Postoperative Effects of Conventional Ultrafiltration on Adult Cardiac Surgery Patients

by

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Abstract

For years, ultrafiltration has been used during cardiac surgery involving cardiopulmonary bypass (CPB) in order to minimize hemodilution. Despite this, current research on the effects of conventional ultrafiltration on adult patients is limited and those studies that do exist often have contradicting results. The purpose of this study was to investigate the postoperative effects of conventional ultrafiltration on lung function, kidney function, the need for blood transfusions, bleeding, and length of intensive care unit stay in adult patients.

Data were collected retrospectively from patient charts and the Society of Thoracic Surgeons database for 40 patients that underwent myocardial revascularization, valve repair or replacement, or a combination of those surgeries at Aurora St. Luke's Hospital in Milwaukee, Wisconsin, between January 1, 2017 and October 12, 2017. Half of these patients received conventional ultrafiltration during surgery and the other half did not (controls). In order to determine the postoperative effects of conventional ultrafiltration, postoperative hematocrit, blood loss, platelet count, ventilation time, length of intensive care stay, creatinine levels, urine output, and the amount of red blood cell transfusions were compared between the two groups.

This study found no statistically significant differences between the two groups of patients except for the variable of urine output on postoperative day one, which was higher in the control group. Although there were no differences identified for most measures, a few adverse events were noted. One patient in the control group did suffer from a pleural effusion requiring drainage postoperatively and one patient in the ultrafiltration group suffered from acute kidney failure. The results of this study lead to the conclusion that while there are no obvious benefits to conventional ultrafiltration on this particular patient group, it is not detrimental to patient health. A much larger study should be conducted in order to verify these results.

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Several people helped to make this project a reality and without them it would not have been possible. I would like to thank Dr. Ronald Gerrits for his constant guidance throughout the creation of this project as well as for his help in editing and revising my paper. I would also like to thank Dr. Larry Fennigkoh for his guidance in performing statistical analysis of the data used in this study. A thank you also goes out to Gary Shimek for his help in formatting and proofreading the final document. Also deserving recognition and thanks is Matt Hietpas for collecting data and Jonathan Howard for help throughout the entirety of this project from idea to proofreading the final document.

Table of Contents

List of Figures

List of Tables

Introduction

Since its creation, the use of cardiopulmonary bypass (CPB) has presented a variety of challenges for patients and healthcare workers. One of these challenges is the high use of blood products that historically accompanied the larger fluid volumes that are necessary when using CPB. One solution to this problem is to allow hemodilution of the patient instead of adding additional red blood cells. Today, hemodilution is an accepted way to reduce the need for banked blood during circuit priming as well as to improve oxygenation during CPB [1, 2, 3]. Unfortunately, hemodilution also has some adverse effects, such as hypoxia, hypotension, decreased colloid oncotic pressure, interstitial edema, and hypocoagulation [4]. In order to combat these negative effects, ultrafiltration can be used [5].

Ultrafiltration is a technique where excess water and solutes are filtered out of the blood across a semipermeable membrane driven by a positive transmembrane hydrostatic pressure [6, 7]. This method of volume management during CPB can minimize some effects of hemodilution, such as edema, and may reduce the need for blood transfusion [5]. Although there is much research regarding the impact of ultrafiltration on postoperative lung function, renal function, bleeding, transfusion requirements, recovery time, and the inflammatory response, findings are often conflicting. Additional research is required to determine what the postoperative effects of ultrafiltration are. The goal of this project was to compare postoperative patient data from two groups of CPB patients, those that underwent ultrafiltration and those that did not, in an effort to further study the effects of this technology on patients. This study specifically investigated clinical

markers used to assess lung function, renal function, transfusion requirements, and recovery time.

Background

The main purpose behind ultrafiltration while on CPB is to separate excess water from the blood [8]. Separation occurs across a semipermeable membrane. The pore size of the membrane also allows some small molecules, usually less than 65,000 Daltons, to be filtered out of the blood as well. These small molecules include potassium, sodium, chloride, creatinine, glucose, and inflammatory mediators [6, 8]. Some of the larger molecules that are not filtered out of the blood by a hemoconcentrator (the device used to carry out the process of ultrafiltration) are albumin, hemoglobin, and fibrinogen [8]. Table 1 lists the sizes of various molecules found in the blood.

Table 1: Molecular Sizes of Blood Components and Other Substances [9].

Molecule	Size (Daltons)
Sodium Potassium Chloride Urea Creatinine	< 10,000
Albumin	69,000
Hemoglobin	68,000
Fibrinogen	341,000
Leukocytes Platelets Red Blood Cells	> 341,000

In addition to molecular size, removal of solutes during ultrafiltration is also determined by the concentration gradient between blood and the filtrate. For molecules that are freely filtered, it means that the filtrate and blood will end up with the same concentration of the molecule, assuming adequate time to reach equilibrium. For larger molecules that might only be partially filtered, the concentration of the molecule in the

filtrate is determined by the sieving coefficient, which represents the ratio of the solute concentration in the filtrate compared to that in the plasma. Solutes that are freely filtered have a sieving coefficient of 1.0 [2]. The sieving coefficient for several molecules, along with their approximate sizes, is shown in Figure 1.

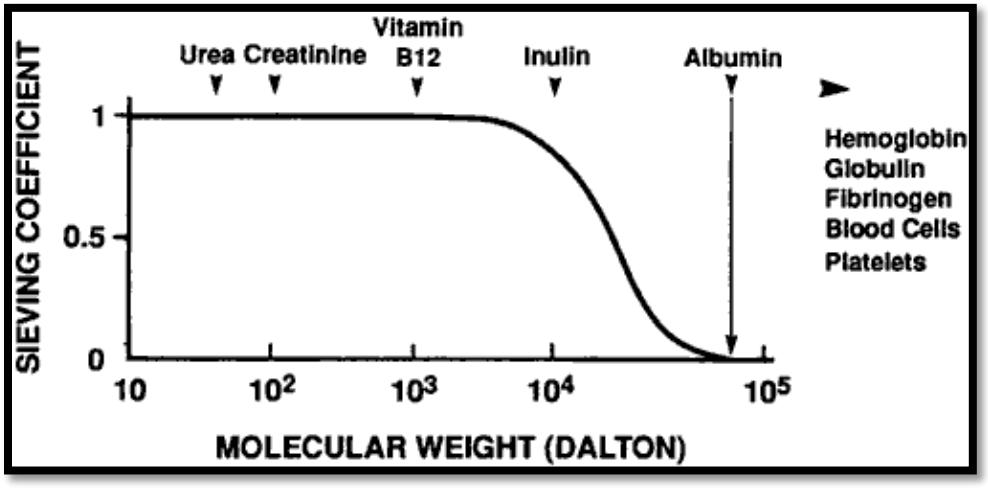

Figure 1: Sieving Coefficient of Various Molecules [10].

The rate that filtered molecules are removed is dependent upon the transmembrane pressure (TMP) [8]. TMP is based on the blood inlet pressure (P_A), blood outlet pressure (P_v), and negative pressure applied to the effluent, or runoff, side of the hemoconcentrator (P_S) and, according to Gravlee *et al*. [6], it can be expressed by the equation

$$TMP = [(P_A + P_V)/2] + P_S.$$

The effect of TMP alone on the rate of ultrafiltration (K_{UF}) is shown in Figure 2 [11]. As TMP increases, so does the rate of ultrafiltration at all blood flow rates, although the relationship is not linear over a large range of TMP. Other factors affecting filtration rate

include blood flow volume, thickness of the membrane, quantity and size of the pores in the membrane, hematocrit, and temperature [8].

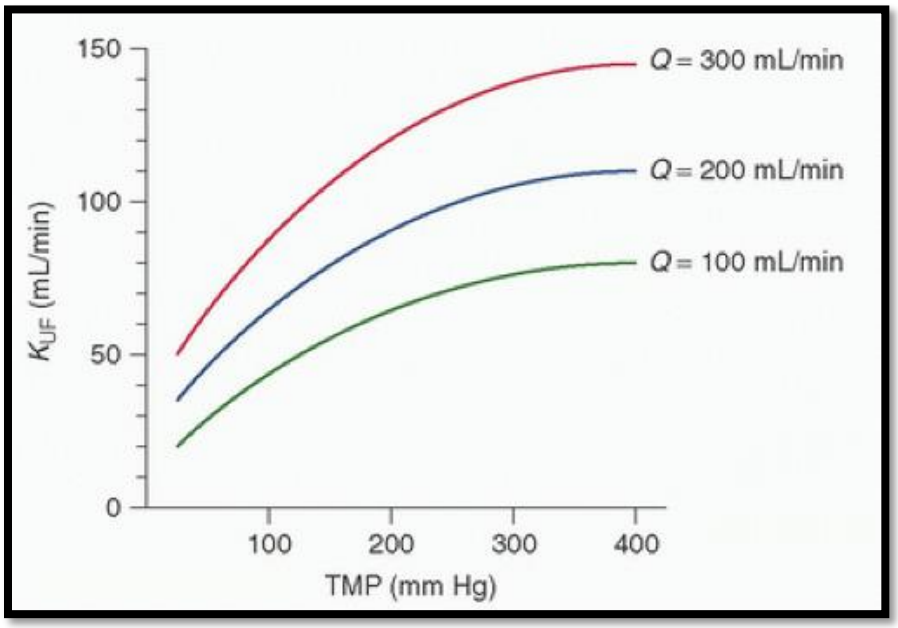

Figure 2: Relationship Between Transmembrane Pressure (TMP) and Ultrafiltration Rate (K_{UF}) at Various Flows (Q) [11].

There are multiple forms of ultrafiltration including conventional, modified, and zero balance, but the focus of this paper and study is conventional ultrafiltration. Conventional ultrafiltration is a method that can be used at any point during surgery involving CPB. In conventional ultrafiltration, the hemoconcentrator is in parallel with the CPB circuit and, in the most common circuit, the inflow comes from the arterial line and the outflow joins with the venous return line (Figure 3) [6]. The benefit of this method is that the patient's time on CPB is not extended, but the disadvantage is that the

amount of filtrate is limited because of the amount of fluid necessary to keep the circuit primed [8, 12].

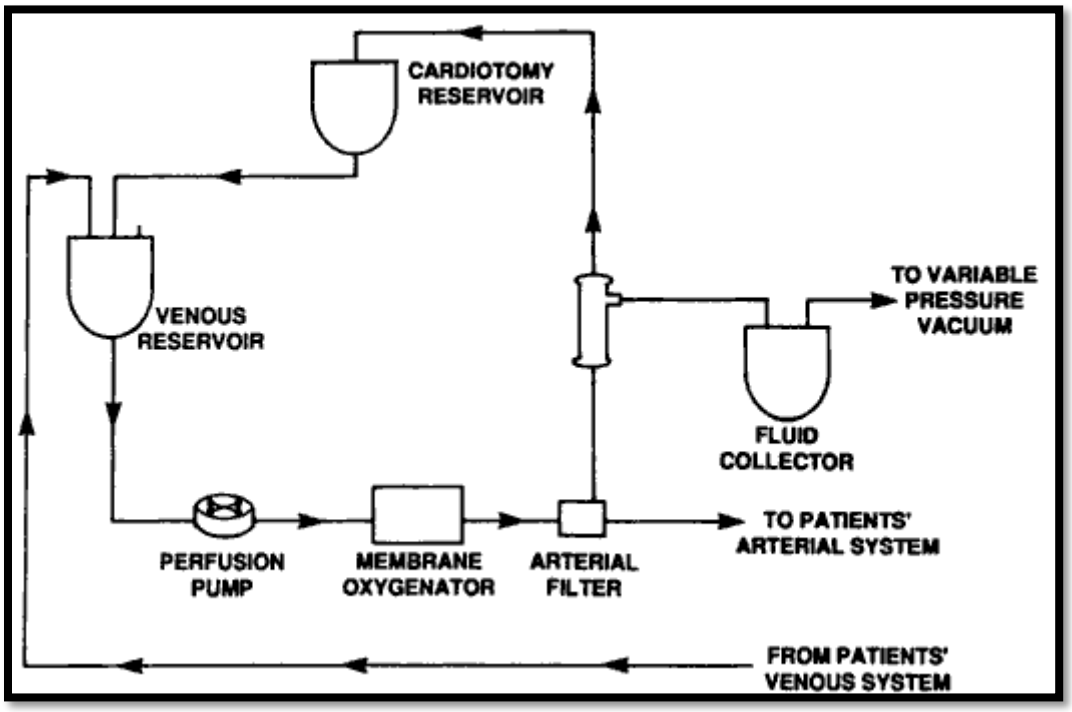

Figure 3: Hemoconcentrator in a Parallel Circuit with CPB [6].

Using ultrafiltration during cardiac surgery to alleviate the negative effects of CPB, particularly those related to hemodilution, has become common [13]. Yet this technique remains controversial amongst perfusionists in regards to adult cardiac surgery [14]. This is likely because research on postoperative benefits and disadvantages to adult conventional ultrafiltration is lacking, and the research that is available is often conflicting. Persisting concerns related to the postoperative effects associated with ultrafiltration use include its impacts on the need for blood transfusions [15], coagulation and bleeding [15], systemic inflammatory response syndrome (SIRS) and pulmonary

function [16], kidney function [15, 17], and length of stay in the intensive care unit (ICU) [15, 18].

The need for blood transfusions following cardiac surgery is common [19]. This is despite the fact that transfusions increase the risk of a patient having a negative outcome or side effect [20]. Some of these negative effects include infections, allergic reactions, febrile reactions, transfusion related acute lung injury, transfusion associated circulatory overload, non-ABO hemolytic transfusion reactions, and transfusion-related immune modulation [21]. Many researchers have documented an increased postoperative hematocrit in patients who received ultrafiltration while on CPB compared to patients who did not [16, 17, 22, 23], although a smaller number of studies reported no significant difference in postoperative hematocrit between patients who did and did not receive ultrafiltration [15, 24]. It would seem logical that researchers who saw an increased hematocrit also saw less need for blood transfusions in these same patients, such as Boodhwani *et al*. [25] did in their research, but this is not always the case. For instance, Maningding *et al.* [22] observed an increase in postoperative hematocrit in ultrafiltrated patients but no difference in the rate of transfusions between those patients and the patients not ultrafiltrated. In general, research so far has shown an array of outcomes in regard to the need for blood transfusions postoperatively in patients who were ultrafiltrated compared to those who were not, as summarized in Table 2. With these mixed results, it is still unclear what the impact of ultrafiltration is on the need for blood transfusions, if any.

Table 2: Summary of Research into Relationship Between Ultrafiltration and Need for Blood Transfusion. UF = ultrafiltration, MUF = modified ultrafiltration, HC = hemoconcentrated, CUF = conventional ultrafiltration.

Study	Data	Conclusions
Maningding *et al.* [22]	• UF n= 10 • Non UF n= 10 • All patients underwent either coronary artery bypass grafting, aortic valve replacement, or mitral valve plasty	No significant difference in amount of blood transfused between HC patients and those that were not.
Babka *et al.* 1997 [15]	• UF n= 30 • Non UF n= 30 • All patients underwent coronary artery bypass grafting	No significant difference in amount of blood transfused between HC patients and those that were not.
Boodhwani *et al.* 2006 [25]	• Combined a total of 10 studies for a total of n= 1004 between the different groups.	Found CUF is associated with a reduced use of red blood cell products, although MUF further reduces usage.
Leyh *et al.* 2001 [26]	• CUF n= 16 • MUF n= 16 • Non UF n=16 • All patients underwent coronary artery bypass grafting.	Patients receiving CUF plus MUF had less need for transfusion when compared to the control group.
Tesdahl *et al.* 2017 [27]	• UF n= 42,515 • Non UF n= 55,424	Found ultrafiltration was associated with an increased rate of red blood cell transfusion.

In addition to red cells, other large components of blood are also concentrated when ultrafiltration is used. Examples of these components include platelets and clotting factors like factor VII and fibrinogen [28]. The concentration of these hemostatically active molecules may lead to a decrease in postoperative blood loss [8, 28, 29, 30], although this is not supported by all studies [15]. In particular, platelet counts are not always found to increase after ultrafiltration, as summarized in Table 3. The majority of studies that measured postoperative blood loss reported a decrease after ultrafiltration

[25, 29, 30, 31], although one study found no statistically significant differences in their patient population [15].

Table 3: Summary of Research on the Relationship Between Ultrafiltration and Platelet Levels. UF = ultrafiltration, MUF = modified ultrafiltration, CUF = conventional ultrafiltration.

Study	Data	Conclusions
Naik *et al.* 1993 [30]	• UF n= 24 • Non UF n= 24 • Patients underwent various surgeries.	Found MUF causes factors including platelet levels to increase.
Kiziltepe *et al.* 2001 [32]	• UF n= 20 • Non UF n= 20 • All patients underwent either coronary artery bypass grafting or valve repair/replacement.	Found combined CUF and MUF patients showed higher platelet levels.
Babka *et al.* 1997 [15]	• UF n= 30 • Non UF n= 30 • All patients underwent coronary artery bypass grafting.	Found no statistically significant difference between the ultrafiltration group and the control group.
Hopeck *et al.* 1981 [33]	• UF n= 35 • Non UF n= 24 • All patients underwent either coronary artery bypass grafting or valve repair/replacement.	Found no significant difference between the ultrafiltration group and the control group.
Santarpino *et al.* 2009 [34]	• UF n= 12 • Non UF n= 12 • All patients underwent either coronary artery bypass grafting or valve repair/replacement.	Found similar results in the ultrafiltration group and the control group in regard to platelet count.

It is well documented that CPB leads to a systemic inflammatory response syndrome (SIRS) due to the extensive contact between a patient's blood and the foreign surface of the CPB circuit [6, 35, 36]. This inflammatory response leads to capillary leak and interstitial edema that can cause organ dysfunction, particularly in the lungs [35, 37,

38, 39, 40]. Ultrafiltration has been shown to combat SIRS by removing inflammatory mediators, such as IL-6, IL-8, TNF-alpha, C3a, and C5a [41]. Ultrafiltration also increases plasma colloid oncotic pressure because albumin is too large to filter out of the blood. This also helps to combat SIRS by reducing interstitial edema [16]. One of the benefits of this reduction in SIRS is improved pulmonary function. It has been demonstrated that ultrafiltration leads to benefits in pulmonary compliance [42], airway resistance [42], and gas exchange [16, 32, 42], and in some instances, decreases length of mechanical ventilation [32, 42]. This last point, though, is debated with other researchers finding opposing results [43].

Another organ believed to be affected by ultrafiltration while on CPB is the kidney. The effects of ultrafiltration on the kidneys have been theorized to be both good and bad. Some researchers believe that CPB without ultrafiltration will lead to a fluid overload and the resultant tissue edema may cause injury to the encapsulated kidneys [44]. On the other side of the argument, some researchers believe ultrafiltration leads to acute kidney injury, because it causes fluid shift imbalances and renal hypoperfusion [15, 45, 46]. Research so far into the subject has ended with a variety of results, which are summarized in Table 4. While heavily disputed, research into ultrafiltration and kidney function has given no clear results.

Table 4: Summary of the Relationship Between Ultrafiltration and Postoperative Kidney Function. UF = ultrafiltration, MUF = modified ultrafiltration, CUF = conventional ultrafiltration.

Study	Data	Conclusions
Foroughi *et al.* 2014 [46]	• UF n= 87 • Non UF n= 72 • All patients underwent either coronary artery bypass grafting or valve replacement.	Found no significant difference between CUF group and control group in terms of renal insufficiency.
Kuntz *et al.* 2006 [45]	• CUF n= 49 • Non UF n= 47 • All patients underwent coronary artery bypass grafting or valve replacement.	Found a significantly lower adjusted 24-hour creatinine associated with CUF.
Paugh *et al.* 2015 [17]	• CUF n= 1,362 • Non UF n= 5,045 • All patients underwent coronary artery bypass grafting.	Found an increased risk of acute kidney injury postoperatively in patients that received ultrafiltration.
Babka *et al.* 1997 [15]	• UF n= 30 • Non UF n= 30 • All patients underwent coronary artery bypass grafting.	Found ultrafiltration improved outcomes in patients with preoperative kidney disease but has no significant effect on patients without preoperative kidney disease.

With all the theorized effects of ultrafiltration during CPB on patients postoperatively, it would be expected that the length of stay in the ICU should also be affected. In their research, Lakshmanan *et al*. [18] found that both the need for inotropic support and ICU stay were reduced in patients who received ultrafiltration. However, both Babka *et al*. [15] and Wang *et al*. [43] found no difference in ICU stay between ultrafiltrated patients and those who were not. Some research has even found that patients who had ultrafiltration needed an extended stay in the ICU [17]. With all the

conflicting reports on postoperative effects of ultrafiltration, additional research would be beneficial.

Project Goal

Based on conflicting data related to patient outcomes after the use of ultrafiltration, additional research is necessary. The goal of this project was to analyze postoperative patient data in order to determine what effects conventional ultrafiltration has on adult patient outcomes. The specific hypothesis tested was that there would be no statistically significant differences between patients who received ultrafiltration and those who did not, in terms of postoperative bleeding, transfusion requirements, lung function, kidney function, and length of stay in the ICU.

Methods

After obtaining approval from the Institutional Review Board, retrospective data were obtained from 40 patients who underwent cardiac surgery requiring cardiopulmonary bypass at St. Luke's Medical Center in Milwaukee, Wisconsin, between January 1st, 2017, and October 11th, 2017. While there were more patients available to choose from for this study, only the 40 randomly selected patients were included in order to reasonably conclude the study under the time restraints for this project. Inclusion and exclusion criteria are summarized in Table 5. All data were obtained either from the Society of Thoracic Surgeons Database or the patient's chart in EPIC. Normal cardiopulmonary bypass protocols were used on patients involved in the study. Patients may have had either the Terumo System 1 centrifugal or roller pump used on them during surgery, as well as Terumo's Capio FX25 oxygenator. Type of cannulation used during surgery was not noted, but would have been left to the surgeon or perfusionist to choose. Lab values were recorded by following the hospital's protocols. The decision to use a hemoconcentrator was left to the perfusionist to decide, and for any patients who received conventional ultrafiltration, the Sorin SH14 hemoconcentrator was used. The amount of filtrate removed was based on the decision of the perfusionist.

Table 5: Patient Inclusion and Exclusion Criteria.

Inclusion Criteria	Exclusion Criteria
All patients underwent either myocardial revascularization, valve repair or replacement, or a combination of these.	Any aortic, ventricular assist device, or heart transplantation surgery
Status in the Society of Thoracic Surgeon database listed as elective	History of preoperative kidney disease
Microplegia was used as the cardioplegia during surgery	Redo operations
Surgery occurred between January 1, 2017 and October 11, 2017	History of myocardial infarction
	Any type of ultrafiltration besides conventional

Various preoperative and intraoperative variables (Table 6) were compared among the patient groups in an effort to ensure that these variables were not responsible for any changes identified in postoperative outcomes, as described by others [47, 48, 49]. All postoperative variables analyzed are also discussed in Table 6.

Table 6: Preoperative, Intraoperative, and Postoperative Variables Analyzed.

System Evaluated	Variables	Notes
Blood/Vascular	• Hematocrit (Preoperative and 3 days postoperative) • Platelet Count (Preoperative and 3 days postoperative) • Blood Loss through Chest Tubes (2 days postoperative) • Amount of Red Blood Cell Transfusions and Number of Patients Receiving Transfusions • Lowest Intraoperative Hemoglobin	• Blood Loss was measured by dividing total loss over a 24-hour period by the patient's weight
Lung	• Postoperative Ventilation Time • Any Adverse Postoperative Pulmonary Events	• Any patients with noted preoperative lung disease were left out of the study • Any patients extubated in the OR were left out of the study • One patient in the control group was left out of the study as they experienced a postoperative pneumothorax
Kidney	• Urine Output (3 days postoperative) • Creatinine (Preoperative and Day 3 postoperative) • Any Incidence of Postoperative Acute Renal Failure or Need for Dialysis	• Urine Output was measured by dividing total output over a 24-hour period by the patient's weight • One patient in the ultrafiltration group was left out as the urine output studies as the output was charted at such large values there was some doubt whether they had been charted correctly
Other	• Intraoperative Perfusion Time • Intraoperative Aortic Cross Clamp Time • Length of Stay in the Intensive Care Unit • Any Need for Postoperative Mechanical Support • Any Need for a Patient to be Readmitted	

Statistical Analysis

Statistical analysis of the data was performed using Minitab 18 Statistical Software. The two-sample student's t-test was used to perform all data analysis, except for evaluating the number of patients requiring a postoperative red blood cell transfusion, with p-values less than or equal to 0.05 considered to be significant. For perfusion time, aortic cross clamp time, blood loss on postoperative day two, platelet count on postoperative day two, urine output on postoperative day two, creatinine level on postoperative day three, and length of ICU stay, it was necessary to use the base 10 logarithm transformation in order to meet the normality and equal variances assumptions, which are indicated in the next section. To analyze the number of patients requiring a red blood cell transfusion, the two proportions test was used with a p-value less than or equal to 0.05 considered to be significant. In some cases, certain patient data were left out of the analysis for various reasons (as noted in the results), such as possible errors in patient charting. Because of the retrospective nature of this study, not all data points were available in every patient's chart, resulting in numbers less than 20 per group in some tests. Tabulated data are presented as means ± SD when applicable.

Results

Data were collected for a total of 40 patients with 20 patients in the control group and 20 patients in the ultrafiltration group. Out of the 40 patients, two died within 30 days of surgery, one from each group; but because no reason was given to believe that their causes of death could have affected the data collected, both were included in the statistical tests. Table 7 includes preoperative patient characteristics for both groups of patients and shows that there were no statistical differences between the preoperative variables considered in the study. As shown, the group sizes were the same and the gender mix was almost identical between the two groups. Intraoperative data (Table 8) also show no significant difference between groups for the variables evaluated.

Table 7: Preoperative Patient Data.

Characteristic	Control Group	Ultrafiltration Group	p-value
Number of Patients	20	20	
Gender	M- 12 F- 8	M- 13 F- 7	
Creatinine Levels (mg/dL)	0.86 ± 0.166	0.935 ± 0.305	0.342
Platelet Count (per Liter)	208,800 ± 60808	224,350 ± 65,457	0.441
Hematocrit (%)	40.31 ± 4.54	39.87 ± 4.81	0.765

Table 8: Intraoperative Patient Data.

Characteristic	Control Group	Ultrafiltration Group	p-value
Lowest Hemoglobin (g/dL)	8.79 ± 1.13	9.15 ± 1.55	0.414[a]
Perfusion Time (minutes)	100.3 ± 56.7	104.3 ± 39.7	0.398[a]
Aortic Cross Clamp Time (minutes)	76.5 ± 45.1	81.3 ± 34.0	0.342[a]

[a]Note: The base 10 logarithm transformation was necessary to meet the t-test assumptions of normality and equal variance.

No statistically significant differences were found between the groups in any of the variables used to assess blood loss and the need for blood transfusions, as shown in Table 9. The amount of red blood cell transfusions was the same for both groups at seven units. There was also no significant difference found in the number of patients in each group requiring a red blood cell transfusion, with five requiring at least one in the ultrafiltration group, and six requiring at least one in the control group.

Table 9: Postoperative Blood Data.

Characteristic	Control Group	Ultrafiltration Group	p-value
Hematocrit (%) Postoperative Day 1	27.02 ± 4.60 n = 20	27.45 ± 4.53 n = 20	0.773
Hematocrit (%) Postoperative Day 2	26.47 ± 4.86 n = 18	26.85 ± 4.11 n = 18	0.800
Hematocrit (%) Postoperative Day 3	26.20 ± 4.22 n = 18	27.12 ± 3.88 n = 18	0.503
Platelet Count (/L) Postoperative Day 1	141,300 ± 55,200 n = 20	128,600 ± 35,600 n = 20	0.392
Platelet Count (/L) Postoperative Day 2	130,100 ± 36,000 n = 18	113,300 ± 40,400 n = 18	0.186[a]
Platelet Count (/L) Postoperative Day 3	143,800 ± 37,300 n = 18	126,800 ± 48,500 n = 18	0.248
Blood Loss (cc/kg) Postoperative Day 1	7.85 ± 3.82 n = 20	6.06 ± 4.63 n = 20	0.189
Blood Loss (cc/kg) Postoperative Day 2	4.13 ± 4.53 n = 19	3.35 ± 3.29 n = 17	0.569[a]
Patients Requiring a Red Blood Cell Transfusion (proportion)	0.30 n = 20	0.25 n = 20	0.723

[a]Note: The base 10 logarithm transformation was necessary to meet the t-test assumptions of normality and equal variance.

Time spent on a ventilator postoperatively was analyzed to evaluate the effect of ultrafiltration on lung function. As shown in Table 10, no statistically significant difference was found between the two groups in regard to ventilation time. It is important to note that none of the patients in either group required reintubation, although one patient in the control group also experienced a postoperative pleural effusion that required drainage.

Table 10: Postoperative Ventilation Time.

Characteristic	Control Group	Ultrafiltration Group	p-value
Postoperative Ventilation Time (hours)	4.40 ± 1.37 n = 11	4.30 ± 2.62 n = 12	0.907

Of the variables assessed to determine kidney function, only urine output on postoperative day one was found to be significantly different, with the ultrafiltration group having a lower output (Table 11, Figure 4). It is also worth noting that out of all 40 patients, only one patient (in the ultrafiltration group) developed acute renal failure postoperatively, but did not require dialysis.

Table 11: Postoperative Kidney Function.

Characteristic	Control Group	Ultrafiltration Group	p-value
Urine Output (cc/kg) Postoperative Day 1	24.21 ± 9.34 n = 20	18.36 ± 8.08 n = 19	0.031
Urine Output (cc/kg) Postoperative Day 2	19.2 ± 12.7 n = 20	16.8 ± 12.0 n = 19	0.558[a]
Urine Output (cc/kg) Postoperative Day 3	20.2 ± 11.6 n = 19	18.0 ± 12.0 n = 18	0.589
Creatinine Level (mg/dL) Postoperative Day 3	0.846 ± 0.220 n = 16	1.209 ± 0.828 n = 17	0.160[a]

[a]Note: The base 10 logarithm transformation was necessary to meet the t-test assumptions of normality and equal variance.

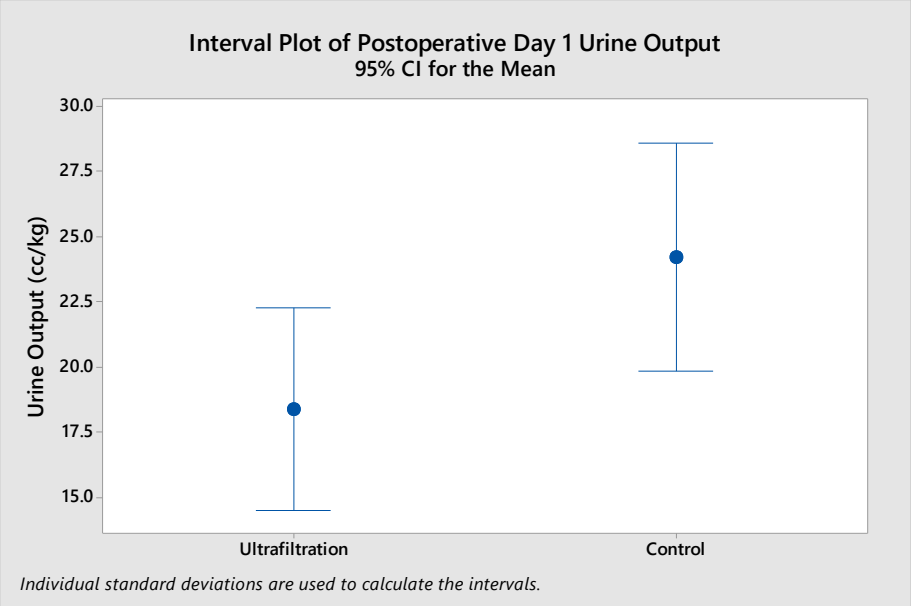

Figure 4: Urine Output Postoperative Day One.

Length of stay in the intensive care unit was also analyzed to determine if ultrafiltration had an effect. Table 12 shows the results of that analysis with no statistically significant difference. None of the patients needed an intra-aortic balloon pump or ECMO postoperatively, although one patient in the control group did need to be readmitted later on.

Table 12: Postoperative Length of ICU Stay.

Characteristic	Control Group	Ultrafiltration Group	p-value
Length of ICU Stay (hours)	68.9 ± 37.3 n = 20	73.5 ± 40.8 n = 20	0.687[a]

[a]Note: The base 10 logarithm transformation was necessary to meet the t-test assumptions of normality and equal variance.

Discussion

For many years, ultrafiltration has been used during cardiac surgery in order to combat the negative effects of hemodilution. Both positive and negative effects have been theorized to be caused by ultrafiltration, yet research into adult conventional ultrafiltration is limited and data are often conflicting [5]. The goal of this study was to further investigate the postoperative effects of hemoconcentration on adult cardiac surgery patients. To start, it was necessary to compare the groups preoperatively in order to rule out differences. In this study, although the group sizes were small, the groups did not differ in any of the pre- or intraoperative variables used to describe the patient populations. Therefore, it is less likely that preoperative differences would impact postoperative results.

It has previously been shown that ultrafiltration use during cardiac surgery can raise the hematocrit of the patient [6]. It is debated, however, whether the higher hematocrit persists after surgery. Because of this, postoperative hematocrit for days one, two, and three were evaluated. No statistically significant differences were found between the two groups on any of the three days (Table 9). This likely means that ultrafiltration has no lasting effect on hematocrit. Likewise, there was no difference in the amount of red blood cell transfusion usage between the two groups, which agrees with the research by both Maningding *et al.* [22] and Babka *et al.* [15], although it differs from studies by Boodhwani *et al.* [25] and Tesdahl *et al.* [27], who found a decreased need for red blood cell transfusions and an increased need, respectively. It is hard to determine a reason for the differences found. The benefits of the studies by both Boodhwani *et al.* and Tesdahl *et al.* are the large sample sizes, although these were

obtained by pooling data from several clinical sites and included multiple types of ultrafiltration. The studies by Babka *et al.* [15] and Maningding *et al.* [22] are similar to the current study, with small sample sizes, and data were collected from a single location. When comparing the various studies, it is important to note that Boodhwani *et al.*'s [25] meta-analysis looked heavily at modified ultrafiltration rather than just conventional ultrafiltration. It is also important to note that, at least in the research done for this study, Tesdahl *et al.*'s [27] study appears to be the only one finding that ultrafiltration leads to an increase in the need for red blood cell transfusions. Taken together, studies generally indicate that ultrafiltration either lessens, or does not lead to additional, transfusions.

It would be reasonable to assume that platelets and other clotting factors would become more concentrated in the ultrafiltration group as they are too large to be filtered during ultrafiltration [28]. This study found no significant difference between postoperative platelet counts for the two groups, although interestingly, the ultrafiltration group tended toward a lower platelet count. Blood loss for postoperative days one and two were also evaluated, but found to not be significantly different between the two groups. This finding makes sense if clotting factors are not actually being concentrated in the ultrafiltration group as was demonstrated by Babka *et al*. [15]. It is important to note, however, that many studies found ultrafiltration leads to a decrease in blood loss postoperatively [25, 29, 30, 31]. One possible reason that there was no significant differences found in this study is because its small size may not be adequately representative of the larger patient population. Additionally, it could be that standard ultrafiltration produces results that differ from those of modified ultrafiltration, which make up a large majority of the ultrafiltration cases included in the larger studies. In fact,

Boodhwani *et al.* [25] found that, while still considered significant, there was a much smaller reduction in postoperative blood loss when patients only received conventional ultrafiltration rather than that combined with modified ultrafiltration. Despite the difference in the results of the studies discussed here, none of them found an increase in blood loss associated with conventional ultrafiltration in adult cardiac patients.

It has been demonstrated that modified ultrafiltration, particularly in pediatrics, leads to a decrease in inflammatory mediators [6] which may lead to increased postoperative lung function [16, 32, 50]. But similar research on the effects of conventional ultrafiltration on adult lung function has not been studied in detail. To evaluate postoperative lung function, total ventilation time was analyzed. This study found no statistically significant difference between the ventilation time for the two groups (Table 10). None of the patients in either group required reintubation, although one patient in the control group also experienced a postoperative pleural effusion that required drainage. The limited data set used in this study makes it hard to draw strong conclusions about the impact of ultrafiltration on lung function postoperatively and additional research is warranted.

In order to assess kidney function, postoperative urine output for the first three days as well as creatinine levels on postoperative day three were evaluated. The only significant difference identified was urine output for postoperative day one with the ultrafiltration group having a lower output (Table 11). This seems reasonable because the ultrafiltration group likely had additional fluid removed prior to the end of surgery, reducing body fluid volume, although this study is limited by not having compared that data.

Although not significant, there was a slight trend for the ultrafiltration group to have a lower average urine output on postoperative days two and three. Because intraoperative fluid output and diuretic use was not included in this study, creatinine levels are likely the best indicator of postoperative kidney function, which did not vary between the two groups. Although no patient in either group required postoperative dialysis, one patient in the ultrafiltration group did suffer from acute renal failure postoperatively. In their much larger study, Paugh *et al*. [17] found an increased risk of acute kidney injury in patients receiving ultrafiltration. Complicating this finding was that their ultrafiltration group had a much higher incidence of preoperative vascular disease, prior myocardial infarction, and congestive heart failure than the control group. Ideally, a larger study could be conducted in which the groups do not differ in preoperative variables.

Similar to other researchers [15, 43], this study did not find a significant difference for length of stay in the ICU between the two groups. Neither group had any patients requiring other postoperative mechanical support and each group had one patient die within the first 30 postoperative days as well. Overall, this study found no differences between the two groups. Based on the results of this study, there seems to be no obvious benefit to the use of conventional ultrafiltration during adult cardiac surgery on total ICU stay. Despite this, there were also no obvious detrimental effects of conventional ultrafiltration in this study so there is no reason to discourage its use and it should be considered safe to use at the discretion of the perfusionist.

Conclusion

The results of the study support the hypothesis that there are no significant differences between patients who received ultrafiltration and those who did not in terms of postoperative bleeding, need for blood transfusions, pulmonary function, kidney function, and length of ICU stay. This means that, at least within the confines of the variables evaluated in this study, ultrafiltration does not appear to have harmful effects on patients. Although the results of this study are not consistent with some of the other studies investigating similar interventions and outcomes, differences in patient populations, types of ultrafiltration analyzed, and failure to rule out preoperative comorbidities, makes it a challenge to make direct comparisons. But taken collectively, there doesn't seem to be significant disadvantages to standard ultrafiltration and perfusionists should feel free to use it when desired, such as when trying to avoid an intraoperative red blood cell transfusion on a small patient or when a patient is volume overloaded.

Limitations

This small study was aimed at investigating the effects of ultrafiltration on common variables used to assess blood status and function of the lungs and kidneys as well as other possible adverse postoperative outcomes. The strength of this study is that the preoperative and postoperative variables did not differ between the groups, but the study also had significant limitations. The main weakness is the small sample sizes. Including a much larger number of patients would increase the statistical power and have a greater chance of representing the larger populations as well as capturing infrequent

adverse events. Another limitation is that while all patients with preoperative kidney disease were excluded and patients with history of lung disease were excluded from the ventilation analysis, other comorbidities, such as diabetes, cancer, or history of smoking, were not taken into consideration.

The retrospective nature of this study also calls into question the integrity of the data used and limits what data were available. Only one patient had data that seemed to be charted in error and that was in the ultrafiltration group. The urine output for postoperative day one for that patient was charted as a reasonable number but the urine output for postoperative days two and three were charted at unnaturally high values. There is no way to know if the data were actually an error but to be safe it was left out of the study. If the data were correct, and included, the statistical results may have changed. Four patients were also missing data for hematocrit on postoperative days two and three and platelet count on postoperative days two and three. Data were also missing for day three postoperative urine output for two patients, creatinine postoperative day three for seven patients, and blood loss on postoperative day two for four patients.

Recommendations for Future Studies

To improve this study, a larger sample size as well as a prospective study is necessary. Beyond this, other variables should be considered as well, such as the amount of filtrate removed during surgery. By evaluating this, more groups could be created to see if there is a certain ultrafiltration threshold that, when reached, has an effect on patients. The analysis of the effects of ultrafiltration on kidney function could be strengthened by looking at diuretic usage in the patients postoperatively. Another consideration for future research should be a study comparing the incidence of postoperative adverse events, such as ECMO, pleural effusions, and acute kidney failure.

There are also other areas of postoperative patient health that could be affected by conventional ultrafiltration that were not evaluated in this study. For example, a recent study by Soliman *et al*. [51] found that in patients receiving ultrafiltration during cardiac surgery, serum lactate levels were increased postoperatively leading to metabolic acidosis. The study also found that patients receiving ultrafiltration during cardiac surgery also had lower mixed venous saturations. These data could mean that these patients are not receiving adequate tissue perfusion. While the authors of that study have theories as to why these results were found, more research is needed into this topic.

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Appendix A: Raw Data

Table A-1: Ultrafiltration Group Data- Part 1.

Patient	Height (cm)	Weight (kg)	BSA	History of Lung Disease	Preop Creatinine Level (mg/dL)	Preop Platelet Count (per L)	Preop Hct (%)	Preop Hemaglobin (g/dL)
1	170.21	97.4	2.08	No	0.92	203,000	46.7	15.5
2	192.99	141	2.67	No	1.35	155,000	45.9	14.8
3	178	88	2.06	No	1.01	221,000	39.7	13.8
4	134.59	72.7	1.55	no	0.71	286,000	42.8	14.3
5	163.8	74.6	1.81	Lung disease documented, severity unknown	0.68	210,000	34.1	10.6
6	165.1	104.6	2.1	Mild	0.7	273,000	37.5	13.1
7	165.1	90.5	1.98	No	0.88	222,000	41	13.1
8	182.91	136.2	2.53	No	1.9	181,000	25.9	8.2
9	165.1	117.1	2.2	No	0.86	235,000	40.5	13.4
10	172.69	68.9	1.82	No	0.59	313,000	35.3	10.9
11	168	84	1.94	No	0.77	206,000	40.8	13.6
12	157.51	67.6	1.69	No	1.25	164,000	39.4	13.1
13	177.8	94.9	2.13	no	0.82	195,000	43.6	15.2
14	182.91	102.6	2.25	Mild	0.97	195,000	45.6	15.7
15	170.21	64	1.74	No	0.66	443,000	40.2	14.2
16	170.21	120.2	2.28	Lung disease documented, severity unknown	0.89	210,000	34.7	11
17	170.21	72.4	1.84	No	0.78	153,000	40.1	14.2
18	172.69	97.4	2.11	No	1.1	217,000	42.3	14.9
19	172.69	92.7	2.06	No	1.14	214,000	38.5	12.7
20	167.59	93	2.02	No	0.71	200,000	42.7	14.7

Table A-2: Ultrafiltration Group Data- Part 2.

Patient	Lowest Intraop Hemoglobin (g/dL)	Procedure	Perfusion Time (min)	Aortic Cross Clamp Time (min)	Extubation in OR	Postop Vent Time (hours)	Postop Pleural Effusion	Postop Pneumo-thorax
1	9.7	AVR + CAB	96	73	No	5.3	No	No
2	11.6	MV Replace	129	105	Yes	0	No	No
3	9	AVR+CAB	97	80	No	10.87	No	No
4	8.6	MV Repair	95	61	No	2.73	No	No
5	5.7	AVR+CAB	68	46	No	8.75	No	No
6	10.7	AVR	236	186	No	7.73	No	No
7	10	AVR+MV Replace	145	126	Yes	0	No	No
8	7	CAB	61	42	No	6.7	No	No
9	10.3	AVR	98	63	No	3.55	No	No
10	9	MV Replace	67	51	No	1.73	No	No
11	8.6	AVR	116	85	No	3.73	No	No
12	7	CAB	92	78	No	5.55	No	No
13	10.7	AVR	77	68	Yes	0	No	No
14	12	MV Repair	138	124	No	2.18	No	No
15	8.3	AVR+CAB	94	73	No	1.63	No	No
16	8	AVR	72	59	No	4.6	No	No
17	8.6	AVR+CAB	78	59	No	4.73	No	No
18	9.3	AVR+CAB	118	76	No	1.97	No	No
19	9.3	CAB	130	104	Yes	0	No	No
20	9.6	AVR	80	66	No	3.1	No	No

Table A-3: Ultrafiltration Group Data- Part 3.

Patient	Initial ICU Stay (hours)	Readmitted	Mortality Status 30 Days Postop	Postop Urine Output Day 1 (cc/kg)	Postop Urine Output Day 2 (cc/kg)	Postop Urine Output Day 3 (cc/kg)	Postop Creatinine Day 3 (mg/dL)	Postop Acute Renal Failure
1	44.4	No	Alive	15.97	10.16	20.94	0.93	No
2	71.3	No	Alive	8.58	11.45	10	1.12	No
3	98.9	No	Alive	22.05	13.18	16.19		No
4	69.2	No	Alive	37.41	20.5	7.29	0.52	No
5	48.5	No	Alive	24.33	14.41	5.36	0.94	No
6	49.4	No	Dead	17.11	13.19	26.96	0.5	No
7	148.7	No	Alive	12.04	661.05	128.23	3.31	Yes
8	68.7	No	Alive	14.17	7.42	4.22	2.07	No
9	146.2	No	Alive	13.71	3.54	1.58	2.99	No
10	47.6	No	Alive	15.31	15.31	17.05		No
11	168.4	No	Alive	19.64	25.42	28.87	0.72	No
12	81.1	No	Alive	17.31	22.26	15.31	1.32	No
13	30.2	No	Alive	19.6	40.25	38.46	0.7	No
14	51.2	No	Alive	10.92	49.07	21.59		No
15	25.8	No	Alive	32.58	27.73	45.31	0.54	No
16	104.3	No	Alive	11.19	10.19	15.93	1.06	No
17	50.1	No	Alive	31.84	6.49		0.71	No
18	68.8	No	Alive	14.03	11.55	27.67	1.33	No
19	28.3	No	Alive	9.92	3.45	4.85	1.08	No
20	68.3	No	Alive	13.12	12.68	17.31	0.72	No

Table A-4: Ultrafiltration Group Data- Part 4.

Patient	Postop Hct Day 1 (%)	Postop Hct Day 2 (%)	Postop Hct Day 3 (%)	Postop Platelet Day 1 (per L)	Postop Platelet Day 2 (per L)	Postop Platelet Day 3 (per L)	Postop Blood Loss Day 1 (cc/kg)	Postop Blood Loss Day 2 (cc/kg)	Red Blood Cell Transfusions (units)
1	37.7	36.4	37.6	141	135	142	2.05	0.62	0
2	29.5	29.2	28.5	100	75	88	4.54	4.68	1
3	26.4	23.9	29.2	98	68	89	23.18	13.52	2
4	24.7	26.2	25.9	142	147	175	6.81	5.78	0
5	25.3	25.5	28	141	106	133	4.02	8.04	0
6	32		30.8	161		192	2.83	1.05	0
7	28.5	23.8	22.6	160	80	68	2.43	4.09	0
8	26.5	25.8	23.5	145	153	150	5.03	2.72	0
9	25.8	25.4	25.6	120	126	115	6.92	1.96	0
10	21.8	19.8	23	158	105	108	6.39	2.32	2
11	22.5	30.8	28.5	80	92	117	7.46	0.83	1
12	19.9	21.5	22.4	114	97	120	6.07	0.98	1
13	35.4		31.6	144		144	5.9		0
14	33.5	34.2		113	102		2.53	2.34	0
15	26.8	27.2	27.4	231	238	269	9.69	2.66	0
16	25.1	26.4	25.7	110	104	100	2.87		0
17	29.5	29.8	29.6	72	70	75	9.63	3.18	0
18	23.1	24.2	23.4	98	102	91	5.75	1.44	0
19	27.7	27.9		137	143		2.66	0.76	0
20	27.2	25.3	24.8	106	97	106	4.41		0

Table A-5: Control Group Data- Part 1.

Patient	Height (cm)	Weight (kg)	BSA	History of Lung Disease	Preop Creatinine level (mg/dL)	Preop Platelet Count (per L)	Preop Hct (%)	Preop Hgb (g/dL)
1	168	122	2.27	No	0.76	236000	45	15.5
2	149.91	64	1.59	No	0.81	98000	44.6	15.6
3	183.01	100	2.22	No	1.08	188000	45.6	16
4	151.99	94	1.89	No	0.62	241000	40.8	13.7
5	162.99	86	1.92	No	0.83	262000	34.6	11.4
6	165	76	1.83	No	0.65	190000	39.6	13.3
7	180.29	91.4	2.12	No	1.1	183000	40.3	13.7
8	177.8	107.7	2.25	No	0.76	89000	41.2	14.5
9	182.91	120.4	2.4	No	1.1	192000	36.2	12.7
10	167.59	61.9	1.7	No	0.75	298000	48.2	15.8
11	163.8	63.7	1.69	Mild	0.69	180000	40.1	13.6
12	177.8	105	2.22	Mild	1.13	190000	43.8	15.2
13	175.31	58.6	1.72	No	0.7	183000	29.5	9.7
14	163.8	65.1	1.71	Lung disease documented, severity unknown	0.7	231000	40.3	13.5
15	172.69	81.6	1.95	No	0.9	338000	39.6	13.3
16	170.21	85.2	1.97	Mild	0.77	164000	38.9	13.6
17	157.51	119.9	2.15	Lung disease documented, severity unknown	0.86	239000	34.4	11.2
18	180.29	76.7	1.96	Mild	1.04	281000	42.4	13.6
19	170.21	79.4	1.91	No	1	166000	45	14.9
20	165.1	80.1	1.88	No	0.94	227000	36.1	11.9

Table A-6: Control Group Data- Part 2.

Patient	Lowest Intraop Hgb (g/dL)	Procedure	Perfusion Time (min)	Aortic Cross Clamp Time (min)	Extubated in OR	Postop Vent Time (hours)	Postop Pleural Effusion	Postop Pneumo-thorax
1	9.3	CAB	79	56	No	4.52	No	No
2	8.3	AVR	190	138	No	1	No	No
3	11.3	CAB	67	37	No	5.37	No	No
4	7.8	MV Replace	269	208	No	82.57	No	Yes
5	7.7	AVR + CAB	97	86	Yes	0	No	No
6	8.2	CAB	87	67	No	4.62	No	No
7	9	AVR	113	100	No	5.92	Yes	No
8	10	AVR	158	110	No	4.87	No	No
9	7	CAB	61	48	No	5	No	No
10	9.7	MV Replace	99	83	No	3.05	No	No
11	9	AVR	132	118	Yes	0	No	No
12	9.3	CAB	45	33	No	4.32	No	No
13	7	MV Repair	131	114	No	0	No	No
14	8.8	CAB	80	60	No	5.27	No	No
15	9	CAB	62	43	No	4.18	No	No
16	8.7	CAB	72	59	No	3.75	No	No
17	8.3	CAB	34	22	No	1.62	No	No
18	9.3	CAB	127	71	No	5.57	No	No
19	10.7	CAB	40	27	No	4.32	No	No
20	7.5	CAB	62	50	No	5.57	No	No

Table A-7: Control Group Data- Part 3.

Patient	Initial ICU Stay (hours)	Readmitted	Mortality Status 30 Days Postop	Urine Output Postop Day 1 (cc/kg)	Urine Output Postop Day 2 (cc/kg)	Urine Output Postop Day 3 (cc/kg)	Creatinine level Postop Day 3 (cc/kg)	Postop Acute Renal Failure
1	54.4	No	Alive	9.06	4.04	7.89	1.34	No
2	42.3	No	Dead	33.98	24.77			No
3	28.1	No	Alive	20.37	14.68	6	0.87	No
4	101.4	No	Alive	35.48	41.12	43.94	1.13	No
5	102.3	No	Alive	25.41	14.77	29.59		No
6	28.3	No	Alive	23.42	8.68	15.79	0.83	No
7	106.8	No	Alive	25.98	3.5	26.48		No
8	83.2	No	Alive	13.32	6.69	22.7	0.62	No
9	146.8	No	Alive	13	20.22	13.91	1.26	No
10	51.3	No	Alive	29.05	36.19	2.75	0.62	No
11	48	No	Alive	37.33	22.06	17.27	0.58	No
12	70.7	No	Alive	21.38	32.33	22.71	0.87	No
13	30.1	No	Alive	33.77	50.43	46.93		No
14	53.1	No	Alive	28.42	8.06	19.97	0.8	No
15	33.1	No	Alive	22.37	14.77	21.75	0.83	No
16	144.2	Yes	Alive	29.05	10.68	19.84	0.73	No
17	26.7	No	Alive	0.63	20.14	4.8	0.67	No
18	98.8	No	Alive	24.71	20.47	15.58	0.79	No
19	73.9	No	Alive	27.05	19.96	24.75	0.76	No
20	54.3	No	Alive	30.34	10.05	20.6	0.84	No

Table A-8: Control Group Data- Part 4.

Patient	Hct Postop Day 1 (%)	Hct Postop Day 2 (%)	Hct Postop Day 3 (%)	Platelet Postop Day 1 (cc/kg)	Platelet Postop Day 2 (cc/kg)	Platelet Postop Day 3 (per L)	Postop Blood Loss Day 1 (cc/kg)	Postop Blood Loss Day 2 (cc/kg)	Red Blood Cell Transfusion (units)
1	34.1	30.5	27.8	161	141	155	8.39	2.46	0
2	25.2			176			12.5	18.44	1
3	32.3	33.5	34.2	121	114	109	4.95	1.1	0
4	22.9	22.7	25.3	71	94	159	7.23	1.28	0
5	25.1	25	24.7	274	174	241	9.42	0	1
6	25.5	26.9	27.1	140	134	142	5.7	2.24	0
7	27.2	26	23.7	195	174	152	6.52	2.52	1
8	26.9	22.6	24.8	54	59	90	6.04	5.76	1
9	21.7	21.3	21.1	107	120	142	6.23	4.65	0
10	21.8	21.3	22.5	145	133	146	18.17	10.99	0
11	26	24.5	22.9	101	86	93	9.39		0
12	28.9	30.6	30.8	127	137	140	7.9	1.71	0
13	23.3		21.7	77		110	4.44	0.26	1
14	28	28	27.7	105	119	132	13.01	2.3	0
15	26.3	23.8	23.8	168	147	165	6.69	1.72	0
16	18	17	20.8	77	65	107	10.25	9.51	2
17	30.4	27.6	28.6	205	173	160	0.58	0.83	0
18	28.6	29.9		163	154		3.78	4.43	0
19	37.7	37.2	35.3	147	141	140	6.01	3.24	0
20	30.6	28	28.8	212	177	205	9.86	5.12	0

Perfusion

Thesis Approval Form

Master of Science in Perfusion – MSP

Milwaukee School of Engineering

This thesis, entitled "Postoperative Effects of Conventional Ultrafiltration on Adult Cardiac Surgery Patients," submitted by the student Alyssa Myers, has been approved by the following committee:

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