfusion (as described in a recent metaanalysis[16]).

In the current study, we defined clear transfusion criteria based on a hematocrit of 17% during CPB (a hematocrit of 20% in approximately one third of our patients who were considered at risk of potential increased mortality rate after CPB and patients aged > 75 yr, with previous cardiac surgery, diabetes, or ventricular arrhythmias[14]). The strictly applied hematocrit transfusion level has probably been determinant in lowering the percentage of patients transfused in the control group of the current study (29%) as compared with the 43% described recently in a previous study in our institution (without transfusion criteria).[15] This fact has contributed to lower the power of the current study designed to reduce the percentage of allogeneic transfusions by 30%. In addition, in a third of patients subjected to ANH, at least one unit of the collected blood had to be restituted already during CPB, and in four patients, all of the collected blood was restituted during this period, thus eliminating the potential benefit of not exposing part of blood elements and coagulation factors to the CPB circuit in these patients.

Despite a comparatively large amount of collected blood during ANH, ranging from 10 to 40% of the patients' estimated blood volume to aim at a pre-CPB hematocrit of 28%, the whole procedure was safe in terms of clinical cardiovascular, respiratory, renal, as well as

biologic parameters. Even hematologic and coagulation profiles were not significantly influenced by hemodilution, except for the transient pre- and per-CPB reduction in hematocrit and prolongation in prothrombin time, with these variables being immediately restored at the end of surgery after reinfusion of the collected blood. There were no adverse effects during institution of the ANH procedure, the duration of anesthesia and surgery was not prolonged, and no statistical difference in the type and rate of postoperative complications between both treatment groups was noted during the whole hospital stay.

There are several reasons that may explain the absence of a beneficial effect of ANH in the current setting. First, to avoid the confounding effects of aprotinin, intraoperative cell saving, and external heating at the end of CPB, all shown to be very effective in reducing bleeding and transfusion needs in cardiac surgery with CPB,[15,17] we applied all of these methods in both groups of patients. This may have masked a possible beneficial effect of ANH alone in reducing allogeneic transfusions, by reducing by themselves the net surgical blood loss. These results support the concept that multimodality blood conservation strategies are probably not superior in terms of blood transfusion sparing, as shown in a recent study in which the association of ANH and tranexamic acid was not superior to aprotinin alone.[18]

Second, the transfusion trigger that we chose, lower than previously used in our institution, probably resulted in a relatively low transfusion rate in both groups of patients in the current study, compared with results previously reported in our institution.[15] Patients are indeed allowed to bleed more before they are transfused. That fact enhances the importance of determining a transfusion trigger in a multimodal program intended to lower transfusion in surgical patients. It must nevertheless be noted that the number of allogeneic blood products administered per transfused control patient remained the same compared with that previous study.

Third, the stringent exclusion criteria that were applied also contribute to explain the absence of a positive effect of ANH in our selected patients. We have excluded 43% of patients about to have cardiac surgery, according to consensus-established criteria of increased risk of myocardial ischemic complications secondary to the ANH procedure.[19] These excluded patients may have benefited from ANH, but we thought we might expose them unduly to complications caused by the hemodilution-induced critically decreased hematocrit.[14,20] We voluntarily kept the heterogeneity of cardiac surgical patients in this study to reflect our daily practice, with coronary and valvular patients being evenly distributed within both groups. Revision cardiac surgery was infrequent (one and three patients in the control and ANH groups, respectively; $P$ = nonsignifi-

cant) and has most probably not influenced the observed results.

Fourth, there may have been a postoperative relative allogeneic overtransfusion in ANH patients because of a dilution phenomenon associated with the strict hematocrit trigger criterion for transfusion. Postoperative hematocrit may have been indeed relatively lower in ANH patients because of persistent hemodilution by hydroxyethylstarch received before CPB. In a recent study in patients subjected to ANH, measured postoperative blood volume was higher than preoperative blood volume, with plasma volume being higher and erythrocyte volume lower than during the preoperative period.[21] Moreover, hydroethylstarch may have a negative effect on blood coagulation[22] and promote hemorrhage. However, whereas ANH patients received statistically more hydroxyethyl starch than control patients (27 ml/kg in ANH *vs.* 17 ml/kg in control patients; $P < 0.001$), they did not bleed more than control patients, and there was no significant difference in perioperative standard blood coagulation tests between both groups.

Finally, ANH patients took more diuretics than control patients, a fact that could have led to a relative preoperative hemoconcentration in these patients, making them more susceptible to hypovolemia and lowering their hematocrit during vascular filling. Indeed, in the ANH group, 5 of the 12 patients who were taking diuretics had to be transfused with allogeneic blood, whereas both control patients taking diuretics were not transfused, supporting this finding. In addition, preoperative heparin administration could also have influenced our results. However, only two patients presented an effective effect of heparin anticoagulation on the morning of surgery, because in the other patients heparin administration was stopped several hours before surgery; these two patients were in the ANH group and were not transfused.

In conclusion, the results of the current study demonstrate that, in elective cardiac surgical patients who are not at high risk for coronary ischemia, there is no benefit of adding ANH to intravenous aprotinin, intraoperative cell saving, and external heating. However, it is possible that ANH in a multimodality strategy for saving allogeneic blood transfusion might be effective in patients who were not included in the current study, *i.e.*, patients with combined coronary and valvular surgery, emergency surgery, patients receiving anticoagulant therapy, or those with known coagulopathy risk. That potential benefit of ANH will have to be balanced with the increased cardiovascular risk of performing this procedure in these particular patients and needs to be evaluated further.

evaluate the efficiency of thrombocytapheresis during cardiac surgery. Before undertaking this project, we designed the current investigation to determine transfusion needs and the efficacy of standard ANH in our cardiac surgical patient population. There is no other association between one of the authors and Biosafe Corporation. The authors also thank Michèle Brunet, B.S. (Laboratory Technician, Department of Anesthesiology, Pharmacology and Surgical Intensive Care, University Hospital of Geneva, Geneva, Switzerland) for excellent technical assistance.

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