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Post-cardiotomy exploration for bleeding, when and where but what if 'negative exploration' encountered

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Abstract: Background: It is greatly disappointing to just finish a lengthy open-heart surgery then find out surgical exploration is necessary after few hours because of continuous blood loss. It is significantly pivotal to understand the causes behind post-cardiotomy bleeding as well as current measures to control bleeding. **Methods**: Through single year interval, all patients who had open-heart operation were included. Our techniques were unified in all patients regarding heparinization and protamine policy. All patients were closed similarly and we used prophylactic moderate PEEP with gentle suction on chest drains during ICU stay. **Results**: A 341 patients underwent resternotomy for bleeding, accounting for 7.03% of the total open-heart operations. The mean time to resternotomy was shorter in the ICU group (10.2 Vs 14.3 hours) but it was not significant ($p = 0.410$). The ICU group had a significantly higher rate of cardiac tamponade before resternotomy (52.5% Vs 9.8%, $p < 0.0001$) and had a higher incidence of cardiopulmonary resuscitation (CPR) before resternotomy (44.4% Vs 16.5%, $p < 0.0001$). The mean operative time for bleeding control was shorter significantly in the ICU group (105.8 vs 144.3 min, $p < 0.001$). No significant statistical difference was found in chest tube drainage for 24 hours after resternotomy ($p = 0.669$) **Conclusion**: Unified surgical plan is used for all cardiac surgery cases aiming to decrease reopening for bleeding. The medical reasons should be investigated and targeted then exploration if needed to correct any surgical causes. The negative exploration is beneficial and needed even if we don't seem to agree upon.
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1. Introduction:

A considerable percentage of postcardiotomy patients are at risk of blood loss with hemodynamic instability necessitating volume replacement and inotoropes, attention towards preventing cardiac tymponade through providing adequate care to the drainage tube, management of hemostatic abnormalities. But if bleeding continues, reexploration is required. It accounts for 3% to 5% but in redo situations or in complex procedures, it increases to 7% [1,2]. Exploration for postcardiotomy bleeding is clearly costly but it's really a time and effort-consuming as well, with many patients had no detectable surgical cause [3]. In this retrospective study we looked for reasons behind postcardiotomy bleeding as well as current interventions to control bleeding; and to find out what does negative exploration mean.

This research was undertaken at cardiac surgery unit**, Nasser institute** of research and treatment. when the authors worked together in the same institution.

2. Materials and Methods

Utilizing data base of cardiac surgery unit at Nasser institute[1] for research and treatment (PATS) during period from 1st of January, 2018 till 31th December, 2018. All open heart patients through one year period were included for the study of postoperative bleeding. In all patients, our techniques were unified; heparinization was reversed with equal dose of protamine. All patients were closed using the same techniques and prophylactic use of PEEP (5cm) soon after tightening the sternal wires with gentle continuous suction applied on their chest drains. PEEP continued for 6 hours or till extubation. With early check on hemoglobin level and CXR upon coming into ICU, before extubation and next morning.

While in the intensive care unit, if blood loss is ≥ 200 ml/hour for 3 consecutive hours was investigated for any abnormalities in clotting variables to be corrected. Abnormalities in platelet counts, prothrombin times, or partial thromboplastin times were corrected. Hypothermia and acidosis were also corrected. Hypertension was controlled with nitroglycrin or sodium nitroprusside. The amount of collected blood both in drains and suction was measured hourly and totaled at 8 hours. PEEP was increased by 2-3 cm until bleeding reduced or haemodynamiclly disturbed or hitting 10cm.

Gradually, blood loss tapers over several hours, as aggressive pharmacological treatment can arrest "medical bleeding" But if persistent loss or haemodynamic instability, we went for early exploration. We cared for the chest tubes to be always patent because blocked drains mask the ongoing hemorrhage and blood got retained within the pericardium leading to tymponade or drained into pleural cavity. We agreed to reopen if total bleeding amount had exceeded 1000 mL or was more than 400 mL/h for 1 hour or more than 300 mL/h for 3-4 consecutive hours. Some cases with severe hemorrhage or suddenly arrested or rapidly deteriorating haemodynamics were re-explored on bed inside the ICU with as much sanitation as it could be provided, while those with stable conditions enabled us to go to OR. Thus it was logical to divide them into 2 groups; the stable / OR group and unstable / ICU group.

Abbreviations: OR: operative room **ICU:** intensive care unit **PEEP**: positive end-expiratory pressure **cm**: centimeter **mL/h**: milliliter per hour **LAD**: left anterior descending artery **CXR**: chest X radiography **IABP**: intra-aortic balloon pulsation **MVR**: mitral valve replacement **CPR**: cardiopulmonary resuscitation **PT**: prothrombin time **APTT**: activated partial thrombin time **rfVIIIa**: recombinant factor VIIIa **FDP**: Fibrin degradation product **ACT**: activated clotting time.

3. Statistical analysis:

For statistical analysis, we used SPSS version 21. Continuous variable data were presented as the mean ± standard deviation. Student's t-test was used for statistical comparisons between the two groups for continuous variables and for categorical variables, we used chi-square test. Statistically significant variable if p value is less than 0.05.

4. Results:

A total of 341 patients underwent re-sternotomy for the reason of bleeding control after cardiac surgery between 1st January 2018 and 31st December 2018. They represented 7.03 % of all open-heart done during that period at cardiac surgery unit, Nasser institute[1], Cairo, Egypt. Various categories of cardiac surgeries were performed including aortic artery surgery, coronary, valvular and combined procedures. The monthly rates of resternotomy during this period are shown in Figure 1.

We divided them into 2 groups according to where we did explore; 260 patients in the OR and 81 in the ICU. Preoperatively, there was no significant difference of mean age or sex between the two groups (p = 0.746, 0.674) and so with other preoperative variables. The preoperative characteristics are shown in Table 1.

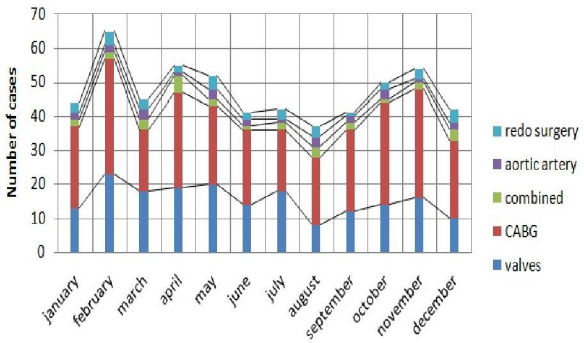

Fig. 1: Monthly rate of re-opening in major 5 cardiac surgeries categories.

The most common type of primary operation was coronary artery bypass graft surgery in both groups then aortic artery surgery comes second in the ICU group while valve surgery is the second in OR group. This might be due to the growing elderly patients seeking revascularization that exceeded the number of the endemic rheumatic valvular category. See table 2.

From the operative variables, no significant difference was found in the bypass or cross clamp time (p = 0.754). Also no significant difference in amount of blood loss before resternotomy (p =0.672). the units of transfused blood were almost the same in both groups. The mean time to resternotomy was shorter in the ICU group (10.2 Vs 14.3 hours) but it was not statistically significant (p = 0.410). The ICU group had a significantly higher rate of cardiac tamponade before resternotomy (44% Vs 16.5%, p < 0.0001) and had a higher incidence of haemodynamic instability and cardiopulmonary resuscitation (CPR) before resternotomy (27.5% Vs 3.3%, p < 0.0001). See table 3.

According to the source of bleeding, we classified patients into two main types: surgical category which included cardiac and non-cardiac sources of bleeding, and a second category which

included medical subcategory where we couldn't find surgical source but witnessed generalized ooze from extracardiac tissues with altered profile of coagulation but those named negative exploration subcategory that included those of undetermined cause both surgical or medical.

In the OR group, the most common type was surgical non-cardiac source (68 of 146 patients). Conversely, the surgical cardiac source was significantly more common in the ICU group 47 of 55 but still no significance (p = 0.542). Of 81 patients in the ICU group, 10 (24.4%) had bleeding at the cannulation sites and nine (22.0%) at the suture lines (See figure 3). The mean operative time for bleeding control was significantly shorter in the ICU group (105.3 vs 144.6 min, p < 0.0001). No significant difference was found in chest tube drainage for 24 hours after resternotomy (p = 0.669) and the amount of red blood cells transfused after bleeding control (p = 0.247), see Table 4.

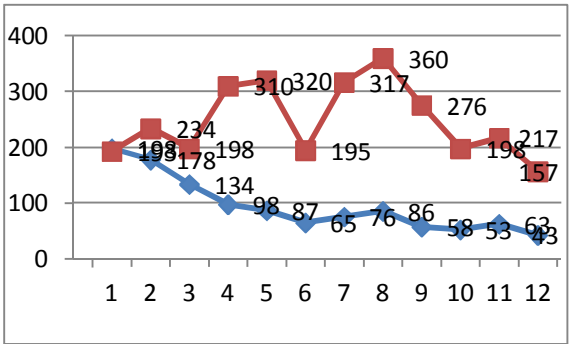

Fig. 2: Median amount of blood loss in millimeter per hour pre & post-exploration. Red line represents the median pre-operative loss in millimeter per hour. Blue line represents the median post-operative loss in millimeter per hour.

The frequency of second resternotomy was seen higher among ICU group where 4 cases of aortic artery surgery and 2 cases of aortic valve replacement, one case had Nick's procedure (p = 0.148). While almost three cases of OR group went back for a 2nd resternotomy for non bleeding causes, where a second graft was inserted over the LAD in one case and sternal dehiscence in other 2 cases.

The total ICU stays in OR group was quite shorter (p = 0.300), and hospital stays (p = 0.289) as well compared to the ICU group which is biased by the seriousness and complexity of the cardiac pathology rather than the bleeding consequences.

The postoperative outcomes are in Table 5. No significant difference with respect to the rate of bacterial growth in blood culture between two groups (p = 0.674). The prevalence of superficial wound dehiscence was relatively high in the ICU group (12.5% vs 4.9%), but it was not statistically significant (p = 0.168). The rate of renal shut down was slightly higher in the ICU group (4.9% vs 2.5%) but there was no significant difference between two groups (p = 0.542). Hepatic hypoperfusion happened almost equally in both groups (13% and 17.4%). IABP was used in 28 patients (10.7%) in OR group and 16(19.7%) in ICU group but still non-significant.

In-hospital mortality was 3.1% in the OR group and 12.5% in the ICU group. There was no significant difference in both groups (p = 0.218). However, there was only three patients who died from an infection-related complication in OR group while four patients died from mediastinitis in the ICU group. In the ICU group, five patients who died were placed on IABP during the perioperative period. Three patients were placed on IABP prior to the exploration and two were placed following the exploration. They eventually died from non-infectious causes, multi-organ failure or stroke. In OR group, there were two deaths from cardiac arrest which occurred during the wait for transportation for exploration. In the ICU group, three patients died from cardiac arrest during a transfer to the OR, (p = 0.192). But this did not reach statistical significance.

Table 1: Preoperative variables between the 2 groups and the general postcardiotomy population.

Characteristics	OR group =260	ICU group =81	Control group =2059	P Value
Age	18-72 Mean 46±3.9	22-74 Mean 49±4.3	20-76 Mean 39±7.1	p = 0.746
Gender	M=210 (80.7%)	M=64 (79.01%)	M=1683 (81.7%)	p = 0.674
Urgent surgery	5(1.9%)	2(2.46%)	56 (2.7%)	P= 0.564
Diabetes	31(11.9%)	16(19.7%)	1023 (49.7%)	P=0.371
Hypertension	54(20.7%)	23(28.35)	1503(72.95)	P=0.561
COPD	11(4.2%)	7(8.6%)	65(3.2%)	P=0.429
Obesity	41(15.7%)	10(12.3%)	158(7.6%)	P=0.813

Table 2. Various types of cardiac surgery needed exploration for bleeding.

Characteristics	OR group =260	ICU group =81	Control group =2059	P value
CABG only	137 (52.7%)	52 (64.2%)	1098 (53.3%)	p = 0.532
Valve only	73 (28.1%)	8 (9.8%)	670 (32.5%)	p = 0.591
Aortic artery surgery	22 (84.6%)	15 (18.5%)	73 (3.5%)	p = 0.457
Combined procedure	28 (10.7%)	6 (7.4%)	164 (7.9%)	p = 0.342
Redo surgery	6 (2.3%)	4 (4.9%)	54 \ (2.6%)	p = 0.365

Table 3. Showing the operative variables.

Characteristics	OR group =260	ICU group =81	Control group =2059	P Value
X clamp time	35-115	45-125	24-134	p = 0.503
CPB time	50-135	60-145	38-164	p = 0.754
HD instability episode	260	81	389	p < 0.001
CPR before explore	43 (27.5%)	36(3.3%)	63	p < 0.001
Tamponade signs	174 (52.5%)	18 (9.8%)	0	p < 0.001
Bleeding Time pre-exploration	6-24 Mean14.3±1.5	4-18 Mean 10.2±2.8	5-9 Mean 6.3±3.4	p = 0.410
Bleeding amount pre-exploration	900-1700mL Mean 1143±233	800-1900 Mean 1345±437	600-1100 Mean 765±354	p = 0.672
Blood transfusion pre-exploration	4-6unit	5-8	1-6	p = 0.236

Table 4. The different causes of bleeding.

Characteristics	OR group =260	ICU group =81	P value
Surgical cause (cardiac+noncardiac)	146(56.1%)	55(68%)	p = 0.542
ACT disbalance	67(25.7%)	15(18.5%)	p = 0.365
Platelets abnormality	28(10.7%)	9(11.1%)	p = 0.344
Negative exploration	19(7.3%)	2(2.4%)	p = 0.185
Operative time for bleeding control	68-176 Mean 144.6±21.9	57-131 Mean 105.3±13.8	p < 0.001
Bleeding time post-exploration	2-6h Mean 5.1±3.2	1-7 Mean 4.6±2.7	p= 0.467
Bleeding amount post-exploration	400-1000 Mean 455±95.6	500-1200 Mean 623±85.3	p = 0.669
RBC transfusion after control	1-3unit	1-5	P= 0.247

Table 5. The post-exploration outcomes.

Characteristics	OR group =260	ICU group =81	Control group =2059	P value
Open chest	2(0.7%)	8(9.8%)	27(1.3%)	p = 0.581
IABP	28(10.7%)	16(19.7%)	117(5.6%)	p = 0.322
Second re-exploration	3(1.15%)	6(7.4%)	-------	p = 0.148
ICU stay (days)	3-14 (Mean 4.9±1.1)	3-28 (Mean 7.4±2.7)	2-9 (Mean 4.3±2.6)	p = 0.300
Hospital stay (days)	7-18 (Mean 6.8±2.1)	8-34 (Mean 8.6±4.2)	6-19 (Mean 7.9±3.5)	p = 0.289
Positive blood culture	12(4.65)	7(8.6%)	16(0.7%)	p = 0.674
Superficial wound dehiscence	49(18.8%)	18(22.2%)	302(14.6%)	p = 0.168
Deep Sternal infection	9(3.4%)	4(4.95)	41(1.9%)	p = 0.426
Renal shutdown	11(4.2%)	2(2.46%)	176(8.5%)	p = 0.542
Hepatic dysfunction	34(13%)	14(17.3%)	123(5.9%)	p = 0.451
Mortality	9(3.1%)	17(12.5%)	92 (4.46%)	p = 0.218

Discussion:

Controversies about reopening for bleeding continue. While studies suggested amelioration of the final results upon early exploration, other studies highlighted the risks of transfusion, acquired hepatitis, associated risk of sternal fracture with wound infection [1,2].

Causes behind post-cardiotomy bleeding are categorized into surgical and medical. And there are two categories of medical bleeding, one with abnormal hemostatic profile, the other has normal hemostatic profile and represents what is called the 'negative exploration'; the abnormality exists locally in the collected mediastinal blood that consumes the natural and the given clotting factors and actually in this situation, bleeding begets bleeding.

Reasons behind medical bleeding are rebound or residual heparin, thrombocytopenia or thrombocytoathenia, clotting factor deficiency or fibrinolysis. [3] The orthodoc management of bleeding depended on administration of hemostatic pharmacologic agents and the various blood components with gentle internal compression through using PEEP. Should also we understand that correction of hypothermia and acidosis if detected earlier will augment any targeted management. [4]

If the prothrombin time (PT) and activated partial thromboplastin time (APTT) are one and half the baseline value or more, fresh-frozen plasma (FFP), cryoprecipitate or factor VIII concentrates should stop the active bleeding. [4]

Reversing any residual effect of intraoperatively administered heparin or heparin released from binding tissues postoperatively using protamine in appropriate doses can control bleeding [5]. The dose of protamine can vary from 20 to 60 mg as excess protamine may increase platelet dysfunction or complement activation. [12]

Since the introduction of rfVIIa as a rescue management, various reports documented rapid decrease of bleeding, lesser need for blood components and eventually no need for reexploration. The used dose was 60µg/kg. Another agent used in excessive bleeding is vasopressin which is beneficial in setting as post-cardiotomy or uremia induced platelets dysfunction at 0.4 lg/ kg/ over 30 min to minimize hypotension. [5,6]

Most of re-explored cases for surgical causes were found to be correctable through ligation, clipping or cauterization; sources such as the side branches of the conduits both internal thoracic artery or saphenous vein grafts, or at graft anastomoses sites, cannulation sites, atriotomy or aortotomy sites, or from substernal soft tissues, sternal wires sites, bone marrow, periosteum, raw surfaces caused by previous surgery or pericarditis, which attributed to the experience of the operating surgeons, the nature of the patient's disease and the complexity of the procedure or the duration of cardiopulmonary bypass. [4,5]

In certain cases, no identifiable source of bleeding and apart from generalized ooze, thus the only benefit of going for exploration will be to evacuate the collected mediastinal blood, irrigate the mediastinum and electro-coagulate the raw surfaces. In one third of our patients; there was no identifiable surgical source. [4] Not surprisingly, after a negative exploration, bleeding will taper over few hours then stop. Like if there is "magic in exposure to night air of OR''. [10]

Basically, the pericardial blood doesn't clot but they become partially defibrinated by the effects of mechanical forces of heart beats and consumption of clotting factors. With a proved markedly elevated fibrinolysis in the mediastinal blood, through measuring the levels of fibrinogen, FDP, plasminogen activator inhibitor-1, and a2-antiplasmin levels that confirmed that fibrinolysis is a main mechanism for nonclotting of such blood [10]. This would explain the magic of the negative exploration, where only irrigation and clots removal reduced the fibrinolytic process; this may allow the bleeding ends of capillaries and small vessels to thrombose and bleeding to stop. [10]

Thus, our policy shifted towards preoperatively unified plans for all cardiac surgery candidates, where stopping any medications affecting clotting mechanism, assessing the clotting profile and optimizing the conditions before surgery. See table 6. Careful revision of anastomotic sites and all side branches before careful and meticulous sternal closure. Adequate heparin neutralization to return to baseline ACT value. Administer blood, its component, hemostatic drugs postoperatively and to be patient, vigilant and watchful then exploring.

Table 6: Policy for management of postoperative bleeding in ICU.

ICU Policy for Postoperative Bleeding
Obtain immediate postoperative chest x-ray as baseline of mediastinum and pleurae.
Quantify and register the amount of bleeding hourly.
Optimize hemodynamic status
Ensure that chest tubes are patent
Warm patient to normothermia
Control hypertension, agitation, and shivering
Obtain coagulation studies:
a. PT/INR, PTT, platelet count, fibrinogen level
b. Platelet function testing
c. Thromboelastogram, if available
Protamine 25 mg IV for two doses if elevated PTT
Packed cells if hematocrit<26
Platelet transfusion if count <150x103
Fresh frozen plasma, 2-4 units
Cryoprecipitates, 6 units
Recombinant factor VIIa, 60µg/kg (in persistent bleeding)
Consider use of 10 cm PEEP
Check results of coagulation studies
Repeat coagulation studies after blood products administered if still bleeding
Repeat chest x-ray if concerned about tamponade or undrained collected pleural blood
Obtain TEE if concerned about tamponade and cardiac function.
Explore early for significant ongoing bleeding or tamponade.

5. Conclusion:

Unified plan for postcardiotomy bleeding should be used for all cardiac surgery cases aiming to decrease reopening. This should be translated into institutional protocol. The medical reasons should be investigated and targeted then re-exploration if needed to correct any surgical causes. The negative exploration is beneficial and needed even if some surgeons don't seem to agree upon.

Disclosure:

The authors have nothing to disclose.

Conflict of interest:

The authors have no conflicts of interest to disclose.

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Authors' contributions:

All authors: 1) have made substantial contributions to conception, design, acquisition of data, analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; and 3) have given final approval of the version to be published.

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