

Blood Transfusion Utility During Cardiopulmonary Bypass and Correlation with Key-Biochemical Laboratory Findings: A New Approach to Identify Preventive and Risk Factors (1-Year Practice at University Hospital Hassan-II of Fez)

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Abstract

Background: Blood transfusion (BT) can be mandated during cardiopulmonary bypass (CPB)-aided surgery, although it poses a risk for morbidity and mortality. However, inconsistent BT-strategies have long been documented among clinical settings; thereby limiting its prognostic utility and an evidence-based rational decision there-from.

Methods: Accordingly, we investigated the incidence of BT during (CPB) in 105 cardiac-patients and further assessed its impact/association with demographic data, clinical history data, key biochemical-laboratory findings, in-hospital outcomes, incidence of hemofiltration and CPB parameters. Statistical significance and correlations were determined with the SPSS-program-package.

Results/conclusion: 12% of patients received RBC-transfusion during CPB. Parametric analyses indicated significant association between BT and preoperative urea, preoperative creatinine, post-operative urea, and Nadir-hematocrit% during CPB. Furthermore, non-parametric Chi-square analysis positively associated BT with combined-surgery, coronary surgery and hemofiltration. Lastly, logistic regression analysis identified Nadir-hematocrit value on CPB to inversely correlate with (a negative predictor of) BT, while the history of coronary surgery was found to positively associate with (a risk-factor of) BT during CPB. Thus, BT decision during CPB should be individualized based on weighing the risk/benefits anticipated with anemia and BT and assessing the impact of engaged variables. In this context, while many determinants coexist, Nadir hematocrit and incidence of coronary surgery stand as crucial triggers of a rational decision on BT during CPB.

Keywords: RBC transfusion; CPB; Biochemical-Laboratory findings; Nadir hematocrit during CPB; Coronary surgery; Risk and preventive factors; Patient demographic data

Introduction

Cardiopulmonary bypass (CPB) is a technique that temporarily takes over the function of the heart and lungs during surgery, maintaining the circulation of blood and the oxygen content of the patient's body. The CPB pump itself is often designated as a heart-lung machine or "the pump". Accordingly, the advent of cardiopulmonary bypass (CPB), also permitting open-heart surgery, is considered a breakthrough in medicine in the 20th century [1]. Since the advent of CPB, hemo-dilutional anemia has been frequently used to reduce blood viscosity and prevent arterial hypertension [2-4]. Accordingly, this will result in lowering of patient's hematocrits during CPB, thereby entailing risk of acute anemia and its sequelae [5]. Despite major advances in blood conservation strategies in reducing the requirement for red cell blood transfusion (BT), transfusion rates in cardiac surgery remain inevitable in some cardiac surgical patients to control life-

threatening hemorrhage [6,7]. With the witnessed higher frequency of CPB operations, rates of BT have been likewise escalating [8,9].

However, BT is associated with an increased risk of morbidity and mortality pertaining to risk of bleeding for per-operative transfusion and/or transfusion- and hypo-perfusion-evoked injuries to vital organs [10,11]. In addition, it may pose risks of infections, allergy and immune-reactions (especially with multiple BT). Besides, containment of blood products and costs are additional concerns to rationalize BT. Therefore, BT must be viewed as a scarce and onerous resource that carries both risks and benefits that should accordingly mandate intense scrutiny and restrictive strategy [12,13]. On the other hand, for better guidelines on indication of BT, certain patient variables should be considered to unequivocally predict or guide a decision on the utility of BT during CPB, which, in many settings, has been more dubious than certain. For instance, in Morocco, only a few studies, if any; have attempted to address the utility, management, and caveats of blood transfusion in patients undergoing cardiac surgery, and these have been managerial rather than applied/clinical studies [14].

Therefore, this study handled and analyzed, retrospectively; data on patients who had undergone open heart surgery and required transfusion in the period from January 2015 to December 2015, with the objectives of:

Assessing the incidence of BT, and its association with demographic, laboratory outcomes, and surgery type/characteristics of Moroccan patients who had undergone open heart cardiac surgery.

Investigating the differential contributions and extent of association of the aforementioned variables in transfused versus non-transfused patients, to determine their ultimate ability to dictate or modulate decision on blood transfusion during CPB.

Patients and Methods

Patients

Data were collected retrospectively on 105 consecutive patients undergoing cardiopulmonary bypass in open heart surgery between January and December 2015, at Department of cardiac surgery, Hassan II University Hospital. The study was formally approved by the ethical committee at the university of Fez (June 2015). Data used in this study also included the following methods:

Demographic data

Patient age, gender, and body surface area (BSA), kind of medical insurance, ABO group and Rh group.

Laboratory variables

The following biochemical and hematological parameters; urea, creatinine, CRP pre- and postoperative, preoperative hematocrit; lowest hematocrit during bypass, postoperative hematocrit, were performed with the Architect C 8000 system and Sysmex XE 5000, respectively. Hematocrit in operation room was measured with OPTI CCA, Blood Gas Analyzer, OPTIMedical; cassette; OPTI CCA cassettes. Prothrombin time was measured with the ACL TOP FAMILY system.

Haemostatic management performed

Hemofiltration and transfusion.

In hospital outcomes

Return to bypass after initial separation, return to the operating room, surgical site infection, vital status at hospital discharge, and length of stay in hospital.

CPB parameters

Pump time and clamp time.

Statistical evaluations

Statistical studies were performed using SPSS Statistical program package, version 20.0. T-test test was applied to assess the extent of difference among parametric variables. Chi-square test was employed to judge the differences among non-parametric variables. Logistic regression was used as a power means to determine the significance and direction of association between transfusion and other variables.

Results

This retrospective study involved 105 patients undergoing CPB in open heart surgery. All patients are holders of Health Card. As can be inferred from (Figure 1) gender distribution shows 65% of women and 35% of men, thereby indicating a significantly higher proportion of females. The average age of patients was 45.21 years (range, 17-72). Surgical site infection has occurred in 1% of patients. Reoperation was performed for 1% of patients. A death rate of 3.8% of patients has been recorded. The return frequency to CPB after separation was observed in 1.9% of patients. Furthermore, 7% of patients underwent combined cardiac surgical procedures; while 2% of patients performed a redo cardiac surgery. All patients were undergoing elective surgery except one patient who underwent emergency surgery. Besides, 74% of patient underwent valvular surgery, 23% of patient underwent coronary surgery, 7% performed congenital surgery, and 3% underwent aortic surgery (Figure 2).

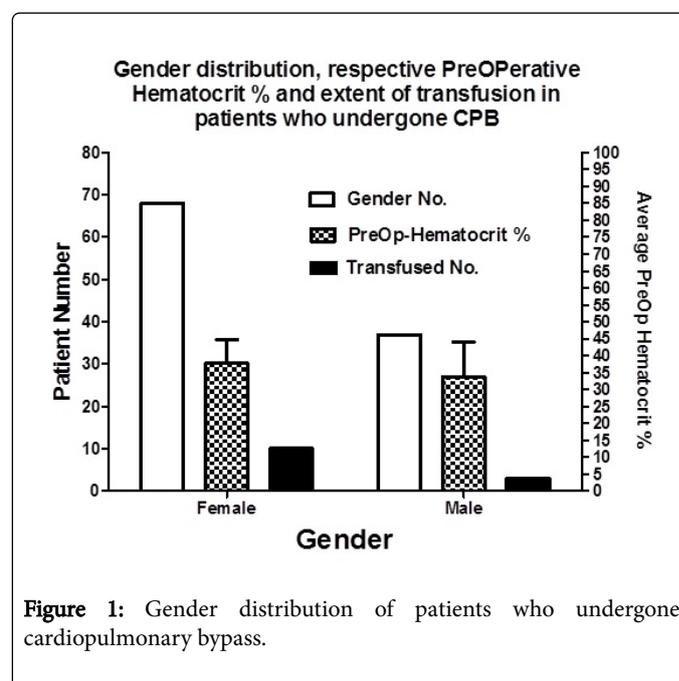
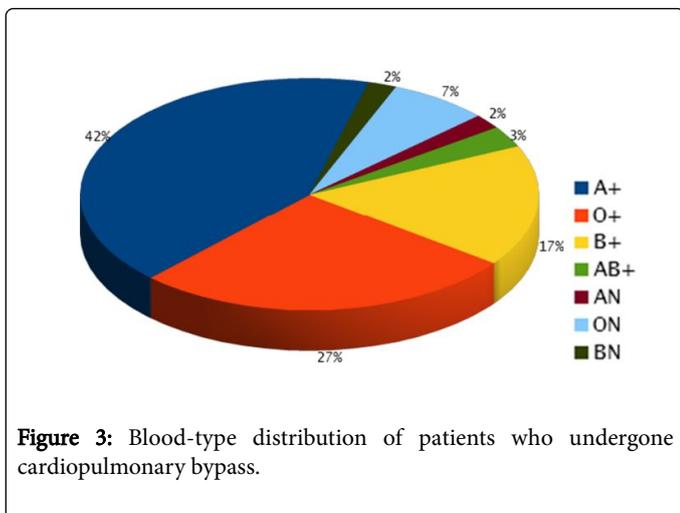
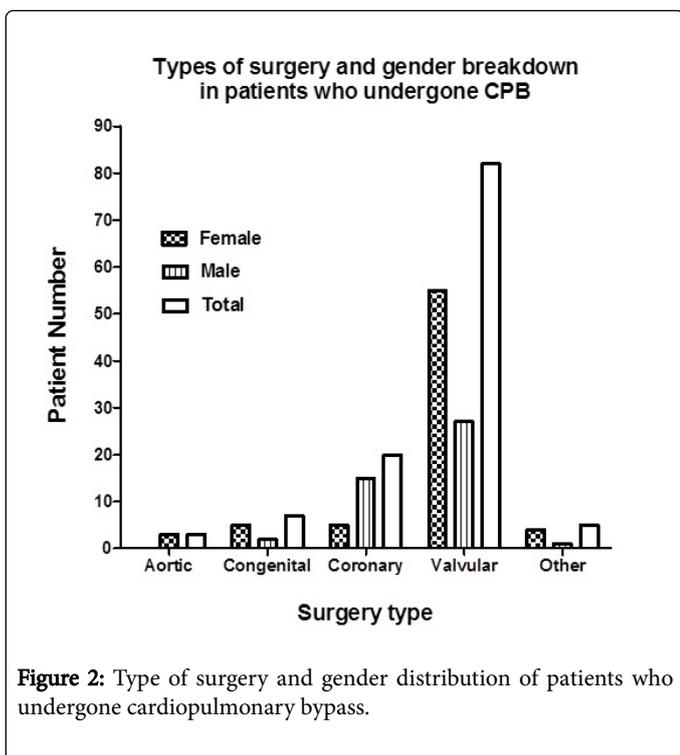


Figure 1: Gender distribution of patients who undergone cardiopulmonary bypass.

The average age of patients undergoing valvular surgery was 42.3 years, 52.78 years for coronary surgery, 39.2 years for congenital surgery and 58 years for aortic surgery. The average age of patients undergoing other type surgery was 38 years.

Mitral heart Valve Replacement was performed for 21% of patients. Aortic Valve Replacement was performed for 9.5% of patients. 8.6% of patients underwent triple bypass. 7.6% of patients underwent double valve replacement. Atrial septal defect closure was performed for 1% of patients. Excision of atrial myxoma and hydatid cyst was occurred in 2% of patients. The remaining patients were required an association of 2 or 3 surgical acts. The distribution of blood type among patients undergoing CPB in 2015 is illustrated in the charts (Figure 3). (A+) Rh positive Blood-type was surprisingly the most common (42%), followed by (O+, 27%), among patients undergoing CPB, 12.4% of patients required a hemofiltration.



Prothrombin time Post-op	69.619 (+/-) 19.22
Urea Pre-op (g/l)	0.36 (+/-) 0.34
Urea Post-op (g/l)	0.33 (+/-) 0.28
Creatinine Pre-op (mg/l)	8.73 (+/-) 4.1
Creatinine Post-op (mg/l)	8.05 (+/-) 4.03
CRP Pre-op (mg/l)	6.21 (+/-) 14.27
CRP Post-op (mg/l)	198.32(+/-) 69.78
Pump T (min)	98.44 (+/-) 40.64
Clamp time (min)	67.8 (+/-) 29.83

Table 1: Patient demographic, hematological, CPB, and biochemical characteristics.

Outcomes in transfused patients

Of the 105 patients undergoing CPB, 12% (13) of patients received red blood cell (RBC) transfusion (On CPB), while (88%) of patients did not. Gender breakdown showed that 77% of transfused patients were women and 23% were men, indicating higher count for females, yet it was not statistically different, taking the total gender counts into consideration (Figure 1 and Table 1). The average age of transfused patients was 50.3 and 44.50 years for non-transfused patients. Of the total transfused patients, 47% had hematocrit (Hct) levels below 30%. Gender distribution of transfused patients showed a proportion of 77% for females and only 23% for males. Average male and female Hct levels were (27 +/- 8.2) and (30.1 +/- 5.7); respectively, thereby affording a statistically insignificant difference (P= 0.46).

In total, 17 units of RBC were used on CPB. The average amount of RBC transfused to each patient was 1.3 units per patient (range, 1-3). 61.5% of patients had type O+ blood, 23% of patients had type A + blood, 2% had type B+ blood, and 2% had type ON blood. One death occurred among the transfused patients, compared to non-transfused patients. 43% of transfused patients underwent combined surgery.

Transfused patients had already demonstrated significantly lower preoperative hematocrit, where their average Hct scored 29.4% (range, 18-36). Nadir hematocrit, defined as the lowest scored Hct, was 20% (range, 17-23) for transfused patients. 12.3% of patients underwent cardiac surgery with hemofiltration during CPB, 46% of them received also RBC transfusion. The volume average of hemofiltration was 1540 ml (range, 200-2000 ml). The transfused patients demonstrated a higher stay length average in ICU. The average was 4 days (range, 2-13). The average of pump time was 113 min (range, 52-174). The variables of transfused and non-transfused patients are summarized in Table 2. The difference between transfused and non-transfused group is not statistically significant for most variables. By contrast, differences in preoperative Urea/Creatinine, postoperative urea, preoperative-Hematocrit and Nadir Hematocrit on CPB values were statistically significant. Furthermore, non-parametric, Chi-square, analysis positively associated BT with combined-surgery, coronary surgery and hemofiltration (Table 3). Moreover, the more powerful logistic regression analysis identified Nadir-hematocrit value on CPB to inversely correlate with BT, while the history of coronary surgery was found to positively associate with BT during CPB, suggesting the two latter variables as robust dictators of the BT decision during CPB.

Variable	Average
Age	45.21
BSA (m ²)	1.66 (+/-) 0.23
Stay Length Pre-op (days)	10.63 (+/-) 7.53
Stay Length ICU (days)	2.71 (+/-) 1.41
Stay Length Post-ICU (days)	10.63 (+/-) 4.64
Hematocrit Pre-op (%)	35.92 (+/-) 6.1
Nadir Hematocrit on CPB (%)	25.28 (+/-) 4.72
Hematocrit Post-op (%)	28.1 (+/-) 3.76
Prothrombin time Pre-op	70.88 (+/-) 20.17

Variable	Transfused	SD	Non-transfused	SD	P (T-test)
Age (years)	50.31	14.08	44.5	13.66	0.846
SL pre-op (days)	10.69	7.718	10.63	7.55	0.551
SL ICU (days)	3.38	3.042	2.62	1.004	0.062
SL post ICU(day)	10.38	6.475	10.67	4.371	0.191
Pre-op haematocrit %	29.38	6.117	36.84	5.534	0.0001*
Nadir hematocrit on CPB %	20	1.871	26.03	4.527	0.007*
Post-op haematocrit %	28.44	4.008	28.05	3.748	0.984
Pre-op PT %	74.62	20.127	70.36	20.235	0.659
Post-op PT %	70	15.454	69.57	19.772	0.365
Pre-op urea (g/l)	0.56	0.875	0.33	0.144	0.02*
Post-op urea (g/l)	0.47	0.68	0.31	0.159	0.001*
Pre-op creatinine (mg/l)	10.85	10.351	8.43	2.093	0.0001*
Post-op creatinine (mg/l)	9.62	7.332	7.84	3.329	0.13
Pre-op CRP (mg/l)	9.15	17.464	5.84	13.819	0.415
Post-op CRP (mg/l)	171.31	67.744	202.14	69.571	0.136
Pump time (min)	113	53.852	96.39	38.358	0.161
Clamp time (min)	69	31.131	67.63	29.818	0.899
BSA (m2)	1.58	0.132	1.67	0.232	0.54

Pre-op= preoperative; Post-op= post-operative; BSA= Body Surface area; SL= Stay Length; ICU = Intensive Care Unit. * P< 0.05, statistically significant.

Table 2: Association of patient surgical history, hematological parameters, biochemical laboratory findings, CBP-parameters and demographic profiles with incidence of blood transfusion.

Variable	P	OR	IC 95%
Nadir hematocrit during CPB	0.0001	0.605	0.459 – 0.798
Coronary surgery	0.002	14.951	2.740 – 81.571

OR= Odds Ratio coefficient

Table 3: Logistic regression analysis of pivotal characteristics of patient undergoing BT during CPB.

Discussion

Cardiovascular disease (CVD) comes as the leading cause of death all over the world, for having prime interactions with all body organs and synergy with coexisting anomalies like diabetes, cancer and obesity. Therefore, not surprisingly, research targeting prevention, diagnosis, and management of CVD has been exponentially surging [15-17]. The first successful open heart procedure on a human utilizing the heart lung machine was performed by John Gibbon on May 6, 1953 at Thomas Jefferson University Hospital in Philadelphia. He repaired an atrial septal defect in an 18-year-old woman [18]. Gibbon's machine was further developed into a reliable instrument by a surgical team led by John W. Kirklin at the Mayo Clinic in Rochester, Minnesota in the

mid-1950s [19]. Per se, CPB is not entirely benign and some potential anomalies can be anticipated, which encompass hemolysis, capillary leak syndrome, clotting, embolism and respiratory distress. Thus, CPB is only used during the several hours a cardiac surgery may take [20]. BT can add an additional risk, if not rationally deployed. The present retrospective study was marshaled to evaluate the utility of BT in a group of heterogeneous cardiovascular patients who have undergone CPB for different surgery indications.

Currently, this study indicates that BT was circumstantially associated with preoperative urea, preoperative creatinine, post-operative urea and Nadir hematocrit. BT incidence also correlated with history of coronary and combined surgeries as well as hemofiltration, during CPB. Of these diverse, potentially contributing factors, the power logistic regression analysis crucially elected coronary surgery and Nadir-hematocrit as the most coherent variables to dictate a decision on BT during CPB.

While current findings revealed insignificant effect for prolonged ICU stay in both transfused and non-transfused patients, Azarfarin and colleagues reported that patients with > 96 hours of ICU stay received more blood transfusion and intravenous inotropes [21], thus possibly reflecting the involvement of an interplay among many variables that could differ among groups of patients and location of clinical service. Presently, also, the parametric analysis showed a

significant relationship between BT and renal function. Renal and/or hepatic insufficiencies are defined as a major risk factor for the incidence of bleeding [22]. Postoperative serum urea and serum creatinine were significantly lower in comparison to preoperative values, consistent with improved circulation and hemodynamics following CPB. Many studies, that targeted relevant clinical settings have unequivocally substantiated the present observations via both direct and circumstantial evidence [23-25].

Our study showed an insignificant association between transfusion and pump time. However, the impact of transfusion on patient hemostatic profiles has been controversial. Thus, a study reported that prolonged pump time can pose a major risk factor for bleeding [22]. Conversely, a study by Rivera showed that prolonged pump time is independent of bleeding-risk in CPB [26]. An also observation in this study showed the association of low Nadir hematocrit with transfusion needs. In adult bypass, the nadir hematocrit can vary widely with body size and pre-bypass hematocrit variations, yet its adverse effects on perioperative organ dysfunction and patient outcomes remained elusive during the past decade [27]. Subsequently, however; Loor and coworkers reported that Nadir hematocrit during CPB was associated with end-organ function and mortality in non-transfused patients. Although RBC transfusion carries an associated morbidity risk, there must be a tradeoff between adverse effects of low-hematocrit during cardiac surgery and those of transfusion [28]. An interesting study, in this vein, sought to elucidate the effects of anemia, transfusion, and their combination on end-organ disruption and mortality. They assessed markers of vital organ functions like glomerular filtration rate, troponin, ventilatory support time, length of stay, and mortality.

Results indicated that although individual exposure to anemia or RBC-BT alone was linked to some risk, it was usually milder than that of the joint anemia and RBC exposure [29]. The second major determinant in this study to permit a BT was coronary surgery. A plethora of studies has attempted to delineate the risk of BT in such patients and revealed that BT can entail some adverse sequelae like stroke and neurological complications, which in other studies were suggested to be partially influenced by the length of RBC storage [30,31]. Thus, for many decades, the decision of BT was based upon the "10/30 rule": transfusion was used to keep a blood hemoglobin (Hgb) level above 10 g/dL (100 g/L) and a Hct above 30%. However, many concerns, as stated before, spurred a re-examination of transfusion practices in the 1980s. The 1988 NIH-Consensus-Conference on Perioperative BT advised that no single criterion is adequate to entail BT, rather; multiple factors based on the patient's clinical condition and oxygen delivery requirements should be considered. During the subsequent 25 years, a big body of clinical evidence was created to guide for BT with the broad goal to balance the benefit of treating anemia with the avoidance of harms due to unnecessary BT [32,33]. In this study, while some patients had Hct levels above 30% (upto 36%), they mostly had history of either repeated bleeding and/or deficiency in oxygen delivery.

Conclusion

Conclusively, in this retrospective regional study on patients undergoing CPB in open heart surgery, we demonstrated that BT can directly relate to vital biochemical markers, like Nadir hematocrit and blood urea, as well as surgery type; but is independent of prothrombin-time and patient age or BSA. Furthermore, BT decision during CPB should be individualized based on weighing the risk/benefits anticipated with anemia and BT. While the ultimate decision can be multifactorial as

well, and involves renal function, scrutinized analyses showed Nadir hematocrit and coronary surgery as the most sagacious and coherent dictators to guide a rational decision of BT during CPB.

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