Arterial versus venous blood samples for monitoring of activated clotting time during open heart surgery and its correlation with postoperative bleeding and reopening

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Objective
The aim of this study was to compare between arterial and venous sampling for activated clotting time (ACT) monitoring during cardiac surgery, and to record incidence of postoperative bleeding and reopening in both the situations.

Patients and methods
This prospective, comparative, double-blind study was conducted on 100 patients with heart disease undergoing open heart surgery, using systemic heparinization, cardiopulmonary bypass, and protamine reversal. Patients were randomly allocated into two equal groups. In group I, arterial ACT was used as a guide for heparinization and heparin reversal. In group II, venous ACT was used as a guide for heparinization and heparin reversal. Each patient in both groups had simultaneous arterial and venous ACT carried out at the following time points: baseline, after heparinization, 10 min after heparinization, and after protamine administration. All patients were monitored for the amount of bleeding from the chest tube during the first 3 h postoperatively and the incidence of reopening after surgery for the first 24 h postoperatively.

Results
Baseline venous ACT was significantly higher than arterial ACT, whereas after heparinization and after blood collection, venous ACT became significantly lower. After administration of protamine, venous ACT was nonsignificantly lower than arterial ACT. Blood loss was significantly increased in the venous group than in the arterial group. With regard to the incidence of reopening, there was an increase in the rate of reopening in the venous group than in the arterial group.

Conclusion
There is great individual variability between the venous and arterial ACT measures. The use of arterial samples for ACT measurement had lesser rates of postoperative bleeding and reopening.

Keywords:
arterial activated clotting time, bleeding, open heart surgery, reopening, venous activated clotting time

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Introduction

Anticoagulation is an important step before cardiopulmonary bypass (CPB). The hemostatic management of patients undergoing cardiac surgery is a complex issue, because there is a need to maintain a delicate balance between anticoagulation for CPB and hemostasis after CPB [1]. These two opposing goals must be managed carefully and modified with respect to the patient's initial hematologic status, specific timing during cardiac surgery, and desired hemostatic outcome. Anticoagulation is monitored by activated clotting time (ACT). ACT is usually carried out using venous blood samples. Surprisingly, the arterial samples used for monitoring of ACT showed a great difference. Leyvi and Zhuravlev [2] found that during the period of systemic anticoagulation, there is great individual variability between ACT measures obtained from the venous and arterial samples (aspirated from nonheparinized line) . The aim of this study was to compare between arterial and venous samples in monitoring ACT during cardiac surgery and its correlation with postoperative bleeding and reopening.

Patients and methods

After obtaining institutional ethical committee approval and informed written consent from patients, this prospective, comparative, double-blind study was conducted on 100 patients, 47 male and 53 female, American Society of Anesthesiologists (ASA) II, III, and IV, aged between 16 and 77 years, undergoing open heart surgery using systemic heparinization, CPB, and protamine reversal.

Each patient had simultaneous arterial and venous ACT performed upon at the following time points:

baseline before heparinization, after heparinization, 10 min after blood collection, and after protamine administration.

Then these patients were randomly allocated by sealed envelope assignment into two equal groups:

Group I (50 patients): Arterial ACT was used as a guide for heparinization and heparin reversal.

Group II (50 patients): Venous ACT was used as a guide for heparinization and heparin reversal.

Both groups were monitored postoperatively for:

(1) Amount of bleeding from the chest tube for the first 3 h after surgery (primary outcome)
(2) Incidence of reopening after surgery for the first 24 h.

Patients receiving oral anticoagulants, patients suffering from coagulation abnormalities, patients with liver and/or renal impairment, or patients who received any drugs interacting with heparin, such as acetyl salicylate, ibuprofen, indomethacin, and antiplatelet drugs, were excluded from the study.

ACT values were obtained as part of routine care. Vascular access was obtained; the venous and arterial sheaths were chosen according to the patient's weight. Heparin bolus of 300 IU/kg was administered, aiming to keep the ACT level above 480 s. Heparin was injected into the central line.

ACT was carried out using a dual-chambered Hemochron blood coagulation timing system (Hemochron Model 801) K-ACT (aktalyke) tube-containing activator (14 mg), glass tube with yellow flip in, and barcode label. 2.0 ml blood sample. These tubes were stored at temperature of 15–30°C as recommended by the manufacturer [3].

All surgical procedures were performed by the same surgical team.

All patients were administered general anesthesia, with fentanyl, midazolam, pancuronium, and isoflurane titrated to hemodynamic effects.

All patients were monitored using the standard ASA modalities as well as invasive hemodynamic monitors.

Re-exploration was considered when chest tube outputs were greater than 400 ml/h for 1 h, greater than 300 ml/h for 2–3 h, 200 ml/h for 4 h, or if signs of tamponade or hemodynamic instability developed. Tamponade was considered in the presence of hypotension, tachycardia, elevated filling pressures, increasing inotrope requirements, pulsus paradoxus, and/or equalization of right and left atrial pressures.

Hemodynamic instability was considered when mean blood pressure decreased more than 20% of the original level, heart rate increased more than 20–30% of the original level, and urine output decreased to less than 0.5 ml/kg/h.

Statistical analysis

Analysis of data was performed by using SPSS version 16 (IBM, New York, USA) as follows:

(1) Sample size was calculated according to the primary outcome, which was the amount of bleeding from the chest tube for the first 3 h after surgery.
(2) Quantitative variables were presented as mean ± SD.
(3) Qualitative variables were presented as number and percentage.
(4) Student's *t*-test was used to compare quantitative variable.
(5) χ^2-Test was used to compare qualitative variables.
(6) *P*-value less than 0.05 was considered significant.
(7) *P*-value less than0.01 was considered highly significant.

Results

Demographic characteristics showed nonsignificant difference between groups in terms of age, weight, height, sex, and ASA physical status (Table 1).

Table 2 showed nonsignificant difference between the groups with regard to the type of operation.

Table 1 Demographic characteristics of patients

Item	Group I	Group II	Test of significance	*P*-value
Age (years)	40.56 ± 15.35	42.56 ± 16.42	t = 1.34	0.764
Weight (kg)	78.16 ± 14.96	78.82 ± 13.59	t = 2.56	0.098
Height (cm)	164.69 ± 9.31	163.5 ± 8.555	t = 0.26	0.762
Sex [*n* (%)]				
♂	23 (46)	24 (48)	χ^2 = 0.040	0.841
♀	27 (54)	26 (52)		
ASA [*n* (%)]				
II	12 (24)	10 (20)	χ^2 = 0.39	0.82
III	30 (60)	33 (66)		
IV	8 (16)	7 (14)		

Data are represented as mean ± SD for age, weight, and height and as *n* (%) for sex and ASA. ASA, American Society of Anesthesiologists. *Significant. **Highly significant.

With regard to comparison between arterial and venous ACT, it was found that venous baseline ACT was significantly higher than arterial baseline ACT, whereas arterial ACT after heparin and after blood collection was significantly higher than venous ACT. After administration of protamine, venous ACT was nonsignificantly lower than arterial ACT (Table 3).

With regard to blood loss, there was a significant increase in mean blood loss in group II (448.8 ml) than in group I (380.6 ml) (Fig. 1).

With regard to the incidence of reopening, the study showed a decrease in the rate of reopening in group I (two cases) in comparison with that in group II (five cases).

Table 2 Types of operations

Item	Group I	Group II	χ^2	*P*-value
Aortic valve replacement	9 (18)	6 (12)	0.3	0.75
Mitral valve replacement	11 (22)	14 (28)		
Double valve replacement	7 (14)	7 (14)		
Coronary artery bypass grafting	20 (40)	16 (32)		
CABG+MVR	1 (2)	3 (6)		
Atrial septal defect	1 (2)	3 (6)		
Ventricular septal defect	1 (2)	1 (2)		

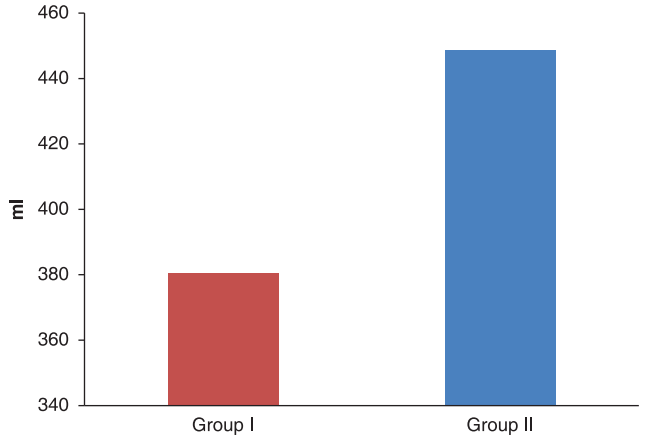
Data are represented as *n* (%). CABG, coronary artery bypass grafting; MVR, mitral valve replacement. *Significant. **Highly significant.

Table 3 Arterial versus venous activated clotting time in group I

Item	Arterial	Venous	*t*-test	*P*-value
Baseline	112.9 ± 13	120.13 ± 15.05	2.57	0.011*
After heparin	636.4 ± 80.7	540.9 ± 130.7	4.4	<0.001**
After blood collection	614.9 ± 132	519.5 ± 104.7	4	<0.001**
After protamine	115.8 ± 20.3	110.45 ± 15.15	1.5	0.14

Data are represented as mean ± SD. *Significant. **Highly significant.

Figure 1



Comparison between groups with regard to blood loss.

Discussion

This study showed that baseline ACT values derived from venous blood samples were higher than those obtained from the arterial line, denoting that the difference was related to the sample site as reported by Leyvi and Zhuravlev [2], who studied anticoagulation in 44 patients undergoing coronary artery bypass grafting, use of CBP and systemic heparinization, and target ACT of 480 s. Venous group baseline showed that the venous ACT measures were statistically significantly higher than the arterial ACT measures, which goes with the present study. Warner *et al.* [4] studied 115 patients who had undergone coronary angioplasty in a catheterization laboratory and received 100 IU/kg of heparin in femoral sheath; the study showed that baseline venous ACT was higher in only 55% of the patients. Pesola *et al.* [5] also found similar results: at baseline, venous ACT was slightly but significantly greater than arterial ACT.

Zisman *et al.* [6] studied ACT in open heart surgery using samples from heparin-flushed arterial line and central venous heparin-free line, and they found baseline arterial ACT to be higher than venous ACT.

After heparin administration, our study showed that arterial ACT samples were significantly higher than venous samples by a difference ranging from 20 to 600 s, as reported by recent studies on adult patients undergoing coronary angioplasty; these studies noted that there are differences between venous and arterial ACT values. Warner *et al.* [4] investigated the variability between samples taken from arterial versus venous blood after one bolus injection of heparin in patients undergoing coronary angioplasty. They found that arterial ACT values were significantly higher than venous ACT values in 70% of the patients.

Zeevi *et al.* [7] conducted studies on a large group of pediatric and adult patients with congenital heart disease undergoing cardiac catheterization to reduce the risk of thromboembolic complications. Systemic anticoagulation was used to maintain ACT above 200 s. They demonstrated that studies on adult patients undergoing percutaneous coronary angioplasty have demonstrated differences in venous and arterial ACT [8,9]. On the contrary, studies on children with congenital heart disease undergoing cardiac catheterization have not made any distinction between arterial and venous ACT values; the mean ACT value at 10 min was above 200 s in both the venous and arterial samples, although there were values below that. At 60 min and above, they administered an additional bolus of 30–75 IU/kg of

heparin, depending on the plan and progress of the procedure. Manspeizer *et al.* [10] examined arterial/venous differences in thromboelastography (TEG). They reported stronger (larger maximal amplitude) and slower (shorter reaction time, *K* value, wider α angle) clot formation in samples obtained from the arterial access compared with those collected from the side port of the pulmonary artery catheter. These investigators suggested that the oxygen content and the viscosity of the arterial blood, or possibly platelet activation associated with the shear stress of the withdrawing of arterial blood through the arterial catheter, could contribute to arterial/venous TEG differences [11].

The research group used the arterial samples to guide protamine administration and return of ACT to baseline in group I, and used venous samples in group II to guide protamine administration and follow-up for ACT. Frumento *et al.* [12,13] showed that arterial/venous TEG differences could be attributable to shear stress. Moreover, they suggested that shear stress causes platelet aggregation and influences TEG values. This effect was most mitigated in samples obtained from the side port of the sheath introducer.

Zisman *et al.* [6] noted a shorter ACT obtained from central venous pressure at baseline. Conversely, any heparin leached from the pulmonary artery catheter could elevate the venous baseline ACT. After systemic heparinization, the effect would be minimized by the large systemic bolus.

After protamine administration (arterial ACT was used as a guide for protamine dose according to heparin response curve) in the arterial group, the results show significant difference between arterial and venous ACT, whereas in the venous group (ACT was used as a guide for protamine dose according to heparin response curve) there was a significant difference between arterial and venous ACT, where ACT in group I was significantly higher.

After protamine reversal, differences between mean arterial and mean venous ACT values and individual differences were minimal, using the Bland–Altman analysis. Perhaps protamine neutralizes any leached heparin as well. The second possible explanation is that CPB platelets are already significantly destroyed so that the effects of shear stress on the ACT are minimized [14].

We followed up on the patients after operation for 3 h in the postoperative care unit with regard to bleeding denoted by collection of blood in chest drains. A comparison was made between the arterial and venous groups, demonstrating that bleeding in the venous group was significantly higher than the arterial group.

Follow-up was also done in postoperative care unit for reopening in the first 24 h, and patients found to have surgical bleeding were excluded from the study.

The research group found that the number of reopened cases in the arterial group was significantly lower than that in the venous group, where three patients in the arterial group were reopened because of nonsurgical bleeding and normal coagulation profile, whereas in the venous group five patients were reopened because of nonsurgical bleeding.

Conclusion

There is great individual variability between ACT measures obtained from the venous and arterial samples. It is clear from these results that the use of arterial samples for ACT measurement had better rates of postoperative bleeding and reopening.

Recommendations

Further studies are required to analyze the cause of differences at different sites and times and the best site for sampling ACT during open heart surgery.

Acknowledgements

Conflicts of interest

None declared.

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