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An audit of the intraoperative usage of blood products in patients undergoing cardiac surgery on cardiopulmonary bypass

Kenyaditswe Charity Petronella Phokontsi

A research report submitted to the Faculty of Health Sciences,
University of the Witwatersrand,

in the fulfillment of the requirements for the degree

of

Masters of Medicine in the branch of Anaesthesiology

Johannesburg, 2018

Declaration

I, Kenyaditswe Charity Petronella Phokontsi, declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Anaesthesiology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

_____

Candidate's signature

_____

Date

Abstract

Title: An audit of the intraoperative usage of blood products in patients undergoing cardiac surgery on cardiopulmonary bypass.

Background: Transfusion of blood products is increasingly recognised as an independent predictor of poor outcome after cardiac surgery. The study aims to audit blood transfusion usage in a cardiothoracic unit, at a tertiary academic centre.

Methods: A descriptive, retrospective, contextual audit. A consecutive convenience sampling method was used. One hundred and twenty-two adult patients who underwent their first elective cardiac surgery on cardiopulmonary bypass were enrolled.

Results: The mean age of the population studied was 46.7 (16.2) years. Patients were predominantly male (60.7%). The mean (SD) body mass index was 21.4 (5.6) kg/m^2. Their mean (SD) preoperative haemoglobin and platelet count was 12.8 (2.3) g/dL and 274.4 (121.9) 10^9/L respectively. Following a clear fluid prime cardiopulmonary bypass technique, with a median (IQR) priming volume of 1500 (1000 - 2000) ml, the first mean (SD) haemoglobin on cardiopulmonary bypass was 8.9 (1.6) g/dL. Overall, 110 (90.2%) patients received donor blood products. Eighty-five (77.3%) patients received red blood cells,103 (93.6%) fresh frozen plasma, and 35 (31.8%) platelet transfusion. A total of 255 red blood cell, 225 fresh frozen plasma and 37 platelet units were transfused. The cell salvage technique was used in 94 (77.0%) patients. The median (IQR) volume of salvaged blood was 535 (250–754) ml.

Conclusion: A high rate of homologous blood product transfusion was found in patients undergoing cardiac surgery in the study.

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List of abbreviations

CPB	cardiopulmonary bypass
RBC	red blood cells
FFP	fresh frozen plasma
Hb	haemoglobin
Hc	haematocrit
Plt	platelet
DIC	disseminated intravascular coagulopathy
USA	United States of America
DO_2	oxygen delivery
CaO_2	oxygen content
CO	cardiac output
ICU	intensive care unit
AKI	acute kidney injury
CABG	coronary artery bypass graft
WHO	World Health Organisation
TRALI	transfusion related lung injury
PAD	preoperative autologous donation

Section 1

Literature review

1.1 Introduction

Blood transfusion has been the cornerstone of circulatory support and haemodynamic management during the perioperative period (1, 2). From the early 20th century, the development of blood saving techniques has been credited with saving lives of many (3).

This chapter will discuss concerns associated with the usage of blood products in cardiac surgery including an overview of the physiology, blood components, benefits and complications of blood transfusion. It highlights blood transfusion triggers and blood conservation strategies and reviews guidelines related to blood product usage in cardiac surgery.

1.2 The history of blood transfusion

William Harvey discovered the circulation of blood in 1616 (4). Following his experimental work on animal subjects, he published a book titled “An anatomical study of the heart and of the blood in animals”. In this book, he describes the circulation and the properties of blood.

Although met with some scepticism, his discoveries sparked interest in the field. Following many failed and often fatal transfusion attempts, Richard Lower successfully resuscitated a dog with fresh blood drawn from another dog in 1665 (5). Jean-Baptiste Denis performed the first animal to human transfusion. He transfused a 15 year old boy and later a “labourer” with blood drawn from a sheep, both patients survived the transfusions (4, 5). The first successful human blood transfusion was performed in 1818, by James Blundell, saving the life of a patient with post-partum haemorrhage (4, 5).

In the 1900s, Karl Landsteiner led to the discovery of ABO blood groups by performing experiments on blood samples drawn from his staff members. Subsequent developments in coagulation, advances in blood storage and cross-matching techniques as well as the institution of blood banks have made transfusion of blood safer and more accessible.

It is reported that the first blood bank was established in 1937, in Chicago, United States of America (4-6). Voluntary donation of blood for later use was started in the 1920s. The significance of blood transfusion as a life-saving procedure was demonstrated during World War II, where blood transfusion is reported to have saved the lives of many wounded soldiers.

1.3 The physiology of blood

Blood is the fluid component of the cardiovascular system. It is made up of plasma and cellular components. Plasma constitutes about 55% of the total blood volume, which in turn comprises 90% water, 8% plasma proteins, with the remaining 2% consisting of electrolytes and organic compound. Haemoglobin containing red blood cells, white blood cells and platelets make up the cellular component.

Blood has many important homeostatic functions, and in addition to the transportation of oxygen, carbon dioxide, nutrients and waste products, it possesses an immune function and is also involved in acid base balance. Haemostasis is achieved through a series of highly interwoven, complicated and intricate processes. Blood is a complex substance which forms part of a highly efficient system which possesses properties that are vital for life (7).

1.4 Blood components

Blood is collected as whole blood and then separated into its constituents.

Whole blood is considered to be an complex matter from which appropriate components are processed (8). Each unit of whole blood is separated and fractionated to provide red cell concentrates, fresh frozen plasma, platelets, cryoprecipitate and clotting factor concentrates (9). Use in this manner maximises utilisation of blood bank resources.

1.4.1 Red cell concentrates

A closed sterile system is used to prepare red cell concentrates from whole blood by centrifugation of plasma. The prepared units can be stored at 1-6° Celsius, for up to 45 days. Administration requires an appropriate blood administration set and warming prior to transfusion. Blood transfusion must be completed within four hours.

The haematocrit content in each unit of red blood cells (RBC) is roughly 70%. Transfusion of a single unit of packed RBC may increase the level of haemoglobin (Hb) by 1 g/dL and the haematocrit by 3%. The main indication for transfusion of RBC is to restore oxygen carrying capacity (8, 10, 11). The oxygen carrying capacity is low when anaemia is present. Anaemia is defined according to the World Health Organization (WHO) as a Hb of less than 12.0 g/dL (9).

1.4.2 Platelets

Platelet concentrates are available as random donor pooled platelets or single donor apheresis platelet concentrates. Random donor units are prepared from the buffy layer of whole blood donations within eight hours of collection. Single donor units are collected from a donor through the process of apheresis. Units are stored at 20–22° Celsius for up to five days.

The expected rise in platelet count after a standard adult dose is 20–40 X 10^9/L. The increment may vary in patients with splenomegaly, disseminated intravascular coagulation (DIC) and septicaemia.

Transfusion of platelet concentrates is a form of treatment for thrombocytopenia associated bleeding or platelet dysfunction in conditions such as dilutional thrombocytopenia in massive transfusion, DIC and bone marrow failure. Thrombocytopenia is defined as a platelet count of less than 150 X 10^9/L (9). The risk for major postoperative bleeding exists when the platelet count is 50 X 10^9/L and less (8, 10, 11).

1.4.3 Fresh frozen plasma

Fresh frozen plasma (FFP) is prepared from the plasma obtained from anti-coagulated whole blood separated by centrifuging in a closed sterile system, and then frozen at -18°C. It contains all the coagulation factors at normal physiological levels.

Administration of FFP requires thawing of the unit at 30–37°C. The unit must be transfused within 30 minutes of thawing as labile factor deteriorates soon after reconstitution. It is administered in patients who require replacement of multiple coagulation factors such as those seen in DIC, massive blood transfusion and liver disease (10, 11). Above therapeutic levels of anticoagulation therapy are a common indication for transfusion of FFP. Transfusion requirements are indicated by the presence of a raised international normalised ratio.

1.4.4 Factor concentrates

Cryoprecipitate is the insoluble portion of FFP. It is acquired by liquefying FFP at 0–4°Celsius. It is stored at -18°C for up to one year. It contains factors VII and XIII, fibrinogen and Von Willebrand factor in concentrated amounts. Indications for cryoprecipitate transfusion include: haemophilia, DIC and congenital or acquired hypofibrinogenaemia. Other factor concentrates are available and are indicated in patients with haemorrhagic disorders due to coagulation factor deficiencies (10, 11).

1.5 The goals of transfusion therapy

The main goal of transfusion is to reduce the complications related to inadequate oxygen delivery due to tissue injury that results from surgery (12). The objective of blood transfusion is based on the relationship between oxygen delivery (DO_2), cardiac output (CO) and oxygen content (CaO_2). This relationship is best described by the following equation:

$$DO_2 = (CO \times CaO_2)$$

Oxygen is carried in the blood in two forms; as a bound or dissolved component. The bound component is associated with the haem group of Hb within the RBC, while a proportion of oxygen is dissolved in plasma. These components constitute the CaO_2 part in the equation:

$$CaO_2 = (SaO_2 \times Hb \times constant) + (PaO_2 \times constant)$$

SaO_2 is the oxygen saturation of Hb, Hb is a protein in RBC that carries oxygen. PaO_2 is known as the partial pressure of oxygen in arterial blood. The constant is known as Hüfner's constant.

With these equations in mind, one can see that in an anaemic patient, the CaO_2 can be increased through blood transfusion, which would result in increased DO_2. An increase in DO_2 in turn ensures that the delicate balance between the DO_2 and oxygen consumption is maintained. The maintenance of this balance results in prevention or reversal of ischaemia (13-15).

Oxygen delivery and metabolic demands vary with age, body mass index, gender, comorbidities and the presence of active bleeding. Oxygen delivery is reported to be adequate in a healthy patient at an Hb of 8g/dL.

In a patient with comorbidities or poor cardiopulmonary reserve, a level of 10 g/dL is generally acceptable (16). Pre-existing anaemia has been shown to increase the risks of transfusion (17).

1.6 The complications of blood transfusion

Similar to drugs, transfusion of blood products has the propensity to cause side effects (18). Transfusions are increasingly recognised as a potential risk factor for unfavourable sequel following cardiac surgery (19, 20). Transfusions were also seen to cause unwarranted morbidity and mortality (21).

In this review, these side effects are grouped as general complications comprising of the infectious and non-infectious adverse events; complications of blood transfusion in cardiac patients and complications related to storage.

1.6.1 General complications of blood transfusion

Infectious complications of blood transfusion

Until 1983 routine surveillance for viral infection was not performed. To date, in accordance with recommendations by WHO, donated blood is screened routinely using sensitive assays in most blood banks in developed countries. This has subsequently decreased the risk of viral infections transmission through transfusion of blood. These include the human immunodeficiency virus (HIV), hepatitis B and C viruses and syphilis (14, 16, 18, 22, 23).

Risks of transmission may be higher in some developing countries including sub-Saharan WHO regions as some blood banks' are not compliant with the recommended WHO standards (23). A summary of these infections and incidences thereof is presented in Table 1.

Table 1: Infectious complications of blood transfusion (24).

Complication	Estimated risk per unit blood
Hepatitis B virus	1 in 350,000
Hepatitis C virus	1 in 1.8 million
Human T-lymphotropic virus 1 or 2	1 in 2 million
Human immunodeficiency virus	1 in 2.3 million
Creutzfeldt-Jakob disease	Rare*
Human herpes virus 8	Rare*
Malaria	Rare*
Pandemic influenza	Rare*
West Nile virus	Rare*

*Exact risk unknown.

Non-infectious complications of blood transfusion

Haemolytic transfusion reactions

The frequency of haemolytic transfusion reactions is estimated to be 1 in 10 000 to 1 in 50 000 of transfusions (25). Most haemolytic transfusion reactions involve the ABO and rhesus (Rh) systems (21). Transfusion of incompatible RBC will result in intravascular haemolysis and may further complicate with increased vascular permeability and hypotension, DIC, renal failure, and death (26).

Allergic reactions

Allergic transfusion reactions occur in 1 in 20 000 to 1 in 50 000 of transfusions. These reactions range from mild urticaria to life threatening anaphylaxis. Anaphylaxis occurs in response to recipients' pre-sensitisation to a range of proteins in donor plasma (14, 21).

Post-transfusion purpura

Post transfusion purpura is a serious, but fortunately rare complication of transfusion said to occur in fewer than 300 reported cases (25). The majority of cases are said to be due to platelet specific antigens. It occurs in 5 to 10 of transfusions, mostly affecting multiparous females (26).

Graft-versus-host disease

Graft-versus-host disease associated with transfusion is a result of a multiplication of donors' lymphocytes, leading to an immune mediated destruction of the recipients' tissues and organs. It is fatal in more than 90% of the cases; fortunately it is a rare complication of transfusion (14, 26).

Massive transfusion

Massive transfusion is historically defined as the transfusion of 10 units of blood, or complete replacement of the circulating blood volume over a 24 hour period (16). It is also defined as transfusion of four units of blood in one hour or replacement of 50% or more of the patient's blood volume in three hours. The latter definitions are useful during management of an actively bleeding patient (27). Massive transfusion is associated with hypothermia, dilutional coagulopathy, citrate toxicity, hypocalcaemia, hyperkalaemia and acid base disturbances (26). These and other non-infectious transfusion adverse effects are listed in Table 2.

Table 2: Non-infectious complications of transfusion (25).

Immune mediated
Haemolytic transfusion reactions
Febrile transfusion reactions
Allergic/Urticarial/anaphylactic transfusion reactions
Transfusion-associated graft-versus-host disease
Microscherism
Transfusion-related immunomodulation
Alloimunisation
Non-immune mediated
Septic transfusion reactions
Non-immune haemolysis
Transfusion-associated circulatory overload
Metabolic derangements
Coagulopathic complications of massive transfusion
Complications from red cell lesions
Over/under transfusion
Iron overload

1.6.2 Complications of blood transfusion in cardiac patients

Cardiac surgery is one of the major fields necessitating blood transfusion (28).

Blood transfusion is a recognised risk factor for adverse outcome after cardiac surgery (2, 19, 21, 28-31). Literature extending over a decade indicates significant risks of adverse outcomes in cardiac patients who were transfused as opposed to those who were not (2, 19, 21, 28-31).

Several studies looking at the association of transfusion in cardiac surgical patients with morbidity and mortality have suggested an immune based aetiology. The three main systems affected adversely by transfusion are the cardiac, pulmonary and renal systems (2, 19, 21, 28-31).

Cardiovascular adverse effects

Cardiac complications related to transfusion include ischaemic events, atrial fibrillation and heart failure (2, 28, 29). Potential mechanisms for transfusion related cardiac ischaemic complications include pro-inflammatory effects and storage defects (2, 13, 28). Stored red blood cells are deficient in 2.3 diphosphoglycerate (DPG) thus are less proficient at delivering oxygen. The cells become less flexible which can possibly lead to slugging and occlusion of capillaries (28).

Pulmonary adverse effects

Transfusion related lung injury (TRALI) is defined as a new acute lung injury characterised by non-cardiogenic pulmonary oedema occurring within six hours of blood transfusion (14, 26, 28). In 2011, Tuinman et al. (32) explored the effects of blood transfusion on the pulmonary system in a group of 60 mixed surgical critically ill intensive care unit (ICU) patients. All the patients had received blood transfusion intraoperatively. Indirect bronchoalveolar lavage fluid specimen was collected within three hours of admission to ICU and later processed for the presence of pro-inflammatory cytokines. Their results showed that blood transfusion is associated with marked pulmonary inflammatory changes and this occurred partly in a dose dependent manner.

Renal system adverse events

Acute kidney injury (AKI) is an important complication of cardiac surgery with cardio pulmonary bypass (CPB) (33). It is a common complication and rates of up to 30% have been reported.

Observational studies have been conducted looking at various variables as risk factors for this kidney insult (34, 35). Up until recently, the effect of blood transfusion as a risk factor had not been considered.

Karkou et al. (36) suggested that the irreversible morphological and biochemical changes that occur during storage as resulting in the pro-inflammatory state, impairment of oxygen delivery and exacerbation of tissue oxidative stress. This can cause AKI in susceptible patients undergoing cardiac surgery with CPB.

Deep surgical wound infection

Surgical site infection is a serious complication, which is associated with high morbidity and mortality. Definitions vary, but it is commonly described as wound infection that occurs within 30 days of operation. It is characterised by the presence of a purulent discharge, wound dehiscence or a positive wound swab culture. The known risk factors include obesity, diabetes mellitus and advanced age. Several studies have suggested that there is a strong association between blood transfusion and infection after cardiac surgery (28, 29, 31). The risk of these infections has been documented to be as high as 80% in a study done in the United Kingdom, by Murphy et al. (29).

Horvath et al. (31) conducted a large multicentre study in United States of America and Canada. A total of 5158 patients were prospectively studied in 2010 over eight months. The primary objectives of the study were to investigate the association of RBC and post-operative infection as well as to identify patient and operative risk factors for infection. Patients were then followed for 65 days after surgery, with post-discharge assessments at days 30 and 60 after surgery. The end points were evidence of deep incisional surgical site infection. Their study demonstrated that there is a strong association between RBC transfusion and infection. This relation is dose dependent, increasing by an estimated 29% with each unit transfused.

Risk of mortality

Blood transfusion is a recognised risk factor for major adverse outcomes after cardiac surgery. In 2001, Mikkola et al. (20) investigated the effects of blood transfusion after coronary artery bypass surgery. A total of 2235 patients were included in the study. A 30-day all-cause mortality was the end point. The study demonstrated that transfusion increased the risk of short-term mortality. In 2002, Engoren et al. (30) retrospectively studied 1915 patients who underwent isolated coronary artery bypass operations over a period of five years. This study confirmed that blood transfusion was associated with an increased risk of mortality. Five-year mortality rates were found to be twice as high in transfused patients compared to those who were not transfused.

These findings were consistent with the findings of a study conducted by Murphy et al. (29) in 2007 showing that an association of blood transfusion with short and long term mortality exists. More recently, two studies done in 2013 by Poane et al. (21) and Shaw et al. (19) showed similar outcomes and also demonstrated the occurrence of other adverse outcomes such as postoperative myocardial ischaemia, new onset arrhythmias and organ failure associated with blood transfusion (2, 21, 28-30, 37).

Complications related to cardiopulmonary bypass

Excessive bleeding remains an important cause of morbidity and mortality after cardiac surgery. Abnormal bleeding after CBP is a common complication of cardiac surgery (38). The nature of coagulation disorders after CBP are multi-factorial and several triggers have been identified (38-40). These include; consumption of coagulation factors due to activation of the coagulation system which results in thrombin generation and impairment of platelet function; blood contact with CPB circuit surfaces and coagulation factor adsorption onto CPB lines; ischaemia-reperfusion injury; hypothermia; activation of the inflammatory system and surgical trauma itself (41, 42).

On pump surgery, particularly if CBP times exceed 60 minutes, and the use of a clear prime fluid have been found to be associated with an increased tendency to bleed (43). Takai et al. (44) prospectively randomised 288 coronary bypass graft (CABG) procedures over four years and demonstrated that using low volume prime techniques was associated with fewer blood transfusions, less blood loss and faster recovery times.

Complications related to storage of blood

The aim of research in blood storage techniques has been to try to prolong the shelf life of RBC in order to maximise the availability of a perishable resource (45). Modification of storage techniques and processing procedures have increased the shelf life of RBC to the current 35-42 days (10, 46).

Although RBCs are commonly given with the goal of increasing oxygen delivery to tissues, their ability to accomplish this is often significantly more limited than appreciated. As stored blood ages, RBCs undergo significant degradation referred to as the storage lesion. These changes occur after two to three weeks of storage and accumulate progressively with time (47). This results in morphologic and biochemical changes, which adversely affect their ability to deliver oxygen.

Biochemical changes include a low P50 as well as a progressive loss of 2.3 DPG. This results in enhanced Hb affinity for oxygen and impairment in the ability of Hb to offload oxygen at cellular level, resulting in leftward shift of the oxyhaemoglobin dissociation curve. Morphologic deterioration results in a reduced ability to transverse the microcirculatory bed. Stored blood cells may lyse, resulting in a release of free Hb and a variety of other biologically active substances that can trigger an inflammatory response and induce vasoconstriction, further reducing the microcirculatory perfusion (13, 28, 45, 48).

Koch et al. (47) conducted a study testing the hypothesis that transfusion of RBCs older than two weeks was associated with serious complications and mortality. Records of patients who underwent various cardiac surgical procedures over eight years were examined. Patients who received a combination of newer and older units were excluded. Those who received blood units older than two weeks were found to have greater in-hospital mortality and multiple adverse effects. Wang et al. (49) conducted a meta-analysis which included 21 studies that showed that transfusion of older blood was associated with a significantly increased risk of death.

1.7 The cost implications of blood transfusion

In an environment in which blood can be lifesaving, the economic impact and cost of transfusion therapy mandates a careful understanding of the indications for its use and the development of appropriate decision-making processes (29, 50, 51).

There are direct and indirect costs associated with transfusion of blood products. Directs costs are considerable, especially in cardiac surgery as it accounts for a significant proportion of all RBC transfusions as reported in a USA citing, that 20% of their blood bank's inventory was consumed by cardiac surgery patients (29, 30, 52). The indirect costs are due to blood transfusion related adverse effects. The occurrence of these complications leads to prolonged ICU admissions, escalation of treatment, re-operations and an overall increase of the duration of admission (29, 30, 37, 42, 53).

In 2007, Murphy et al. (29) retrospectively investigated 8518 adults having cardiac surgery over a period of seven years. The aim of their study was to quantify associations of blood transfusion with clinical outcomes and cost in cardiac surgery patients. Their study demonstrated a strong association between transfusion and occurrence of side effects.

They suggested that avoiding transfusion could have prevented over 50% of the adverse effects found in their patients and they believed this would have in turn reduced the non-operative costs of admission by 40%.

1.8 Blood conservation strategies in cardiac surgery

Annually, an estimated 1.25 million patients undergo cardiac surgery worldwide (54). Consumption of blood products in this population is reported to be high (51, 55). With increasing evidence demonstrating an association of blood transfusion with a series of untoward effects, it is important to ensure that these products are used optimally.

The clinical problems posed by transfusion of blood have encouraged the development of blood conservation strategies in cardiac surgery (56, 57). Preoperative identification of patients at risk of high transfusion requirements is an essential first step in employing conservation strategies efficiently. Pharmacological conservation strategies include the preoperative use of haematinics, erythropoietin and intraoperative administration of antifibrinolytic agents.

Advanced blood conservation techniques such as autologous blood donation (PAD), cell salvage and acute normovolaemic haemodilution have been shown to be effective (6, 9, 51, 58, 59). Surgery related factors and employing haemostatic adjuncts are important measures in reducing excessive blood loss and the need for transfusion. Implementing institution specific clinical guidelines and the application of point of care testing ensures an efficient use of available resources (6, 9, 51, 58, 59).

1.8.1 Preoperative risk assessment tools

Predicting blood transfusion requirements helps clinicians to anticipate patients' requirements and guides appropriate blood management strategies.

Blood-conservation techniques may be expensive; hence directing their use to high-risk cases would be more cost effective. A predictive scoring system guides the use of such strategies in the target risk groups and may potentially reduce costs of the care needed. A number of pre-operative clinical variables have been identified that independently predict the likelihood of requiring blood transfusion in patients undergoing cardiac surgery (6).

In 2006, Alghamadi et al.(6) developed the Transfusion Risk Understanding Scoring Tool used to stratify cardiac surgery patients' transfusion requirements. These variables included preoperative Hb, weight, female gender, emergency surgery, re-do surgery and combined procedures. More recently, in a 2013 study by Sandoughadaran et al. (43) on-pump surgery was added to the list of predictors for blood product requirement.

1.8.2 The use of antifribrinolytic agents

Three drugs play a role in blood conservation during the perioperative period. They include aprotinin, epsilon-aminocaproic acid and tranexamic acid.

Aprotinin

Aprotinin is a bovine pancreatic trypsin inhibitor with antifibrinolytic properties. Its efficacy in limiting excessive requirements for blood transfusion has been demonstrated in several studies (60-62). This however, has been overshadowed by adverse events which ultimately led to its withdrawal from routine use during cardiac surgery due to concerns that it may predispose patients to micro-vascular thrombosis, increasing the risks of cardiovascular complications and death (55). Its use is currently being reviewed.

Epsilon-aminocaproic acid

Epsilon-aminocaproic acid is classified as lysine analogue.

It inhibits fibrinolysis through its inhibitory effects of plasminogen inhibitor and to a lesser degree through its antiplasmin activity. It is cost effective, has low side effect profile and has been shown to be effective in lowering CBP related blood loss.

Tranexamic acid

Tranexamic acid is an antifibrinolytic agent that works by completely inhibiting the activation of plasminogen to plasmin. It has a similar mechanism of action as epsilon-aminocaproic acid but is approximately 10 times more potent. It is well known for its ability to reduce blood loss, blood transfusion requirements as well as reducing risk of mortality as shown in the CRASH II trial and most recently the WOMAN trial (63, 64). It is important to note that although these studies were conducted in non-cardiac surgery patients, their results have led to an improved understanding and renewed interest in tranexamic acid. Studies conducted in the cardiac surgery population have also shown positive reports, as indicated by decreased chest tube drainage with the use of tranexamic acid (55, 59).

1.8.3 The use of erythropoietin

Erythropoietin is an endogenous glycoprotein hormone produced by the kidney. It stimulates formation of red blood cells in response to hypoxia and anaemia. It has been shown to be an effective treatment in anaemic patients (51). It is administered subcutaneously and several doses can be given over a period of two to three weeks prior to surgery. A typical erythropoietin regime is reported to be costly and as such uncertainty about its cost effectiveness exist (28, 51, 65).

Vaislic et al. (66) retrospectively studied outcomes in 500 consecutive Jehovah's Witness patients who underwent cardiac surgery over a period of 21 years. Several conservation strategies including an erythropoietin regime were employed.

They concluded that application of the erythropoietin regime and other conservation strategies made bloodless open-heart surgery possible.

1.8.4 Cell salvage technique

The cell salvage procedure involves recovering the patient's own blood lost during surgery and re-infusing it back. Using cell salvage during cardiac surgery may reduce exposure to donor RBC significantly (67-69). Several methods of intra-operative cell salvage are commercially available. The most widely used salvaging technique involves collection of blood that has been suctioned from the operating field, mixing the collected blood with heparin to prevent clotting then processing it by centrifugation. The centrifuged product is then returned to the patient without platelets and clotting proteins.

There seems to be contrasting views over the routine use of the cell savage technique. It has been shown to reduce donor blood transfusion, however this comes at the risk of potentially increasing clotting factor and platelet requirements. Some reports have expressed concerns regarding the high cost of consumables when weighed against the costs of donor blood transfusion (67).

Studies implicating re-infused cell salvaged blood as a potential cause of coagulopathy are increasing (70-72). Campbell et al. (73), conducted a study in 20 coronary artery bypass graft patients assessing clot formation and integrity following reinfusion of cell saved processed blood using a point of care testing device. They concluded that cell salvaged blood not only reduced platelet count, but also reduced clot firmness, and prolonged time to clot formation. In 2016, Shen et al. (70) added that cell saved blood further impaired coagulation by reinfusion of blood with residual heparin that is devoid of clotting factors.

It has been noted that reinfusion of cell saved blood may increase the risk of bleeding and the need for transfusion of clotting factors and platelets (70, 74, 75).

1.8.5 Acute normovolemic haemodilution

Acute normovolaemic haemodilution is a blood conservation modality that has been used successfully in cardiac surgery. It is achieved by collecting blood from the patient before instituting CPB, maintenance of normovolaemia through infusion of clear fluids following by reinfusion of the collected blood after surgery. This technique however may have limited usefulness in patients with significant pre-operative anaemia or reduced blood volume, which may be present in high-risk patients undergoing CPB (52).

1.8.6 Preoperative autologous donations

Autologous transfusion involves the collection and subsequent reinfusion of the patients' own blood or blood products. The different methods of autologous transfusion include preoperative blood donation, blood salvage systems and acute normovolaemic haemodilution. Cell salvaged blood, and mediastinal shed and re-infused blood are also forms of auto-transfusion. The latter however is not recommended (51, 55).

1.8.7 Point of care devices

Point of care testing means the availability of a testing device in the clinical setting, with results being made available in real time and subsequent therapy being tailored appropriately. These tools are designed to mitigate the common time limitations of a busy laboratory, to facilitate prompt treatment, and to avoid misuse or inappropriate use of resources. Standard laboratory tests for coagulopathy are impractical to carry out intraoperatively, however point of care devices, such as the thromboelastogram are able to assess global coagulopathy and avail results within minutes.

The benefits of such a test are that it saves time, resources and it encourages a more appropriate usage of blood products (70).

1.8.8 Surgery related conservation strategies

Management of haemostasis is a key factor of any surgical procedure. Between 3-14% of patients with significant bleeding requires re-exploration and a surgically correctable cause of bleeding is found to be present in 50-67% of patients. Bleeding as well as surgical re-exploration are both independent predictors of an unfavourable outcome. Meticulous control of surgical bleeding is essential (76).

Dixon et al. (54) looked at the association between the operating surgeon and the risk of bleeding post cardiac surgery. They retrospectively studied 2575 patients who underwent cardiac surgery performed by five surgeons over a period of six years between the years 2002–2008. The study defined chest tube blood losses of more than 1000 ml recorded over 24 hours of ICU admission as their marker for potentially life-threatening bleeding. The operating surgeon was found to be an independent predictor of the amount of chest tube drainage. They concluded that management of surgeon specific factors may offer the possibility of reduced bleeding, fewer transfusions, and improved patient outcomes.

1.8.9 Blood transfusion guidelines in cardiac surgery

Practice guidelines are recommendations that help the practitioner to make evidence based clinical decisions. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints (77). Considering the untoward effects associated with blood transfusion, the current practice in cardiac surgery is moving towards a more conservative approach (77).

The Society Of Cardiothoracic Surgery and The Society of Cardiovascular Anaesthesiologist developed a set of rigorous evidence based blood conservation guidelines with specific considerations for the cardiac patient (51). The use of these guidelines has been credited with significant improvements in practice and cost reductions (2, 15, 28, 56, 69, 78, 79). Several articles cited these guidelines and welcomed the proposed methods (2, 3, 14, 15, 19, 21, 28, 56, 68, 69).

In 2009, Reddy et al. (69) conducted an audit of the use of homologous blood and blood products in patients undergoing open-heart surgery by a single surgical team using in-house protocol for blood conservation. A total of 310 adult patients scheduled for open-heart surgery, over a period of eight months took part in this study. The group developed a blood conservation protocol adapted to suit their institutions' availability of resources, using The Society of Cardiothoracic Surgery and The Society of Cardiovascular Anaesthesiologist clinical practice guidelines, and other international guidelines. Following the application of a comprehensive in-house blood conservation protocol, a reported 50% reduction in blood utilisation was observed.

Andreason et al. (56) retrospectively evaluated the impact of instituting a multimodal blood sparing techniques in reducing blood transfusion rates in their centre. At total of 450 cardiac surgery patients who had their surgery during 2004, 2008 and 2010 were reviewed. They reported a 17% reduction in overall transfusion rates and further reductions in inappropriate blood utilisation rates from 37% to 16%.

1.9 Research in blood utilisation practices in cardiac surgery

Owing to their considerable cost, the limited availability and potentially harmful effects associated with perioperative transfusion of blood products, appropriate utilisation is essential (80).

It is reported that there are considerable variations in transfusion practices, between different countries and between cardiac surgery centres (12, 81-87). Snyder-Ramos et al. (88) investigated 70 cardiac centres in 16 countries prospectively. The study showed intraoperative variations ranging between 9–100% between the 16 countries studies and between centres within a country. The rate of RBC transfusion varied by more than 12-fold intraoperatively among the 16 countries investigated.

Several other audits have consistently demonstrated the significant variability in transfusion practices between cardiac surgery centres internationally. Brevig et al. (89) conducted a re-audit of blood transfusion in cardiac surgery patients at a community hospital in 2008. The initial audit performed five years earlier showed a blood transfusion rate of 43%. The authors reported RBC transfusion rate of 18% after the re-audit, the 50% reduction in blood usage was attributed to implementation of a transfusion protocol.

In 2009, two blood transfusion audits conducted in different cardiac centres in India by Reddy et al. (69) and Dushyant et al. (18) reported overall transfusion rate of 17.4% and 2,5% respectively. Andreason et al. (56) conducted a series of audits in Denmark in 2004, 2008 and in 2010. The authors reported RBC transfusion rates of 62.2%, 55.8% and 46.9% for each respective year studied, showing improvements.

A 2011 study by Stokes et al. (53) in the United States of America reported an incidence of transfusion rates of 43% in cardiac surgery patients. In the same year, a national audit in the United Kingdom by Murphy et al. (82) reported wide variations in transfusion practices between the 25 cardiac centres audited. The author reported variations of 20–60% for RBCs and 5–45% for FFPs.

Zafiropoulos et al. (90) conducted a single centre, retrospective audit in 100 cardiac patients undergoing CABG and valve replacements in 2014. The authors reported an overall transfusion rate of 66%. Transfusion rates per blood product type were reported to be 45.75%, 41.5% and 38.9% for RBC, FFP and PLT respectively. McQuilton et al. (91) conducted a large retrospective multicentre audit in Australia. The authors reported variation in transfusion of 22–67%, 11– 48% and 11–39% for RBC, FFP and PLT respectively.

In 2015, Geissler et al. (85) conducted a large single centre retrospective audit over a period of 4 years in Germany. Transfusion rates of 55.6–61.9% were reported. The study further showed overall transfusion rates of 50% RBC, 25% FFP and 20% PLT units. Another Australian study by Scott et al. (92) reported overall rate of transfusion of 46.2%. Intraoperative cell salvage rates of 12.3% were reported, these rates were attributed to selective use of cell salvage method, which was reserved for high-risk patients in their institution.

More recently, a 2016 multicentre inter-hospital comparison study by Bouwers et al. (84) confirmed findings consistent with earlier studies. The author reported variations ranging between 43–54% in patients undergoing CABG surgery, 54–67% in valve surgery and further reported findings in valve combined with CABG surgery to be ranging between 80–88%. The authors concluded that in all the hospitals studied, the variations persisted in the number and the combination of blood products used.

These wide differences have been attributed to reasons such as: different patient population; differences in procedure related factors; traditions or norms associated with transfusions; the use of a wide variety of algorithms; and a lack of adherence to international recommendations. These marked variations may also be attributed to a possibility of inappropriate use of blood products (37, 79, 80, 93).

1.10 Conclusion

Blood transfusion is a unique form of therapy with proven lifesaving properties notwithstanding the potential adverse effects. It is an extremely scarce commodity. Regrettably, indiscriminate use of blood is on the rise (79). This demonstrates a lack of consensus as to what the best approach to blood transfusion practices is, and hence the need for change to better standardise this process (88). Monitoring blood usage, instituting multimodal conservation strategies and adhering to up to date evidence based recommendations may alleviate this crisis.

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Section 2

Cardiothoracic journal of Africa: Authors Guidelines

Article submission

All categories of manuscripts for the Cardiovascular Journal of Africa must be submitted on-line to Editorial Manager. You will be assigned your own password and user name. This will allow complete interaction between the editor and authors. Internally, reviewers will be approached to review material in their field of expertise and assigned with similar interaction. All information will be entirely protected and confidential.

All submissions should be written in a clear and succinct manner, following the style of the Journal. Title page should include a descriptive title; authors' surname and forename, address of each author and full address, telephone, fax and e-mail contacts for the corresponding author. In text: tables and figures are either inserted as part of sentence, for example Table 1, or in parentheses, for example (Fig. 1). Each table should carry a descriptive heading.

Editorial Manager will clearly indicate which aspects of the submission must be supplied off-line (**download off-line document**). This must be provided to the Journal by mail (PO Box 1013, Durbanville, South Africa, 7551) or e-mail to **info@clinicscardive.com**

All images MUST be at or above intended display size, with the following image resolutions: Line Art 800 dpi, Combination (Line Art + Halftone) 600 dpi, Halftone 300 dpi Image files also must be cropped as close to the actual image as possible.

Preferred Image Format	
Image Format	.tif
Image Width	Greater than or equal to intended display size
Colorspace	RGB
DPI	500+
Alpha Channels	None
Layers	Flattened

Alternative Image Format	
Image Format	.jpg
Image Width	Greater than or equal to intended display size
Colorspace	RGB
DPI	500+
Compression Quality	Maximum

References numbered in the order of appearance in the text, according to Vancouver style. For articles: Author AB, Author C, Author M.

The title of the article. Abbreviated journal title 1999; 14: 172–183. For book chapters: Author AB, Author CD. The title of the chapter. In: Editor A, Editor BC, ed. Title of the book, 2nd edn. Location: Publisher, 1999: 133 –139. DOI Numbers / PMID (Pubmed ID / PMC ID) must be added to all references to facilitate tagging for PubMed Central.

Original articles: Title page as above. Abstract (150 words) a short inclusive statement suitable for direct electronic abstracting, identifying the purpose of the study, key methods, the main results and the main conclusion. Keywords: maximum of six keywords for indexing. Introduction: concise description of background, sufficient for the non-specialist to appreciate the context of the work. Clear statement of the purpose of the study. Methods: a brief description of study design, procedures, analytical techniques and statistical evaluation.

Results: a clear account of the study findings using quantitative language where possible and cross-referenced to tables and figures. Discussion: an interpretation of the study placed within the context of current knowledge, leading to specific conclusions where possible. Acknowledgements. References, figures and tables as above.

Reviews

Title page as above. Abstract (150 words) setting out the scope, key messages and conclusions of the review. Body of text liberally partitioned with headings and subheadings leading to a synopsis with conclusions at the end. Key messages in a separate box itemising two to five short principal statements. Acknowledgements, references, tables and figures as above.

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Section 3

Draft article

An audit of the intraoperative usage of blood products in patients undergoing cardiac surgery on cardiopulmonary bypass

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Keywords: Transfusion, cardiac surgery, cardiopulmonary bypass, audit

Title: An audit of the intraoperative usage of blood products in patients undergoing cardiac surgery on cardiopulmonary bypass.

Background: Transfusion of blood products is increasingly recognised as an independent predictor of poor outcome after cardiac surgery. The study aims to audit blood transfusion usage in a cardiothoracic unit, at a tertiary academic centre.

Methods: A descriptive, retrospective, contextual audit. A consecutive convenience sampling method was used. One hundred and twenty-two adult patients who underwent their first elective cardiac surgery on cardiopulmonary bypass were enrolled.

Results: The mean age of the population studied was 46.7 (16.2) years. Patients were predominantly male (60.7%). The mean (SD) body mass index was 21.4 (5.6) kg/m^2. Preoperative haemoglobin and platelet counts were 12.8 (2.3) g/dL and 274.4 (121.9) 10^9/L respectively. Following a clear fluid prime cardiopulmonary bypass technique, with a median (IQR) priming volume of 1500 (1000 - 2000) ml, the first haemoglobin on cardiopulmonary bypass was 8.9 (1.6) g/dL. Overall, 110 (90.2%) patients received donor blood products. Eighty-five (77.3%) patients received red blood cells,103 (93.6%) fresh frozen plasma, and 35 (31.8%) platelet transfusion. A total of 255 red blood cell, 225 fresh frozen plasma and 37 platelet units were transfused. The cell salvage technique was used in 94 (77.0%) patients. The median (IQR) volume of salvaged blood was 535 (250–754) ml.

Conclusion: A high rate of homologous blood product transfusion was found in patients undergoing cardiac surgery in the study.

Introduction

Annually, an estimated 1.25 million patients undergo cardiac surgery worldwide. [1] In this population, consumption of blood products is reported to be higher than in other surgical groups. [2, 3] Cardiac surgery is often accompanied by acute blood loss which affects blood volume, haemoglobin and clotting factors. The premise behind blood transfusion is to replace volume, enhance oxygen delivery and improve haemostasis. [4]

Although the current study did not investigate the relationship between transfusion and outcome, it is important to note that transfusions are increasingly recognised as a risk factor for adverse outcome after cardiac surgery. [5] Several studies have shown an association between blood transfusion, morbidity and mortality in patients undergoing cardiac surgery. [6-12] Blood transfusion has been found to be an independent predictor of poor outcome. [13, 14]

It is reported that considerable variations exist in transfusion practices between different countries and between cardiac surgery centres within those countries. [15-19] This demonstrates a lack of consensus and hence the need for continuous review of these practices. [20] Evidence suggests that transfusion guidelines may reduce unjustified transfusions. [15, 16, 21] The considerable cost, limited availability and potentially harmful effects associated with the perioperative administration of blood products are all reasons to make appropriate utilisation mandatory. [22, 23]

Promoting appropriate blood use is one of the major objectives of the World Health Organization (WHO). The key factors recommended by the WHO can be achieved by monitoring of blood use through serial audits, development of local guidelines and protocols, and incorporating haemovigilance programmes. [24]

At our institution, an audit to determine the utilisation of blood products during cardiac surgery has not been previously undertaken. The aim of the current study was to audit the intraoperative usage of blood products in adult patients undergoing cardiac surgery on cardiopulmonary bypass (CPB).

Methods

This was a descriptive, retrospective, contextual audit conducted at Charlotte Maxeke Johannesburg Academic Hospital, a 1088-bedded quaternary referral centre in Johannesburg. Approximately 160 adult cardiac surgeries on cardiopulmonary bypass are done at this institution annually.

The Human Medical Research Ethics Committee approved the study. Other appropriate permissions were sought and granted. Consecutive records of 122 adult patients who underwent their first elective cardiac surgery on CPB were analysed. Anonymised data were retrieved from records completed by the anaesthetist, perfusionist and intensive care unit doctors. The data collected included demographics, perioperative blood profile, aspects regarding the use of cardiopulmonary bypass and the blood products used. The information collected was used to create a single database, and the data were collected by one author (CP).

A descriptive statistical analysis was performed using Microsoft Excel^{TM} 2007. Descriptive statistics included the mean, standard deviation (SD), median, inter quartile range (IQR), frequencies, numbers and percentages where appropriate.

Results

Between January and December 2013, a total of 138 participants underwent cardiac surgery on CPB. Fifteen participants (12.2%) were excluded. Amongst those excluded, three had emergency surgery and twelve had missing data.

Records of 122 participants were eligible for the analysis. A summary of the participants' demographics is shown in Table 1.

Table 1: Participants' demographic and surgical data

Demographics	**mean**	**SD**
Age (years)	46.7	16.2
Weight (kg)	70.9	17.9
Height (m)	1.6	0.1
BMI (kg/m^2)	21.4	5.3
Gender	**n**	**%**
Male	74	60.7
Female	48	39.3
Diagnosis	**n**	**%**
Coronary artery disease	28	22.9
Valve disease	83	68.0
Myxoma	4	3.3
Aneurysm	7	5.7
Surgical Procedures	**n**	**%**
Single valve repair/replacement	36	29.5
Double valve repair/replacement	37	30.3
Triple valve repair/replacement	7	5.7
Isolated CABG	28	22.9
Single valve repair and CABG	3	2.5
Myxoma removal	4	3.3
Aneurysm repair	7	5.7

*BMI-body mass index, CABG-coronary artery bypass graft

Haemoglobin levels and platelet counts were assessed perioperatively. These findings are shown in Table 2.

Table 2: Perioperative haemoglobin and platelet counts

Blood results	**Mean (SD)**	**Range**
Haemoglobin (g/dL)		
Preoperative	12.8 (2.3)	7.7–18.8
Intraoperative: First on CPB	8.9 (1.6)	5.4–16
Last on CPB	9.9 (1.3)	6.8–13
Postoperative: Intensive care unit	11.1 (1.6)	7–13.5
Platelets 10^9 /L		
Preoperative	274.4 (121.9)	34–838
Postoperative	172.9 (71.3)	42–308

*CPB-cardiopulmonary bypass

In the current study, anaemia was found to be present in 48 (40%) patients and thrombocytopenia in 11 (9%) patients preoperatively. The mean (SD) preoperative platelet count was 274.4 X 109/L (121.9). Postoperatively, the mean (SD) platelet count was 172.9 X 109/L (71.3). A small proportion (8%) of patients had platelet counts below 150 X 109/L postoperatively. Overall, 57 (46.7%) patients received preoperative anticoagulation therapy. Of these, 36 (63.1%) were on coumadin while 21 (36.9%) were on acetylsalicylic acid and enoxaparin. Enoxaparin was commenced in hospital, and both enoxaparin and coumadin were discontinued appropriately preoperatively.

The CPB machine was primed with a crystalloid in all patients. The median (IQR) priming volume was 1500 (1000–2000) ml. The anticoagulant used on CPB in all the patients was heparin and the mean (SD) dose given was 90 (0.91) mg.

The overall median (IQR) time on CPB was 117 (95–145) minutes. In total, 97 (79.5%) received cell saved blood and the median (IQR) volume of salvaged blood was 535 (250–754) ml. The time on CPB and volume of blood salvaged for each surgical group are presented in Table 3.

Table 3: Time on cardiopulmonary bypass and blood salvaged

Type of Surgery	**Time on CPB (min) median (IQR)**	**Cell saved blood (ml) median (IQR)**
Single valve repair/replacement	113 (88–135)	682 (108–875)
Double valve repair/replacement	117 (96–139)	600 (327–900)
Three valve repair/replacement	145 (135–170)	306 (250–650)
Isolated CABG	117 (97–150)	500 (200–678)
Single valve and CABG	115 (102–202)	600 (570–700)
Myxoma removal	75 (62–98)	426 (184–712)
Aneurysm repair	130 (81–240)	500 (0–700)

*CPB-cardiopulmonary bypass, CABG-coronary artery bypass graft

Overall, 110 (90.2%) patients were transfused donor blood products. Among those transfused, 85 (77.3%) received red blood cells (RBC), 103 (93.6%) fresh frozen plasma (FFP) and 35 (31.8%) received platelet transfusion. A total of 255 RBC, 225 FFP and 37 platelet units were transfused. Of these products, the anaesthesiologists transfused 107 (41.9%) RBC, 171 (76.0%) FFP, and all 37 (100%) of platelet units. The perfusionists transfused 148 (58.0%) RBC, 54 (24.0%) FFP and 0 (0%) platelet units. A per patient mean (SD) number of units transfused was 3.14 (2.2) RBC, 1.8 (1.5) FFP and 0.3 (0.4) platelet units.

A summary of the types of surgery performed, number of patients and percentage, the type and the number of blood products used is presented in Table 4.

Table 4: The total number of product units per type of surgery

Type of Surgery	Pts n(%)	RBC n(%)	FFP n(%)	PLT n(%)
Single valve repair/replace	36 (29.5)	79 (30.9)	70 (31.1)	10 (27.0)
Double valve repair/replace	37 (30.3)	60 (23.5)	59 (26.2)	12 (32.4)
Triple valve repair/replace	7 (5.7)	18 (7.1)	11 (4.9)	1 (2.7)
Isolated CABG	28 (22.9)	51 (20.1)	46 (20.4)	6 (16.2)
Single valve and CABG	3 (2.5)	9 (3.5)	10 (4.4)	2 (5.4)
Myxoma removal	4 (3.3)	16 (6.3)	11 (4.9)	2 (5.4)
Aneurysm repair	7 (5.7)	22 (8.6)	18 (8.0)	4 (0.1)

*Pts-Patients, Replace-replacement, PLT-platelet, RBC-Red blood cells, FFP-Fresh frozen plasma, CABG-coronary artery bypass graft

A breakdown of product units used per patient according to the type of surgery performed is shown in Table 5.

Table 5: The number of product units per patient per surgical group

Type of surgery	Pts n(%)	RBC mean (SD)	FFP mean (SD)	PLT median (IQR)
Single valve repair/replace	36 (29.5)	2.2 (2)	1.9 (0.5)	0 (0-1)
Double valve repair/replace	37 (30.3)	1.6 (1.9)	1.6 (1.2)	0 (0-2)
Triple valve repair/replace	7 (5.7)	2.6 (0.9)	1.6 (0.9)	0 (0-0)
Isolated CABG	28 (22.9)	1 (0-3) #	1.6 (1.3)	0 (0-0)
Single valve and CABG	3 (2.5)	3 (2.6)	3.3 (2.3)	0 (0-2)
Myxoma removal	4 (3.3)	4 (3.2)	2.6 (1.6)	0.5 (0-1)
Aneurysm repair	7 (5.7)	2 (0-4) #	2.6 (2.2)	0 (0-1)

* Pts-Patients, replace-replacement, RBC-Red blood cells, FFP-Fresh frozen plasma, PLT-platelet, CABG-coronary artery bypass graft, # - median(IQR)

Discussion

Overall, 110 (90.2%) patients were transfused donor blood products. Among those transfused, 85 (77.3%) patients received RBC transfusions, 103 (93.6%) received FFP transfusions and 35 (31.8%) patients received platelet transfusions. In a large prospective multicentre study by Snyder-Ramos et al. [20], a 12-fold variation in intraoperative transfusion was shown between 16 countries studied. The average rate of transfusion of all blood products was much lower in their study comparatively, with rates of (41.5%) RBC, (10.9 %) FFP and (9.2%) platelet transfusion.

Varying transfusion rates have been demonstrated in multiple international studies. [10, 18, 20, 21, 25-32] These vast differences have been attributed to different patient populations; differences in procedure-related factors; traditions and norms associated with transfusions; the use of variable protocols; and a lack of adherence to international recommendations. [20]

Several other audits have consistently demonstrated the significant variability in transfusion practices between cardiac surgery centres internationally. [27] Most reported transfusion rates are still lower compared to those found in our study despite the considerable variation in their reported rates.

Andreason et al. [27] conducted a series of audits in Denmark in 2004, 2008 and in 2010. The authors reported RBC transfusion rates of 62.2%, 55.8% and 46.9% for each respective year studied, thus showing a reduction in rates. A 2011 study by Stokes et al. [33] in the United States of America reported an overall transfusion rate of 43%. In the same year, a national audit in the United Kingdom by Murphy et al. [17] reported variations of 20–60% for RBC and 5–45% for FFP between the 25 cardiac centres audited. In 2015, Geissler et al. [19] conducted a large single-centre retrospective audit and reported transfusion rates of 50% RBC, 25% FFP and 20% platelet units. Similarly, a multicentre audit by McQuilton et al. [26] showed transfusion rates ranging between 22–67%, 11–48% and 11–39% for RBC, FFP and platelet units respectively.

Independent preoperative clinical variables that predict the likelihood of exposure to blood transfusion in patients undergoing cardiac surgery have been identified. These variables include preoperative haemoglobin (Hb), weight, female gender, emergency surgery and combined procedures. [34, 35] The mean (SD) age of the population studied was 46.7 (16.2) years, predominantly male (60.7%), with a mean (SD) preoperative Hb of 12.8 (2.6) and a body mass index of 21.4 (5.6) kg/m^2. In comparison to the current study, the patient profile in a comparative study had older patients at 64.1 (9.8) years, who were overweight with a body mass index of 27.6 (4.5) kg/m^2, and however, with lower transfusion rates. [20] Emergency surgeries were included in other studies, which also reported lower transfusion rates than those found in the current study. [25, 32, 35, 36]

Given the low-risk nature of the population in the current study, and that emergency surgery was excluded, the risk for transfusion was anticipated to be lower. The current results suggest that there may be other factors that could explain this trend.

Analysis of blood use by surgical procedure in the current study showed that the single valve repair patients received the highest number of RBCs (30.9%) and FFPs (31.1%) compared to other surgical groups. The group that received the least number of RBCs and FFPs (3.5% and 4.4% respectively) was the combined CABG and valve surgery. Scott et al. [35] also reported transfusion rates by surgical group. The CABG and valve surgery group showed a higher transfusion rate (69.8%) compared to lower transfusion rates (33.9%) found in the valve surgery group. This is in contrast to the current study.

The multi-centre study by Snyder-Ramos et al. [36] investigated rates during CABG surgery and showed a RBC transfusion frequency of 38.3%, 8.8% for FFP and 7.1% for platelets amongst the 70 centres studied. In the current study, in the CABG subgroup, the frequency for RBC transfusion was lower (20.1%), however, FFP (20.4%) and platelets (16.1%) were comparatively higher.

On-pump surgery, particularly if CBP times exceed 60 minutes, together with the use of a clear prime fluid, has been associated with an increased tendency to bleed. [37] In the current study, valve surgery was the procedure performed predominantly (68.0%), and 116 (95.1%) of the valve surgery patients had CPB times exceeding 60 minutes. A clear fluid, standard prime volume 1500 (1000–2000) ml was used. The decrease in preoperative Hb levels from a mean (SD) of 12.3 (2.3) to 8.9 (1.6) shown by the first Hb on CPB could be due to haemodilution during pump prime.

Takai et al. [38] prospectively randomised 288 CABG procedures and demonstrated that using low-volume prime techniques was associated with less blood loss and fewer blood transfusions. In the current study, aspects related to the use of CPB were found to be largely uniform. Modifying the current CPB priming technique may lower transfusion rates. [39-41]

Bleeding in cardiac surgery patients is multi-factorial. Transfusion of FFP and platelets is used to manage bleeding. The FFP and platelet transfusion rates were found to be 93.6% and 31.8% respectively in the current study. These rates are higher than those found in one study. [25] Zafiropoulos et al. [25], showed FFP and platelet transfusion rates of 41.5% and 38.9% respectively. Glasgow et al. [32] found FFP transfusion rates to be 38.3% in their study. The difference between these studies and the current study is that the FFP and platelet use was guided by a protocol [25] and by point of care testing. [32] This could possibly explain the differences in the rates of transfusion.

Standard laboratory tests for assessing coagulopathy are impractical to carry out intraoperatively, however, point of care devices such as the thromboelastogram are able to assess global coagulopathy and yield results within minutes. [42] In the setting of the current study, point of care testing for transfusion of FFPs and platelets was not used.

FFPs and platelets were therefore transfused without prior testing to guide therapy, suggesting that transfusions were given empirically. In a 2016 multicentre inter-hospital comparison study by Bouwers et al. [18], the authors concluded that in all the hospitals studied, the variations in blood transfusion persisted not only in the number of patients transfused but also in the number and the combination of blood products used. In the absence of a protocol and a point of care testing, it is possible that FFP and platelet transfusion were not administered in correct ratios, which may explain the current high volume of the products used and the number of patients transfused in the current study.

Enoxaparin was used in 36.9% of the patients in this study. Preoperative enoxaparin has been linked with a tendency to increase intraoperative bleeding. [42] This effect is observed if the surgery is performed less than 12 hours after the last administered dose. [43] The effect of anticoagulants on bleeding was not assessed in this study. It is assumed that as all the cases in this study were elective, the enoxaparin and coumadin therapy had been discontinued appropriately. These anticoagulants are therefore not expected to have contributed to a current high usage of blood products.

Clinical complications posed by transfusion of blood have led to the development of blood conservation strategies in cardiac surgery. [27, 44] Studies [2, 34, 45-47] have summarised conservation strategies as preoperative autologous blood donation, use of erythropoietin, intraoperative use of antifibrinolytic agents, cell salvage and acute normovolaemic haemodilution. The Society Of Cardiothoracic Surgery and The Society of Cardiovascular Anaesthesiologists developed guidelines for blood transfusion, with specific consideration for the cardiac patient. [2] The use of these guidelines has been credited with significant improvements in practice and cost reductions. [22, 27, 48-51] The use of cell saver is a class 1A recommendation by this group. [45] The routine use of the cell salvage technique and its cost effectiveness in low risk patient has been challenged. [35, 52]

The cell salvage and reinfusion technique was used in 94 (77.0%) patients in the current study. The median (IQR) volume of blood reinfused was 535 ml (250–764). In comparison, an overall autologous transfusion frequency of only 9% was shown in a 2008 multi-centre Snyder-Ramos et al. study [20]. In one country in that study, no patient received autologous blood. In a 2015 study by Scott et al. [35], cell salvage rates of 12.3% were reported. The authors [35] attributed these rates to selective use of the cell salvage method, which was reserved for high-risk patients in their institution.

Cell salvage techniques are helpful in reducing RBC transfusion, however, the processing of blood leads to loss of plasma and platelets, which may in turn lead to increased FFP and platelet requirements. [53, 54] This effect was not assessed in the current study. There was an increased rate of factor and platelet transfusion and an increased volume of salvaged blood in the current study. A relationship between cell salvaged blood and impaired coagulation has been shown. [55] This could be an area to explore as the reason for the FFP and platelet transfusion trend. The indiscriminate use of cell salvage in the current study may explain the current FFP and platelet transfusion rates.

Campbell et al. [56] conducted a study in 20 CABG patients assessing clot formation and integrity, following reinfusion of cell salvaged processed blood using a point of care testing device. The author concluded that cell salvaged blood reduced not only platelet count but also clot firmness, and prolonged time to clot formation. In 2016, Shen et al. [55] demonstrated similar findings and added that cell salvaged blood further impaired coagulation by reinfusion of blood with residual heparin that is devoid of clotting factors. It is suspected that reinfusion of cell salvaged blood may increase the risk of bleeding and the need for transfusion of clotting factors and platelets. [53, 55, 57] Reports regarding the use of cell salvage in the literature are conflicting, but the consensus is that in the correct setting its use is associated with a decreased rate of transfusion. [27, 52, 58]

Anaemia is present when the Hb < 12.0 g/dL for females and <13.5 g/dL for males. [47] Oxygen delivery and metabolic demands vary with age, BMI, gender, comorbidities and the presence of active bleeding; therefore, a single universal number cannot describe anaemia. [15] Oxygen delivery is said to be adequate in a healthy patient at an Hb of 8g/dL; conversely, in a patient with poor cardiopulmonary reserve, a level of 10 g/dL is generally acceptable. [57]

Preoperative anaemia was found to be present in 48 (40%) of the patients in the current study. Pre-existing anaemia has been shown to increase the risks of transfusion. [59] In a study by Scott et al. [35] preoperative anaemia was present in 24.2% of their population and their blood transfusion rates were lower. In the current study, the mean (SD) Hb in ICU was found to be 9.9 g/dL and 82% had a postoperative Hb of > 10g/dL. Appropriate transfusion thresholds as well as target transfusion Hb are a matter of ongoing debate. [60-63]

Thrombocytopenia is defined as a platelet count of less than 150 X 10^9 /L [47] .The risk for major postoperative bleeding exists when the platelet count is 50 X 10^9 /L and less. [64] In the current study, thrombocytopenia was found in 11 (9%) patients preoperatively, however, none of the thrombocytopenic patients were below the bleeding threshold. A total of 35 (31.8%) patients received platelet transfusion intraoperatively despite the lack of intraoperative assessment of platelets.

Transfusions are increasingly recognised as a risk factor for adverse outcome after cardiac surgery. [6, 8, 9, 49, 65-68] Several studies looking at the association of transfusion in cardiac surgery patients with morbidity and mortality have suggested an immune-based aetiology. The three main systems affected adversely by transfusion are the cardiac system, the pulmonary system and the renal system. [6, 7, 9, 50, 51, 69, 70] The current study did not look at morbidity and mortality outcomes related to blood product transfusion.

Conclusion

The blood transfusion practice has not been assessed in the current study's setting before.

Management of haemoglobin was consistent with practice in other studies, however, the use of high volumes of cell salvaged blood was seen. Despite the high priming volume, the mean on-pump Hb was 8 (1.6) g/dL. In the absence of point of care testing, FFP and platelet transfusions were empiric and some may be unjustified. These factors may have contributed to the current transfusion rates observed. Transfusion guidelines and protocols may reduce unjustified incidents of transfusion as evidenced in previous studies. (15, 21, 22, 27, 48, 71, 72)

Introducing a locally adapted, in-house transfusion protocol based on published recommendations may lead to reductions in the incidence of transfusion. Employing the use of a point of care service, changing CPB priming techniques and using the cell salvage reinfusion technique in selected high-risk patients in our institution may lead to a change in the current blood transfusion practice. A study looking at outcomes related to blood transfusion is also recommended.

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Section 4

Appendices

Appendix 1: Human Research Ethics Committee (Medical) approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Academic & Research)

MEMORANDUM

TO: **Dr Charity Phokontsi**
Department of Anaesthesiology
E-mail: phokontsi@gmail.com

FROM: **Ms Zanele Ndlovu**
Administrative Officer: Human Research Ethics Committee (Medical)
Tel: 011 717-1252
e-mail: zanele.ndlovu@wits.ac.za

DATE: 19 September 2014

REF: ***R14/49*** *(This is not your protocol number)*

The protocol below was considered at a meeting of the Human Research Ethics Committee (Medical) **on Friday 29 August 2014.** The Committee requires the following amendments/corrections/information from you before your application can be approved.

Protocol no: **M140834** *(Please quote this reference number in all correspondence relating to this study)*

Project Title: An Audit of the Intraoperative Usage of Blood Products in Patients undergoing Cardiac Surgery on Cardiopulmonary Bypass

Conditions: **Approved subject to:**
- Providing written permission to do the study from the hospital CEO
- Application: January 1, 2013 – December 31, 2013. Not clear why approval is sought in 2014 if study commences only in April 2015. Please clarify

NB:

1. **Please submit a covering letter, highlight any changes made and send two hard copies to this office**
2. **Amendments must be delivered at Faculty of Health Sciences, Phillip Tobias Building, second floor, Cnr York Road and Princess of Wales Terrance**
3. **Office hours: 08h30–17h00**

R14/49 Charity Phokontsi

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140834

NAME: (Principal Investigator)	Charity Phokontsi
DEPARTMENT:	Anaesthesiology Charlotte Maxeke Johanesburg Academic Hospital
PROJECT TITLE:	An Audit of the Intraoperative Usage of Blood Products in Patients undergoing Cardiac Surgery on Cardiopulmonary Bypass
DATE CONSIDERED:	29/08/2014
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Juan Scribante and Palesa Motshabi
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	11/05/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.

I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee **I agree to submit a yearly progress report**.

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 2: Postgraduate approval

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Dr KCP Phokontsi
PO Box 2467
Lichtenburg 2740
South Africa

Dear Dr Phokontsi

Master of Medicine: Approval of Title

Private Bag 3 Wits, 2050 Fax: 027117172119 Tel: 02711 7172076

Reference: Ms Thokozile Nhlapo E-mail: thokozile.nhlapo@wits.ac.za

27 November 2014 Person No: 1032635 PAG

We have pleasure in advising that your proposal entitled *An audit of the intraoperative usage of blood products in patients undergoing cardiac surgery on cardiopulmonary bypass* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 3: Approval letter from Chief executive officer

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries: Ms. Lefentse Mapaisa
Office of the Clinical Executives
Tel: (011)488-3710
Fax: (011)488-3947
28 November 2014

Dr. Charity Phokontsi
Registrar: Department of Anaesthesiology
University of the Witwatersrand

Dear Dr. Phokontsi

RE: An audit of blood transfusion practices in adult cardiac surgery patients, on cardiopulmonary bypass

Permission is granted for you to conduct the above recruitment activities as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic hospital will not in anyway incur or inherit costs as a result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall be observed at all times.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the Head of Department and Unit Manager or Sister in Charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Supported / ~~not supported~~

Dr. M.I. Mofokeng
Clinical Director
DATE: 1/12/2014

Approved / not approved

Ms. G. Bogoshi
Chief Executive Officer
DATE: 2/12/2014

Appendix 4: Approval letter from Gatekeeper

Appendix B: Request to the gatekeeper for access of anaesthetic records

Dr. Charity Phokontsi
Department of Anaesthesiology
University of the Witwatersrand
24. July. 2014

Attention: The Gatekeeper

Re: Request to the gatekeeper for access of anaesthetic records

Dear Dr. Krubin Naidoo

I am a registrar at the department of Anaesthesiology and completion of a research project is a requirement. The title of my research is, **An audit of blood transfusion practices in adult cardiac surgery patients, on cardiopulmonary bypass, at CMJAH**

It is a retrospective study reviewing blood usage using anaesthetic, perfusionist and ICU charts. No patients or clinicians names will be included in the study. The records will be reviewed at the department and will not be removed from the hospital premises.

I would like to request permission to access these records.

Yours Sincerely

Dr. Charity Phokontsi

0724172989

phokontsi@gmail.com

APPROVAL GRANTED

K NAIDOO
FC(Cardio(SA)
25/07/2014

Appendix 5: Data collection sheet

Data collection sheet A: Demographics

Study no.	Age	Gender	Race	Diagnosis
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				

Data collection sheet B: Procedural parameters

Study no.	Date of op	Type of op	Duration of op	CBP time	Prime volume

Table C: Haemoglobin trends

Study no.	Preoperative	Intraoperative Anaesthetist	Intraoperative Perfusionist Hb 1	Perfusionist Hb2	Postoperative
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

Data sheet D: Blood components

Study no.	Red blood cell	Platelets	Fresh Frozen plasma
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			

Section 5

Proposal

An audit of the intraoperative usage of blood products in patients undergoing cardiac surgery on cardiopulmonary bypass

Kenyaditswe Charity Petronella Phokontsi

1032635

Supervisor	**Palesa Motshabi** **Department of Anaesthesiology**

1. Introduction

In 1818, James Blundell, a British obstetrician performed the first successful blood transfusion using freshly drawn human blood. Since that time, blood transfusion has become a vital component of clinical medicine globally (1). In the 21st century, according to the World Health Organizations' (WHO) 2011 blood safety report, approximately 92 million blood donations are collected around the world, annually (2).

Blood banking techniques have evolved dramatically since the times of lamb blood transfusions in humans (3). Whole blood is separated into its components and then stored appropriately. Each unit of whole blood is fractionated by centrifugation to provide red cell concentrates, fresh frozen plasma, platelets, cryoprecipitate and clotting factor concentrates (4). Use in this manner maximizes utilization of blood bank resources.

Annually, an estimated 1.25 million patients undergo cardiac surgery worldwide (5). Consumption of blood products in this population is reported to be high (6, 7). Cardiac surgery is often accompanied by acute blood loss affecting the blood volume, haemoglobin and clotting factors. The premise behind blood product transfusion is to enhance oxygen delivery and improve haemostasis (8). There have been suggestions regarding the limitations of these benefits with debates in this regard still ongoing (8-14).

Transfusion of blood products is not without risks (9-11). Numerous significant complications associated with transfusions have been demonstrated (13, 15-18). Infectious and non-infectious adverse effects have been of concern for decades. Although modern blood banking techniques including routine surveillance for human immunodeficiency virus (HIV), syphilis and hepatitis B virus as well as hepatitis C have led to notable reductions in their transmission, the risk exists still (4, 19).

Transfusion of red blood cells is a recognised risk factor for adverse outcome after cardiac surgery. Literature extending over a decade ago has accumulated, indicating significant risks of adverse outcomes in cardiac patients who were transfused as opposed to those who were not.

In 2001, Mikkola et al. (20) investigated the effects of blood transfusion after coronary artery bypass surgery and demonstrated that transfusion increases the risk of short term mortality. Six years later, Edgoren et al. (10), in retrospective study stated that blood transfusion is associated with increased risk in long term mortality. More recently, two studies in 2013 by Paone et al. (13) and Shaw et al. (16) confirmed these findings and also demonstrated other adverse outcomes such as postoperative myocardial ischaemia, new onset arrhythmias and organ failure (9, 11, 13, 14).

It is reported that there are considerable variations in transfusion practices between different countries and between cardiac surgery centres (21-23). Snyder-Ramos et al. (24) investigated 70 centres in 16 countries prospectively. The study showed intraoperative variations of transfusion practices ranging between 9-100% between the 16 countries studied and between centres within a country. This demonstrated a lack of consensus as to the best approach to blood transfusion practice and a need standardise this practice (24).

The clinical problems posed by transfusion of blood have prompted the development of blood conservation strategies in cardiac surgery (25, 26). Several authors (4, 6, 27-29) have summarised conservation strategies as preoperative autologous blood donation (PAD), the use of erythropoeitin with or without PAD, intraoperative use of antifibrinolytic agents, cell salvage and acute normovolaemic haemodilution. Alternatives to blood transfusion have been shown to be safe and cost effective in some studies (30, 31).

Herbert et al. (32), conducted a multicentre, randomised controlled clinical trial in 1999 comparing effects of restrictive versus liberal transfusion strategies on critically ill patients. The restrictive method was found to be superior, with fewer adverse outcomes. In 2006, Alghamadi et al. (27) developed the Transfusion Risk Scoring Tool (TRUST) to stratify cardiac patients according to their blood transfusion needs. Using eight preoperative variables, this clinical scoring tool was validated by the group.

Practice guidelines are systematically developed recommendations that assist practitioners to make evidence based clinical decisions (33). There are several international guidelines (4, 6, 10, 28, 34), among these, the Society Of Cardiothoracic Surgery and The Society of Cardiovascular Anaesthetist developed guidelines for blood transfusion specific for the cardiac patient. The use of these guidelines has been associated with significant improvements in practice (14, 18, 25, 35, 36) and cost reduction (25, 35, 37).

“First do no harm” is a fundamental principle in medical practice. Used appropriately, blood transfusion can be life-saving but the mounting evidence highlighting adverse effects related to its use warrants improvement.

2. Problem statement

Cardiac surgery and cardiopulmonary bypass carry a substantial risk of blood loss and therefore of blood transfusion. Many studies have shown that an association exists between blood transfusion and morbidity and mortality in cardiac patients undergoing cardiac surgery (11, 13, 16, 20).

There is significant variability of transfusion practices between cardiac surgery units and between clinicians (38). Several studies have demonstrated high incidences of inappropriate blood use (39-41). Evidence suggests that transfusion guidelines may reduce unjustified transfusion (21, 22, 42).

Furthermore, some studies have demonstrated significant reductions in the use of blood products following formulation and introduction of locally adapted, in-house transfusion protocols based on published recommendations (25, 35).

There is a perception that blood products are used liberally during cardiac surgery at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), however no audit to determine the utilisation of blood products has been done. There is currently no standard blood transfusion protocol for use during cardiac surgery at CMJAH.

3. Aim

The aim of this study is to audit the intraoperative usage of blood products in adult patients undergoing cardiac surgery on CPB at CMJAH.

4. Objectives

The objectives of this study are to:

- determine the patients preoperative Hb and platelet count
- Describe the preoperative anticoagulant therapy
- determine the type and number of blood products used intraoperatively by the anaesthetist and those used by the perfusionist
- describe the priming of CPB machine (type and volume of prime fluid) used and determine the time duration on CPB
- determine the first and the last Hb on CPB
- determine the patients first Hb and platelet count in ICU.

5. Research assumptions.

The following definitions will be used in this study.

Adult: patients 18 years and older.

Anaesthetic chart: a clinical record completed manually by the anaesthetist for each anaesthetic given and a record of events occurring during the anaesthetic.

Perfusionist chart: a clinical record completed manually by the perfusionist for each patient during surgery and a record of events related to CPB.

Intensive care unit charts: a clinical record completed by ICU health care professionals and a record of events occurring during their care in ICU.

Blood components: In this study, this includes red cell concentrates, platelets and fresh frozen plasma.

Gatekeeper: The person who regulates access to records, in this study, the Head of the Cardiothoracic Department granted the researcher access to records required.

6. Demarcation of study field

The research will be conducted using charts of patients who had cardiac surgery on CPB at CMJAH. CMJAH is a central hospital with 1088 beds and is affiliated to the University of the Witwatersrand, Johannesburg.

Approximately 160 cardiac surgeries on CPB are done yearly, in adults, at this hospital.

7. Ethical considerations

Approval to conduct this study will be obtained from the Graduate studies Committee and the Human Research Ethics Committee (43) of the University of the Witwatersrand. Permission to conduct the study will be requested from the CEO of CMJAH (Appendix A). Written permission to access perfusionist and ICU charts of patients included in this study was obtained from the gatekeeper in the Department of Cardiothoracic Surgery (Appendix B).

As this study is a retrospective audit no patient consent is required. Anonymity and confidentiality will be maintained as names and other identifiers will be removed from patients' records. Only the researcher and the supervisors will have access to the raw data. Data will be stored securely for six years following completion of the study.

This study will be conducted in accordance with the principles of the Declaration of Helsinki (44) and the South African Good Clinical Practice Guidelines (44).

8. Research Methodology

8.1 Study design

A descriptive, retrospective and contextual study design will be used in this study.

A descriptive study defines the characteristics of the sample under investigation. The researcher of such a study does not manipulate any of the variables (45). In this study, the use of blood product in cardiac surgery patients on CPB will be audited in order to describe practice.

A retrospective study measures variables based on past events (45). This study is deemed as such because the records from January to December 2013 will be audited.

A contextual study is one that examines data collected from a specific location or area (46). Only records of patients admitted to CMAJH, Department of Cardiothoracic Surgery will be included.

8.2 Study population

All the records of adult patients who underwent cardiac surgery on CPB at CMJAH will constitute the population for the study.

8.2 Study Sample

All the records of adult patients who underwent cardiac surgery on CPB at CMJAH from the 1st January to 31st December 2013 will constitute the sample for the study.

Sample Size

The sample size of this study, as determined by the number of cases that were done during the study period, was 153.

Sampling method

A consecutive, convenience sampling method will be used.

Convenience sampling, a form of non-random sampling, uses the most easily accessible individuals or units in a study. Consecutive sampling is a version of convenience sampling where every available individual or event within the accessible population is selected for inclusion in the study. It is the best choice of non-random sampling (45, 46).

Records of all the patients who had cardiac surgery on CPB during the year 2013 will be included in the study.

Inclusions and exclusions

The following inclusion and exclusion criteria will apply.

Inclusion criteria:

- records of adult patients 18 years and older
- who underwent cardiac surgery on CPB.

Exclusion criteria:

- incomplete set of records
- congenital heart conditions
- records of patients belonging to the Jehovah's Witness religious group.

8.4 Data collection

Written permission to access perfusionist and ICU charts of patients included in this study was obtained from the gatekeeper in the Department of Cardiothoracic Surgery. The gatekeeper will provide the researcher with the list of patient names that fulfil the inclusion criteria. The researcher will then review the records for completeness and will allocate each eligible patient's records a study number.

The collected data will be directly recorded onto a Microsoft Excel™ spreadsheet (Appendix C). The following data will be recorded:

- demographics (age, gender, weight, type of surgery)
- preoperative anticoagulant therapy
- preoperative Hb and platelet count

- type and number of blood products used intraoperatively by the anaesthetist and those used by the perfusionist
- priming used for CPB machine (type and volume fluid and anticoagulant)
- CPB time
- first and last Hb on CPB
- first Hb and platelets in ICU.

8.5 Data analysis

Data will be analysed in consultation with a biostatistician using descriptive and inferential statistics, Stata® version 13.1. Categorical variables will be described using numbers and percentages and continuous variables using means and standard deviations or medians and interquartile ranges as appropriate.

9. Significance

Promoting appropriate blood use is one of the major objectives of the WHO. The key factors recommended by the WHO can be achieved by monitoring blood use through serial audits, development of local guidelines and protocols and incorporating haemovigilence programs (47).

Cardiac surgery and cardiopulmonary bypass carry a substantial risk of blood loss and therefore of blood transfusion. Blood transfusion carries with it significant risks and there is growing evidence that demonstrates that an association exists between blood transfusion and mortality in this population group (16-18).

There is significant variability of transfusion practices between cardiac surgery units and between clinicians. Several studies have demonstrated high incidences of inappropriate blood use (39, 40).

Evidence suggests that transfusion guidelines may reduce unjustified incidents of transfusion (21, 37, 41, 42). Furthermore, some studies have demonstrated significant reductions in the use of blood products following formulation and introduction of locally adapted, in-house transfusion protocols based on published recommendations (25, 35).

This audit will draw attention to blood product usage and may lead to the introduction of protocols at CMJAH which could ensure the appropriate use of this scarce resource in patients undergoing cardiac surgery on CPB in future.

10. Validity and reliability

With any research data set quality checks are necessary to determine the reliability and validity of the data. When a research study design is being developed it is important to take into account these formal evaluations of measurement error. Measurements are assessed in terms of reliability and validity (48).

Validity indicates whether the conclusions of a study are justified based on the design and interpretation, validity refers to the degree to which a measurement represents a true value (48).

Reliability represents the consistency of the measure achieved ,meaning that if a valid measuring tool is applied to different groups under similar circumstances, it should be able to produce the same result (48).

The validity and reliability of this study will be ensured by:

- using an appropriate study design
- data being collected by a single research to ensure consistency
- strict application of inclusion and exclusion criteria
- checking every tenth data entry to ensure accuracy

- analysing data in consultation with a biostatistician.

11. Potential limitations of the study

This study requires information from patients' records including charts from anaesthetist, perfusionists' and the ICU. There may be difficulties in acquiring all three charts for each patient.

Record keeping is a known problem in many institutions. All the data to be collected depends on others for accurate record keeping. Incomplete records or missing data can impede the progress of data collection and also affect the sample size.

As the study is contextual the results may not be generalisable to other hospitals.

12. Project outline

12.1 Time frame

	Jun ‘14	Jul ‘14	**Aug ‘14**	**Jan ‘15**	**Feb ‘15**	**Mar ‘15**	**Aug ‘16**	**Sep ‘16**	**Oct ‘16**	**Nov ‘16**	**Dec ‘16**
Chapter 1-3	X	X									
Proposal	X	X									
Ethics Submission			X								
Postgrad submission			X								
Data Collection				X	X	X					
Data analysis							X	X			
Chapter 4-5									X	X	
Submit											X

12.2 Financial plan

The Department of Anaesthesiology will fund all paper and printing costs incurred in this study.

The proposed budget for this study is illustrated below.

Description	Price per item	Amount of items	Total
Printing of proposal	R1 per page	+/- 400	R400
Printing research report	R1 per page	+/-1000	R1000
Binding of final research report	R200	+/-3	R600
Total			**R2000**

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Appendix 1: Letter to the CEO

Appendix A: Request to the CEO of Charlotte Maxeke Johannesburg Academic Hospital

Dr. Charity Phokontsi
Department of Anaesthesiology
University of the Witwatersrand
28 November 2014

Attention: The CEO of Charlotte Maxeke Johannesburg Academic Hopsital

Re: An audit of blood transfusion practices in adult cardiac surgery patients, on cardiopulmonary bypass, at CMJAH

Dear Ms Gladys Mogodi-Bogoshi

I am a registrar at the department of Anaesthesiology. My research is a retrospective study. I propose to assess the usage of blood transfusion and blood products in the cardiac surgery unit at Charlotte Maxeke Academic Johannesburg Hospital. Ethics approval has been received from the Human Research Ethics Committee.

Patients' medical records will be used in the study. The gatekeepers' permission has been granted. Patient identifiers will be removed from records to assure anonymity. The records will be reviewed at the department and will not be removed from the hospital premises.

There will be no costs to Charlotte Maxeke Johannesburg Academic Hospital or the Gauteng Provincial Department of Health. A copy of the final report will be made available to you, at your request.

Attached, please find proposal, gatekeepers' permission and HREC clearance permission certificate.

Yours Sincerely

Dr. Charity Phokontsi
0724172989
phokontsi@gmail.com

Appendix 2: Letter to the gatekeeper

Dr. Charity Phokontsi
Department of Anaesthesiology
University of the Witwatersrand
24. July. 2014

Attention: The Gatekeeper

Re: Request to the gatekeeper for access of anaesthetic records

Dear Dr. Krubin Naidoo

I am a registrar at the department of Anaesthesiology and completion of a research project is a requirement. The title of my research is, **An audit of blood transfusion practices in adult cardiac surgery patients, on cardiopulmonary bypass, at CMJAH**

It is a retrospective study reviewing blood usage using anaesthetic, perfusionist and ICU charts. No patients or clinicians names will be included in the study. The records will be reviewed at the department and will not be removed from the hospital premises.

I would like to request permission to access these records.

Yours Sincerely

Dr. Charity Phokontsi
0724172989

phokontsi@gmail.com

Appendix 3: Data collection sheets A, B, C, and D

Data collection sheet A: Demographics

Study no.	Age	Gender	Race	Diagnosis
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				

Data collection sheet B: Procedural parameters

Study no.	Date of op	Type of op	Duration of op	CBP time	Prime volume

Table C: Haemoglobin trends

Study no.	Preoperative	Intraoperative Anaesthetist	Intraoperative Perfusionist Hb 1	Perfusionist Hb2	Post operative
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					

Data sheet D: Blood components

Study no.	Red blood cell	Platelets	Fresh Frozen plasma
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			