Effect of hypothermic versus normothermic cardiac bypass in patients undergoing coronary artery bypass grafting surgery on coagulation: a randomized controlled trial

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Objectives
To assess and compare early postoperative (PO) hematological and coagulation profile of patients undergoing on-pump coronary artery bypass grafting surgery with hypothermic (HT) versus normothermic (NT) cardiopulmonary bypass.
Patients and methods
A total of 86 patients were divided into two equal groups: NT group included patients who received warm bypass and HT group included patients who received cold bypass. PO monitoring included changes in 2-h PO hematological and coagulation profile in relation to preoperative profile and amount of PO daily blood loss and number of transfused blood units and its relation to change in coagulation profile.
Results
Mean activated clotting time estimated before wound closure was significantly longer in patients of HT group. At 2-h PO, hemoglobin concentration and platelet count (PC) were significantly lower, ADP-induced platelet aggregation (IPA) was significantly decreased, whereas activated partial thromboplastin time (aPTT) and international normalized ratio (INR) were significantly increased in HT patients. Estimated activated clotting time, IPA, INR, aPTT, and PC showed a negative significant correlation with the use of HT. The amount of PO daily bleeding and number of transfused units showed a positive significant correlation with the use of HT, 2-h PO aPTT, and INR, whereas showed a negative significant correlation with 2-h PO estimated IPA and hemoglobin concentration Regression analysis and receiver operating characteristic curve analysis defined the use of HT and prolonged aPTT as significant predictors for development of PO bleeding.
Conclusion
On-pump coronary artery bypass grafting surgery deleteriously affects hematological and coagulation profiles of patients, and this effect was accentuated by the use of HT. Two-hour PO altered PC and function and prolonged clotting times correlated with amount of PO daily bleeding and number of transfused blood units, but prolonged aPTT is the best predictor for these events.

Keywords:
coronary artery bypass grafting surgery, coagulation profile, cold blood cardioplegia, platelet function

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Introduction

Coronary artery bypass grafting (CABG) is a common procedure to circumvent the obstruction of coronary arteries when stents are unsuitable [1]. Bleeding complications after cardiac surgery are common and are associated with increased morbidity and mortality [2]. However, routine laboratory tests have been demonstrated to have a low ability to predict perioperative bleeding [3].

Etiology of surgical bleeding complications is multifactorial, and treatment decisions are time sensitive [2], so better understanding of hemostatic function during surgery would lead to identification of high-risk patients for bleeding [3]. CABG is a very traumatic surgery, and hemodilution, hypothermia (HT), fibrinolysis, and acidosis showed differential effects on clot formation and platelet function [4].

Maintaining perioperative normothermia (NT) reduces blood loss and transfusion requirement by

clinically important amounts [5]. Mild therapeutic HT is considered standard care in the treatment of patients resuscitated from cardiac arrest [6]; however, even mild HT (<1°C) significantly increases blood loss by ~16% and increases the relative risk for transfusion by ~22% [5]. The relationship between deep HT duration and perioperative bleeding is dependent on cardiopulmonary bypass (CPB) time [7].

In cardiac surgery, blood loss is directly influenced by reduced pre-CPB thrombin generation rate, increased post-CPB consumption and dilution of clotting factors, as well as inadequate post-CPB clot stabilization [8]. Impaired platelet function may underlie bleeding associated with CPB [9], and the effects of HT on platelet function have been studied [6], but the results are inconsistent and may be related to the circumstances during which HT is achieved [6] or is incompletely evaluated with existing diagnostic technologies [9].

Hypothesis

HT may alter coagulation profile of patients undergoing CABG surgery, thus, affecting patients' outcome.

Aim

The study aimed to assess and compare the immediate postoperative (PO) hematological and coagulation profile of patients undergoing on-pump CABG with cold versus warm CPB.

Design

A prospective randomized, controlled, double-blinded clinical trial was conducted,

Setting

The study was conducted at the Departments of Anesthesia and Cardiac Surgery at Nasser Institute and Clinical Pathology at Cairo University Hospitals.

Patients and methods

This randomized controlled study was conducted in Departments of Anesthesia and Cardiac Surgery and Clinical Pathology at Nasser Institute and Cairo University Hospitals from February 2019 till June 2019, after approval of the Ethical committee and written patients consent concerning anesthetic and surgical procedures and mode of CPB fluid temperature. Study was registered in ClinicalTrials.gov (ID: NCT04148404).

Patients were allocated to the study groups using a computer-generated random list, and the group assignments were sealed in opaque envelopes that were opened after the induction of anesthesia.

Inclusion criteria included patients with ischemic heart disease of both sexes, aged 50–65 years, who were assigned for first-time, elective and isolated on-pump CABG surgery. Exclusion criteria included pre-existing coagulopathy, hemostasis disorders, anemia, redo or emergency CABG, re-exploration for surgical-cause PO bleeding, other associated pathologies, hepatic or renal impairment, and/or maintenance on antiplatelet therapy during the last 10 days before surgery. A total of 86 patients who fulfilling the inclusion criteria were randomly, using sealed opaque envelopes prepared by an assistant blinded about the study targets and chosen by patient him/herself, allocated into two groups:

(1) NT group included patients who underwent CABG under warm CPB using warm blood cardioplegia (NT CBP).
(2) HT group included patients who underwent CABG under cold CPB using cold blood cardioplegia (HT CBP).

Preoperative assessment included collection of demographic data, ASA grading, clinical findings, and grading of angina according to the Canadian Cardiovascular Society classification, and cardiac function was assessed using the New York Heart Association classification and by preoperative determination of the ejection fraction (EF%) by echocardiography. All patients underwent preoperative laboratory tests including full blood count, induced platelet aggregation (IPA) test using ADP-stimulated platelet aggregometry, activated clotting time (ACT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT).

Collected operative data included number of vessels grafted, aortic cross-clamp time, CBP time and total operative time, and frequency of the need for transfusion of blood or blood product. PO collected data included PO blood loss as judged by the amount collected through chest tube drainage since chest wall closure till time of its removal, transfusion requirement as judged by number of units and type of blood products used, and the frequency of chest re-exploration for bleeding.

Anesthetic technique

All patients were premedicated with oral diazepam (0.1 mg/kg) the night before surgery and

intramuscular morphine (0.1 mg/kg) before transfer to the operating theater. Anesthesia was induced with fentanyl (0.002–0.005 mg/kg) and propofol (1–2 mg/kg) or midazolam (0.15 mg/kg) in patients with left ventricular EF less than 35%. Muscle relaxation was provided by intravenous pancuronium bromide (0.1 mg/kg). Anesthesia was maintained with incremental doses of fentanyl up to 0.015 mg/kg, and isoflurane 1–1.5% before and after bypass, and an infusion of propofol in a dose of 6–10 mg/kg/h during bypass. Muscle relaxation was provided with pancuronium according to requirements. No patients had isovolumic hemodilution or received perioperative antifibrinolytic drugs.

Surgical protocol

All patients underwent surgery through a full median sternotomy. The left internal thoracic artery was harvested in each patient with a conventional pleurotomy access. Additional conduits were obtained by harvesting the radial artery, or segments of the great saphenous vein.

Cardiopulmonary bypass

CPB was instituted using ascending aortic cannulation and two-stage venous cannulation of the right atrium. A standard circuit was used: Dideco tubing set, Stockert roller pump, and a hollow-fiber membrane oxygenator (Sorin Biomedica, Midhurst, UK). The extracorporeal circuit was primed with 1500 ml of Ringer's solution, 0.5 g/kg mannitol 20%, and 10 000 IU of heparin. Nonpulsatile flow was used, and flow rates throughout bypass were 2.4 l/m^2/min. On completion of all distal anastomoses, the aortic cross-clamp was removed, and the proximal anastomosis was performed with partial clamping.

Normothermic technique

Intermittent warm blood cardioplegia was conducted for patients of NT group as described by Calafiore *et al.* [10] using blood taken directly from the oxygenator and infused into the aortic root by means of a roller pump, and potassium solution (1 mmol of potassium/ml) was given using a syringe pump. The first dose of blood was given through 2 min at a flow rate of 200–300 ml/min; the syringe pump rapidly pushed 2 ml of the potassium solution in about 20 s, and then the blood flow rate was adjusted at 150 ml/ min for a final concentration of about 20 mmol. Every 10 min, another dose was given at a flow rate of 200–300 ml/min of blood and 120 ml/h of potassium solution for 2 min with keeping systemic temperature more than 35°C although the operation.

Hypothermic technique

Cold blood cardioplegia was conducted for patients of HT group as described by Robinson *et al.* [11] using a mixture of blood and cold crystalloid in a ratio of 3 : 1, respectively provided at a rate of 10–15 ml/kg for induction with 30 mEq/l of potassium, sodium bicarbonate 13 mEq/l, and magnesium 1 mg/l, with 60 mg xylocaine injected into the aortic root after aortic cross-clamping. Every 30 min during aortic cross-clamping, the same mixture was given at volume of 10 ml/kg with topical myocardial cooling to keep systemic temperature in range of 30–32°C.

Anticoagulant therapy

In both groups, heparin was administered before distal transection of the left internal mammary artery in a dose of 300 IU/kg to achieve a target ACT of more than or equal to 480 s before commencement of CPB, and additional 5000 IU of heparin was administered to achieve the targeted ACT. ACT was monitored every 30 min during the bypass period, and an additional 5000 IU of heparin was administered if required. On completion of all anastomoses, heparin was reversed with protamine sulfate at a ratio of 1 mg : 100 IU, with further doses of 25 mg protamine given to obtain an ACT equal to baseline.

Fluid management

The extracorporeal circuit was primed with 1500 ml of Ringer's solution, 0.5 mg/kg mannitol 20%, and 10 000 IU of heparin. During CPB, when additional volume was required, Ringer's solution was administered if the hematocrit level was more than 22% or red blood cell concentrates (PRCs) were given if the hematocrit level had dropped below 22%. PO, Ringer's solution was infused at a rate of 1 ml/kg/h. To manage hypovolemia, hydroxy-ethyl starch 130/0.4 (Voluven 6%; Fresenius Kabi, Egypt) in dose less than 1500 ml during the first two PO days or Ringer's solution was given if hematocrit level above 24% or red blood cell concentrates (PRCs) if a hematocrit level dropped below 24%.

Postoperative monitoring and management of bleeding

Postoperative monitoring

A minimum of two chest drains were placed in the mediastinum and left pleura whenever the internal thoracic artery was harvested. Continuous negative pressure suction at −10 to −20 mmHg was applied to the drains to ensure tube patency. PO blood loss was measured and recorded hourly immediately after ICU admission, and drains were removed when amount of drainage was less than 100 ml during the last 12 h. On

ICU arrival, all patients underwent estimation of platelet count (PC), INR, aPTT, and full blood count.

Management of bleeding

Bleeding management was indicated if there was excessive bleeding, defined as chest tube drainage of more than 150 ml/h over two consecutive hours, elevation of ACT values for more than 30 s compared with baseline ACT, PC <80.000/μl, and/or hematocrit value was less than 24%. Surgical re-exploration for bleeding was indicated if there is blood loss of more than 500 ml during the first PO hour, more than 300 ml for two consecutive hours, more than 200 ml for three consecutive hours, or 100 ml/h in an increasing not decreasing manner or collection more than 1 l during the first eight-PO hours. Moreover, a falling hematocrit level, a rising central venous pressure, and hemodynamic compromise are another indication for decision making concerning re-exploration.

Laboratory parameters

Blood sampling

Preoperative blood samples were collected by clean venipuncture 24 h before surgery, whereas PO samples were obtained from the central venous catheter (first 10 ml discarded) at 2, 12, and 24-h PO. Samples obtained for platelet aggregation were obtained immediately preoperative by clean venepuncture and 2-h PO from the central line.

Assay methods

Hemoglobin, hematocrit, PCs, and MPV were measured with a semiautomated blood analyzer Coulter-STKS (Coulter Electronics Inc., Hileah, Florida, USA). All determinations of PT and PTT variables were performed with a fully automated coagulometer (STA4; Diagnostica Stago, Asnier sur Seine, France). The INR was then calculated, based on the International Sensitivity Index of the given thromboplastin reagent.

Study outcomes

Primary outcome included coagulation and hematological profile, which is the amount of blood loss.

Secondary outcomes included amount of blood loss in 24 h PO, frequency and amount of blood transfusion, and the frequency of re-exploration for bleeding.

Statistical analysis

In a pilot study on 10 patients, the ADP-IPA was 57 ±15% in warm blood cardioplegia group, whereas in cold cardioplegia group, it was 44.3±16%. Using MedCalc software, version 14.10.2 (MedCalc software bvba, Ostend, Belgium), it was calculated that a sample size of minimum number of 80 patients (40 patients per group) was calculated to have a study power of 80% and alpha error of 0.05. The number was increased to 86 patients (43 patients per group) to compensate for possible drop-outs.

Results

The study included 86 patients assigned for CABG surgery and were divided into two equal groups.

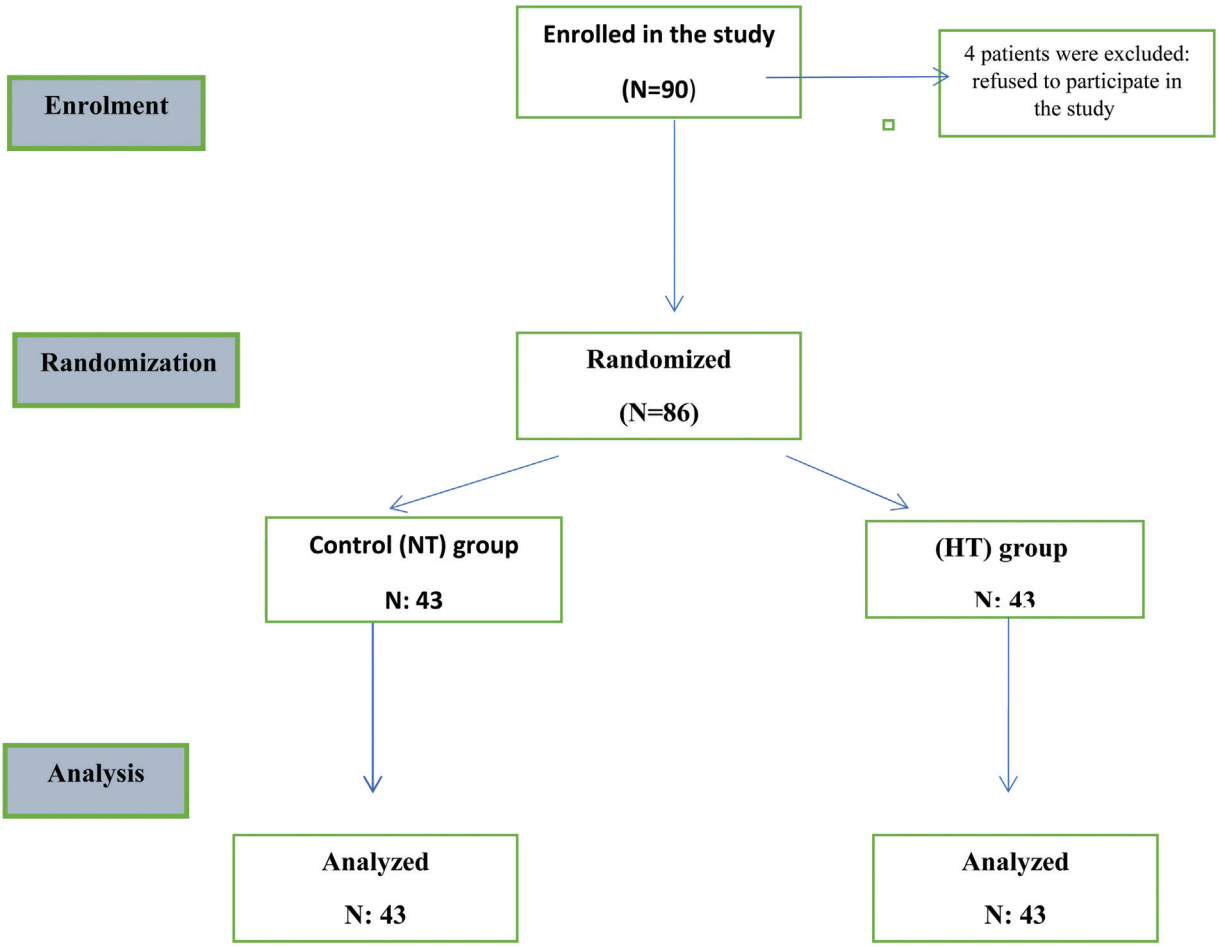
Figure 1 shows consort flow diagram.

Detailed data of enrolled patients as illustrated in Table 1 showed nonsignificant difference ($P>0.05$) between both groups.

Aortic cross-clamping and CPB times were nonsignificantly ($P>0.05$) longer, and number of distal anastomoses was nonsignificantly ($P>0.05$) higher, whereas total operative time was significantly ($P=0.0022$) shorter in patients of NT versus HT group. Mean ACT estimated before sternal wound closure was significantly ($P=0.001$) longer in patients of both groups compared with their preoperative ACT, which showed nonsignificant ($P>0.05$) difference between both groups. Mean ACT time estimated before wound closure was significantly ($P=0.001$) longer in patients of HT group versus NT group. Throughout PO period, PO daily amount bleeding and number of transfused blood product units were significantly higher in patients of HT group versus NT group. However, seven patients required reopening for development of bleeding (two in NT and five in HT groups), with nonsignificantly ($P>0.05$) higher frequency among patients of HT group than NT. Details of operative and immediate PO data of included patients are shown in Table 2.

Hemoglobin concentration (Hb Conc) and PC determined 2-h PO were significantly ($P=0.001$) decreased in patients of both groups compared with their preoperative estimates and were significantly lower in patients of HT group than patients of NT group. The 2-h PO estimated IPA was significantly decreased, whereas aPTT and INR were significantly increased in all patients compared with their preoperative measures. However, such PO changes were significantly worse in patients of HT group versus patients of NT group. Details of PO

Figure 1



Consort flow chart.

laboratory findings in studied patients are shown in Table 3.

Estimated ACT before sternal wound closure, IPA, INR, aPTT, and PC determined 2-h PO showed a negative significant correlation with the use of cold blood cardioplegia, in decreasing order of significance. The amount of PO daily bleeding showed a positive significant correlation with the use of cold blood cardioplegia, 2-h PO aPTT, and INR, whereas showed a negative significant correlation with 2-h PO estimated IPA and Hb Conc, in decreasing order of significance. The amount of transfused blood product units showed a positive significant correlation with the use of cold blood cardioplegia, 2-h PO aPTT, and INR, whereas showed a negative significant correlation with 2-h PO estimated Hb Conc and IPA, in decreasing order of significance (Table 4).

Regression analysis defined the use of HT CPB during CABG surgery and the development of prolonged aPTT as persistently significant predictors for development of PO bleeding complications (Table 5). However, receiver operating characteristic curve analysis defined the development of prolonged aPTT and the use of HT CPB during CABG surgery as the significant sensitive predictors for development of PO bleeding complications (Table 5 and Fig. 2).

Discussion

The current study showed the deleterious effect of on-pump CABG surgery on hematological and coagulation profiles of studied patients manifested as significant decrease of Hb Conc and PC and IPA evaluated 2-h PO with concomitant significant prolongation of ACT and aPTT and increased INR in comparison with preoperative values of these parameters. Similarly, Selimović Čeke *et al.* [12] found the values of aPTT and INR tend to increase immediately after CABG surgery, but the increase was significantly higher with on-pump versus off-pump technique. Moreover, Roy *et al.* [13] reported that on-pump surgery was associated with excessive

fibrinolytic activity immediately after operation, whereas the off-pump patients demonstrated less activation of coagulation and fibrinolysis. Moreover, Lako *et al.* [14] detected that after on-pump CABG, the average values of erythrocytes, Hb Conc, and hematocrit declined to reach lower values on day 3 PO and the average PC decreased to the lowest value on day 2 PO.

Unfortunately, these deleterious effects of on-pump CABG had been worsened by the use of cold blood cardioplegia (HT) that induced more alterations of hematological and coagulation profiles with significant difference in comparison with patients who received warm blood cardioplegia (NT). Moreover, ACT, IPA, INR, aPTT, and PC determined PO showed a negative significant correlation with the use of HT. These findings go in hand with Zentai *et al.* [15], who, using experimental animal model, found HT down to 33.5°C and hemodilution led to severe coagulopathy as measured by thromboelastometry (TEG) and coagulation parameters, and with Brinkman *et al.* [16], who found that in ICU patients admitted after cardiac arrest and treated with mild therapeutic HT, blood samples analyzed at 32°C showed a significant longer clotting time than at 37°C. Moreover, Durila *et al.* [17] detected, in healthy volunteers, that 30°C HT-induced coagulopathy can be detected both by TEG and TEG and be corrected by fibrinogen concentrate. Recently, Van Poucke *et al.* [18] experimentally demonstrated considerable decline in platelet function during HT without uniform recovery of platelet function observed after rewarming. Moreover, Trąbka-Zawicki *et al.* [19] found the use of mild therapeutic HT in patients after out-of-hospital cardiac arrest who are undergoing primary percutaneous coronary intervention was associated

Table 1 Patients' enrollment data

	NT group	HT group	*P* value
Age (years)			
Age group			
≤40	3 (7)	5 (11.6)	0.266
41-59	33 (76.7)	26 (60.5)	
≥60	7 (16.3)	12 (27.9)	
Mean age	53.7±6.8	54.7±7.4	0.708
Sex			
Males	27 (62.8)	25 (58.1)	0.659
Females	16 (37.2)	18 (41.9)	
BMI data			
Weight (kg)	81.9±10.5	80.7±11.2	0.608
Height (cm)	170±3.9	169.4±3.4	0.453
Mean BMI (kg/m^2)	28.3±3.6	28.1±3.5	0.085
Clinical findings			
NYHA class			
I	13 (30.2)	11 (25.6)	0.631
II	30 (69.8)	32 (74.4)	
CCS			
2	28 (65.1)	32 (74.4)	0.348
3	15 (34.9)	11 (25.6)	
EF (%)			
<40	5 (11.6)	8 (18.6)	0.366
>40	38 (88.4)	35 (81.4)	
Mean	51.9±8.9	47±10	0.338

Data are presented as *n* (%) and mean±SD. CCS, Canadian Cardiovascular Society; EF, ejection fraction; HT, hypothermic; NT, normothermic; NYHA, New York Heart Association. *P* value more than 0.05 indicates nonsignificant intergroup difference.

Table 2 Operative and immediate postoperative data of patients of both groups

	NT group	HT group	*P* value
Operative data			
Aortic cross-clamping time (min)	51.5±17.9	48.3±14.2	0.353
Cardiopulmonary bypass time (min)	80.4±20.3	72.4±17	0.080
Total operative time (min)	178±35.1	200±29	0.0022
Number of distal anastomoses	2.9±0.8	2.7±0.9	0.319
ACT (s)			
Preoperative	106.02±14.539	103.79±11.595	0.433
Before sternal closure	133.65±10.312	149.49±7.814	0.001
P value	0.001	0.001	
Bleeding data			
Total bleeding (ml/24 h)	396.7±202	643.7±262	0.001
Transfusion requirement			
PRBC (U)	0.19±0.5	1.09±1.27	0.002
FFP (U)	0.47±1.01	1.93±1.67	0.003
PLTC (U)	1.37±2.37	4.07±5.01	0.002
Total (U)	2.02±2.73	7.09±6.08	0.001
Reopening for bleeding	2 (9.3)	5 (14)	0.236

Data are presented as mean±SD and *n* (%). ACT, activated clotting time; FFP, fresh frozen plasma; HT, hypothermic; NT, normothermic; PLTC; PRBC, packed red blood cells. *P* value more than 0.05 indicates nonsignificant difference. *P* value less than 0.05 indicated significant difference.

Table 3 Laboratory findings determined 2-h postoperative in patients of both groups

Estimated parameters	Time of estimation	NT group	HT group	*P* value
Hb Conc (g%)	Preoperative	13.8±0.55	14±0.47	0. 689
	2-h PO	12.62±1	12.19±1.09	0.001
	P value	0.001	0.001	
Platelet count ($\times 10^9$/l)	Preoperative	273.38±39.59	285.98±29.76	0.336
	2-h PO	188.3±24.7	177.5±23.4	0.041
	P value	0.001	0.001	
ADP-induced platelet aggregation (%)	Preoperative	70.5±15.2	65.5±17.2	0.392
	2-h PO	58.4±13.4	37.7±12.2	0.001
	P value	0.001	0.001	
aPTT (s)	Preoperative	38.35±3.11	39.09±3.49	0.433
	2-h PO	51.91±4.97	64.65±7.27	0.001
	P value	0.001	0.001	
INR	Preoperative	1.16±0.21	1.13±0.15	0.861
	2-h PO	1.378±0.11	1.655±0.18	0.001
	P value	0.001	0.001	

Data are presented as mean±SD. aPTT, activated partial thromboplastin time; Hb Conc, hemoglobin concentration; HT, hypothermic; INR, international normalized ratio; NT, normothermic; PO, postoperative. *P* value more than 0.05 indicates nonsignificant difference. *P* value less than 0.05 indicated significant difference.

Table 4 Correlation between the use of hypothermic cardiopulmonary bypass, 2-h postoperative laboratory findings, amount of daily postoperative bleeding and need for transfusions in patients underwent on-pump coronary artery bypass grafting

	Use of hypothermic CPB	Amount of PO bleeding (ml/24 h)	Number of transfused blood product (U)
Use of hypothermic CPB		0.471 (<0.001)	0.478 (<0.001)
ACT before sternal closure	–0.659 (<0.001)	–0.130 (0.235)	–0.196 (0.379)
2-h PO			
Platelet count	–0.221 (0.021)	–0.134 (0.672)	–0.137 (0.207)
Platelet aggregation	–0.633 (<0.001)	–0.298 (0.005)	–0.306 (0.004)
INR	0.396 (<0.001)	0.350 (0.001)	0.317 (0.003)
aPTT	0.396 (<0.001)	0.529 (<0.001)	0.602 (<0.001)
Hb%	–0.206 (0.057)	–0.283 (0.043)	–0.328 (0.002)

Data are presented correlation coefficient and its *P* values are in parenthesis. ACT, activated clotting time; aPTT, activated partial thromboplastin time; CPB, cardiopulmonary bypass; Hb Conc, hemoglobin concentration; INR, international normalized ratio; PO, postoperative. *P* value more than 0.05 indicates nonsignificant difference. *P* value less than 0.05 indicated significant difference.

Table 5 Regression and receiver operating characteristic curve analyses of the use of hypothermic and 2-h laboratory findings as predictors for development of postoperative bleeding in patients underwent on-pump coronary artery bypass grafting

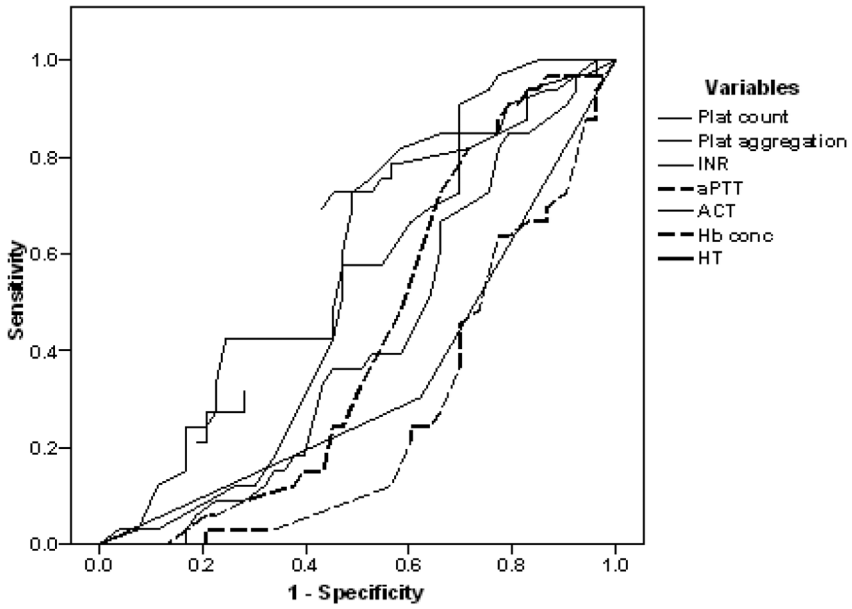
Regression analysis					ROC curve analysis			
Model	Variable	β	*t*	*P*	Variable	AUC (±SE)	*P*	95% CI
1	aPTT	0.366	4.080	<0.001	HT	0.340 (0.06)	0.013	0.221–0.459
	HT	–0.241	4.135	<0.001	ACT	0.524 (0.063)	0.706	0.401–0.648
	Hb%	0.482	–2.864	0.005	Platelet count	0.573 (0.062)	0.258	0.451–0.695
	ACT	0.313	2.849	0.006	Platelet aggregation	0.606 (0.062)	0.100	0.484–0.727
2	aPTT	0.390	4.191	<0.001	INR	0.413 (0.061)	0.178	0.294–0.533
	HT	0.272	2.890	0.005	aPTT	0.264 (0.053)	<0.001	0.160–0.369
	Hb%	–0.215	–2.464	0.016	Hb%	0.428 (0.061)	0.265	0.308–0.548
3	aPTT	0.406	4.252	<0.001				
	HT	0.310	3.238	0.002				
4	aPTT	0.529	5.715	<0.001				

β, standardized coefficient; ACT, activated clotting time; aPTT, activated partial thromboplastin time; AUC, area under curve; CI, confidence interval; Hb%, hemoglobin concentration; HT, hypothermia; INR, international normalized ratio; ROC, receiver operating characteristic. *P* value less than 0.05 indicates significant value.

with a reduced rate of clot formation, increased weakness of clot strength, and disturbances of fibrinolysis.

In a trial to explore the mechanisms underlining these effects of CPB using cold blood cardioplegia, Worel *et al.* [20] found induction of HT caused

Figure 2



ROC curve analysis for the use of HT and postoperative levels of estimated laboratory parameters as predictors for postoperative bleeding. HT, hypothermic; ROC, receiver operating characteristic.

thrombocytopenia, increased fibrin degradation products, prolonged clotting time, alteration in coagulation factors, and increased liver enzymes and assumed that HT-induced liver impairment might play crucial role in coagulation disturbances. Experimentally, De Robertis *et al.* [21] found acidosis and HT progressively impair platelet aggregability and clot formation, where acidosis increases fibrinogen breakdown, whereas HT impairs its synthesis.

The effect of HT was manifested as significantly longer total operative time, secondary to time consumed for hemostasis before wound closure, significantly higher PO daily amount of blood wound drainage and amounts of transfused blood products, and nonsignificantly higher need for reoperation to deal with this bleeding. Moreover, the amount of PO bleeding and transfused blood product showed positive significant correlation with the use HT, PO prolonged aPTT, and increased INR, but negative significant correlation with platelet aggregation.

These correlations coincided with Coakley *et al.* [22] who suggested that preoperative defects in the propagation phase of hemostasis are exacerbated during CPB, contributing to post-CPB bleeding, and with Pekelharing *et al.* [23], who found fibrinogen concentration and aPTT had the best correlation with the amount of first-hour blood loss. Recently, Mazzeffi *et al.* [24] found that after CPB, ADP-induced aggregation correlates with PO bleeding, and Van Poucke *et al.* [25] found arachidonic acid-IPA increases to higher levels during the first 24-h PO, and this might be important for early initiation of antiplatelet therapy after CABG to prevent the possibility of development and control PO bleeding. Moreover, Spiezia *et al.* [26] found lower PO PC is a possible risk factor for PO bleeding and consumptive coagulopathy might cause a strong predisposition to PO bleeding in children undergoing cardiac surgeries with CPB.

Statistical analyses defined prolonged 2-h PO aPTT, among other estimated laboratory parameters, as the most significant independent predictor for the possibility of getting excessive amount of PO bleeding. In line with this finding, Pekelharing *et al.* [23] found TEG did not show better correlation with PO bleeding than conventional clotting tests. Recently, Ranucci *et al.* [27] documented that a combination of aPTT of 50–70 s, INR of 1.5–2.5, and ACT more than 185 s may be useful to manage anticoagulation during postcardiotomy extracorporeal membrane oxygenation, and the best positive predictive value for prompting therapeutic decision is provided by a combination of ACT and viscoelastic tests.

Conclusion

On-pump CABG surgery deleteriously affects hematological and coagulation profiles of patients, and this effect was accentuated by the use of cold

blood cardioplegia. Two-hour PO altered PC and function and prolonged clotting times correlated with the amount of daily PO blood wound drainage and number of blood products units used, but prolonged aPTT is the best predictor for these events.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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