

Comparison of sternal intramedullary bleeding prevention strategies in cardiac surgery

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Aim: Sternal intramedullary bleeding is an important contributor to postcardiac surgery hemorrhage. The aim of this study is to investigate the effects of bone wax, oxidized regenerated cellulose, and electrocoagulation on sternal intramedullary hemostatic control.

Materials and methods: A total of 142 patients undergoing on-pump coronary bypass surgery were prospectively studied. The patients were randomized into 3 groups; bone wax concomitant with electrocauterization, oxidized regenerated cellulose concomitant with electrocauterization, and electrocauterization alone. The amount of postoperative hemorrhage was noted at the 1st, 2nd, 3rd, 6th, 12th and 24th hours. Rates of reexploration for hemorrhage and number of units of blood and its products used were also studied.

Results: The mean age of the patients was 64.23 ± 5.81 years. There were 114 (79.7%) male patients. The patients were comparable regarding preoperative demographics except age and intraoperative variables. The amount of postoperative hemorrhage was lowest in the oxidized regenerated cellulose and highest in the electrocauterization alone group. The number of fresh frozen plasma and erythrocyte suspension used was also lowest in the oxidized regenerated cellulose group.

Conclusion: To overcome hemorrhage originating from the sternal intramedullary space, oxidized regenerated cellulose use concomitant with electrocauterization is effective and can be safely used immediately before closing the chest in open heart surgery.

Key words: Sternum, hemorrhage, electrocoagulation, cellulose, oxidized, bone wax

1. Introduction

Postoperative bleeding is still one of the most important issues following open heart surgery. The reexploration rate for hemorrhage was reported as between 2% and 6% following coronary artery bypass grafting (CABG) (1). Surgical and hematological etiologies should be distinguished to give an exact decision for reexploration. Multiple surgical sites may cause bleeding, including distal and proximal anastomoses, cannulation sites, branches of arterial and venous grafts, the internal thoracic wall where the internal mammary artery is harvested, anterior mediastinum, and others. Postoperative bleeding results in increased mortality and morbidity rates and health care costs (2). Excessive blood loss requiring heavy transfusion is also a well-known risk factor for wound infections and

subsequent sternal dehiscence (3). During the healing process in the sternotomy incision site, a spectrum of complications from simple seromas to dehiscence of all layers with instability of the thoracic wall and severe osteomyelitis, purulent pericarditis, and mediastinitis may occur (3). Some hemorrhage may result from the sternal intramedullary area. In this clinical study, we aimed to emphasize the importance of intramedullary bleeding control while comparing different management strategies.

2. Materials and methods

A prospective, controlled, and randomized study was carried out. The study was approved by the local ethics committee, and written informed consent was obtained from every patient. From January 2010 to December 2011, 252 on-pump CABG

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operations were performed in a single center. The patients were randomized into 3 groups according to chronological order. The first group received bone wax (Bone-wax®, Aesculap Inc., USA) concomitant with electrocauterization, the second group received oxidized regenerated cellulose (ORC) (Surgicel® Absorbable Hemostat, Johnson & Johnson, Ethicon Inc., USA) concomitant with electrocauterization, and electrocauterization alone was performed in the third group.

All anticoagulant and antiplatelet medications were stopped 1 week prior to the surgery. Preoperative and postoperative routine coagulation tests including activated partial thromboplastin time, international normalized ratio, and platelet counts were performed. After all perioperative data were gathered, to maintain homogeneity of the data and prevent bias, patients with very long cardiopulmonary bypass (CPB) times (>100 min), coagulation test abnormalities, and urgent and emergent procedures and patients who underwent reexploration for hemorrhage with surgical bleeding sites of other than sternal origin were excluded from the study. After that, 47 patients remained in the first group, whereas 53 remained in the second group and 42 in the third group. Drainage amounts were noted at the postoperative 1st, 2nd, 3rd, 6th, 12th and 24th hours. The amount of units of blood and its products used were also studied.

All patients were operated on-pump with administration of heparin, 4 mg/kg, with standard aortic cross-clamping. The left internal mammary artery was harvested in each case. Only venous bypass grafts were used concomitant with the mammary artery. Antegrade, intermittent crystalloid cardioplegia was administered from the aortic root and venous bypass grafts. Proximal anastomoses were performed with single-side clamping. Bone-wax was spread by digital pressure on the sternal surfaces immediately after sternotomy and before closing the chest. ORC was cut and laid along the sternotomy over the intramedullary area before closing the chest (Figure). The activated coagulation time levels were measured

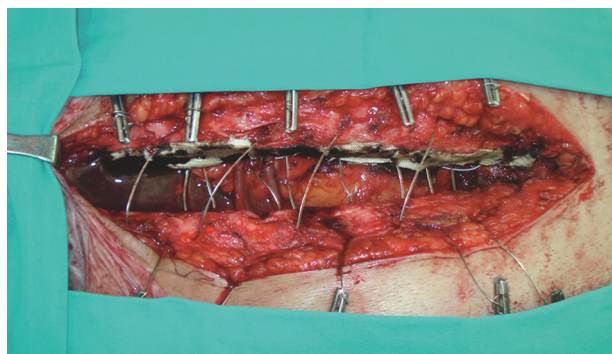


Figure. Oxidized regenerated cellulose was cut and laid along the sternotomy over the intramedullary area before closing the chest.

and adjusted between 100 and 120 s postoperatively. All patients received prophylactic systemic antibiotic therapy (Cefazolin Na, 3 g/day). Salicylic acid or clopidogrel was begun on the postoperative second day if adequate hemostasis was achieved and no further bleeding was expected.

2.1. Statistical analyses

Statistical analyses were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean values \pm standard deviation (SD). Categorical variables were expressed as numbers and percentages. Categorical variables were compared using the chi-square test. For comparison of continuous variables, the Kruskal–Wallis test was used. In cases of significant difference the Bonferroni adjusted Mann–Whitney U test was used to explore the more efficient group. Statistical significance was set at $P < 0.05$.

3. Results

There were 142 patients included in the study. The mean age of the patients was 64.23 ± 5.81 years in the whole study group. The mean age of the patients was higher in the third group compared to first and second groups ($P = 0.015$). There were 114 (79.7%) male patients. There were no statistically significant differences between the groups regarding preoperative demographic characteristics (Table 1). The CPB times and mean number of grafts anastomosed did not differ between the groups.

When the amount of postoperative hemorrhage (mL) was explored, in the 1st, 2nd, 3rd and 24th hours, the drainage amount was the lowest in the second group, and it was lower in the first group compared to third group. In the 6th and 12th hours, the drainage was again the lowest in the second group, but there was not a statistically significant difference between the first and third groups (Table 2).

The number of fresh frozen plasma and erythrocyte suspensions used was lowest in the second group, but there were not statistically significant differences between the first and third groups (Table 2).

No superficial wound infections (postoperative 30-day period) were observed throughout the study period. Reexploration for hemorrhage due to sternal bleeding sites was performed only in the electrocauterization alone group in 3 cases and in none in the other 2 groups ($P = 0.026$).

4. Discussion

The issue of hemostasis has been widely studied in all kinds of surgery and numerous hemostatic agents and agents preventing bleeding have been used. A hemostatic agent is defined as one intending to produce hemostasis by accelerating blood coagulation (4). Apart from the hemostatic

Table 1. Comparison of the 3 groups by preoperative and intraoperative variables.

Factor	Bone wax + EC Mean ± SD	ORC + EC Mean ± SD	EC Mean ± SD	P-value*
Age	63.28 ± 6.48	63.36 ± 5.08	66.38 ± 5.43	0.015
BMI (kg/m ²)	28.00 ± 2.98	28.96 ± 2.89	28.26 ± 2.97	0.242
LVEF (%)	44.00 ± 2.98	42.51 ± 4.81	42.29 ± 4.86	0.119
CPB time (min)	85.96 ± 24.64	90.57 ± 22.31	81.19 ± 21.20	0.141
Graft #	3.11 ± 0.84	3.09 ± 0.74	3.17 ± 0.66	0.888
	n (%)	n (%)	n (%)	P-value**
Patient total	47 (100.0)	53 (100.0)	42 (100.0)	
Male sex	37 (78.7)	41 (77.4)	36 (85.7)	0.565
Diabetes mellitus	21 (44.7)	22 (41.5)	15 (35.7)	0.686
Hypertension	32 (68.1)	33 (62.3)	31 (73.8)	0.488
Dyslipidemia	16 (34.0)	21 (39.6)	17 (40.5)	0.786
Peripheral arterial disease ^a	10 (21.3)	12 (22.6)	12 (28.6)	0.695
Renal dysfunction	2 (4.3)	3 (5.8)	4 (9.8)	0.056
Hepatic dysfunction	-	5 (9.4)	1 (2.4)	0.05
COPD/asthma	9 (19.1)	11 (20.8)	12 (28.6)	0.527

*: Kruskal–Wallis test, **: chi-square test.

^a: History of therapeutic vascular intervention, history of claudication, or angiography/noninvasive proven peripheral arterial disease. EC: electrocauterization, ORC: oxidized regenerated cellulose, BMI: body mass index, LVEF: left ventricular ejection fraction, CPB: cardiopulmonary bypass, COPD: chronic obstructive pulmonary disease.

Table 2. Comparison of the 3 groups by postoperative variables.

Drainage	Bone wax + EC Mean ± SD	ORC + EC Mean ± SD	EC Mean ± SD	P-value*
1 hour (mL)	138.83 ± 77.99	99.25 ± 36.45	194.79 ± 51.98	<0.001
2 hours (mL)	213.30 ± 103.76	131.04 ± 39.41	307.17 ± 151.97	<0.001
3 hours (mL)	252.34 ± 57.93	191.06 ± 39.84	293.86 ± 91.52	<0.001
6 hours (mL)	352.94 ± 67.71	243.92 ± 42.26	375.71 ± 113.46	<0.001
12 hours (mL)	477.36 ± 83.71	287.43 ± 40.26	472.17 ± 139.72	<0.001
24 hours (mL)	622.15 ± 102.71	353.00 ± 49.48	695.88 ± 199.98	<0.001
FFP used	1.87 ± 0.76	1.60 ± 0.49	2.52 ± 0.55	<0.001
ES used	2.62 ± 0.61	1.62 ± 0.59	2.83 ± 0.49	<0.001
	n (%)	n (%)	n (%)	P-value**
Patient total	47(100.0)	53 (100.0)	42 (100.0)	
Reexploration for hemorrhage	-	-	3 (7.1)	0.026

*: Kruskal-Wallis test, **: chi-square test.

EC: electrocauterization, ORC: oxidized regenerated cellulose, FFP: fresh frozen plasma, ES: erythrocyte suspension.

effect, some also have wound healing and antiinfective properties (5). In this context, bone wax may be considered as an agent physically preventing bleeding; oxidized cellulose and electrocauterization are hemostatic agents.

Electrocauterization (unipolar or bipolar) is a popular method in terms of preventing surgical bleeding. It is generally used for soft and adipose tissues. Although electrocauterization is very effective on the soft tissue, it is ineffective on the bone tissue. Bipolar cautery is most frequently used for coagulation of the small vessels and has minimal efficacy on diffuse capillary bleeding, as in the case of sternal intramedullary bleeding.

Profuse bleeding from the sternal marrow after sternotomy is routinely controlled with bone wax in many heart centers. It is effective, cheap, and therefore favorable (6). However, some constituents of wax material are not absorbed by spongy tissue and bacterial implantation may occur. Complications have been reported considering the bone wax used as a physical barrier to aid hemostasis on the surface edge of sternum (3). Bone wax may produce a giant cell reaction, which may subsequently lead to any form of sarcoma induction in humans and also to a fibrous reaction that could prevent osteosynthesis (3). It inhibits osseous fusion and may promote infection formation (6). Authors conclude that it should be used sparingly and suggest avoidance of excessive application of bone wax to prevent sternotomy dehiscence (3,6). Increased risk of mediastinitis with wax use was reported (3). Bone wax should not be used excessively and should be avoided in patients at high risk for infection (6). In particular, bone wax might not even be effective in elderly patients and those with osteoporosis. The spongiosa scaffold of the marrow cavity might absorb large quantities of bone wax with still enhanced bleeding. Prziborowski et al. reported that bone wax is not an independent risk factor concerning early resternotomy, sternum stabilization, sternal infection, early mortality, and blood and blood product consumption (7). Conversely, Mair et al. showed that it inhibits osseous fusion, causes infections, and may even be responsible for embolization from sternotomy incisions to the lung (8). We did not encounter any wound infections or sternal instability due to wax use in our study.

ORC was developed in 1960 and it was manufactured from wood pulp, which contains about 50% cellulose. It generates an artificial clot lowering pH and causing a caustic effect (9). The clot is brownish because it has acid hematin (10). It has different mechanisms of action. It creates a physical and a mechanical barrier. It absorbs serum and expands. It returns to the gelatinous formation. It activates extrinsic hemostatic pathway and platelets. The most important advantage of the ORC is definitely its resistance to the pathogenic organisms in vivo and in vitro (9). This product is applied topically and can effectively control diffuse capillary oozing (11).

Supporting the osteoinductive effect of ORC, Mair et al. placed ORC strips to the preoperatively existent sternal fractures in 38 patients with weak sternal bones. None of the patients required reoperation for bleeding or sternal instability. They reported that superficial wound infection developed in 2 patients, who were treated with topical dressing, and deep sternal wound infections did not occur (8).

It is different from the bone wax because it is absorbed (11). Since it is a chemically altered form of cellulose, it is first dissolved and then turned into a continuous fiber (12). It is supplied as a knitted strip that can be easily trimmed to any size. It swells and expands to the sternal corpus. One major advantage of oxidized cellulose over wax is its definite and potent action against a wide variety of pathogenic organisms, both in vivo and in vitro. This beneficial effect is immediate and is exerted by a low pH effect. The current theory is that this chemical hemostasis reduces the effective initial inoculum with an acid hostile ambient, allowing the host's natural defenses to overcome the organism (13). It has also been shown to reduce *Staphylococcus aureus* growth in in vitro set-ups (14).

For comparison of wax and ORC, Finn et al., in an experimental study, produced surgical defects in the iliac crests of 4 dogs. Bone wax caused a marked foreign-body reaction and lack of bone reformation. They concluded that ORC might be adequately used in iliac bone procurement, whereas wax seemed to be contraindicated (15).

The present study clearly demonstrates that ORC decreases sternal intramedullary bleeding and does not increase the infection rates. The reexploration rates were also shown to be decreased with ORC use. When the number of fresh frozen plasma and erythrocyte suspensions used were studied, the requirements were lowest in the ORC group compared to others. However, there are many factors affecting postoperative blood and its products use, and those many parameters were not taken into account during the study, so any conclusion related with this subject derived from these data could not be made.

In conclusion, hemorrhage originating from the sternal intramedullary space may cause too much blood loss, which may or may not necessitate revision. To overcome this undesired complication, ORC concomitant with electrocauterization can be used safely immediately before closing the chest in open heart surgery.

Although the exact origin of bleeding cannot be determined unless revision is not required due to excessive blood loss, the homogeneity of the data was maintained to overcome bias. Cost analysis was not made during the study, which could have reflected the cost-effectiveness of ORC use more objectively. Additionally, regarding the use of blood and its products, more variables should be taken into account.

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