
Oxygenator Volume Control by Parallel Ultrafiltration to Remove Plasma Water

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Abstract

A technique of hemoconcentration during and after cardiopulmonary bypass using parallel ultrafiltration (hemodiafiltration) is described and evaluated. Fifty-nine (59) adult patients were evaluated with thirty-five (35) being ultrafiltered intra-operatively and twenty-four (24) not being ultrafiltered. The technique of ultrafiltration is presented as a viable method of achieving significant hemoconcentration ($p < .001$). The ultrafiltered group demonstrated a drop in hematocrit between pre-pump and post-pump samples of 11%, whereas the group which was not ultrafiltered demonstrates a 16% drop in hematocrit between the same two samples. Operative fluid balance index is also significantly lower in the ultrafiltered group ($p < .001$), which had a positive index of 727 ml/m² as compared to the non-ultrafiltered group which had a positive index of 1206 ml/m². Comparisons of platelet counts, fibrinogen levels and plasma hemoglobin levels between the groups indicate no significant disruption of formed elements of plasma proteins associated with the use of ultrafiltration. There were no system failures during this series and no complications attributed to the use of parallel ultrafiltration.

Introduction

Hemodilution during extra-corporeal circulation is

a widely used technique, and its advantages are well documented.^{1(p.255),2,3} The management of the dilutional status of a patient can normally be accomplished quite uneventfully if the perfusionist understands the limitations of the technique.

There are however, many instances in which a technique of hemoconcentration is necessary.

A. *Excessive hemodilution* may occur as a result of the administration of large volumes of cardioplegic solution, or the mismanagement of fluid administration. Excessive hemodilution may result in oxygen carrying capacities below tolerable limits,^{4(p.224)} severe compromise of the body's hemostatic abilities by dilution of plasma proteins as well as other clotting factors,⁵ and systemic edema due to decreased intravascular oncotic pressure.^{1(p.216),6-8}

B. *Pre-operative or intra-operative anuria or oliguria* may limit the body's ability to hemoconcentrate on its own and thereby limits the patient's tolerance to fluid administration.

C. Some patients may present with an *expanded circulating blood volume*^{1(p.110),6(p.352)} upon initiation of cardiopulmonary bypass which would be advantageous to concentrate.

Hemoconcentration during extracorporeal circulation is normally accomplished by one of three methods: 1) increasing the urine output: although the most physiologic method of hemoconcentration, hemodynamic changes and medication administration intended to increase urine output are not always as effective as desired,^{4(p.244),9} especially in the face of pre-operative anuria or oliguria; 2) bank blood administration: this is dependent on availability and subject to negative aspects of bank blood administration;^{2(p.345)} 3) mechanical washing and concentrating: although this is

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very effective at hemoconcentrating, plasma constituents are lost in the process.^{3,10}

The purpose of this paper is to present our experience with a fourth method of hemoconcentration which is isolated ultrafiltration in parallel with cardiopulmonary bypass. The effective use of isolated ultrafiltration for treatment of fluid overload is described in the literature^{9,11-13} as is the concurrent use of hemodialysis during cardiopulmonary bypass.¹⁴ The technique herein described is a safe and simple procedure which provides the perfusionist an additional tool to accomplish hemoconcentration and maintain better control of the level of fluid in the oxygenator.

The technique should not be confused with dialysis as ultrafiltration does not require the flow of a dialysate fluid with its inherent complexities, but merely involves the creation of a transmembrane pressure gradient across a suitable device to accomplish water and electrolyte removal from the blood.

Theory of Operation

The ultrafilter is an artificial kidney. Blood enters into the ultrafilter and flows through parallel hollow fibers of cellulose acetate ($\approx 10,000$ fibers/ultrafilter). Each parallel fiber has an inside diameter of $195 \mu\text{m}$ and a wall thickness of $40 \mu\text{m}$. The walls have an effective pore size of approximately 30 Angstrom which provide a molecular weight cut-off of approximately 20,000 (that is, 90% of particles with a molecular weight of 20,000 will not pass through the pores of the ultrafilter). This cut-off permits the passage of water and electrolytes but not the formed elements of the blood or plasma proteins.^{15(pp.36,37)} The hollow fibers are surrounded by air space and a rigid plastic outer housing. This space between the hollow fibers and the outer housing will be referred to as the "ultrafiltrate path."

Ultrafiltration or hemodiafiltration^{15(pp.62-63)} occurs as a result of a pressure gradient from the blood to the ultrafiltrate path ("transmembrane pressure" or TMP) which causes water to move from the blood compartment to the ultrafiltrate compartment. The ionic concentration of this water or "ultrafiltrate" is the same as that of plasma water.¹²

The rate of ultrafiltration is primarily affected by two factors: 1) ultrafilter surface area and 2) transmembrane pressure.^{15(pp.49-50)} In any given procedure, the surface area of the ultrafilter is constant. Hence the rate of ultrafiltration is primarily dependant

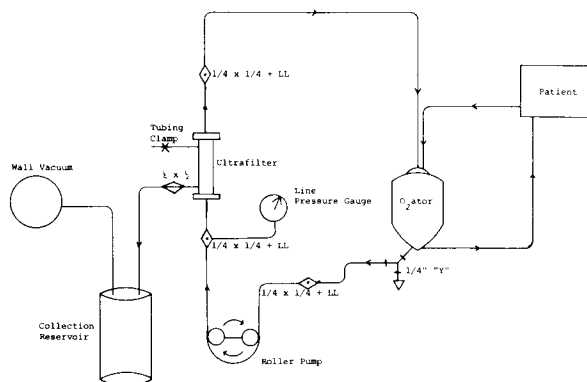


FIGURE 1.

on the TMP. TMP is defined as:

$$\Delta \bar{P}_m = \frac{P_{bi} + P_{bo}}{2} - \bar{P}_u$$

where \bar{P}_m = mean TMP, P_{bi} = pressure at blood inlet, P_{bo} = pressure at blood outlet, \bar{P}_u = mean ultrafiltrate compartment pressure.^{15(pp.49-50)}

P_{bi} and P_{bo} are functions of the blood flow rate, resistance of the ultrafilter and its distal circuitry. Increases in TMP can be accomplished by partial occlusion of the tubing distal to the ultrafilter, however, since this can cause hemolysis^{1(p.255),4(p.224),16} due to an increase in shear force,^{1(p.134),4(p.266),16} it was elected not to utilize this method to increase TMP. Hence blood path pressures were constant in this series at approximately 30-50 mmHg at 250 ml/min blood flow rate. TMP was maintained at approximately 250-500 mmHg in this series by application of vacuum to the ultrafiltrate path (P_u).

Materials and Methods

The ultrafiltration circuit is assembled as a parallel circuit around the cardiopulmonary bypass circuit. (See Figure 1). An adaptor line is connected to the coronary perfusion outlet of the oxygenator which allows access to the oxygenator volume for ultrafiltration and also provides a blood spike for bagging post-bypass hemoconcentrated oxygenator volume. The circuitry consists of $1/4" \times 3/32"$ tubing* throughout the entire blood path. The blood flows from the coronary perfusion port

* William Harvey Inc., Santa Ana, CA. 92705

of the bubble oxygenator,** or a modified reservoir outlet in the membrane system,*** through a low flow roller pump,**** through the ultrafiltration device and returns to the bubble oxygenator via the rapid prime port, or to the top of the membrane reservoir. Three luer-lock connectors are provided to allow access for rinsing of the ultrafilter and blood path pressure monitoring.

The ultrafilter used in this series is a hollow fiber artificial kidney, Model C-DAK 4000,***** with an effective surface area of 1.4 square meters. The hollow fiber ultrafilter was chosen because it has a fixed priming volume of approximately 109 ml and a high ultrafiltration capability (3.4 to 3.7 ml/hr/mmHg transmembrane pressure). At a maximum TMP of 750 mmHg,¹⁷ this allows plasma water to be removed at the rate of approximately 2.55 to 2.775 L/hour. The bottom port of the ultrafiltrate path is connected to a stub of 1/2" x 3/32" tubing which is reduced with a 1/2" x 1/4" connector.† This connector is attached to a 1/4" x 3/32" drain line which empties into a sealed graduated reservoir‡ for quantitating removed volume. A variable vacuum source is also connected to the reservoir to allow adjustment of TMP. Negative pressure is developed in the ultrafiltrate path by connection of a small stub of 1/2" x 3/32" tubing to the top ultrafiltration path port and occluding it with a tubing clamp.

The decision as to which patients would be ultrafiltered was based upon their anticipated need for extra-corporeal hemoconcentration during the cardiac surgical procedure. The following criteria were arbitrarily established as indications for the use of intra-operative ultrafiltration: 1) pre-operative oliguria or anuria or 2) an estimated minimal hematocrit of less than 24%.

The **estimated minimal hematocrit** was calculated using circulating blood volume, estimated from Allen's formula,¹⁸ pre-operative hematocrit, known extra-corporeal circuit prime volume, an estimate of the amount of fluid administered prior to bypass by anesthesia and an estimate of the amount of cardioplegic solution required during bypass.

** Model No. BOS-10, Bentley Laboratories, Inc., Irvine, CA. 92714

*** Model Nos. 2500-2A, 3500-2A, 4500-2A, Sci-Med Life Systems, Inc., Minneapolis, MN. 55441

**** Sarns, Inc., Ann Arbor, MI. 48103

***** Cordis Dow Corp., Miami, FL. 33145

† Cardio-Systems, Inc., Hayward, CA. 94545

‡ Sorenson Research Co., Salt Lake City, UT. 84115

Laboratory determinations of hematocrit, fibrinogen level and platelet count were done preoperatively, immediately prior to bypass, and as bypass was terminated. Free hemoglobin levels were also determined¹⁹ immediately prior to and upon termination of bypass. The patient's fluid balance was calculated in the intensive care unit upon admission.

The ultrafilter was rinsed with lactated Ringer's as per the manufacturers specifications.¹⁷ After rinsing, recirculation of the oxygenator contents through the ultrafilter allowed for final debubbling and protein coating of the sub-system prior to use.

During cardiopulmonary bypass, ultrafiltration was accomplished using a TMP of 250–500 mmHg and a blood flow rate of approximately 250 ml/min. While ultrafiltering, vacuum was never applied unless blood was flowing through the ultrafilter, to avoid hemolysis and coagulation of the fibers.¹⁷

Statistical data from both groups of patients were analyzed using Student's "t" test.²⁰

Results

Fifty-nine (59) adult patients were included in this series with thirty-five (35) meeting a criterion for intra-operative ultrafiltration (Group I) and twenty-four (24) not meeting a criterion (Group II). Table 1 summarizes the patient population data. The sex, type of procedure, and oxygenator used are expressed in numbers of patients and percent of the total group. Data are summarized in Table 2 for the each category and the mean of each group is given with the level of

TABLE 1
Patient Population

Category	Group I (N = 35)	Group II (N = 24)
Sex		
Male	22 (63%)	21 (88%)
Female	13 (37%)	3 (12%)
Procedure		
CABG	32 (91%)	21 (88%)
valve replacement	3 (9%)	1 (4%)
CABG + LVA	—	1 (4%)
Septal myotomy	—	1 (4%)
Oxygenator		
bubble	26 (74%)	17 (71%)
membrane	9 (25%)	7 (29%)

CABG = coronary artery bypass graft

LVA = left ventricular aneurysmectomy

TABLE 2
Group Data Comparisons

Category	Group I (N = 35)	Group II (N = 24)	Level of Significance
Body Surface Area (m ²)	1.79	2.02	<.001
Perfusion Time (min)	100	116	NS
Fluid Balance (ml)	1292	2437	<.001
Fluid Balance Index (ml/m ²)	727	1206	<.001
Priming Volume (ml)	2000	2048	NS
Estimated Minimal Hematocrit (%)	19	26	<.001
Hematocrit			
pre-op	39	45	<.001
pre-pump	35	40	<.001
post-pump	24	24	NS
Fibrinogen Level			
pre-op	348	357	NS
pre-pump	271	277	NS
post-pump	170	161	NS
Platelet Count			
pre-op	250	247	NS
pre-pump	208	214	NS
post-pump	160	157	NS
Plasma-Free Hemoglobin			
pre-pump	4.0	3.7	NS
post-pump	16.0	23.0	<.05

significance between the means. The mean body surface area, estimated minimal hematocrit, pre-operative and pre-pump hematocrit were significantly lower in Group I as compared to Group II ($p < .001$). There was no significant difference between the groups in post-pump hematocrit levels. There was also no significant difference between the groups in fibrinogen level, platelet count or free hemoglobin level at any sampling point. Total circuit priming volume as well as perfusion time were comparable for the two groups.

The operative fluid balance as well as the operative fluid balance index (operative fluid balance/body surface area (BSA)) were significantly less positive for Group I as compared to Group II ($p < .001$). There were no ultrafiltration system failures during this series nor any complications associated with the use of this sub-system.

Discussion

This study demonstrates the ability of an ultrafilter to effectively hemoconcentrate the circulating blood volume during cardiopulmonary bypass without loss of plasma proteins or other coagulation factors and without the administration of bank blood.

The patients in Group I had significantly lower he-

matocrits prior to bypass than did the patients in Group II. In addition, Group I patients had a significantly smaller mean BSA than did Group II. These two factors would cause the estimated minimal hematocrit of Group I to be less than that of Group II. The fact that the hematocrit in both groups of patients was the same at the end of bypass demonstrates the ability of the ultrafilter to concentrate the red blood cell volume of group I to a level equal to that of Group II. It should be noted at this point that in both groups, an average of less than one unit of bank blood was administered during bypass.

Group I did demonstrate a significantly lower operative fluid balance and fluid balance index. This was an unexpected positive aspect since fluid overload is a classic complication of cardiopulmonary bypass.^{8,21} Increased plasma protein concentrations, specifically albumin which is the major component in developing intra-vascular oncotic pressure, might explain this decreased volume overload^{6(pp.236-239),8} although it would seem that the fibrinogen levels would be somewhat of an indicator of increased albumin levels. However as the data show, fibrinogen levels were comparable between the two groups. Perhaps there are transient periods of increased plasma protein concentration during the procedure with ultrafiltration, such

as between intermittent cardioplegic infusions, which limit third space fluid shifting.

Pre-pump free hemoglobin levels were comparable between the two groups. However Group II had a higher post-pump free-hemoglobin level as compared to Group I. The authors believe that this difference is probably linked to variations in the use of the cardiomy suction system.^{4(pp.266),16} The data does however indicate that the use of ultrafiltration was not associated with any appreciable increase in hemolysis.

Post-bypass concentrating of residual volume was easily accomplished by continued recirculation through the ultrafiltration circuit. By simple calculations the time required to concentrate the residual volume to any desired hematocrit can be derived. The advantages of this type of concentration include:

- 1) retention of plasma-proteins and other coagulation factors;
- 2) maintenance of primed extra-corporeal circuit should bypass need to be reinitiated;
- 3) precise and rapid concentration capabilities.

Due to its heterogeneous nature, heparin has a molecular weight that varies between 6,000 and 20,000.²² As such it is removed with the plasma water and electrolytes during ultrafiltration. This did not present a problem during this series as anticoagulation therapy is managed by activated clotting times and heparin titration. However, institutions using fixed dosage protocols should be aware that circulating heparin is being removed with plasma water, and some mode of monitoring heparin activity should be considered.

Addendum

Since the time this series was completed, Cordis Dow has begun marketing a new artificial kidney, under the tradename "HEMOCONCENTRATOR." This kidney has an ultrafiltration capability several times the capability of the unit used in our series. The "HEMOCONCENTRATOR" has an ultrafiltration index of 12 ml/hr/mmHg.²³ At maximum TMP (750 mmHg) this would allow the removal of plasma water at a rate of approximately 9 liters per hour.

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