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Impact of Postoperative Hypothermia on Bleeding Postoperatively in Coronary Artery Bypass Surgery

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Abstract

Background: Hypothermia is known for its adverse effects on coagulation cycle that could be of clinical significance for patients undergoing elective coronary artery bypass surgery.

Aim of Study: The aim of this prospective study was to evaluate the influence of core temperature on postoperative amount of blood loss, transfusion requirements, coagulation profile and the length of hospital stay in patients undergoing elective on pump coronary artery bypass grafting operations

Patients and Methods: As regarding the methodological approach for the intended research, well formulated objectives are made with study design of prospective observational comparative study at Ain Shams University cardiothoracic hospital, from May 2022 till August 2022. Regarding the sample size: By using PASS 11 program for sample size calculation, setting power at 99%, alpha error at 5% and after reviewing previous study results showed that the amount of blood loss was significantly larger in hypothermic group (185.667±41.34) compared with normothermic group (516.033 ±41.536). Based on that: A sample size for 60 patients undergoing coronary artery bypass surgery (divided into 2 groups- 30 patients in each group) will be sufficient to achieve study objective. The patients will be divided into 2 groups. In normothermic group (n=30) patients will be warmed by warming fluids and mattresses warmers, however patients whom belong to the hypothermic group (n=30), will be allowed to develop hypothermia. Exclusion criteria includes patients with pre-existing hypothermia (<36 C) or hyperthermia (>38 C), a postoperative temperature >38 C.

Results: The amount of blood loss (bleeding) was much larger in hypothermic group than normothermic group ($p<$). The amount of blood units transfused was significantly higher in hypothermic group than normothermic group. The PTT and PT were more prolonged in hypothermic group compared with normothermic group. There was a noticed correlation as in increased length of hospital stay in hypothermic group compared with normothermic group.

Conclusion: The study demonstrates that hypothermia is associated with increased amount of postoperative bleeding/blood loss and the number of blood units transfused in patients underwent elective on pump coronary artery bypass grafting surgery.

Key Words: *Hypothermia – Bypass – Bleeding – Transfusion.*

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Introduction

HYPOTHERMIA is defined as a core body temperature less than 35 **[1]**. Although hypot hermia is known to decrease the metabolicdem and of the body and promotes impairment in various systems causing Decrease oxygen release to tissues.

Hypothermia results in impairment of the coagulation cascade and the white cell count also decreases **[2]**, hypothermia impairs immune function so nosocomialpneumonia will occur in over half of patients who are hypothermic for more than 7 days **[3]**. Hypothermia-induced increase in catecholamines leads to an increase in cardiac output and oxygen demand **[4]**.

As a result of prolonged hypothermia, bleeding time will be increased due to its effects on platelets count and function **[5,6]**. Platelets also are been sequestrated through RES system (liver/spleen) **[7,8,9]**.

Postoperative bleeding and transfusion occur few hours after surgery 6-24 hrs, so we monitor carefully the body core temperature (BMT) in ICU for the first 6 hours postoperatively.

The aim of this prospective study was to evaluate the influence of core temperature on postoperative amount of blood loss, transfusion requirements, coagulation profile and the length of hospital stay in patients undergoing on pump coronary artery bypass grafting surgery.

Patients and Methods

As regarding the methodological approach for the intended research, well formulated objectives are made with study design of prospective observational comparative study.

Regarding the sample size: By using PASS 11 program for sample size calculation, setting power at 99%, alpha error at 5% and after reviewing previous study results showed that the amount of blood loss was significantly larger in hypothermic group (185.667±41.34) compared with normothermic group (516.033±41.536).

Based on that: A sample size for 60 patients undergoing coronary artery bypass surgery (divided into 2 groups - 30 patients in each group) will be sufficient to achieve study objective.

The patients will be divided into 2 groups. In normothermic group (n=30) patients will be warmed by warming fluids and mattresses warmers,however patients whom belong to the hypothermic group (n=30), will be allowed to develop hypothermia. Exclusion criteria includes patients with pre-existing hypothermia (<36C) or hyperthermia (>38C), a postoperative temperature >38C.

Inclusion criteria:

- Age group: Adult patients from age of 45 years to 70 years.
- Sex: Both sexes.
- Elective open heart surgeries for coronary bypass grafting.
- Same cardioplegia of custodial.
- Bypass time less than 3 hours.

Exclusion criteria:

- Patients refuse to givein formed consent.
- Emergency open heart CAB Gsurgeries
- Patients with Renal or hepatic affection leading to coagulation problems and non surgical bleeding measured by lab investigation INR, PT, PTT.
- Previous open heart surgery.
- Patients with known hematological disorder that affects coagulation cascade.
- Patients with echopreop showing EF% less than 35% with normal range for lab investigations of INR, CBC, renal and liver function tests.
- Patients with pre-existing hypothermia (<36C) or hyperthermia (>38C), a postoperative temperature >38C.

Sampling method:

Patients will be randomly allocated by computer generated randomization into two groups A and B, each group includes 30 patients.

- Group A (control): Patients with normothermia.
- Group B: Patients suffering from hypothermia less than 36.

Preanaesthetic check and investigations as CBC, coagulation profile, echocardiography and coronary angiography were done and on night of surgery preoperative evaluation was performed. Priorto anesthesia & induction, a baselineb laboratory evaluation was done including prothrombin time, hemoglobin, hematocrit and renal function tests and liver function tests. Core body temperature, urine output, arterial blood gases, total amount of blood loss and transfusion requirements were monitored during operations. After surgery all patients were transferred to the ICU during the perioperative period.

Measured parameters:

Pre-operative: Assessing the pre op cardiac function & EF and preop INR and liver enzymes, also to assess preop ACT done.

Intra-operative: Assessing the ACT before and after heparin in fusion before bypass and ACT after bypass. Also assessing and comparing cross clamp time and bypass time not exceeding 3 hours comparing results for affecting platelets and coagulopathy.

Postoperative: Assessed postoperative variables included amount of blood loss, length of stay in the ICU, PT and PTT (prothrombin time and partial thromboplastin time).

The time points at which temperature was measured, were 1,2,4,6 and 10 hours postoperatively. Assessing postoperative labs for renal and liver function tests and CBC.

The primary outcome measure is to compare the amount of postoperative blood loss between patients of normothermic group (temp >36C) and hypothermic group (temp <36).

The secondary outcome measure was to compare:

Transfusion requirements, the length of stay in the hospital, ICU stay, Ventilation time, incidence of surgical site infection among the study group, ACT time after bypass surgery in both groups, also comparing postoperative echo follow-up EF%.

In order to measure PT and PTT, blood samples were collected via arterial catheter **[10]**.

Sample size justification:

By using PASS 11 program for sample size calculation, setting power at 99%, alpha error at 5% and after reviewing previous study results (Ali and shokri, 2020) and a previous study by Mircea I, et al. **[11]** showed that the amount of blood loss was significantly larger in hypothermic group (185.667±41.34) compared with normothermic group (516.033±41.536) thus a sample size of 30 patients is pergroup enough to find such a difference.

Statistical analysis:

The collected data was coded, tabulated, and statistically analyzed using SPSS program (Statistical Package for Social Sciences). Descriptive statistics were done for numerical parametric data as mean±SD (standard deviation), while they were done for categorical data as number and percentage. Inferential analyses were done for quantitative variables using in dependent *t*-test in case soft woin dependent groups with parametric data.

Results

The previous table shows that there was no statistically significant difference between normothermic and hypothermic group regarding age, gender, weight, height and BMI of the studied patients.

The previous table shows that there was no statistically significant difference between normothermic and hypothermic group regarding number of stents of the studied patients.

The previous table shows that there was statistically significant difference between normothermic and hypothermic group regarding temperature variations after the first hour in ICU postoperatively of the studied patients.

The previous table shows that there was statistically significant difference between normothermic and hypothermic group postoperative regarding blood lost, postoperative PT, ICU stay, Hospital stay, blood units of the studied patients and No statistically significant difference between normothermic and hypothermic group postoperative regarding sternal wound infection of the studied patients.

The previous univariate logistic regression shows that blood loss >250ml, ICU stay >3 days, hospital stay >8 days and blood units >1 unit were associated with hypothermia. The multivariate logistic regression analysis shows that blood loss >250ml and ICU stay >3 days were the most associated factors with hypothermia.

Table (1): Comparison between normothermic and hypothermic group regarding demographic data of the studied patients.

	Normothermia group No. = 30	Hypothermia group No. = 30	Test value	*p*-value	Sig.
Age:					
Mean ± SD	56.90±6.55	58.37±6.84	–0.848•	0.400	NS
Range	44-69	44-70			
Gender:					
Female	6 (20.0%)	5 (16.7%)	0.111*	0.739	NS
Male	24 (80.0%)	25 (83.3%)			
Weight (kg):					
Mean ± SD	85.07±15.22	81.33±14.78	0.964•	0.339	NS
Range	56-111	55-120			
Height (cm):					
Mean ± SD	165.70±9.59	165.40± 8.04	0.131•	0.896	NS
Range	140-185	144-180			
BMI:					
Mean ± SD	30.96±4.92	29.68±4.75	1.023•	0.311	NS
Range	24.22-41.5	21.8-44.08			

p-value >0.05: Non significant. *p*-value <0.05: Significant. *p*-value <0.01: Highly significant.
*: Chi-square test. •: Independent *t*-test.

Table (2): Comparison between normothermic and hypothermic group regarding number of stents of the studied patients.

No. of stents	Normothermia group No. = 30	Hypothermia group No. = 30	Test value	*p*-value	Sig.
2	4 (13.3%)	7 (23.3%)	1.018*	0.601	NS
3	24 (80.0%)	21 (70.0%)			
4	2 (6.7%)	2 (6.7%)			

p-value >0.05: Non significant.
p-value <0.05: Significant.
p-value <0.01: Highly significant.
*: Chi-square test.

Table (3): Comparison between normothermic and hypothermic group regarding temperature variations in first 6 hours of the studied patients.

Temperature	Normothermia group No. = 30	Hypothermia group No. = 30	Test value	*p*-value	Sig.
Post T0:					
Mean ± SD	35.30±0.28	35.33±0.32	–0.431•	0.668	NS
Range	35-36	35-36			
Post T1:					
Mean ± SD	36.98±0.18	35.42±0.18	33.834•	0.000	HS
Range	36.7-37.3	35.2-35.7			
Post T2:					
Mean ± SD	37.00±0.20	35.63±0.29	21.150•	0.000	HS
Range	36.6-37.3	35.2-36.1			
Post T3:					
Mean ± SD	37.01±0.14	36.35±0.22	13.759•	0.000	HS
Range	36.8-37.2	35.5-36.6			
Post T4:					
Mean ± SD	37.02±0.19	36.81±0.20	4.149•	0.000	HS
Range	36.7-37.3	36-37			
Post T5:					
Mean ± SD	37.10±0.19	36.74±0.65	2.961•	0.004	HS
Range	36.8-37.4	36.2-39.9			
Post T6:					
Mean ± SD	37.06±0.25	36.88±0.16	3.288•	0.002	HS
Range	36.7-37.5	36.6-37.2			

p-value >0.05: Non significant.
p-value <0.05: Significant.
p-value <0.01: Highly significant.
*: Chi-square test.
•: Independent *t*-test.

Table (4): Comparison between normothermic and hypothermic group regarding blood lost, postoperative PT, ICU stay, Hospital stay, blood units, sternal wound infection of the studied patients.

	Normothermia group No. = 30	Hypothermia group No. = 30	Test value	*p*-value	Sig.
Blood loss (ml):					
Median (IQR)	150 (100-200)	375 (250-500)	–4.858	0.000	HS
Range	50-300	50-600			
Post PT:					
Median (IQR)	11.90±1.39	17.38±1.76	–13.429•	0.000	HS
Range	10-14	14-20			
ICU stay (days):					
Median (IQR)	3 (2-4)	5 (4-6)	–5.488	0.000	HS
Range	2-4	3-6			
Hospital stay (days):					
Median (IQR)	7.5 (7-8)	9 (7-10)	–3.146	0.002	HS
Range	6-9	7-10			
Blood units:					
Median (IQR)	1 (0-1)	2.5 (2-3)	–5.203	0.000	HS
Range	0-2	0-4			
Sternal wound infection:					
No	27 (90.0%)	25 (83.3%)	0.577*	0.448	NS
Yes	3 (10.0%)	5 (16.7%)			

p-value >0.05: Non significant. *p*-value <0.05: Significant. *p*-value <0.01: Highly significant.
*: Chi-square test. •: Independent *t*-test. : Mann-Whitney test.

Table (5): Univariate and Multivariate logistic regression analysis for factors associated with Hypothermia.

	Univariate				Multivariate			
	p-value	Odds ratio (OR)	95% C.I. for CR		*p*-value	Odds ratio (OR)	95% C.I. for CR	
			Lower	Upper			Lower	Upper
Blood loss >250 (ml)	0.000	58.000	6.871	489.581	0.026	21.851	1.452	328.842
ICU stay >3 (days)	0.000	17.875	4.738	67.434	0.017	10.117	1.517	67.470
Hospital stay >8 (days)	0.019	3.755	1.239	11.385	0.654	0.648	0.097	4.334
Blood units >1	0.000	21.357	5.534	82.427	0.631	1.661	0.210	13.123

Discussion

The current prospective study, showed that hypothermia was associated with an increased postoperative blood loss and transfusion requirement in patients undergoing elective on pump coronary artery bypass surgery.

In previous study, in a case of on pump CABG, 46.7% of the patients were reported to be hypothermic after leaving the operating room. A part from its beneficial influence of providing.

Organ protection against ischemia-reperfusion injury, hypothermia is associated with multiple adverse physiologic alterations in terms of coagulation, hypothermia has been shown to be associated with platelet dysfunction as well as a mild decrease in platelet count **[12]**. Proposed mechanisms include impaired thromboxane A2 release and in habited exposure of P selectin on platelet surface **[13]**. Moreover, hypothermia has been shown to inhibit coagulation enzyme activities delaying the onset of thrombin generation **[14]**. Hypothermia is also accompanied by acidosis which in turn results in profound inhibition of thrombin generation in the propagation phase in a previous study **[15]**. Even mild hypothermia (<0.5ºC) has been shown to be associated with increased blood loss and transfusion require ments in patients undergoing hip arthroplasty of particular interest, a follow-up study reported that aggressive.

Warming reduced blood loss during the some surgical procedure implicating that hypothermia may be a modifiable risk factor of perioperative bleeding and transfusion requirement.

Another study by Mircea, et al., Howed that that postoperative bleeding and transfusion requirements were significantly greater in hypothermia group (p=0.02, p=0.03 respectively, this agreed with our results **[11]**.

A meta analysis based on literature indicates that mild hypothermia significantly increases blood loss by on estimated 16% (CI4-26%) **[16]**.

Another study by Muhammad, et al., showed that systemic warming of the surgical patient is also associated with less perioperative blood loss through preventing hypothermia induced coagulopathy **[17]**.

Nathan H, et al., showed that there was no significant difference in blood product utilization, intubation time, hospital stay, myocardial infarction, or mortality. The mean time in the intensive care unit was 8.4 hours less in the hypothermic group **[18]**, The results of this study were inconsistent with our study.

Multivariate analysis determined that a single intraoperative temperature measurement less than 35°C in dependently increased thesite infection risk 221% perdegree below 35°C,but this did not agree with our study **[19]**.

In our study the amount of postoperative blood loss were significantly greater in the hypothermic group and that agreed with the other studies mentioned before.

Our data showed that the whole body mild hypothermia prolonged APTT and PT consistent with previous studies **[11,15-17]** that demonstrated that mild hypothermia resulted in platelet dysfunction and decreased platelet count.

Conclusion:

This study suggested that postoperative hypothermia assessed by corebodytemp. Was associated with increased blood loss and transfusion requirements and prolonged PT and PTT in patients undergoing elective on pump coronary artery bypass surgery.

Considering the high prevalence of hypothermia and the possibility of hypothermia being a modifiable risk factor of transfusion requirement more aggressive measures should be taken to maintain normothermia in patients undergoing cardiac surgery for better outcomes.

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تأثير انخفاض درجة حرارة المريض على النزيف ما بعد عملية جراحة القلب المفتوح لترقيع الشرايين التاجية للقلب

يُعرف انخفاض حرارة الجسم على أنه درجة حرارة الجسم الأساسية التى تقل عن على الرغم من أن انخفاض حرارة الجسم معروف بقدرته على تقليل الطلب الأيضى للجسم وتعزيز ضعف الأنظمة المختلفة مما يؤدى إلى تقليل إطلاق الأكسجين إلى الأنسجة.

يؤدى انخفاض حرارة الجسم إلى ضعف شلال التخثر وانخفاض عدد الخلايا البيضاء أيضاً، كما يؤدى انخفاض حرارة الجسم إلى إضعاف وظيفة المناعة، لذلك سيحدث الالتهاب الرئوى فى المستشفى لأكثر من نصف المرضى الذين يعانون من انخفاض درجة حرارة الجسم لأكثر من ٧ أيام. تؤدى الزيادة فى الكاتيكولامينات التى يسببها انخفاض الحرارة إلى زيادة النتاج القلبى والطلب على الأكسجين.

نتيجة للانخفاض المطول فى درجة حرارة الجسم، سيزداد وقت النزيف بسبب تأثيره على عدد الصفائح الدموية ووظيفتها. يتم عزل الصفائح الدموية أيضاً من خلال نظام RES (الكبد / الطحال).

يحدث النزيف ونقل الدم بعد الجراحة بساعات قليلة من ٦ إلى ٢٤ ساعة، لذلك نراقب بعناية درجة حرارة الجسم الأساسية فى وحدة العناية المركزة لمدة ساعات بعد الجراحة.

كان الهدف من هذه الدراسة المستقبلية هو تقييم تأثير درجة الحرارة الأساسية على كمية الدم المفقودة بعد الجراحة، ومتطلبات نقل الدم، وملف التخثر، ومدة الإقامة فى المستشفى للمرضى الذين يخضعون لتطعيم مجازة الشريان التاجى.

فيما يتعلق بالمنهج المنهجى للبحث المقصود، يتم وضع أهداف مصاغة جيداً مع تصميم الدراسة للدراسة القائمة على الملاحظة المقارنة.

نتائج دراستنا الحالية:

- كانت كمية الدم المفقودة أكبر بكثير فى المجموعة منخفضة الحرارة منها فى المجموعة السوية (القيمة الاحتمالية = ٠.٠٠٠).
- كان عدد وحدات الدم التى تم نقلها أعلى فى المجموعة منخفضة الحرارة عنها فى المجموعة السوية ($p = 0.000$).
- تم إطالة زمن PT بشكل معنوى فى المجموعة المنخفضة الحرارة مقارنة بمجموعة درجة الحرارة العادية (قيمة $p = 0.000$).
- كانت هناك زيادة فى مدة الإقامة فى المستشفى فى المجموعة منخفضة الحرارة مقارنة بالمجموعة العادية (قيمة $p = 0.002$).
- لا توجد فروق ذات دلالة إحصائية فى وقوع عدوى الجروح القصبية بين مجموعات الدراسة.