A CLINICAL AUDIT OF BLOOD PRODUCT UTILIZATION FOR CORONARY ARTERY BYPASS SURGERY IN THE WESTERN CAPE

By

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DECLARATION

I, Dudley Wolmarans, declare that the content of this dissertation/ thesis represents my own unaided work, and that the dissertation/ thesis has not, been submitted previously for academic examination towards any qualification. Furthermore, it represents my own opinions and not necessarily that of the Cape Peninsula University of Technology.

Signature…….. Date: 05 October 2020

ABSTRACT

Title: A Clinical Audit of Blood Product Utilization for Coronary Artery Bypass Surgery in the Western Cape.

Background:

Numerous international studies have documented variation in transfusion practice for Coronary Artery Bypass (CABG) surgery, despite the widespread availability of clinical guidelines. Optimally, blood management systems seek to streamline utilization with key indicators being patient care and outcome as well as potential waste and cost of blood. To facilitate this view this study sought to audit blood product utilization for Coronary Artery Bypass Graft (CABG) surgery.

Methods:

Blood utilization at both a public and a private hospital in the Western Cape underwent an observational retrospective audit. Participating hospitals completed a data form for fifty consecutive patients undergoing isolated, elective CABG surgery. Information obtained included age, gender, weight, co-morbidities, pre and post-operative international normalized ratio (INR), haemoglobin (Hb), platelet count, serum creatinine, operative details, use of anticoagulants as well as transfusion history. Data was then analysed with the IBM SPSS version 22 statistical package.

Results:

The transfusion rate at the private hospital (56%) was significantly lower than at the public hospital (92%) ($p<0.001$) and these results were carried through to mean number of red cell concentrates transfused (1.9 vs. 3.3; $p<0.001$).

Despite similar pre-operative haemoglobin (Hb) counts at both hospitals, post-operative Hb was considerably higher at the public hospital ($p<0.001$).

The majority of patients at both hospitals were male whose transfusion rates were significantly lower than females (69.8% vs. 100%; $p<0.001$) as was their RCC utilisation (3.6 vs. 2.4; $p<0.005$). Moreover significant differences where noted in the transfusion rates between males at the two hospitals (50% vs. 90%; $p<0.001$).

Furthermore, a significant difference was observable between the ages of transfused and non-transfused patients at both hospitals with the private hospital having significantly older

patients ($p<0.05$) whilst decreased weight was also shown to be a significant factor ($p<0.001$) in predicting transfusion. It was notable that patients at the public hospital where significantly lighter than patients at the private hospital ($p<0.001$). The presentation of ischaemia sufferers was also significantly higher at the private hospital ($p<0.001$) who in addition performed greater quantities of grafts ($p<0.001$) and had greater quantities of pre-operative aspirin usage ($p<0.05$).

Conclusion:

Despite its small size, this study was able to demonstrate that the private sector hospital had a significantly lower transfusion rate than the public sector hospital despite having increased numbers of grafts, older patients with higher levels of ischaemia. In conclusion, the higher transfusion rate demonstrable at the public hospital was probably due to a more liberal transfusion policy. With the inclusion of data from additional studies comparing public and private health care institutions for cardiac surgery, the hope is that protocols detailing patient blood management (PBM) may be developed.

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DEDICATION

This thesis is, dedicated to all my family, especially my wife Leigh, and children, Kayla and Aiden. Thank you so much for all your love, patience and unending support. I cannot thank you enough for all your continued encouragement despite all my ‘grumpiness’ throughout the last few years.

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ABBREVIATIONS AND ACRONYMS

AABB	American Association of Blood Banks
ACS	Acute Coronary Syndrome
AKI	Acute Kidney Injury
aPTT	Activated Partial Thromboplastin
AT	Antithrombin
CABG	Coronary Artery Bypass Graft surgery
CAD	Coronary Artery Disease
CBP	Cardiopulmonary bypass
CHF	Congestive Heart Failure
DM	Diabetes Mellitus
DPG	Diphosphoglycerate
FFP	Fresh Frozen Plasma
Hb	Haemoglobin
Hct	Haematocrit
INR	International Normalised Ratio
MSBOS	Maximum Surgical Blood Ordering Schedule
NHI	National Health Insurance
NHLS	National Health Laboratory Services
PBM	Patient Blood Management
RCC	Red Cell Concentrate
SANBS	South African National Blood Service
SAGM	Saline, Adenine, Glucose, Mannitol
TRALI	Transfusion Related Acute Lung Injury
TITRe2	Transfusion Indication Threshold Reduction trial
TRICS	Transfusion Requirements in Cardiac Surgery trial
TRUST	Transfusion Risk Understanding Tool
TTi's	Transfusion Transmitted Infections
TTP	Thrombotic Thrombocytopaenic purpura
USA	United States of America
WCBS	Western Cape Blood Service
WHO	World Health Organization

GLOSSARY

Term	
Cell salvage	The collection of patient blood intra-operatively which is recycled and re-infused back to the patient
Clinical audit	A quality improvement process in which use is, measured in comparison to agreed standards through systematic review to ensure improvement to patient care.
Co-morbidity	A disease or a condition in addition to a health problem being treated.
Erythropoietin	EPO is a hormone produced primarily by the kidneys. A synthetic version is available. Its function is to stimulate red cell production.
Fresh frozen Plasma	Plasma separated from anti-coagulated whole blood within 18 hours of donation and rapidly frozen to below -18 degrees centigrade. Use of the product is, facilitated by thawing at 37 degrees centigrade. The primary indication for use is the restoration of clotting factors.
Haemoglobin 'trigger'	The ideal Hb point at which the risk of transfusion is less than its potential benefit.
Leucocyte depletion	The process of removing white cells from blood products using filtration.
Patient Blood Management (PBM)	Is an evidence based multidisciplinary outlook whose primary focus is to improve appropriate blood product utilization.
Platelet concentrate	Is a product is, derived from the buffy coat layers of whole blood donation or from designated apheresis donation. Platelets act by initiating clot formation at sites of injury. The primary indication for use is to restore platelet count to prevent bleeding.
Prion	A protein with the ability to cause disease.
Red Cell Concentrate	The red cell component of donated whole blood, which has been, separated from the plasma portion through centrifugation and then reconstituted with SAGM. Primary indication for use is to restore oxygen carrying ability.
Quality control	The process of checking that procedure conforms to specifications in order to determine positive progress.

CHAPTER ONE

1.1 Introduction

Although blood products are the favoured choice for replacing volume, replenishing coagulation factors and for restoring tissue oxygenation, evidence suggests that the use of these products, especially red cell concentrates (RCC) is often inappropriate. The consequent variation found in blood product transfusion, especially in cardiac surgery has been well documented (Bennet-Guerrero et al, 2010:1568-1575; Rogers et al, 2009:37; Camaj et al, 2017:975-980; Tempe, 2018:2743-2745).

Although clinical guidelines are available, its utilisation is often poor as the decision to transfuse blood products largely depends on the clinical situation and experience of the relevant physician. Consequently, significant variation occurs in transfusion practice although the cause for these dissimilarities remains unclear.

Clinical audits are one method utilized to improve quality. The process of a transfusion audit includes the systematic, critical analyses of the appropriate use of resources in patient care and outcome. Additionally, with increased focus on patient blood management (PBM) and the financial burden inherent with transfusion these costs need to be justified in an attempt to improve resource conservation.

Despite a general decrease in transfusion rates in Coronary artery bypass graft (CABG) surgery, this procedure still accounts for a large percentage of blood transfusions given each year (Brouwers et al, 2017:207-214, Nadar et al, 2020:91-98). Considering the small number of previous studies for this procedure in South Africa, an investigation that seeks to ensure appropriate use is justifiable.

1.2 Aim

This thesis aimed to perform a retrospective audit to compare and analyse the use of blood products for CABG surgery at a public and a private institution in the Western Cape.

1.3 Objectives

The objectives of the study were to:

- To compare blood use practices between public and private hospitals in the Western Cape.
- To compare the blood used at these hospitals with the South African clinical guidelines for use.
- To correlate blood usage patterns with patient demographics and clinical features.

CHAPTER TWO

BACKGROUND AND LITERATURE REVIEW

The most common type of open-heart surgery at present is coronary artery bypass surgery (CABG). This procedure described in 1912 using an animal model (Diodata and Chedrawy, 2014) was unfortunately not feasible for humans until the 1960s when technology had developed significantly to enable surgical revascularization (Selke et al, 2010:1031-1037). After these initial advancements, the operation became a viable method for the treatment of patients suffering from coronary artery disease (CAD), a disease in which there is plaque build-up in the arteries providing the heart with blood. With disease progression, plaque hardens causing artery rupture and blood clot formation. Consequently, the heart deprived of oxygen-rich blood becomes ever more ischaemic and ceases to function (Bentzon, 2014:1852-1866). In CABG surgery, healthy veins grafted onto the blockage, bypass the artery and re-store oxygen supply (Aydin et al, 2013:612).

Substantial blood loss is common during major surgeries such as CABG and may cause anaemia, placing further stress on the heart due to an increase in cardiac output (Docherty and Walsh, 2017:61). The most rapid approach to combat anaemia remains blood transfusion (Du Pont-Thibodeau et al, 2014:16).

2.2 Blood transfusion in South Africa

Two companies provide transfusion services in South Africa. These are the Western Cape Blood Service (WCBS) in the Western Cape and the South African National Blood Service (SANBS), which services the provinces of Gauteng, Mpumalanga, KwaZulu-Natal, Free State, the Northern and Eastern Cape, Limpopo and the North West Province.

Both organizations are non-profit companies administered by Boards of Directors and seek to provide safe and sufficient quantities of blood products in a cost-effective, fair manner to patients while still maintaining a high standard of quality (Bird et al, 2014).

2.3 Blood transfusion and its adverse effects

Blood transfusion is the process of receiving blood or blood products intravenously to offset anaemia and inhibit further bleeding (Liumbruno et al, 2009:49-64).

The transfusion of red cell concentrates (RCC) is one of the most extensively used treatments for anaemia and haemorrhage, and is the easiest way to increase oxygen supply to the tissues (Yaddanapudi, 2014:538-542). On average, depending on factors such as weight, it is expected that one unit of blood will increase the total haemoglobin count by 1 g/dL (Naidech et al, 2008:198-203).

Although the expected increase of oxygen carrying capacity is the main objective for red cell transfusion (Napolitano et al, 2009:3124-3157) other uses are to increase circulatory volume although this is only recommended in surgeries that incur massive blood loss as blood transfusion may cause circulatory overload. Under these circumstances, the use of alternatives such as of crystalloid fluid are recommended (Carson et al, 2012:4).

Presently the World Health Organisation (WHO) has set target haemoglobin cut off value of 12.5g/dL. A person below this level is considered anaemic (WHO, 2011).
However, due to the risks involved in transfusion it is, not generally recommended to transfuse solely to maintain this level (Liumbruno et al, 2009:49-64).

Despite the lifesaving properties of blood transfusion, it may be unsuitable under certain scenarios. Inappropriate use includes using blood to expand the circulatory volume, to treat nutritional anaemia's, to facilitate wound healing and in the absence of risk factors, transfusion of patients who have haemoglobin levels above 10 g/dL (Liumbruno et al, 2011:189-217).

The use of alternative strategies to limit transfusion is additionally encouraged. These include limiting transfusion to patients with mild anaemia, reuse of blood through cell salvage equipment, utilisation of small cardiopulmonary priming volume bypass circuits, use of crystalloid fluids to limit haemodilution, increasing pre-operative haemoglobin levels in elective surgery by using iron and vitamin B complex injection and the administration of erythropoietin to stimulate red cell production (Horvath et al, 2013:2194-2201).

Additionally, several models are available to help physicians predict potential blood use. Commonly utilised are the Maximum Surgical Blood Ordering Schedule (MSBOS), a list indicating probable blood usage in a number of surgical scenarios (Lyer, 2014:581-589) while cardiac surgeons often make use of prediction calculators such as the Transfusion Risk Understanding Tool (TRUST) or EuroSCORE to forecast surgical complexity and estimate blood use in cardiac surgeries (Nashef, 2012:734-745:17; Murphy, 2017; Alghamdi, 2006:1120-1129).

Platelet transfusions may be used prophylactically (to prevent bleeding), or therapeutically (to stop active bleeding), in circumstances where either abnormal platelet function or reduced platelet numbers occur.
Several conditions such as post-transfusion purpura and autoimmune thrombocytopaenia are less responsive to platelet transfusion and may be contraindicated (Squires, 2015:221-226).

The clinical indications for fresh frozen plasma (FFP) include use for the replacement of inherited single factor deficiencies particularly when specific factor concentrates are not available, multiple coagulation factor deficiencies, the reversal of warfarin overdose, vitamin K deficiency associated with active bleeding and for thrombotic thrombocytopenic purpura (TTP). Plasma transfusion replaces coagulation factors including fibrinogen, factor II, V, VII, VIII, IX, X, and XI, Antithrombin III as well as glucose, potassium, sodium, chloride and protein C and S (Bird et al, 2014). Its use to enhance wound healing, expand the blood volume, as a nutritional source and to replace immune-globulins is furthermore discouraged (Biu et al, 2018:820-823). Its use in settings such as cardiac surgery requires close analysis of coagulation results and patient clinical condition (Bird et al, 2014).

Although blood transfusion remains a major life-saving therapy, provision of quality blood products in sufficient quantities is often problematic. Organisations such as the Western Cape Blood Service (WCBS) have to face an ageing donor population, increasingly stringent deferral policies and expensive testing procedures to ensure that donated blood is safe. Furthermore, blood products have a finite lifetime and therefore require constant replenishment (Haspel et al, 2012:227-230).

Additionally, transfusion of blood products is not without risk to recipients as it may act as a carrier for several transfusion-transmitted infections (TTi's). The possibility of infection due to the lack of adequate testing or by lack of sensitivity, the so called 'window period' is real and

include potential infection by bacterial, viral and parasitical vectors. Additionally, prions or infectious proteinaceous particles may cause variant Creutzfeldt- Jakob disease (Roback et al, 2008).

Blood transfusion may furthermore cause transfusion reactions that can be immediate or delayed, as well as immune or non-immune (Quinley, 2011:280-284). These include haemolytic, febrile non-haemolytic, urticarial, anaphylactic, transfusion-related acute lung injury (TRALI), transfusion-associated sepsis, circulatory overload, air embolism, hypocalcaemia, hypothermia, alloimmunization, graft vs. host disease, post-transfusion purpura and iron overload (Shander et al, 2012:55-68).

Lastly the impact of storage lesions, the biochemical changes that red cells undergo during storage are also impactful and include decreased 2.3 diphosphoglycerate (2.3 DPG) which leads to a reduction in the oxygen-carrying capacity, elevated potassium and loss of red cell membrane integrity (Tinmouth et al, 2006:2014-2017). Moreover, the anticoagulant sodium citrate used in blood packs is slightly toxic and could affect the viability of the red cell product (Bird et al, 2014).

Therefore, although the use of blood products is necessary and potentially lifesaving, especially in surgeries where intraoperative blood loss is described well, the need for guidelines to advise physicians in its appropriate use are required.

2.4 Transfusion Guidelines

Evidence based clinical guidelines have been published in order to help physicians prescribe the most appropriate blood components in a range of conditions where blood products are commonly used. Variables which may affect these decisions include haemoglobin (Hb) and haematocrit (Hct) levels, the platelet count, international normalized ratio (INR), activated partial thromboplastin time (aPTT), antithrombin (AT), fibrinogen levels as well as estimations of blood loss and a the determination of adequate vital organ perfusion (Luimbruno et al, 2011:189-217).

Rising levels of serum creatinine, an indicator of acute kidney injury (AKI) that could predict cardiovascular morbidity and mortality have also been included (Stein et al, 2012:2455-2456).

Additionally, physicians make use of several predictive models that help in their decisions making process.

2.4.1 Clinical Guidelines for the use of Blood Products in South Africa (5th Edition, 2014)

The South African Clinical Guidelines were published in 2014 (Bird et al, 2014) to assist in transfusion decisions.

These clinical guidelines have proposed appropriate red cell concentrate (RCC) transfusion under the following settings.

- Acute blood loss: Loss of greater 30% volume customarily requires a red cell transfusion.
- General surgery: Where the pre-operative Hb is below 8g/dl and there is an expected loss of 500ml during surgery or if the intra or post-operative Hb falls under 7g/dl.
- Anaemia in acute coronary syndromes: In general, most clinical guidelines do not recommend a liberal or restrictive approach, and further studies are required.
- Anaemia: ideally, the cause of the anaemia is to be identified and a definitive diagnosis made so that it may be managed accordingly. Haemoglobin levels below 8g/dL are indicative for transfusion. In chronic nutritional anaemia's, an Hb of 6g/dl can be well tolerated if there are no other co-morbidities. Commonly, the target Hb for transfusion will be higher in patients where the cause for the anaemia is medical (e.g. chronic renal failure) as opposed to surgical blood loss since as in the latter, the bone marrow function is usually normal whereas in the former this is often not the case.
- Cardiac surgery: Blood transfusion decisions in cardiac surgery are dependent on numerous variables that independently predict potential exposure to blood transfusion. The South African guidelines suggest the use of the transfusion risk understanding scoring tool (TRUST) to analyse potential use.

Platelet transfusions are, recommended under the following conditions.

- Massive haemorrhage: maintain platelet count at above $50x10^9$l
- Cardiopulmonary Bypass: Prophylactic transfusions are not recommended except under conditions where there is abnormal post-operative bleeding for which a surgical cause has been eliminated. This is usually due to thrombocytopaenia or temporary platelet dysfunction. The recommendation is then to transfuse to maintain platelets at $50x10^9$ l.

2.4.2 International guidelines

The American Association of Blood Banks (AABB) have similar criteria to the South African Clinical Guidelines for blood transfusion with the proviso that patients symptoms and characteristics be included in the decision making process when ordering blood (Carson et al,2012:4). In CABG surgery, it suggests maintaining haemoglobin counts of 8g/dL as this may potentially improve patient outcome (Roback et al, 2008) and furthermore suggests that prophylactic platelet transfusion for patients with cardiopulmonary bypass (CPB) should be limited unless symptoms of thrombocytopaenia, peri-operative bleeding or platelet dysfunction becomes apparent (Kaufman, 2015).

British guidelines summarised by the British Committee for Standards in Haematology have similar recommendations with emphasis on restrictive red cell transfusion and target haemoglobin counts of 7g/dL for stable, non-bleeding patients and 8-9g/dL for those with acute coronary syndrome (ACS). Additionally the use of blood product alternatives and the continuous re-evaluation of haemoglobin after every transfusion episode is emphasised (Murphy et al 2015:997-1008).

The Australian Clinical guidelines suggest that transfusion at haemoglobin counts under 7g/dL are likely appropriate, between 7-10g/dL depending on the clinical condition of the patient and that above 10g/dL were likely unwarranted (National Blood Authority, 2012).
The Society of Thoracic Surgeons/ Society of Cardiovascular Anesthesiologists recommend pre-operative haemoglobin levels of 6 g/dL for patients on cardiopulmonary bypass (CPB) and 7gdL for patients at risk of ischaemia, post-operatively on CPB (Murphy et al, 2015:997-1008) whilst the European Society of Anesthesiology recommends haemoglobin levels of 7-9g/dL in bleeding cardiac patients (Kozek-Langenecker et al, 2013:270-382).

2.4.3 Restrictive vs. Liberal Policies

The balance between offsetting increased morbidity and the adverse events associated with both anaemia and transfusion is a fine one (Najafi & Faraoni, 2015:377-382) and one still heavily debated in the literature. On one hand, patients with anaemia are more likely to suffer from cardiovascular events, heart and renal failure, as well as increased levels of morbidity and mortality (Carson et al, 2012:4) compared to the risks posed by transfusion. Transfusion should then, only be considered when the benefit outweighs the risk (Faraoni et al, 2012:919-920).

Despite transfusion guidelines detailing target haemoglobin counts, transfusion at these levels are often problematic as during surgical procedures patient clinical settings may differ (Snyder-Ramos et al, 2008:1284-1299). As such, the literature discussing blood utilisation in cardiac surgery deviates between following restrictive or liberal approaches. As an example, studies such as the International Transfusion Requirements in Cardiac Surgery (TRICS) trial have suggested that transfusion 'triggers' with haemoglobin counts of 7.5 g/dL were not inferior to haemoglobin counts of 9 g/dL (Mazer et al, 2017:2133-2144; Whitman, 2019:1041-1042). Other literature supports this opinion (Hajjar et al, 2010:1559-1567; Curley et al, 2014:2611-2624; Glenn & Whitman, 2019:1041-1042) but in contrast, the Transfusion Indication Threshold Reduction (TITRe2) trial suggests that transfusion at haemoglobin levels of 9 g/dL were more beneficial to patients than transfusion at levels of 7.5 g/dL (Murphy et al, 2015:997-1008; Afifi & Simry, 2015:61).

What is certain however is that patients with pre-operative anaemia are more likely to suffer from morbidities and mortalities post-surgery (Loor et al, 2012:538-546) and some researchers suggest maintaining haemoglobin counts at 10 g/dL, especially for patients at risk of anaemia associated hypoxia (Ranucci et al, 2013:280). This approach has been supported by some researchers who have suggested that this strategy be used until optimal patient based transfusion 'triggers' that take patient characteristics into account are developed (Najafi & Faraoni, 2015:377-382; Scott, 2003:958-963).

2.5 Quality

Although clinicians utilize guidelines and predictive models the use of blood products should still be, monitored. Therefore, a primary objective of transfusion medicine is the improvement of quality standards in aspects of patient care, production and its service to the public. Quality systems are methods used to ensure that high standards are set and continuously improved. These include every function of the blood transfusion service such as organization, procedures, processes, policies and the resources required to reach and bypass certain quality standards (Quinley, 2011:280-284).

An important aspect of quality systems and continuous development is the review and analysis of performance data. This is required to ensure that the processes used are adequate and that potential areas of advancement are identified (Harmening, 2005).

The transfusion audit is a quality improvement process that seeks to improve patient care and outcomes through the systematic review of the use of transfused blood components against transfusion guidelines. It is a systematic critical analysis of the quality of care, which will include the procedures used for the diagnosis and treatment of the patient, the use of available resources as well as the outcome and changes in the quality of life of the recipients. The process aims to create a culture of delivering quality service to patients whereby medical care will be continuously improved (Roback et al, 2008). This is achievable by either removing existing deficiencies in the initial planning process such as unforeseen factors, shifts in customer needs or changes in materials, environmental factors and other variables that could affect the process or by creating better features (Roback et al, 2008).

2.5.1 Rationale for monitoring blood utilization

The primary motivation for monitoring blood utilization is to identify instances when blood component use is less than optimal. This facilitates interventions that can change transfusion practice. Blood is a biological agent associated with many possible adverse events, including infectious and non-infectious complications. Unnecessary complications from inappropriate blood transfusions therefore need to be minimised (Haspel, 2012:227-230).

Secondly, blood components are a scarce and valuable resource as its supply is dependent on a shrinking pool of ageing non-remunerated donors expected to meet the ever-increasing demand. Monitoring blood utilisation may highlight inappropriate use and cause the

implementation of corrective action. This needs to be, followed up with continuous monitoring and assessment to identify further areas of improvement, facilitated by the use of a clinical audit (Pinkerton, 1995:283-286).

2.5.2 Patient blood management and the use of Audits

Blood utilization audits are the prime method of determining appropriate use in specific surgical procedures or clinical situations by comparing them with published guidelines. In this way, optimal use in transfusion practice is improved (Roback et al, 2008).

There are three methods for obtaining audit data. These are retrospective, prospective and concurrent.

Retrospective audits involve the review of data post-transfusion. This type of audit has no impact on the medical treatment of patients during the audit process but may lead to significant changes later. Generally, as these types of audits are performed on a smaller scale and take less time to complete they are often cheaper and furthermore may be better for observing multiple outcomes. The disadvantages are that researchers often have to rely on third parties for record keeping who may be prone to selection bias (Haspel, 2012:227-230).

Prospective audits involve the real-time review of data. In blood transfusion, this entails the review and the validation of the transfusion before blood products are infused. An advantage to this type of study is that the data is often more complete as the collection process has been designed to include all the necessary information. As an example, blood transfusion audits of this type would use structured forms that could be, completed by the time clinicians are ordering blood products. A disadvantage is that it requires the co-operation of all hospital staff, increased funding and often takes more time (Wallis et al, 2002:1-9).

Concurrent audits are often interchangeably with prospective audits. The difference between the two is that while prospective audits involve the planning and recording of data that is collected during treatment, concurrent audits entail data collection while treatment is being provided or in the 12-24 hours following transfusion episodes. The disadvantage in this approach is that this type of audit may only influence future transfusion episodes. The advantage, however, is that the data is often more accurate and the response by ordering personnel less negative (Nel, 2008:61-69).

Audits form an integral part of patient blood management (PBM) defined as the “appropriate use of blood and blood components, with the eventual goal to minimize its use” (Goodnough, 2012:1367-1376). One of the important processes of PBM is to review how blood is used. Two questions should be, considered, is blood usage appropriate and is it in line with peer recommendations (Haspel 2012:227-230; Shander et al, 2013:193-202).

To ensure that blood usage is appropriate, organizations such as the AABB and the WCBS recommend that decisions about transfusion make use of evidence-based transfusion triggers (Savage, 2015:444-447; Carson et al, 2012:4).

It has been proposed that a liberal transfusion policy (using a trigger of 10g/dL for transfusion) compared to a restrictive policy (using a transfusion trigger of 7-8 g/dL) has no significant difference on patient outcome in a wide range of clinical scenarios (Horvath et al, 2013:2194-2201; Carson, 2011:2453-2462; Bennet-Guerrero et al, 2010:1568-1575). Therefore, a suitable transfusion may be described as one in which the treatment of anaemia is balanced against the risk of needless transfusions (Lyer, 2014:581-589).

2.6 Blood usage in Coronary Artery Bypass Graft Surgery

Despite Cardiac surgery being associated with increased blood loss, since the inception of CABG surgery the use of blood products has become far less common due to improved techniques, including the use of cell salvage and the refinement of heart-lung machines (Diodata and Chedrawy, 2014). Additionally, tolerance for anaemic states by surgeons for their patients has become more common-place as the understanding of the potential risks versus the benefits of transfusion continues to grow, including improved knowledge of the dose-dependent relationship between blood transfusion and risks such as morbidity and mortality (Engoren et al, 2011:1180-1186; Moehnle et al, 2011:97-109; and Spiess, 2004:1143-1148).

Despite these trends, cardiac surgery is still associated with significant intraoperative blood loss which has been linked to patient demographics and pre-existing conditions (Tempe and Khurana, 2018:2743-2745; Nelson et al, 2018:850-852) as well as with cardiopulmonary bypass (CPB) priming volume and bleeding caused by coagulopathy or technical factors (Loor et al, 2012:538-546).

One study of 82446 cardiac patients at 408 hospitals reported that the rates of blood transfusion for cardiac surgery ranged from 7.8% to 92% for RCC, 0% to 97% for FFP and 0.4% to 90.4% for platelets. This wide variation remained despite risk factor adjustments (Bennet-Guerrero et al, 2010:1568-1575). Another study of 5185 cardiac surgery patients at 10 centres revealed transfusion rates varying from 33% to 74% (Horvath et al, 2013:2194-2201) whilst a study from South Africa of 30 CABG patients showed transfusion rates of 76.7% with average use off 3 RCC per patient (Nadar et al,2020:91-98). A further examination of 164 consecutive patients at one hospital showed transfusion rates of 86%. This study also reported on the many factors which influenced the decision to transfuse, including increased graft numbers, age of ≥ 62.5 years, female gender, using cardiopulmonary bypass (CBP), combined heart operations and a pre-operative haematocrit lower than 35% (Lako et al, 2014:181-186).

Others have described predisposing risk factors such as decreased weight, a previous history of cardiac interventions and co-morbidities such as hypertension, diabetes mellitus (DM), peripheral vascular disease and renal failure contributing to an overall increase in blood product use (Bennet-Guerrero et al, 2010:1568-1575; Karkouti et al, 2001:1193-1203; Scott et al, 2003:958-963; and Al-Shammari et al, 2005:83-86).

Numerous studies have shown that patient demographics influences the quantity of blood products utilised (Bennet-Guerrero et al, 2010:1568-1575; Scott et al, 2003:958-963; Lako et al, 2014:181-186) and that these demographics could influence the variation in blood use. Additionally, the time-period in which surgeries occurred and geographic locations could affect not only the demographics but the particulars of the operations as well, and this has a significant bearing on blood use (Likosky et al, 2014:3084-3089). Lastly, and potentially the most important cause of variation in blood use are that audits occur at different surgical centres, with varied approaches to handling surgery and anaemia as well as with different surgeons with varying degrees of expertise (Jin et al, 2013:1269-1274).

2.7 Conclusion and rationale for study

South Africa's health care is divided into two systems. The private sector provides medical services to those with medical aids and other sources of funding whilst public hospitals, funded by the government, services the majority of poorer South Africans. The level and quality of service offered by these two tiers of health care differ significantly (Young, 2016). The proposed National Health Insurance (NHI) aims to remedy these inequalities by providing universal coverage to all South Africans (WHO Bulletin, 2010).

Consequently, the hypothesis is that significant dissimilarities exist between blood usage practices of clinicians and hospitals performing CABG surgery in the private sector compared to those in the public sector. This disparity could be caused by numerous factors that may not be in line with approved guidelines.

In South Africa, few studies have been undertaken to document blood product use in cardiac surgery and therefore this thesis aimed to examine the transfusion practices at a private and public sector hospital as well as the clinical features of the patient populations, as these may influence the decision to transfuse. This information could lead to an improvement in blood usage practices.

CHAPTER THREE
STUDY DESIGN AND METHODOLOGY

3.1 Study Design

This was a retrospective study design to determine and compare the rate of blood product use at a private hospital (designated P) and a public hospital (designated T) which performed Coronary Artery Bypass (CABG) surgery in the Western Cape, South Africa.

Review of records commenced as soon as the relevant permissions were obtained from both the public and private hospital as well as from the ethics committee at the Cape Peninsula University of Technology.
This review included an analysis of the records held at the public hospital along with data obtained from Western Cape Blood Service records and a completion of a data form (See Addendum 1) by the private hospital.
The private hospital provided information on surgeries occurring between February- 5 October 2017 and the public hospital on surgeries between April-September 2017, the delay in recording information at the public hospital being due to obtaining permission considerably later.

3.2 Study Subjects

The study population consisted of one hundred patients, fifty from each hospital, selected from patients undergoing CABG. Bias was limited by analysing patient folders consecutively.

Patients were not included in the study if they were undergoing multiple cardiac procedures in addition to CABG surgery such as coronary angioplasty and/or stent insertion, valve replacement, pacemaker insertion and patients undergoing emergency CABG procedures.

Twenty-two patients from the public hospital were consequently not included due to these reasons whilst an additional fourteen with missing or incomplete records could not be analysed.

3.3 Data collection

Patient data was analysed retrospectively. A data collection form detailing the required information was devised (See Addendum 1) and then distributed to the private hospital for completion by hospital staff. Once completed, these forms were forwarded to the investigator for analysis and data capture.

The required data from the public hospital was obtained in the following manner.
Daily review of the work list from the blood bank situated in the public hospital identified cardiac surgery patients. This review of Western Cape Blood Service (WCBS) records furnished basic patient information (age and gender) and detailed the issuing of blood products, including red cell concentrates (RCC), fresh frozen plasma (FFP) and platelets. Any missing data was then obtained by a review of patient checklists, nursing notes, surgery notes and National Health Laboratory (NHLS) records. All information was transcribed onto the data collection form for data capture and analysis. Patients were excluded at this stage if necessary.

Any patients data on transfusion episodes from both hospitals was recorded from the time surgery commenced and concluded at twenty-four hours post-surgery.

The data form included information on the following patient parameters; patient gender, weight, age, details of pre-operative anticoagulants including aspirin, clopidogrel and warfarin and co-morbidities including hypertension, diabetes mellitus, ischaemic heart disease, renal dysfunction, congestive heart failure as well as cerebrovascular disease or stroke.

Additional information requested were details on the procedure itself and included the number of grafts performed, whether the procedure was on or off-pump and the intraoperative use of the anticoagulant heparin and its reversal with protamine. Further information requested details on techniques which may have limited blood loss and included use of cell salvage equipment as well as the use of medications such as aprotinin and tranexamic acid.

A list of the patients pre and post-operative laboratory tests were also included, these were, serum creatinine levels to determine renal function, international normalised ratio (INR), activated partial thromboplastin time (aPTT) and prothrombin time (PT) to determine

coagulation status as well as haemoglobin and platelet counts. Finally, details on the numbers and type of blood products used were requested (see addendum1).

3.4 Ethical and Legal considerations

Confidentially was maintained by ensuring that each hospital, patient and clinical staff details were anonymised. These details were never disclosed during the study. Although the researcher had access to patient records at the public hospital, at the private hospital the only information available was that obtained from the data form. The nursing staff used unique patient identifiers (P1-50) to keep track of patients
For the purposes of the audit, unique study numbers were created for each institution. These numbers were P1-50 for the private hospital and T1-50 for the public hospital. These numbers were linked with the data collection form and subsequently entered into the excel spreadsheet during data capture.

Ethics approval was, obtained from the Cape Peninsula University of Technology's Ethics Committee (Ethics number: CPUT/HW-REC2016/H32, see Addendum 2). Once ethics approval was obtained, permission to perform the study was obtained from the management of the relevant hospitals. These permissions have not been included in the addendums to maintain confidentiality, but are available on request.

3.5 Statistical analysis

All data was transcribed onto a pre-designed excel worksheet with standardized input methods. The use of a double entry method ensured capture accuracy whilst data duplication was limited by the use of unique study numbers. This data was then uploaded to an IBM SPSS version 22 statistical package for analysis. Information obtained in this way included frequency tables, contingency tables as well as descriptive analysis for numeric variables using mean, standard deviation and standard error.

Where deemed suitable, summary statistics were portrayed as means and standard deviations (SD) and average values shown as a mean or median. Performance indicators included the number of patients transfused per hospital as well as the number of units transfused per hospital. The Chi-square test was used to identify the significant differences between two or more groups pertaining to categorical variables or to determine the significant association between two categorical variables. The student t-test was used to

compare the means of a numerical variable between two groups. P Values are given to test the null hypothesis thereby testing the validity of a claim made about a population. These p values given for information purposes were assigned a value of <0.05 as being significant enough to reject a null hypothesis.

3.6 Multivariate Analysis

Working with ordinal variables violates the assumption of normality required for classic linear models. In this study, the dependent variables (red cell concentrates, fresh frozen plasma and platelets) are all ordinal variables but due to scarcity of data for FFP and platelets, these were converted to binary variables, only indicating transfusion or lack thereof. The same process was followed for red cell transfusions, transformed to an ordinal variable with fewer categories for the same reason.

As such a generalized linear model that included analysis of variance as well as regression models was utilised to determine which factors or measurements influenced blood usage.
The three components making up the generalized linear model are a random component, a systematic component and a link function. The assumption of normality is relaxed in the generalized linear model. The distribution of the dependent values can be from any of the class of esponential distributions. The type of data of the dependent variable informs the choice of the link function. In this study the selected link function for the ordinal dependent variables and for the binary variables is the cumulative logit link function. The analysis, in each of the three cases, was repeated until a model that fitted the data well, as indicated by the goodness-of-fit statistics, emerged.

CHAPTER FOUR
RESULTS

4.1 Study Population

The study population included a review of fifty consecutive patients from each hospital undergoing coronary artery bypass graft (CABG), surgery. Some significant differences was observed between the baseline characteristics of the patients at each hospital including weight, which was lower at the public hospital (T) ($p<0.05$), whilst at the private hospital (P) patients were significantly older ($p<0.05$). Additionally a significantly higher number of grafts were performed ($p<0.001$) and higher levels of ischaemia ($p<0.001$) were observed at the private hospital. Although aspirin use was noted at both hospitals significantly more was used at the private hospital ($p<0.05$). There was a significant difference in the numbers of patients who had a history of previous cardiac surgery compared to those who did not ($p<0.05$) at both hospitals.

Table 1 shows the demographics and baseline characteristics.

Table 1: Demographics and Baseline Characteristics

	All patients	P	T	P value
Total no.	100	50	50	
Age (Mean)	60.7	62.8	58.6	<0.05
Weight (Mean)	88,4 kg	94.9 kg	81.9 kg	<0.05
Female Gender	16	6 (12%)	10 (20%)	<0.05
Haemoglobin Pre-Operation Median(IQR)	14.05 (1.8)	14.0 (2.1)	13.8 (1.75)	0.140
Haemoglobin Post-Operation Median(IQR)	11.95 (3.075)	11.2 (2.5)	14.1 (2.9)	<0.001
Co-morbidities				
-Hypertension	71	33	38	0.271
-Diabetes Mellitus	33	13	20	0.137
-Renal dysfunction	5	2	3	1.00
-Ischemic heart disease	53	43	10	<0.001
-Congestive heart failure	2	2	0	0.495
-Cerebrovascular disease/ Stroke	9	4	5	1.00
Pre-operative medication				
-Warfarin	6	2	4	0.678
-Aspirin	67	38	29	0.556
-Clopidogrel	13	5	8	0.372
Previous coronary surgery				0.585
-None	84	41	43	
-CABG	3	0	3	
-Coronary angioplasty	1	0	1	
-Valve replacement	3	1	2	
-Pacemaker	9	8	1	
Graft Number				<0.001
-1-2	30	19	21	
-3	42	17	25	
-4-6	28	24	24	

4.2 Red cell concentrate-analysis

Seventy four percent of patients in the sample population received red cell concentrate's (RCC) either intra-operatively or within twenty-four hours post-operatively. Of these, twenty-eight were from the private hospital and forty-six were from the public hospital. Therefore, twenty-six patients did not receive any red cell concentrate transfusion; twenty-two of these were from the private hospital and only four from the public hospital.

Subsequently, a significant difference in the RCC transfusion rates between the private and the public hospital was noted (56% vs. 92%; $\chi^2 = 16.84$, df = 1, $p<0.001$) as seen by the use of 166 RCC units at the public hospital compared to only 99 RCC at the private. A median (interquartile range) of 2.00 (4) RCC units was utilised per patient at the private hospital compared to 4.00 (2) RCC at the public hospital (Figure 1).

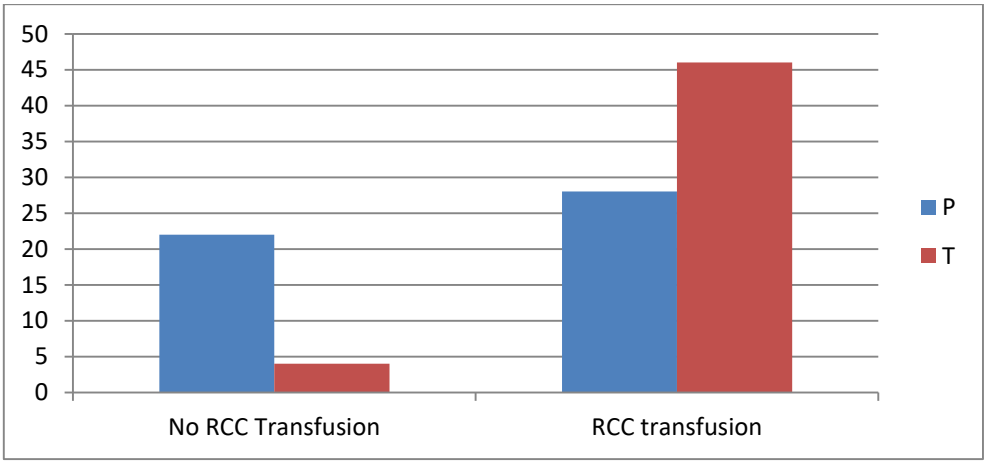

Figure 1: There was a significant difference in the mean number of RCC units per patient between the private and public hospitals (1.5 vs. 3.3 (28 vs. 46); $\chi^2 = 16.84$, df=1, $p<0.0001$)

4.2.1 Haemoglobin concentration analysis

Although there was no significant difference between pre-operative haemoglobin (Hb) levels (14.0 g/dL at the private hospital compared to the public hospital's 13.8 g/dL), shown by the independent samples Mann-Whitney U test. ($p>0.05$), the post-operative Hb results were significantly different (11.2 g/dL vs. 14.1 g/dL; $p<0.001$) (Figure 2)

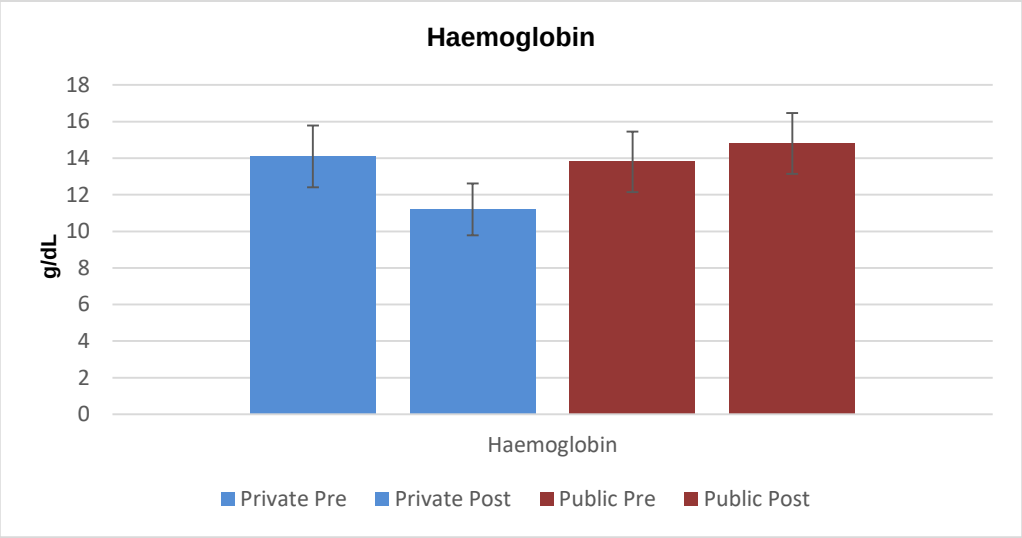

Figure 2: There was no significant difference in the pre-operative haemoglobin counts between the private hospital (mean 14.1g/dL; range 15.8g/dL- 12.4g/dL) and public hospital (mean 13.8g/dL; range 15.2g/dL- 12.4g/dL) ($p>0.05$). However, the post-operative haemoglobin counts at the private hospital (mean 11.2g/dL; range 12.8g/dL- 9.6g/dL) was significantly lower than that at the public hospital (14.8g/dL; range 16.3g/dL- 13.3g/dL) ($p<0.001$).

4.2.2 Variables influencing Red Cell Concentrate (RCC) usage

Before transformation, eight variables emerged as having a significant influence in blood usage by the hospitals, as can be seen in table 2. The most significant factor in the usage of RCC is the type of hospital (p-value<0.001), followed by age (p-value<0.01), number of grafts (p-value<0.05), weight (p-value<0.05), aspirin usage (p-value<0.05), and previous cardiac surgery (p-value<0.05). The usage of clopidogrel (p-value<0.1) and incidence of cerebrovascular disease (p-value<0.1) is significant at the α-level of 0.1.

Table 2: Generalized Linear Model Result for RCC (Likelihood Ration Chi-Square = 54,69, df=15, p-value <0.001)

Independent variables (factors and covariates)	Type III		
	Wald Chi-Square	df	p-value
Cerebrovascular Disease or Stroke	2.977	1	0.084
Hospital	18.330	1	0.000
Aspirin	5.781	1	0.016
Previous Cardiac Surgery	11.191	4	0.024
Graft Number	16.374	5	0.006
Clopidogrel	3.162	1	0.075
Age	9.052	1	0.003
Weight	5.906	1	0.015
Dependent Variable: Red Cell Concentrate			

After transformation to an ordinal variable (Table 3) with fewer categories, RCC_4, the significant difference between hospitals is stronger (χ^2 = 27.35, df=3, p-value<0.0001) with six variables emerging as having a significant influence in blood usage by the hospitals (Table 4). The most significant factor in the usage of RCC was age (p-value<0.001), followed by the type of hospital (p-value<0.01), weight (p-value<0.05), number of grafts (p-value<0.05) and aspirin usage (p-value<0.05). The usage of Warfarin (p-value<0.1) is significant at the α-level of 0.1

Table 3: Frequency table of RCC_4 vs. Hospital Type

	0 units	1 - 2 units	3 - 4 units	5 or more units	Total
P	22	14	3	11	50
T	4	18	21	7	50
Total	26	32	24	18	100

Table 4: Generalized Linear Model Result for RCC_4 (Likelihood Ration Chi-Square = 38.01, p-value <0.001)

Source	Type III		
	Wald Chi-Square	df	p-value
Hospital	10.077	1	0.002
Warfarin	3.571	1	0.059
Aspirin	4.884	1	0.027
Graft Number	13.878	5	0.016
Weight	6.150	1	0.013
Age	11.257	1	0.001
Dependent Variable: RCC transformed into fewer ordinal categories Model: (Threshold), Hospital, Warfarin, Aspirin, Graft Number, Weight, Age			

4.3 Cryoprecipitate, Fresh Frozen Plasma and Platelets

Because cryoprecipitate use occurred only four times in the study period, analyses was not possible, due to the low numbers.

There was a significant difference in the use of Fresh Frozen Plasma (FFP) between the two hospitals (Exact χ^2 = 13.457, df = 4 ; p<0.01) with 37 units used at the public hospital compared to 4 at the private hospital. The two groups have similar median international normalised ratio (INR) results (Mann-Whitney U p-value > 0.05) and activated partial thromboplastin times with both falling within the normal reference range.

The pre and post-operative platelet counts from both institutions support the relatively low use of platelets as only 13 pooled platelets were used at the private hospital and 11 at the public hospital (Exact χ^2 = 1.444, df = 4 ; p>0.05). The median pre-operative platelet count from the public hospital was 263.5 x10⁹/L (Interquartile range: 111) and from the private 233 x10⁹/L (Interquartile range111 x10⁹/L), whilst the median post-operative platelet counts at the private hospital was 189 x10⁹/L (interquartile range: 63 x10⁹/L) and the public hospital 222.5 x10⁹/L (interquartile range: 138 x10⁹/L). Both being well above the recommended reference range for transfusion.

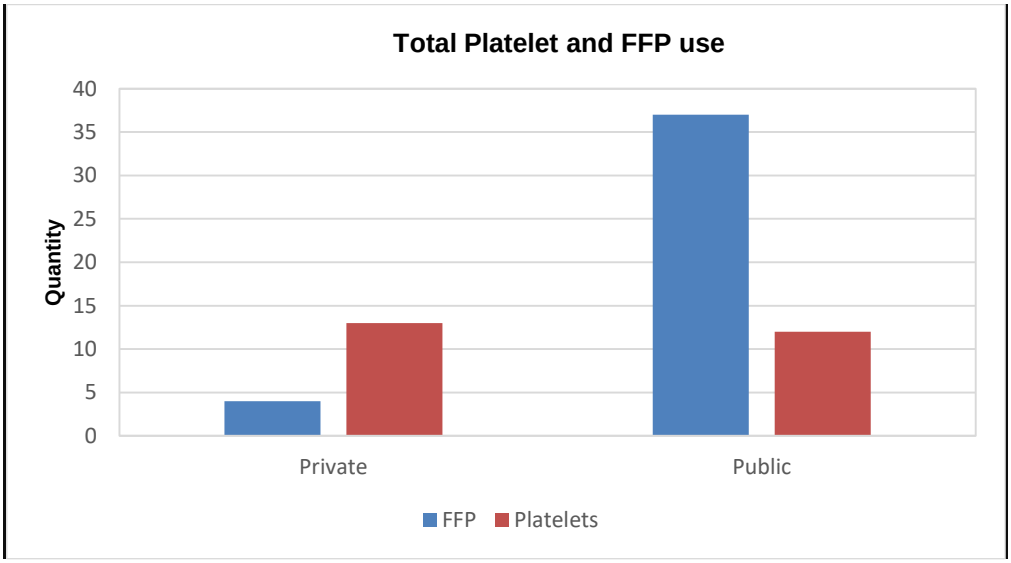

Figure 3: There was no significant difference in the total number of platelet units (p>0.5) used between the two hospitals. However, significantly higher numbers of FFP units were used at the public hospital (37) compared to the private hospital (4) (p<0.01).

4.3.1 Variables affecting fresh frozen plasma (FFP) usage

Due to very small frequencies in some categories, FFP was converted to a binary variable indicating whether FFP was transfused or not (FFP_1). The cross tabulation in Table 1 shows a significant difference in the number of times FFP was transfused between the two types of hospital (χ^2 = 13.28, df=1, p-value<0.0001)

Table 1: No of times FFP transfused by Hospital

Hospital	No FFP transfused	FFP transfused	Total
P	48	2	50
T	34	16	50
Total	82	18	100

The results of the Generalized Linear Model showed that the only significant factor in the number of times FFP was transfused is the hospital type (p-value =0.002) and is depicted in table 6.

Table 2: Generalized Linear Model Result for FFP_1 (Likelihood Ration Chi-Square = 14.80, p-value <0.001)

Source	Type III		
	Wald Chi-Square	df	p-value
(Intercept)	25.230	1	<0.001
Hospital	9.591	1	0.002
Dependent Variable: FFP_1 Model: (Intercept), Hospital			

4.3.2 Variables influencing the transfusion of platelets

Due to a similar scarcity in cells, the platelet variable was transformed to a binary variable, indicating whether the patient received platelets or not (Platelets_2) and the results demonstrated no significant difference between the two types of hospital in the number of times platelets were transfused (χ^2 = 0.22, df=1, p-value>0.5).

Table 3: No of times platelets were transfused by Hospital

Hospital	No Platelets transfused	Platelets transfused	Total
P	37	13	50
T	39	11	50
Total	76	24	100

The generalized linear model showed that two variables influenced the transfusion of the number of platelets, which excluded the type of hospital, confirming the Chi-Square result

. (Table 8)

Table 4: Generalized Linear Model Result for Platelets_2 (Likelihood Ratio Chi-Square = 35.86, p-value <0.001)

Tests of Model Effects			
Source	Type III		
	Wald Chi-Square	df	p-value.
Gender	4.037	1	0.045
Clopidogrel	3.938	1	0.047
Dependent Variable: Platelets_2 Model: Gender, Clopidogrel			

Table 5 compares the factors influencing the number of units of RCC used and the number of times FFP and Platelets were transfused in the hospitals.

Table 5: Summary of factors influencing the use of RCC, FFP and Platelets

	RCC_4	FFP_1	Platelets_2
Age	*		
Hospital	*	*	
Weight	*		
Graft Number	*		
Aspirin	*		
Warfarin	*		
Gender			*
Clopidogrel			*

4.4 Age

Age (range 42-80; SD 9.52) was not shown to influence the transfusion rates for FFP ($p>0.05$) or for platelets ($p>0.05$).

It did however influence the transfusion rates for RCCs. This was demonstrated at the private hospital where the mean age for transfused patients was significantly higher (63.6 vs. 61.7; $p<0.05$) than at the public hospital (59.1 vs. 53.0; $p<0.001$).

Additionally a significant difference was noted between mean patient ages at the private hospital (62.8 y/o) when compared to the public hospital (58.6 y/o) ($p<0.05$).

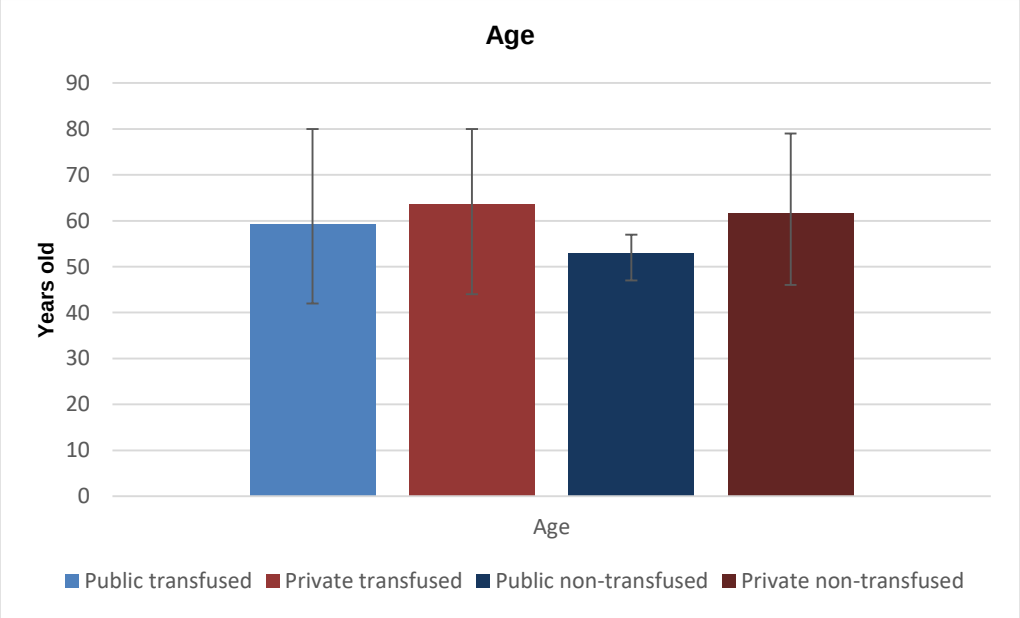

Figure 4: There was a significant difference in the ages of transfused patients at the private hospital (mean 63.6; range 44-80) compared to non-transfused patients (mean 61.7; range 45-79) ($p<0.05$). Similarly, a very significant difference in the ages of transfused patients at the public hospital (mean 59.1; range 42-80) compared to non-transfused (mean 53; range 47-57) was noted ($p<0.001$).

4.5 Weight

Weight ranged from 44 kilograms (kg) to 196 kg (SD 24.2). There was a significant difference in the mean body mass of the patients at the private hospital compared to the participants at the public institution (94.9kg vs. 87.2kg; p<0.001). This had a significant impact on the rate of RCC transfusion, as transfused patients weighed significantly less than non-transfused patients did (84.6kg vs. 99.3kg; p<0.001). Similar results were seen with FFP transfusion (80.8kg vs.90.8kg; p<0.001) and for platelet transfusion (84.3kg vs. 89.6kg; p<0.05).
As expected, female patients weighed significantly less than their male counterparts did. (73.6kg vs. 91.2kg; p<0.001).

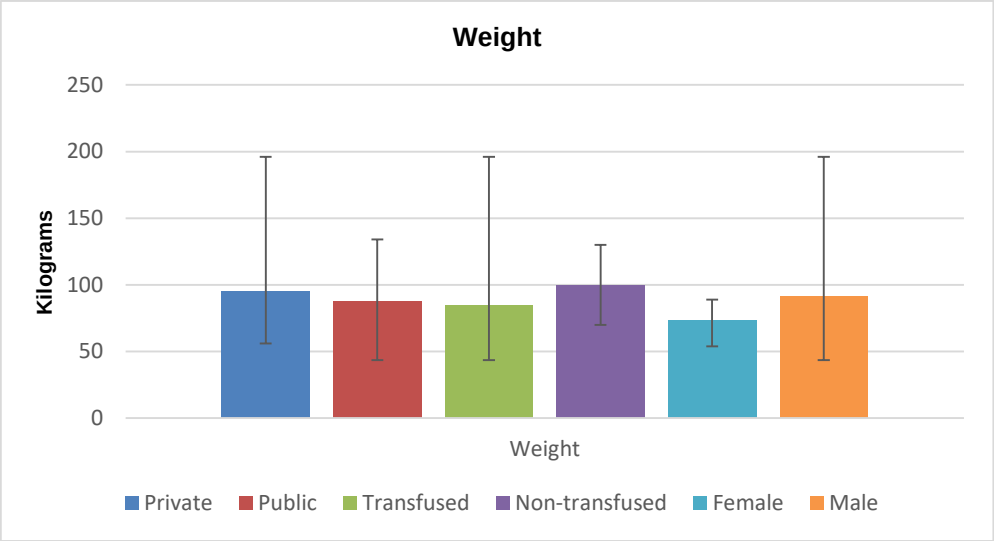

Figure 5: There was a significant difference in the weight between the private (mean 94,9kg; range 56kg-196kg) and the public hospital (mean 87,2kg; range 43,5kg-134kg)(p<0.001). Similarly a significant difference was observed in the weights of transfused (mean 84,6kg; range 43,5kg-196kg) and non-transfused patients (mean 99,3kg; range 70kg-130kg) (p<0.001) as well as between female (mean 73,6kg; range 54kg-89kg) and male patients (mean 91,2kg; mean 43,5kg-196kg) (p<0.001).

4.6 Gender

The majority of patients at both hospitals were male. Females made up only 12% of the patients at the private hospital and 20% of the patients at the public hospital. The transfusion rates for females for RCC use were significantly higher than males (100% vs. 69.8%; $p<0.001$) and similar results were seen for FFP use (50% vs. 39%; $p<0.05$) as well as platelet use (43% vs. 21%; $p<0.05$)

Additionally, the mean utilization of RCC for females was significantly higher than males (3.6 vs2.4; $p<0.005$).

Moreover, significant differences in the transfusion rates between males at the private (50%) and the public hospital (90%) ($p<0.001$) were noted. The mean RCC use for males at the private hospital was 1.8 RCC units as opposed to males at the public hospital with 3.2 RCC ($p<0.005$).

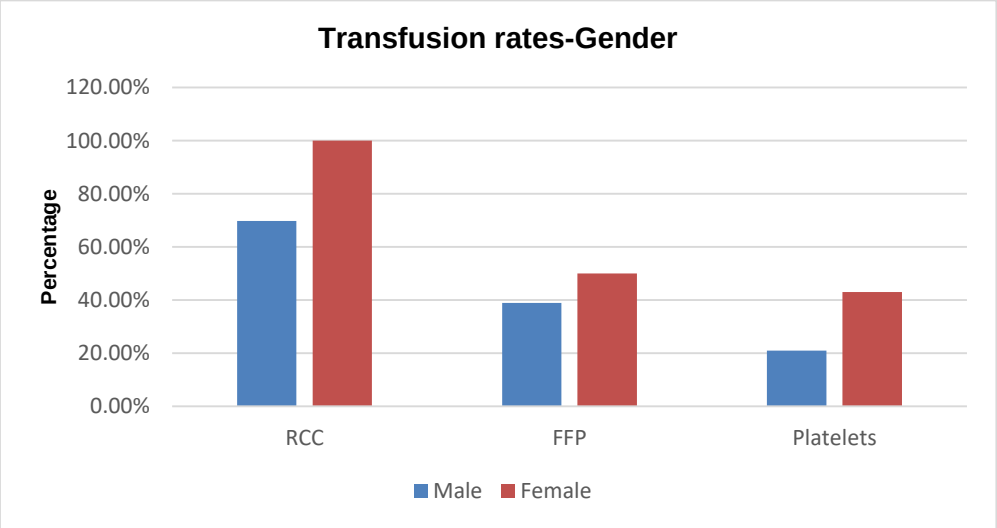

Figure 6: There was a significant difference in transfusion rates between males and females for RCC ($p<0.001$), for FFP ($p<0.05$) and for platelets ($p<0.05$).

4.7 Pre-operative medication

There was little use of the anti-coagulants Clopidogrel and Warfarin at either hospital. The use of aspirin pre-operatively although prevalent at both hospitals, (P, 38 vs. T, 29) was significantly higher at the private hospital ($p<0.05$) where its use showed that patients on aspirin treatment were more likely to receive transfusion (2.2 RCC vs. 1.3 RCC; $p<0.05$) than patients not on aspirin. Aspirin however, did not affect RCC use at the public hospital. Collectively however, aspirin utilization did not affect RCC use (2.7 RCC vs. 2.5 RCC; $p>0.05$). Similarly it did not affect FFP use ($p>0.05$) or platelet use ($p>0.05$).

4.8 Co-morbidities

Ninety-six percent of patients from both centres had co-morbidities. There was however, no significant difference in the incidence of hypertension, diabetes, chronic heart failure, stroke and renal dysfunction between the two hospitals. In contrast, the number of patients with ischaemic heart disease was significantly higher at the private compared to the public hospital (43 vs. 10; $p<0.001$)

Table 10: Number and percentage of patients with co-morbidities.

	All	Private	Public	P value
Hypertension	71	33 (66%)	38 (76%)	NS
Diabetes Mellitus	33	13 (26%)	20 (40%)	NS
Renal dialysis	5	2 (4%)	3 (6%)	NS
Ischaemic heart disease	53	43 (86%)	10 (20%)	P< 0.001
Chronic heart failure	2	2 (4%)	0	NS
Cerebrovascular Disease / Stroke	9	4 (8%)	5 (10%)	NS

4.9 Graft number

There was a significant difference between the number of grafts performed at the two hospitals with >40 patients at the private hospital receiving four or more grafts, as such the private hospital performed significantly more grafts (168) compared to only 129 at the public hospital. ($p<0.001$). Despite this, the use of RCC was significantly higher at the public hospital.

4.10 History of previous cardiac surgery

A significant majority of patients, (84%) had no previous history of cardiac interventions ($p<0.05$).The distribution of patients with either previous history of CABG surgery, angioplasty, valve replacement or stent insertion was evenly distributed between the two hospitals.

CHAPTER FIVE

DISCUSSION, CONCLUSION, RECOMMENDATIONS, LIMITATIONS

5.1 Discussion

This retrospective study compared blood usage in coronary artery bypass graft (CABG) surgery in a tertiary referral university affiliated (public hospital) and a private sector hospital. The results showed that the public hospital had a significantly higher transfusion rate of 92% for red cell concentrate (RCC) use compared to the private hospital with a 56% rate ($p<0.001$). Fresh frozen plasma (FFP) with a 32% transfusion rate at the public hospital and 4% for the private hospital similarly showed a significant different rate ($p<0.01$). No significant difference was noted for platelet use between the 2 hospitals with rates of 26% for the private hospital and 24% for the public hospital respectively ($p>0.05$).
Multivariate analyses indicated that age, weight, the number of grafts and the use of aspirin and warfarin influenced the decision to administer RCC.

Large variations in transfusion rates between institutions are common (Rogers et al, 2009; Stover et al 1998; Kilic and Whitman, 2014:726-734; Cote et al, 2015:297-302). An observational cohort study analysed the blood usage of 102 170 patients undergoing CABG at 796 sites in the United States of America (USA). Transfusion rates ranged from 7.8% to 98.8% for RCC, 0% to 97% for FFP and 0.4% to 90.4% for platelets after adjustment for risk factors including geographic location and hospital volume (Bennet-Guerrero et al, 2010:1568-1575). Another retrospective study of CABG surgery analysed 6359 procedures: RCC usage ranges from 26.2% to 47.5% whilst FFP and platelet use ranges from 16.8% to 33.1% (Brouwers et al, 2017:207-214).

Although similar mean pre-operative haemoglobin (Hb) levels were recorded at both hospitals, 14.0g/dL and 13.8g/dL at the public and private hospital respectively, the mean postoperative Hb levels, however, differed significantly with the private patients having a mean post-operative Hb of 11.2 g/dL and the public hospital of 14.8g/dL ($p<0.001$) (figure 2). This suggests that the private hospital did not require CABG patient discharge when their Hb levels were normal or near normal. A number of studies over the past decade or so have shown that it is not necessary to raise the Hb levels back to normal or near normal (Edwards et al, 2012:2445-2451; Fakhry and Fata, 2004), provided there is no underlying haemopoietic pathology, which is the case in most CABG surgery (Lako et al, 2015:181-186). Alternatively, the “trigger” Hb level for RCC transfusion at the public hospital may be set at a higher level

than at the private hospital. In addition, the patient mix at the public hospital may be different compared to the private hospital as patients are often less able to attend follow up consultations whilst the different patient demographics could also have influenced this.

FFP usage was practically nil (4 units in total) in the private sector, but had significant usage in the public hospital (37 units in total; mean INR of 1.6). Despite a higher mean international normalised ratio (INR) of 1.8 in the private sector, the FFP usage was minimal.
Cryoprecipitate usage was minimal at both hospitals.

Administration of pre-operative anticoagulants aspirin, warfarin and clopidogrel, that could cause bleeding post-operatively (Elbadawi, 2017:18; Biancari et al, 2010:1139-1145; Cao et al, 2014:3092-3098) was not associated with increased blood product usage except in the private hospital where increased RCC usage was seen in patients who were taking aspirin. Curiously, this was not the case at the public hospital. Furthermore, it is not clear why the private hospital, with greater aspirin use compared to the public hospital used less RCC. The reason for this discrepancy is not clear.

Additional factors that were analysed to see if they influenced blood product usage included the co-morbidities hypertension, diabetes mellitus (DM), renal dysfunction, congestive heart failure (CHF), hypertension, ischaemic heart disease and cerebrovascular disease and stroke.
The incidence of co-morbidities showed no significant difference between the two hospitals studied and therefore had no influence on the transfusion rates. However, individual co-morbidities, when analysed have a significant impact on patient outcome and blood product usage (Scrutinio, 2008:379-385, Raza et al, 2015:304; La Par et al, 2016:606-612, Wang et al, 2017:371-375). Apart from hypertension and ischaemic heart disease, the incidence of other co-morbidities was too low to draw any conclusions. Hypertension is common after CABG surgery and has been associated with increased cardiac complications (Yuan et al, 2011; Denault et al, 2010:1-14), and is a risk factor for heart failure, stroke and increased cardiovascular episodes in the peri-operative period (Aronow et al, 2017:227). Hypertension was the most common co-morbidity at both hospitals although no significant difference in the presentation was seen between the two hospitals ($p>0.1$).

Coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention (PCI) are the two primary methods used to revascularize patients with ischaemic heart disease (Deb et al, 2013:2086-2095). In this current study, there were significantly more patients with

ischaemic heart disease at the private hospital than at the public hospital ($p<0.001$). Despite this risk, patients at the private hospital received significantly fewer blood products compared to the public hospital. This suggests that pre-existing ischaemic heart disease had little influence on transfusion rates at this hospital.

A number of earlier studies have shown that an increase in the number of grafts performed during cardiac surgery increases complexity, risk and blood product utilisation (Lako et al, 2014:20-26; Al-Shammari et al, 2005:83-86), due to among others increased total cardiopulmonary bypass time and cross clamp time (Omar et al, 2017:223-229). This study recorded a significant difference in the numbers of grafts per CABG performed. Despite performing more grafts per CABG, the private hospital had a lower transfusion rate suggesting that the additional grafts performed at the private institution did not influence transfusion rates.

Although obesity is regarded as a risk factor for cardiovascular disease in large part due to an increased co-morbidity, profile (De Santo et al, 2018:3719-3727) bleeding tendency is not increased in obese patients (Wigfield et al, 2006:434-440).
There was a significant difference in the mean body mass of the patients at the private hospital compared to the participants at the public institution (94.9kg vs. 87.2kg; $p<0.001$) and this had an influence, as transfused patients weighed significantly less than non-transfused patients did (84.6kg vs. 99.3kg; $p<0.001$). Similar results were seen with FFP transfusion (80.8kg vs. 90.8kg; $p<0.001$) and platelet transfusion ($p<0.05$). This study is therefore in agreement with other published studies that demonstrated that patients with a lower body mass were more likely to receive RCC (Wang et al, 2017:83-90; Ranucci et al, 1999:280-284, Stamou et al, 2011:42-47).

Most studies, (Bennet-Guerrero et al, 2010:1568-1575; Lako et al, 2014:20-26) have shown an increase in blood usage with increased age but attribute this to the increased co-morbidity profile associated with increased age (De Santo et al, 2017:3719-3727; Arias-Morales et al, 2017). Additionally, pre-operative anaemia is associated with age and could influence transfusion levels (Partridge et al, 2013:269-277). Individual analysis of both hospitals showed that age was a significant contributor to increased RCC levels (private $p<0.05$; public p,0.001). Despite this finding the fact that patients at the public hospital were significantly younger ($p<0.005$) suggests that increased age did not affect the difference in transfusion rates of RCC observed between the two hospitals.

As noted earlier, the co-morbidity rates, closely associated with increased age (Nicolini et al, 2017) in both private and public CABG patients were not significantly different so it is unlikely that this was a factor in this study.

A number of publications show female gender as having a significant association with increased blood utilisation (Bennet-Guerrero, 2010:1568-1575; Scot et al, 2003:958-963). The exact cause for this is debatable. It is possible that as clinicians apply the same transfusion triggers for both genders, females could be over-transfused given that females have significantly lower mean Hb reference levels (Stammers et al, 2019:236-245). Similarly, this study also showed an association between increased blood product transfusion (RCC $p<0.001$; FFP $p<0.05$; Platelets $p<0.05$) and female gender. The reason for this gender difference is obscure.

Although previous history of coronary interventions have been linked with an increase in blood product use (Likosky et al, 2018:225-230; Kinnaird et al, 2018:482-492; Biancari et al, 2014:244-252) this study was unable to demonstrate any significant difference due to the low percentage of patients with a previous history.

The use of intra-operative anticoagulants has been shown to lead to increased blood use (Chun et al, 2011:133-138; Rasoli et al, 2012:629-633). Due to the widespread use of heparin in this study and its half dose reversal with protamine, we were not able to make any significant comparison between the two hospitals.

The efficacy of cell salvage, the process whereby blood loss during surgery is minimised by reusing it, has been well documented (Murphy et al, 2017:17; Al-Mandhari, 2015:913-916) despite its detrimental effect on cost (Attaran et al, 2011:824-826). Due to the universal use of this procedure by both hospitals, a comparison of its effect on blood utilisation was not possible.

5.2 CONCLUSION

The scarcity and cost of blood as well as the risks associated with transfusion have promoted the development of Patient Blood Management strategies. These focus on the optimisation of red cells mass, minimisation of blood loss and bleeding as well as the harnessing and optimisation of physiological reserves of anaemia. However the implementation of PBM strategies have not been universally implemented in South African hospitals (Nadar et al, 2020: 91-98).

One of the objectives of this study was to assess whether the blood usage was broadly within the recommendations of the local guidelines. Certainly, the private hospital used fewer blood products but usage was not off the scale in the public hospital and well within the ranges seen in other studies worldwide. The significantly more prevalent use of FFP in the public hospital needs follow up since the mean INR was actually lower than the mean INR in the public sector. However, the wide variation in blood transfusion practice around the world is cause for some concern, given the cost of blood products and potential adverse effects. Although the importance of limiting pre-operative anaemia is recognised, this study found little evidence of this.

Important findings were:

- The significant variability in rates of transfusion of RCC in CABG operations between the two hospitals.
- The significant difference between the two hospitals in terms of FFP usage. Despite having a lower mean INR than the private hospital, the public hospital used considerably more FFP while the private hospital hardly used it at all.
- The mean pre-operative Hb levels were not significantly different but the mean post-operative levels were significantly lower in the private hospital.
- Other factors influencing blood usage were gender (females received more RCC than males); body mass (increased weight was associated with fewer transfusions) and age (older patients were exposed to more transfusions).

5.3 RECOMMENDATIONS

As blood transfusion remains a risk and is associated with worse outcomes in cardiac surgery it is recommended that further investigation which includes more hospitals be conducted, and that regional blood management systems be established to standardise blood product usage.

It is recommended that large hospitals performing complex surgery should establish a Hospital Transfusion Committee. The committee should monitor blood usage in the various units and if there are variations from the recommended guidelines, to ascertain whether the relevant clinician is familiar with the agreed guidelines. It is also suggested that the local blood service has a representative on this committee.

This study has highlighted that blood usage practices are variable and given that the cost of a standard RCC is R 1967, excessive or unnecessary use of blood products is costly. It must however, be the attending clinician who makes the decision to transfuse, by evaluating the individual needs of the patient.

5.4 LIMITATIONS

Although limited by a relatively low sample size, as there are not sufficient resources to mount a large study, nevertheless, this report has shown a couple of anomalies in the use of blood products that will be of use to attending physicians and may require further review.

The results of this study although of value, must however be interpreted in light of a number of limitations. The audit was restricted to only two institutions within the Cape region and therefore is not entirely representative of the Western Cape Province. In light of this, any general conclusions about the blood usage practices in the public and private sector cannot be made and requires the inclusion of more hospitals and centres. In addition, the study only focussed on patients undergoing CABG surgery and excluded other forms of bypass and cardiac surgery, which also are large consumers of blood products. Although every effort was made to include all relevant information, the availability of blood banks in the private hospital and the age and type of bypass equipment were omitted. As many private hospitals do not have blood banks on site and are more likely to have newer and more efficient equipment these factors could have influenced the results.

Despite these limitations, the results of this study suggest that there is a significant variation in the transfusion of RCC and FFP between the two hospitals. The factors influencing this as identified by multivariate analysis, includes age, gender, body mass, the number of grafts performed per surgery and the use of anticoagulant therapy.

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APPENDICES

APPENDIX 1 Data collection form

APPENDIX 2 Ethics Approval

APPENDIX 3 Raw Data Hb Values

APPENDIX 1: Data Collection Form

Clinical Audit
Blood usages for coronary artery bypass surgery
Data Form
Patient study number: _____Hospital:_____

Patient details

Age		
Gender	Male	Female
Weight		

Pre -operative medication

			Date last used
Warfarin	Yes	No	
Aspirin	Yes	No	
Clopidogrel	Yes	No	

Co-Morbidities

Hypertension	Yes	No
Diabetes mellitus	Yes	No
Renal dysfunction	Yes	No
Ischaemic heart disease	Yes	No
Congestive heart failure	Yes	No
Cerebrovascular disease/ stroke	Yes	No

Pre-operative details

History of previous cardiac surgery and type	

Intra-operative details

Graft number		
Procedure on/off pump	On	Off

Intra operative coagulation

Heparin	Yes	No
Protamine	Yes	No
Tranexamic acid or Aprotinin	Yes	No

Please provide detail of the following:

	Pre-op	Post-op (24 hours)
Serum creatinine mg/dL		
INR		
aPTT		
PT		
Haemoglobin d/dL		
Platelet count		

Was, the following method used?

Blood recovery e.g. cell saver	Yes	No

Blood/blood product usage

Date	Time	Order*	Indication	Date	Time	Order*	Indication

*(Number of packed cells/Fresh frozen plasma/Platelets/Cryoprecipitate)
Comments

APPENDIX 2: Ethics Approval

Cape Peninsula University of Technology

HEALTH AND WELLNESS SCIENCES RESEARCH ETHICS COMMITTEE (HW-REC)
Registration Number NHREC: REC- 230408-014

P.O. Box 1906 • Bellville 7535 South Africa
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Tel: +27 21 959 6917
Email: sethn@cput.ac.za

4 October 2016
REC Approval Reference No:
CPUT/HW-REC 2016/H32

Faculty of Health and Wellness Sciences – Biomedical Science Department

Dear Mr Dudley Wolmarans

Re: APPLICATION TO THE HW-REC FOR ETHICS CLEARANCE

Approval was granted by the Health and Wellness Sciences-REC on 15 September 2016 to Mr Wolmarans for ethical clearance. This approval is for research activities related to student research in the Department of Biomedical Science at this Institution.

TITLE: Blood usage practices for coronary artery bypass surgery in the Western Cape

Supervisor: Dr Davison
Co-Supervisor: Dr Bird

Comment:

Data collection permission is required and has been obtained.

Approval will not extend beyond 5 October 2017. An extension should be applied for 6 weeks before this expiry date should data collection and use/analysis of data, information and/or samples for this study continue beyond this date.

The investigator(s) should understand the ethical conditions under which they are authorized to carry out this study and they should be compliant to these conditions. It is required that the investigator(s) complete an **annual progress report** that should be submitted to the HWS-REC in December of that particular year, for the HWS-REC to be kept informed of the progress and of any problems you may have encountered.

Kind Regards

Mr. Navindhra Naidoo
Chairperson – Research Ethics Committee
Faculty of Health and Wellness Sciences

APPENDIX 3: Raw Data Values

STUDY #	AGE	GENDER	WEIGHT	WARFAR	ASPIRIN	CLOPIDO	HYPERTE	DIABETUS	RENALDY	ISCHAEM	CHF	STROKE	HISTORY	GRAFT #	ON/OFF	HEPARIN
P1	70	1	90	2	2	2	1	1	2	1	2	1	0	4	1	1
P2	74	1	56	2	1	2	2	2	2	1	2	2	0	3	1	1
P3	46	1	114	2	2	2	2	2	2	2	2	2	0	5	1	1
P4	67	1	79	2	1	2	1	2	2	1	2	2	5	3	1	1
P5	56	1	86	2	1	2	1	2	2	1	2	2	0	6	1	1
P6	65	1	71	2	1	2	1	2	2	1	2	2	0	3	1	1
P7	61	1	136	2	2	2	2	2	2	2	2	2	0	5	1	1
P8	53	1	103	2	1	2	1	2	2	1	2	2	0	3	1	1
P9	70	1	115	2	2	2	2	2	2	1	2	2	0	1	1	1
P10	68	1	196	1	1	1	2	2	2	1	2	2	5	3	1	1
P11	79	1	85	2	1	2	1	1	2	1	2	2	0	3	1	1
P12	54	1	112	2	1	2	1	2	2	1	2	2	0	2	1	1
P13	55	1	81	2	2	2	1	2	2	1	2	2	0	5	1	1
P14	69	1	80	2	2	2	2	2	2	1	2	2	0	4	1	1
P15	46	1	122	2	2	2	2	1	2	1	2	2	0	5	1	1
P16	63	1	82	2	1	2	1	2	2	1	2	1	0	4	1	1
P17	61	1	66	2	1	2	1	2	2	1	2	2	0	4	1	1
P18	70	2	64	2	1	2	1	1	2	1	2	2	0	4	1	1
P19	76	2	85	2	1	2	1	1	2	1	1	2	5	1	1	1
P20	69	1	96	2	1	1	1	2	1	1	2	2	0	4	1	1
P21	54	1	83	2	1	2	2	2	2	1	2	2	0	4	1	1
P22	65	1	88	2	1	1	1	2	2	1	2	2	5	3	1	1
P23	75	2	66	2	1	2	1	2	2	2	1	2	3	3	1	1
P24	63	1	109	2	1	2	1	2	2	1	2	2	5	2	1	1
P25	61	1	113	2	2	2	1	1	2	1	2	2	0	4	1	1
P26	70	1	119	2	1	2	1	2	2	1	2	2	0	3	1	1
P27	63	1	103	2	1	2	2	2	2	2	2	2	0	4	1	1
P28	58	1	110	2	1	2	1	2	2	2	2	2	0	4	1	1
P29	69	1	110	2	1	2	1	1	2	2	2	2	0	4	1	1
P30	75	2	75	2	1	2	1	2	2	1	2	2	0	1	1	1
P31	59	1	175	2	1	2	1	2	2	1	2	1	0	5	1	1
P32	68	1	85	2	1	2	1	2	2	1	2	2	0	4	1	1
P33	61	1	92	2	1	2	1	2	2	1	2	2	5	3	1	1
P34	45	1	74	2	1	2	1	1	2	1	2	2	0	3	1	1
P35	76	1	93	2	2	2	2	2	2	1	2	2	0	4	1	1
P36	50	1	131	2	1	2	1	2	2	1	2	2	0	2	1	1
P37	80	2	65	1	2	2	1	2	2	1	2	2	0	1	2	1
P38	53	2	63	2	2	2	2	2	2	2	2	2	0	3	1	1
P39	63	1	132	2	1	2	2	1	2	1	2	2	0	2	1	1
P40	73	1	85	2	1	2	1	1	2	1	2	2	0	4	1	1
P41	70	1	62	2	2	2	2	2	2	1	2	2	0	3	1	1
P42	61	1	97	2	1	1	1	1	1	1	2	1	5	4	1	1
P43	76	1	76	2	1	1	1	2	2	1	2	2	0	4	1	1
P44	50	1	88	2	1	2	2	2	2	1	2	2	0	2	1	1
P45	44	1	104	2	1	2	2	2	2	1	2	2	0	4	1	1
P46	56	1	87	2	1	2	1	2	2	1	2	2	5	3	1	1
P47	73	1	80	2	1	2	2	1	2	1	2	2	0	4	1	1
P48	47	1	104	2	1	2	1	1	2	1	2	2	0	3	1	1

P49	63	1	75	2	1	2	1	2	2	1	2	2	0	3	1	1
P50	45	1	82	2	1	2	2	2	2	1	2	2	0	3	1	1
T1	69	2	82	2	1	1	1	2	1	2	2	1	0	2	1	1
T2	61	1	114	2	1	1	1	2	2	1	2	2	0	4	1	1
T3		1	116	2	2	1	1	2	2	2	2	2	0	3	1	1
T4	66	1	43,5	2	1	2	1	2	2	2	2	2	1	4	1	1
T5	70	1	109	2	2	2	2	2	2	2	2	1	0	3	1	1
T6	59	2	65	2	2	2	1	1	2	2	2	2	0	3	1	1
T7	74	2	88	2	2	2	1	2	2	2	2	2	3	2	1	1
T8	61	1	78	2	2	2	1	2	2	2	2	2	0	2	1	1
T9	64	1	54	1	2	2	2	2	2	1	2	2	0	3	1	1
T10	53	1	67	2	2	2	1	1	2	2	2	2	1	3	1	1
T11	68	1	89	2	1	2	1	1	1	2	2	2	1	1	1	1
T12	49	1	86	2	1	2	2	2	2	1	2	2	0	3	1	1
T13	61	1	91	2	1	1	1	2	2	2	2	2	0	3	1	1
T14	52	1	79	2	1	2	1	2	2	2	2	2	0	2	1	1
T15	68	1	81	2	1	2	1	1	2	2	2	2	0	3	1	1
T16	52	1	134	1	2	2	1	2	2	2	2	2	0	2	1	1
T17	54	1	79	1	2	2	2	1	2	2	2	2	3	1	1	1
T18	62	1	74	2	1	2	1	1	2	2	2	2	0	1	1	1
T19	57	1	49,5	2	1	2	1	2	2	2	2	2	0	3	1	1
T20	59	2	78	2	1	2	1	1	2	2	2	2	0	3	1	1
T21	57	1	104	2	2	2	1	1	2	2	2	2	0	1	1	1
T22	47	1	70	2	2	2	1	2	2	2	2	2	0	3	1	1
T23	72	1	87	2	2	2	1	2	2	2	2	2	0	2	1	1
T24	53	1	59	2	2	2	1	2	2	2	2	2	0	3	1	1
T25	75	1	67	2	2	2	1	1	2	2	2	1	0	2	1	1
T26	48	1	99	2	2	2	1	2	2	2	2	2	0	3	1	1
T27	62	2	87	2	1	2	1	1	2	2	2	2	0	2	1	1
T28	48	1	86	2	1	2	2	2	2	2	2	2	0	2	1	1
T29	55	1	118	2	1	2	1	2	2	2	2	2	0	3	1	1
T30	49	1	71	2	1	1	1	2	2	1	2	2	5	3	1	1
T31	72	1	71	2	2	2	1	2	2	2	2	2	0	4	1	1
T32	49	1	70	2	1	2	2	1	2	2	2	2	0	2	1	1
T33	58	1	61	2	1	1	2	2	2	2	2	2	0	3	1	1
T34	54	1	116	2	2	2	2	1	2	2	2	2	0	2	1	1
T35	53	1	72	2	1	2	1	1	2	1	2	2	0	2	1	1
T36	58	2	75	2	2	2	2	2	2	1	2	2	0	3	1	1
T37	50	1	71	2	1	2	2	2	2	1	2	2	0	3	1	1
T38	54	2	73	2	1	2	1	1	2	2	2	2	0	2	1	1
T39	53	2	89	2	1	1	1	1	2	2	2	2	0	2	1	1
T40	54	1	108	2	1	2	1	2	2	2	2	2	0	2	1	1
T41	60	1	74	2	1	1	1	2	2	2	2	2	0	4	1	1
T42	42	1	105	2	1	2	1	2	2	2	2	2	0	3	1	1
T43	49	2	54	2	2	2	1	1	1	2	2	2	0	3	1	1
T44	71	1	94	2	1	2	1	1	2	2	2	2	0	3	1	1
T45	54	1	75	2	2	2	2	1	2	2	2	2	0	3	1	1
T46	54	1	91	2	1	2	1	2	2	2	2	2	0	2	1	1
T47	80	1	77	2	1	2	2	2	2	1	2	2	0	3	1	1
T48	69	1	75	2	2	2	1	1	2	1	2	2	2	2	1	1
T49	58	2	68	1	1	2	1	1	2	1	2	1	0	3	1	1
T50	53	1	73	2	1	2	1	2	2	2	2	1	0	3	1	1

STUDY #	PROT	TRANEX	PRE CR	POST CR	INR	a PTT	PT	PRE HB	POST HB	PRE PLC	POST PLC	CELL SAV	RBC	FFP	PLC	CRYO
P1	1	2	81	81	1	25,3	11,3	14,9	10,9	353	223	1	0	0	0	0
P2	1	2	85	97	1,1	32,4	12,8	14,7	7,6	257	180	1	5	0	0	0
P3	1	2	88	62	1,1	27,9	11,9	14,8	10,8	243	171	1	2	0	0	0
P4	1	2	73	68	1,1	30,6	12,3	13,9	11,7	314	248	1	6	0	0	0
P5	1	2	108	89	1,2	26,7	13	15	8,9	366	189	1	2	0	0	0
P6	1	2	64	61	1	28,2	11,5	14,5	11,5	178	140	1	6	0	1	0
P7	1	2	70	62	1,1	34,5	12,3	14,9	12,1	199	158	1	0	0	0	0
P8	1	1	96	64	1,1	29,7	12,3	14,1	11,4	233	260	1	0	0	1	0
P9	1	2	112	73	1,2	27,4	13,5	14,2	12,2	210	167	1	0	0	0	0
P10	1	2	84	104	1,1	34	12,3	9,1	9	438	195	1	6	0	0	0
P11	1	2	66	64	1	25,4	11	15,8	12,3	300	237	1	0	0	0	0
P12	1	2	93	95	1,2	29,5	13	14,2	11,1	264	251	1	2	0	0	0
P13	1	2	70	65	1	25,6	10,6	13,2	9	366	260	1	6	0	1	0
P14	1	2	77	70	1,1	29,9	30,9	14,8	9,3	178	132	1	2	2	1	0
P15	1	2	80	71	1,1	26,7	12,2	16,4	12,6	193	151	1	0	0	0	0
P16	1	2	75	66	1,1	28,1	12,1	15	11,7	197	165	1	0	0	0	0
P17	1	2	73	69	1	27,6	11,3	14,7	10,1	174	137	1	2	0	0	0
P18	1	2	47	81,4	1,1	30,8	11,9	14,8	10,3	292	236	1	6	0	1	1
P19	1	2	91	89	1,1	27,4	12,3	10,3	12,4	249	280	1	2	0	0	0
P20	1	2	119	115	1,2	28,2	13	15,5	12,5	184	168	1	0	0	1	0
P21	1	2	72	51	1	26,7	10,8	16,7	13,6	254	185	1	0	0	0	0
P22	1	2	72	61				13,4	11,2	388	224	1	2	0	0	0
P23	1	2	81	59	1	26,2	11,7	12,7	10,3	298	90	1	6	0	1	0
P24	1	2	72	72	1	26,7	11,3	13,5	13,3	133	136	1	4	0	1	0
P25	1	2	64	56	1,1	25,9	12	13,2	12,9	201	178	1	0	0	0	0
P26	1	2	86	96	1	29,8	11,6	14,4	9,8	202		1	0	0	0	0
P27	1	2	73	75	1,1	25	12,	15,	14,	16	19	1	0	0	0	0

							6	8	4	5	4					
P28	1	2	64	69	1	33,2	11,8	13,6	8,8	302	279	1	4	0	0	0
P29	1	2	87	102	1	30,2	10,4	13,5	9,4	192	169	1	2	0	1	0
P30	1	2	82	80	1,1	28,9	11,9	14,4	10,6	179	237	1	2	0	1	0
P31	1	2	81	85	1	30	11,5	12,9	9,5	163	189	1	5	0	0	0
P32	1	2	131	108	1	41,9	11,7	15,3	10,9	270	226	1	5	0	0	0
P33	1	2	103	73	1,2	26,9	13,3	14,2	12,8	281	214	1	2	0	0	0
P34	1	2	80	76	1	42,6	11,3	12,6	9,8	216	214	1	1	0	0	0
P35	1	2	98	122	1,2	54,7	13,3	16,6	12,2	255	176	1	0	0	0	0
P36	1	2	73	64	0,9	25,4		12,5	13,6	140	212	1	0	0	0	0
P37	1	2	79	100	1	28,1	11,3	11,3	10,6	219	219	2	1	0	0	0
P38	1	2	84	52	1	30,5	10,4	13,6	10,4	401	161	1	2	0	0	0
P39	1	2	96	95	1,1	28,7	12,9	11,6	12,1	152	201	1	0	0	0	0
P40	1	2	87	67	1	30,9	11,7	13,4	10,4	292	200	1	0	0	0	0
P41	1	2	81	82	1	28,2	10,8	11	8,2	302	202	1	3	0	0	0
P42	1	2	214	296	1,2	29,2	13,9	11	8,9	142	115	1	5	0	1	0
P43	1	2	88	72	1	24,4	10,5	16,5	14	252	140	1	0	0	0	0
P44	1	2	82	58	1,1	32,2	12,9	15,7	14,2	155	160	1	0	0	0	0
P45	1	2	67	66	1,1	40,9	12,4	15,9	12,2	251	175	1	2	2	1	0
P46	1	2	96	65	1	28,2	11,3	15,1	11,7	250	150	1	0	0	0	0
P47	1	2	103	121	1,1	27,2	12	15	9,1	173	128	1	6	0	0	0
P48	1	2	74	51	1,1	34,3	12,9	15,5	11,9	214	244	1	0	0	1	0
P49	1	2	83	62	1	26,9	11,7	12,4	10,9	207	204	1	0	0	0	0
P50	1	2	83	68	1,1	27,5	12,8	15,5	12,7	187	163	1	0	0	0	0
T1	1	2	86	61	1,17	31,6	14	11,8	11,4	300	360	1	4	0	1	0
T2	1	2	122	134	1,07	30,6	12,9	13,2	12,9	270	314	1	2	0	0	0
T3	1	2	80	74	1,25	47,4	15	13,9	13,5	335	231	1	2	2	1	0
T4	1	2	82	68	1,5	180	17,8	12,7	11,7	304	103	1	4	2	0	0
T5	1	2	109	113	1,17	29,4	14	14,6	9	314	164	1	10	2	0	0
T6	1	2	56	47	1,0	28,1	12,	14,	15,	22	26	1	3	0	0	0

					3		4	2	3	4	3					
T7	1	2	105	69	1,12	30	13,5	12,1	12,5	217	154	1	4	2	1	1
T8	1	2	90	134	1,13	29,3	13,6	13,4	15,2	575	294	1	2	0	0	0
T9	1	2	125	110	1,21	31,5	14,5	13,4	9,3	412	225	1	3	0	0	0
T10	1	2	55	56	1,38	40,7	16,4	14,3	117	193	101	1	4	0	0	0
T11	1	2	96	102	1	21,7	12,1	16,7	13,9	170	284	1	2	0	0	0
T12	1	2	121	116	1,07	24,8	12,9	13,7	11	280	126	1	4	0	0	0
T13	1	2	78	81	1,02	22,6	12,3	14,8	15,1	238	219	1	2	0	0	0
T14	1	2	106	69	1,24	33	14,8	13,7	11,1	192	155	1	2	0	0	0
T15	1	2	71	60	0,95	24,2	11,6	13,9	8,1	222	350	1	6	2	1	1
T16	1	2	116	121	1,08	25,3	13	12,7	11,5	175	162	1	2	0	0	0
T17	1	2	79	91	1,01	24	12,2	13,6	15,7	237	300	1	2	0	0	0
T18	1	2	68	83	1,15	24,7	13,8	10,6	11,2	495	404	1	4	0	0	0
T19	1	2	75	61	1,04	23,4	12,5	13,5	13,9	232	150	1	8	6	2	1
T20	1	2	59	62	1,05	28,3	12,6	13,5	13,2	426	349	1	4	2	0	0
T21	1	2	196	184	1,23	29,6	14,7	15,1	14,9	426	449	1	0	0	0	0
T22	1	2	80	92	0,92	18,3	11,1	16,4	15,9	335	319	1	0	2	0	0
T23	1	2	104	86	1,04	22,9	12,5	13,8	11,9	269	162	1	4	2	1	0
T24	1	2	82	97	1,4	177	16,7	14,8	14,2	192	172	1	4	0	0	0
T25	1	2	120	139	1,14	32,6	13,7	14,8	14,1	211	202	1	4	2	0	0
T26	1	2	112	105	1,08	25,3	13	14	13,9	156	129	1	2	1	0	0
T27	1	2	75	168	1,13	27,7	13,6	14,1	12,6	277	83	1	2	0	0	0
T28	1	2	103	52	1,06	24,5	12,8	13,4	8,9	150	74	1	2	0	1	0
T29	1	2	94	66	1,02	22,2	12,3	13,6	10,3	323	220	1	2	0	0	0
T30	1	2	71	66	1,01	22,1	12,2	12,8	9,2	324	192	1	2	0	0	0
T31	1	2	100	148	1,08	45	12,8	12,3	13,5	380	271	1	4	0	0	0
T32	1	2	64	60	1,06	24,1	12,6	14,1	12,2	238	148	1	4	0	0	0
T33	1	2	77	70	1,14	61,8	13,5	15,5	13,6	194	280	1	4	4	1	0
T34	1	2	88	59	1,03	28,3	12,9	16,3	14,9	207	195	1	0	0	0	0
T35	1	2	87	95	0,9	18,5	11,	12,	13,	16	22	1	6	0	1	0

					2		2	9	5	4	2					
T36	1	2	69	64	1,02	22,5	12,3	13,8	12	213	304	1	6	0	0	0
T37	1	2	85	81	1,06	22,8	12,6	16,8	15	323	291	1	4	2	0	0
T38	1	2	64	47	1,04	23	12,3	14,2	10,5	251	234	1	2	0	0	0
T39	1	2	54	67	0,85	15,9	10,4	10,4	11,3	388	373	1	2	2	1	0
T40	1	2	81	87	1,05	36,6	12,6	14,6	14,3	235	276	1	2	2	0	0
T41	1	2	85	98	0,92	18,54	11,2	16	10,1	233	219	1	4	0	0	0
T42	1	2	65	71	1,09	27,4	14,4	13,9	12,5	386	196	1	2	0	0	0
T43	1	2	137	120	0,99	29,4	13,2	12,8	15,2	312	270	1	4	2	1	0
T44	1	2	107	82	0,97	27,6	12,1	13,4	12,8	224	212	1	4	0	0	0
T45	1	2	77	77	0,95	19,6	11,5	14,5	11,4	383	321	1	2	0	0	0
T46	1	2	119	103	1,02	22,5	12,3	15,5	13,3	262	218	1	0	0	0	0
T47	1	2	94	119	1,08	27,7	14,3	12,3	13,8	265	315	1	4	0	0	0
T48	1	2	180	159	1,06	25,6	12,8	11,3	11,5	532	390	1	6	0	0	0
T49	1	2	59	129	1,14	27,9	13,6	12,1	13,3	229	223	1	6	0	0	0
T50	1	2	84	59	1,04	26,7	12,5	13,8	14,5	281	216	1	4	0	0	0

Data Key		
GENDER	1=male2=-female	
WARFAR	WARFARIN: An medication used as an anticoagulant (blood Thinner)	1=yes 2=no
ASPIRIN	ASPIRIN: An medication used to treat pain and inflammation and used for cardiac conditions to prevent stroke due to its anti-platelet properties	1=yes 2=no
CLOPIDO	CLOPIDOGERAL: An medication used often in conjunction with aspirin to reduce the risk of heart disease and stroke due to its anti-platelet properties	1=yes 2=no
HYPERTE	HYPERTENSION: An medical condition in which there is abnormally high blood pressure, an co-morbidity in coronary surgery	1=yes 2=no
DIABETUS	DIABETES: An group of medical conditions characterised by high blood sugar levels over a extended period. An co-morbidity in cardiac surgery	1=yes 2=no
RENAL DY	RENAL DIALYSIS: An process of removing waste from the blood via artificial methods due to lack of adequate kidney function	1=yes2=no
ISCHAEM	ISCHAEMIC HEART DSEASE: A condition that affects the supply of blood to the heart due to narrowing of blood vessels because of cholesterol. An co-morbidity in cardiac surgery	1=yes2=no
CHF	CONGESTIVE HEART FAILURE: A medical condition in which the heart is no longer able to pump sufficient blood. An co-morbidity in cardiac surgery	1=yes2=no
STROKE	CEREBROVASCULAR DISEASE OR STROKE: A disease of the cerebral circulation affecting arteries supply of oxygen to the brain, often resulting in stroke. An co-morbidity in CABG	1=yes 2=n0
HISTORY	PREVIOUS CARDIAC SURGERY: None=0 CABG=1 Coronary angioplasty=2 Valve replacement surgery=3 Pacemaker=4	
GRAFT #	GRAFT NUMBER: Refers to the number of coronary arteries bypassed in the procedure	
ON/OFF	PROCEDURE ON/OFF PUMP: On pump-heart stopped-heart lung machine used/ Off pump-heart still beating- none or minimal heart lung machine usage	1=on pump 2=off pump
HEPARIN	HEPARIN: Anticoagulant used during CABG procedure	1=yes 2=no
TRANEX	TRANEXAMIC ACID OR APROTININ: Medication used to treat or prevent excessive blood loss	
PROTAM	PROTAMINE: An medication used to reverse the effects of Heparin	1=yes 2=no
PRE CR	SERUM CREATINE PRE OPERATION: A waste product synthesized during muscle metabolism. Removed primarily by the kidneys elevated levels may indicate decreased kidney function	
POST CR	SERUM CREATININE POST OPERATION: The level of serum creatine post operation	
INR	INTERNATIONAL NORMALIZED RATIO: An assay used to measure the extrinsic pathway of coagulation	
a PTT	ACTIVATED PARTIAL THROMBOPLASIN TIME: A medical test that characterises blood coagulation or clotting time. aPTT speeds up clotting time and is used to monitor patients response to Heparin	
PT	PROTHOMBIN TIME: An assay measuring extrinsic pathway coagulation with its derived measures of prothrombin ratio and INR	
PRE HB	HEAMOGLOBIN PRE OPERATION: A protein molecule in red blood cells that carries oxygen	
POST HB	HEAMOGLOBIN POST OPERATION: A protein molecule in red blood cells that carries oxygen	
PRE PLC	PLATELET COUNT PRE-OPERATION: Platelets are cell fragments responsible for clot formation when damaged blood vessels are recognised	
POST PLC	PLATELET COUNT POST OPERATION: Platelets are cell fragments responsible for clot formation when damaged blood vessels are recognised	
CELL SAV	CELL SAVER: The process of recovering autologous blood during surgery and re-infusing it into the patient via a cell saving machine	1=yes2=no

RBC	RED BLOOD CELLS: A component issued by the blood bank to replace cells lost during surgery, Red cells carry oxygen via haemoglobin to keep body tissues oxygenated.	
FFP	FRESH FROZEN PLASMA: A Component issued by blood bank. Fresh frozen plasma is the part of blood with the platelets and red cells removed that still contains clotting factors	
PLC	PLATELET: An component issued by blood bank to restore platelet volume	
CRYO	CRYOPRECIPITATE: An component issued by blood bank to restore clotting factors especially factor 8	