

# OPEN HEART SURGERY: MANAGEMENT OF NONSURGICAL BLEEDING IN THE PERI-OPERATIVE PERIOD; 3<sup>1/2</sup>-YEARS INSTITUTIONAL EXPERIENCE.

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## ABSTRACT

**BACKGROUND:** Excessive perioperative bleeding remains a major complication following open heart surgery, resulting in increased morbidity and mortality of some patients in our institution. A study of the principal causes of excessive nonsurgical haemostatic perioperative bleeding, clinical evaluation, treatment and preventive strategies is justified.

**OBJECTIVE/AIM:** To identify the causes of bleeding in patients with haemorrhage that did not require re-exploration and assess the impact on the patient outcomes from different causes of nonsurgical bleeding perioperatively.

**MATERIALS AND METHOD:** For a period of 3 1/2 years (March 2013 – February 2016), the National Cardiothoracic Center of Excellence, UNTH, Ituku/Ozalla, Enugu, Nigeria, partnered with different foreign cardiac missions (USA, UK and India) for the performance of open heart surgery. The case files of the patients managed in the envisaged period were retrieved and analyzed using SPSS, version 2.0 (Chicago). The data analyzed were patients' demographics, the total number of open heart surgery cases, the number that had perioperative nonsurgical bleeding, clinical detection strategies, treatment and preventive modalities as well as the outcome.

**RESULTS:** During the period, a total number of 78 cases of open heart surgery (OHS) were done. There were 43 males and 35 females, with a ratio of approximately 1.3:1. The youngest age was 5 months and the oldest was 74 years, with a mean of 11.1 +/-SD 0.05. Out of these 78 cases, a total of 7 patients had perioperative nonsurgical bleeding, giving a percentage of 9%. 3 patients were noticed intraoperatively in the operating room (OR) while 4 were noticed postoperatively in the intensive care unit (ICU). Treatment included the use of tranexemic acid or aprotinin, fresh frozen plasma (FFP) or fresh whole blood, platelet concentrate and additional doses of protamine, when incomplete reversal of heparin was the cause.

**CONCLUSION:**

Detection of the cause(s) of nonsurgical bleeding without thromboelastography or platelet function analyzer can be quite challenging in our environment. Applying appropriate pharmacologic agents among other interventions can reduce allogenic blood requirements with their attendant complications.

**KEYWORDS:** Perioperative, Open heart surgery (OHS), thromboelastography, platelet function analyzer.

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## INTRODUCTION

Patients undergoing open heart surgery are at the risks of excessive perioperative bleeding, both surgically and nonsurgically leading to increased useage of allogeneic blood and haemostatic blood products with attendant complications<sup>[1]</sup>. Although this patient population represents a relatively small proportion of surgical patients, cardiac surgery consumes about 20% of the available blood supply in the United State<sup>[2]</sup>, with similar number reported worldwide<sup>3,4</sup>.

The principal causes of nonsurgical haemostatic perioperative bleeding are a pre-existing undetected bleeding diathesis which may include failure to recognize and stop patients on anticoagulant medications some days prior surgery and making sure that the coagulation panel, like the international normalized ratio (INR), activated prothromboplastin time (aPTT) and platelet counts are within normal level. Cardiopulmonary bypass (CPB) is known to activate four primary plasma proteins {factor IX, factor IX, prekallikrein and high molecular weight kininogen (HWK)}, through contact with foreign surfaces of the pump. The activated factor IX activates the complement system, intrinsic coagulation and the neutrophils. Furthermore, foreign surface contact of

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the pump also activates the fibrinolytic system and platelet in addition to causing platelet dysfunction. Coagulation abnormality arising from massive blood loss or inadequate doses of heparin can result in disseminated intravascular coagulopathy (disseminated Intravascula Coagulopathy, DIC) and consumption of coagulation factors. Understanding the haemostatic changes occurring in the perioperative period, especially during the cardiopulmonary bypass is crucial in developing new strategies for the management of excessive perioperative bleeding<sup>5</sup>. Drug useages, especially aprotinin, tranexemic acid, desmopressin and increasingly recombinant VIIA are being used prophylactically and therapeutically to stop bleeding<sup>5</sup>. The use of point of care tests like thromboelastography and platelet function analyzer has allowed for more detailed assessment of various steps of haemostasis.<sup>6</sup>

It is important that the surgical and anaesthetic teams realize that many pre-existing so called mild bleeding disorders, eg., VWD(Von Willibrand Disease) are clinically silent from day-to-day and only manifest at times of haemostatic stress such as surgery<sup>7</sup>. One of the key points in minimizing perioperative blood loss is an index of suscipicion and the identification of patients who at increased risk of bleeding<sup>1</sup>. Those undergoing moderate or high risk procedures like open heart surgery should have a PT, APTT and platelet count performed<sup>8</sup>. Simple measures may mean that patients on aspirin is stopped 7 days prior to surgery, other NSAIDS, 2 days and warfarin at least 3-4 days prio surgery, commencing post surgery when haemostasis is secured<sup>9</sup>. Alternatively, if anticoagulation is required patients could be switched over to either intravenous unfractionated heparin for prosthetic heart valves or subcutaneous low molecular weight heparin (LMWH). Perioperative haemostatic changes have been widely studied in complex procedures of open heart surgery, using CPB. Haemostatic activation occurs as a result of the hyperadrenergic state induced by the stress of surgical stimulation. Hyperfibrinolysis is a feature of open heart surgery<sup>3,9</sup>. Consumption of coagulation factors, platelets and physiologic anticoagulants, from bleeding/haemodilution is a feature of the complex procedures in open heart surgery leading to a decrease in platelet count, FVIII, vWF, antithrombin and protein C as well as platelet dysfunction perioperatively<sup>10,11-14</sup>. In fact bleeding time as a measure of impaired haemostasis has a strong linear correlation with the length of bypass and degree of hypothermia<sup>15</sup>.

#### Materials and Method

For a period of 31/2 years (March 2013 – February 2016), the National Cardiothoracic Center of Excellence, UNTH, Ituku/Ozalla, Enugu partnered

with different foreign cardiac missions (USA-VOOM, UK-Save a Heart Nigeria and India-Innova CCH, Hyderabad) for the performance of open heart surgery. A retrospective study was performed to that effect. The case files of the patients managed during the period were retrieved and analyzed using SPSS version 2.0(Chicago). The data analyzed were patients' demographics, the total number of open heart surgery cases, the number that had perioperative nonsurgical bleeding, clinical detection strategies, treatment and preventive modalities as well as the outcome. Those that had surgical bleeding that required intraoperative resuturing for their treatment were excluded from the study.

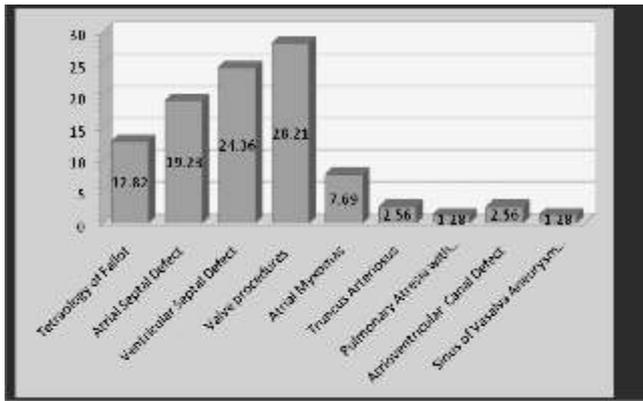
They were identified by excluding surgical bleeding and isolating the haemolysis in the nasogastric tube and the urine as well as derangement it the haemostatic parameters such as APPT, platelet count, clotting factors and PCV.

#### Results

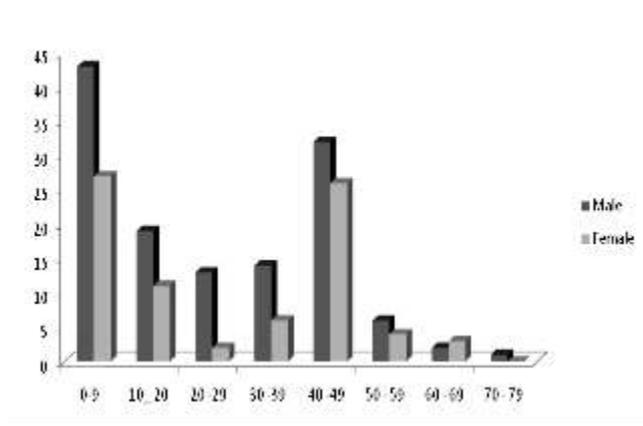
During the period, a total number of 78 cases of OHS were done. There were 43 males and 35 females, with a ratio of approximately 1.3:1. The youngest age was 5 months and the oldest was 74 years, with a mean of 37.8 +/- SD 0.05 Out of these 78 cases, a total of 7(8.97%) patients had excessive perioperative nonsurgical bleeding. 3(3.85%) were noticed intraoperatively in the OR while 4(5.13%) were noticed postoperatively in the ICU. Treatment methods included preoperative preventive strategies like stopping aspirin or other similar drugs few days before operation and making sure that coagulation profile(PT, INR, aPTT) were within normal limit. Others were the use of tranexemic acid or aprotinin, FFP or fresh whole blood, platelet concentrate and additional doses of protamine, when incomplete reversal of heparin was the cause.

Out of the 7 patients managed, 5 died representing 71.4%. Of the 5 patients that died, 3 were females while 2 were males, giving a male to female ration of 2:3, representing 1.7% to 25% respectively.

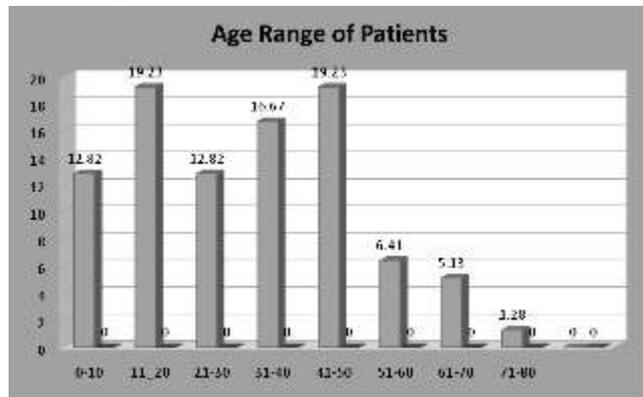
**Figure 1: Indications for the Open Heart Operations Percentages**



**Figure 2: Sex Distributions of Patients**



**Figure 3: Age range of patients Percentages**



**Table 1: Patients that had excessive perioperative nonsurgical bleeding**

Sr	Types of procedure	Number of patients	CPB time (mins)	Degree of hypothermia (°C)	Use of cell saver?
1	valve procedures	3	300-490	32-34	Yes
2	Pericardiotomy + w/procedure	1	490	31	Yes
3	Bicuspid aortic valve excision	1	430	32	
4	valve procedure + resection of L. aorta	1	490	34	Yes
5	Total correction for TOF	1	490	32-34	No
Total		7			

**Table 2: Intra-operative Variables in the affected patients**

Variables/Patients	P1	P2	P3	P4	P5	P6	P7
CPB time	6	5	7	8	8	7 1/2	6
Intraop EBL (ml)	450	600	550	400	750	1200	950
Intraop PRBC (units)	2	3	3	3	4	5	5
Intraop use of surgical/microporous polysaccharide haemostatic (degree)	+	++	++	+	+++	++++	+++
Intraop FFP (units)	2	2	2	2	3	3	3
Intraop platelets (units)	2	2	2	1	2	2	2

**Key:** p = patient, EBL = Estimated Blood Loss, PRBC = Packed Red Blood Cell, FFP = Fresh frozen Plasma

**Table 3: Postoperative variables in the affected patients**

Variable/Patients	P1	P2	P3	P4	P5	P6	P7
CTTD output 24hrs postop (ml)	470	600	750	500	600	450	600
PRBCs (units)							
P: received 1-2 units	2	Yes	-	-	-	Yes	-
P: received > 3 units	-	yes	yes	yes	yes		yes
ICU platelet 24 hrs postop (units)	1	2	2	1	2	1	2
ICU FFP 24-24hr postop (units)	1	3	3	2	3	1	2
ICU median stay	4	2	1	5	4	5	6
30 day mortality	-	2	1	-	-	-	1

**Key:** P= patient, CTTD = chest tube thoracic drainage, ICU = intensive care unit

## DISCUSSION

Expected and unexpected events occur frequently in patients undergoing open heart surgery. Such expected event for instance, is bleeding which could be surgical or nonsurgical. When there is excessive perioperative bleeding that is nonsurgical, it is usually unexpected and it behoves on the managing team to quickly identify the fault and address it so as to have a good outcome. Bleeding after open heart surgery can be broadly divided into 2 groups: surgical (unrecognised bleeding vessels, anatomosis, or suture lines) and nonsurgical bleeding caused by coagulopathy<sup>16</sup>. Factors influencing both can be further broken down into those occurring preoperatively, intraoperatively and postoperatively. A thorough understanding of these factors is necessary to reduce bleeding. This is a desirable clinical goal, because excessive bleeding postoperatively is associated with morbidity and mortality<sup>17</sup>.

In this study, 78 patients had OHS in the envisaged period (figure1). In this study, the male to female ratio is 3:1. The age range of patients that had OHS in our institution ranged from 0-10 to 71-80, with those in the age range of 41-50 with 19.23% being the highest.

The general nonsurgical bleeding tendency in the early postoperative phase can be attributed to mainly 5 factors: viz, platelet function and count, excessive fibrinolysis, heparin rebound and deficiencies in clotting factors as well as hypothermia. Classification of patients into the categories of platelet function and count, excessive fibrinolysis, heparin rebound and clotting factor deficiencies is usually based on platelet function analyzer and thromboelastography. The first test determines the qualitative platelet activity. The second test determines the quantitative platelet activity, degree of fibrinolysis, activated clotting time (heparin rebound) and deficiencies of clotting factors. Unfortunately, these technology was not available to us. Therefore, in our study, FBC(HB< WBC, platelet count), ACT(activated clotting time) and PT, INR were done individually. Tranexemic acid was usually given in anticipation of combating excessive fibrinolysis subjectively. Risks of bleeding increases further if the patient remains in CPB for more than 90 minutes. Analysis of patients based on duration of CPB time. Patients were not analyzed along this line because it was not a constant variable. A few patients with prolonged CPB time did not have coagulopathy while some with prolonged CPB time had.

The average CPB time in our patients with bleeding was more than four hours. The longer a patient's blood is exposed to the mechanical artificial surfaces, the greater the likelihood that platelets malfunction and trigger the clotting cascade leading to bleeding.

Preoperative evaluation excluding bleeding diathesis, patients on anticoagulants or antiplatelets and polycythaemic cyanotic patients will impact favourably in reducing postoperative nonsurgical bleeding<sup>18</sup>.

In this study, out of the 7 patients studied with excessive perioperative bleeding, those patients with valve procedures and total correction for Tetralogy of Fallot(TOF), constituted the highest with 33.33% each. They were followed by those patients with pericardiectomy and valve procedure and valve procedure with resection of left atrial appendage with 8.33% each. In all of them CPB time was prolonged averaging 6-8 hours, see table 1. Two of the 7 patients were on aspirin preoperatively which was stopped 4 days prior to surgery. In other study, it was found that perioperative bleeding complications in cardiac surgery can have multiple aetiologies. Invasiveness of the procedure, induced hypothermia, extended use of CPB, and increasing age, were the major reasons for increased blood loss and the higher incidence of blood transfusions<sup>19</sup>.

In table 1, the intraoperative variables showed parallelism among intraoperative estimated blood loss, intraoperative requirement of packed red blood cell (PRBC), use of local haemostatic agent like surgical or Molyopolysaccharide(Mph), transfusions of fresh frozen plasma (FFP) and platelet concentrate and cardiopulmonary bypass time. The greater the estimated blood loss (EBL), the more the PRBC required with the attendant morbidity and mortality, except in the case of a Jehovah witness, who underwent pericardiectomy with valve procedure. His large EBL was not corrected with PRBC, and this led to patient death. In a similar study, Christensen et al, demonstrated that 22% of patients with excessive perioperative haemorrhage died compared with 6% of patients without excessive perioperative bleeding.<sup>20</sup>

The central mediator in the process of clot formation is the generation of thrombin which acts to convert fibrinogen to fibrin, the basic building block of clot. To prevent thrombosis during CPB, heparin is administered, although some degree of thrombin formation and subclinical clot formation does occur in the presence of adequate heparinisation. All our patients had prebypass heparin achieving an ACT of more than 480 seconds before institution of cardiopulmonary bypass. In prolonged CPB, it can result in consumptive coagulopathy and excessive non surgical bleeding. Average CPB time in the index patients were prolonged, averaging 7 hours/420 mins. Patients undergoing open heart surgery with cardiopulmonary bypass has increased microvascular bleeding by numerous mechanisms. Exposure of blood

to extracorporeal circulation including hypothermia leads to impaired haemostasis and excessive bleeding on account of activation of intrinsic and extrinsic pathways with resultant thrombin and fibrinolytic activity<sup>18</sup>.

The postoperative period, table 3, showed variables such as chest tube output, PRBC requirement some hours in the immediate postoperative period, platelets requirement and intensive care unit median stay as well as 30 day mortality. There were correlations in the chest tube out and PRBC, FFP and platelet requirements. There was also increased morbidity and 30 day mortality was statistically notable in patients with higher output, degree of blood and blood product requirements.<sup>21,22</sup>

During the 3 ½ year period, a total of 78 cases of open heart surgery were done (Figure 1) out of which 7 had perioperative nonsurgical bleeding, representing 10.3%. These patients were managed with blood (red cell) and blood products (platelet concentrate and FFP), see table 2. Correction of hypothermia, and reinfusion of protamine, when adjudged that heparin was inadequately reversed, were used in the management. Also used was tranexamic acid (CRASH 1 & 2)<sup>23,24</sup> and aprotinin. Desmopressin was not used as it was not available. There was also no availability of recombinant FVII (rFVII) in our institution. The off-label use of rFVII in cardiac surgery has increased exponentially in the past 12 years, primarily to treat refractory haemorrhage during or after cardiac surgery<sup>25,26</sup>. Anticipated use of recombinant-activated factor VII is used in preventing postoperative bleeding in cardiac surgery<sup>26</sup>.

In two of the deceased patients, there was associated constrictive pericarditis as a comorbidity. This not only prolonged the bypass time but also provoked a lot of tissue thromboplastin on account of extensive tissue dissection, all leading to consumptive coagulopathy.

#### CONCLUSION:

Excessive perioperative non surgical bleeding following open heart surgery is a haemostatic failure from various causes and its management requires a multidisciplinary approach. Intraoperatively and postoperatively, exclusion of surgical causes is important and presence of complex point of care tests like platelet function analyzer, thromboelastography and rFVII assay will aid in rapid diagnosis of the specific cause(s).

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