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Minimum discard volume to obtain reliable activated clotting time from the heparinized arterial line

Güvenilir aktive pıhtılaşma zamanı ölçümü için heparinize arter kateterinden atılacak minimum kan miktarı

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Background: This study aims to investigate the reliability of activated clotting time (ACT) by using different discard volumes from the heparinized arterial line.

Methods: Between January 2007 and October 2007, 106 of 116 patients (70 males, 36 female; mean age 55.2±15.3 years; range 18 to 81 years) who met inclusion criteria and underwent cardiac surgery were included. Ninety-one patients underwent coronary artery bypass graft (CABG) surgery, including eight with mitral valve replacement and seven with aortic valve replacement. After control ACT was taken from the arterial line, the line was flushed with saline solution containing heparin at a concentration of 2 IU/ml. Blood samples were taken from the arterial line adding different discard volumes to the dead space. Group names were given according to discard volumes. Dead space plus 2 ml discard volumes (group 2), dead space plus 4 ml (group 4), dead space plus 6 ml (group 6), dead space plus 10 ml (group 10), dead space plus 15 ml (group 15), dead space plus 20 ml (group 20) were defined.

Results: The differences between each of the mean heparinized arterial sample and mean control ACT were; in group 2, 40.1 limits of agreement: +87.8 to –7.6, in group 4, 23.5 limits of agreement: +59.6 to –12.6, in group 6, 16.2 limits of agreement: +49.8 to –17.3, in group 10, 12.5 limits of agreement: +40.1 to –15.2, in group 15, 7.4 limits of agreement: +38.4 to –23.6, in group 20, 5.6 limits of agreement: +29.2 to –18. The differences of 10 ml, 15 ml and 20 ml were not significantly different (p=0.17).

Conclusion: In our study, the mean ACT values of heparinized arterial line samples were higher than control ACT. However, due to the normal values of ACT between 80-120, we accept that minimum dead space plus 6 ml discard volume should be withdrawn.

Key words: Activated clotting time; arterial blood sampling; discard volume; heparin.

Amaç: Bu çalışmada heparinize arteriyel yoldan alınan farklı atık hacim değerleri ile aktive pıhtılaşma zamanı (APZ) güvenilirliği araştırıldı.

Çalışma planı: Ocak 2007 - Ekim 2007 tarihleri arasında kliniğimizde kardiyak cerrahi geçiren 116 hastadan çalışma kriterlerine uyan 106 hasta (70 erkek, 36 kadın; ort. yaş 55.2±15.3 yıl; dağılım 18-81 yıl) çalışmaya dahil edildi. Koroner arter baypas greft (KABG) ameliyatı yapılan 91 hastanın sekizine mitral kapak değişimi, yedisine aort kapak değişimi yapıldı. Arteriyel yoldan kontrol ACT alındıktan sonra, bu hat 2 IU/ml konsantrasyonda heparin içeren salin solüsyonu ile yıkandı. Arteriyel yoldan ölü boşluk hacmine farklı atık hacimleri eklenerek kan örnekleri alındı. Gruplar atık hacimlerine göre adlandırıldı. Ölü boşluk + 2 ml atık hacmi (grup 2), ölü boşluk + 4 ml atık hacmi (grup 4), ölü boşluk + 6 ml atık hacmi (grup 6), ölü boşluk + 10 ml atık hacmi (grup 10), ölü boşluk + 15 ml atık hacmi (grup 15), ölü boşluk + 20 ml atık hacmi (grup 20) olarak belirlendi.

Bulgular: Her iki ortalama heparinize arteriyel örnek ve ortalama kontrol ACT arasındaki farklar; grup 2'de 40.1, kabul sınırları: +87.8, –7.6, grup 4'de 23.5, kabul sınırları: +59.6, –12.6, grup 6'da 16.2, kabul sınırları: +49.8, –17.3, grup 10'da 12.5, kabul sınırları: +40.1, –15.2, grup 15'te 7.4, kabul sınırları: +38.4, –23.6, grup 20'de 5.6, kabul sınırları: +29.2, –18. On mililitre, 15 ml ve 20 ml arası fark istatistiksel olarak anlamlı bulunmadı (p=0.17).

Sonuç: Çalışmamızda heparinize arteriyel yoldan alınan örneklerin ortalama ACT değerleri, kontrol ACT'den yüksekti. Ancak 80-120 arasındaki normal ACT değerlerine göre, ölü boşluk hacmine ek olarak minimum 6 ml atık hacminin çekilmesi gerektiği kabul edildi.

Anahtar sözcükler: Aktive pıhtılaşma zamanı; arteriyel kan örneği; atık hacmi; heparin.

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Simple, rapid, and inexpensive assessment of heparin anticoagulation has been made possible with the introduction of the activated clotting time (ACT),[1-3] which is favored for use in the intensive care unit (ICU) and the operating room. Despite the development of new intravenous anticoagulants that affect the thrombin cascade, unfractionated heparin (UFH) remains the most commonly used agent.[4]

In cardiac catheterization laboratories, interventional radiology units, and operating rooms, blood is often taken from the arterial lines for ACT measurements. These lines are usually kept patent manually or by a device which flushes a continuous infusion of a diluted saline solution containing 1-2 IU/ml of heparin. However, there is concern about possible contamination of the heparin from the flushing solution, which could invalidate the ACT measured in the blood.[5] Some authors have shown that significant contamination may be avoided in the coagulation studies if an initial volume of blood is discarded prior to sampling.[6-8] A review of the literature revealed that to the best of our knowledge, no research exists regarding the accuracy of the ACT obtained from an arterial line that is flushed with a heparinized solution.

This study was designed to assess the effect that heparin in the arterial line flushing solution has on ACT measurements in order to avoid extra costs and unnecessary blood loss. To do this, we examined how the results were affected when different discard volumes were taken from the arterial line which had been flushed with a heparinized solution.

PATIENTS AND METHODS

The Hacettepe University Faculty of Medicine Ethics Committee approved this study, which was conducted on 116 patients undergoing cardiac surgical procedures. Informed consent was obtained from all participants. The study consisted of a prospective, controlled experiment with repeated measures. To be eligible for inclusion, patients were required to meet all the following criteria: have a radial 20-gauge cannula with an internal volume of 0.2 ml (BD FloSwitch, Oxford, UK), be over the age of 18, provide informed consent themselves or a legal representative, have hemoglobin levels >8 g/dL, and have received no heparin by any route for 24 hours.

Ten patients were excluded from the study because of incomplete results while eight were not included due mainly to technical problems. One was under 18 years of age, and one was on subcutaneous heparin therapy. The remaining 106 patients (70 males, 36 female; mean age 55.2±15.3 years; range 18 to 81 years) met the criteria for participating in the study. Ninety-one patients underwent coronary artery bypass graft (CABG), eight had mitral valve replacement (MVR) and seven had aortic valve replacement (AVR).

All of the samples were drawn after the anesthesia induction and the radial artery cannulation, and anesthesia management was no different from normal. Each patient was studied only once. The arterial line flushing solution was prepared as 2 IU/ml, and the lines had to be manually flushed. The dead space from the arterial cannula to the sampling three-way stopcock was measured and found to be 2 ml. The ACT was measured in prewarmed tubes on an ACT machine (Hemocrone Jr, Signature+, ITC, Edison, New Jersey, USA) prewarmed to 37 0C. All the measurements were completed before the systemic heparinization for the surgery.

Experimental volumes were selected after considering the current practice in the study institution and examining the volumes supported in the literature. After the arterial catheter was inserted, the control ACT was drawn from the non-heparinized arterial line. Immediately before taking the other samples and after each sampling, the intraarterial catheter was flushed for three-five seconds using the standard flush solution of 2 IU/ml. A 2 ml blood specimen was sampled from the arterial line after the withdrawal of discard volumes of dead space plus 2 ml, dead space plus 4 ml, dead space plus 6 ml, dead space plus 10 ml, dead space plus 15 ml, and dead space plus 20 ml. Seven consecutive samples were drawn from each patient. All of the discard volumes were returned to the patient via a peripheral venous line. Samples were run on the same channel of the Hemochron analyzer (ITC, Edison, New Jersey, USA) to eliminate the possibility of systematic differences between channels of the machine, and the samples were drawn by the same experienced technician to maintain uniformity in procedure, for example the rate of withdrawal and tube agitation. With the largest discard volume, the sample was assumed to be closest to the control value.

Descriptive statistics on patient characteristics were calculated and expressed as mean, standard deviation (SD), and median to allow comparison with other populations. The differences in the ACT values were calculated for each discard volume by subtracting the ACT obtained from the heparinized arterial line from that of the non-heparinized arterial line. The trends in these values with each increasing discard volume were analyzed using repeated measures of analysis

Table 1. Activated clotting time values

	Control	2 ml	4 ml	6 ml	10 ml	15 ml	20 ml
Mean±SD	103.23±8.61	143.37±24.55	126.75±19.06	119.45±18.00	115.71±14.80	110.61±15.27	108.83±11.65

According to the discard volumes; SD: Standard deviation.

of variance (ANOVA). When the trend was found to be significant, the individual discard volume ACT values were compared with the next level of discard volume using post-hoc contrasts for repeated measures. A p-value of 0.05 was used for the level of statistical significance. Differences between two measurements were expressed graphically using the Bland-Altman plot. All analyses were performed using the Statistical Package for the Social Sciences version 11.5 software program (SPSS Inc., Chicago, Illinois, USA).

RESULTS

All ACT values according to the discard volumes are shown in Table 1. The trend in difference from the control ACT values was statistically significant ($p<0.001$, repeated measures ANOVA) (Figure 1). As expected, an increasing discard volume equated to blood results trending exponentially closer to those of the control sample. The post-hoc tests revealed significantly smaller differences in the ACT with increasing discard volume until 15 ml. The differences between 10 ml, 15 ml, and 20 ml were not significantly different ($p=0.17$, repeated contrast post-hoc) (Figure 1).

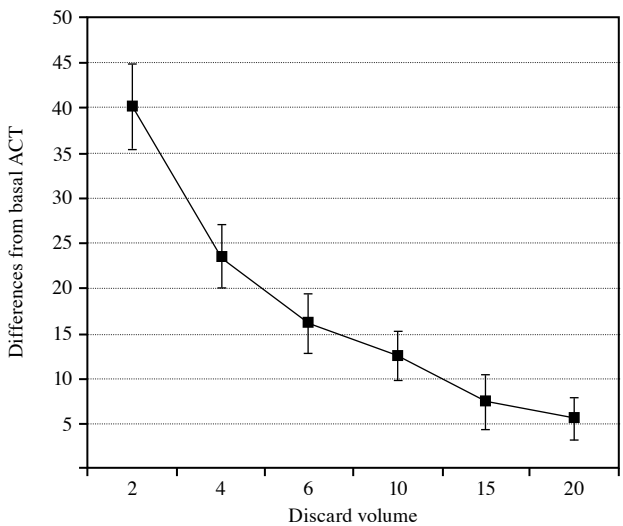

Figure 1. The trend in difference from venous activated clotting time (ACT) values is statistically significant between 4 ml and 6 ml ($p<0.001$, repeated measures ANOVA). The post-hoc tests revealed significantly smaller differences in ACT with increasing discard volume up-till 15 cc. The differences of 10 ml, 15 ml and 20 ml were not significantly different ($p=0.17$, repeated contrast post hoc).

The differences between the 4 ml and 6 ml discard volumes and the mean control ACT are shown graphically in Figures 2 and 3. The biases for samples were the following: 4 ml discard volume: bias +23.5 s, limits of agreement: -12.6 to +59.6 s and 6 ml discard volume: bias +16.2 s, limits of agreement: -17.3 to +49.8 s.

DISCUSSION

Consistent ACT values are important for anticoagulation management during cardiopulmonary bypass (CPB), interventional radiology procedures, and percutaneous transluminal coronary angioplasty (PTCA). Although arterial catheter samples might be contaminated by the heparin flush solution used to maintain patency, it is still a commonly used method of drawing blood for ACT measurements. However, this contamination may cause uncertainties and could lead to administration of excess heparin or protamine, blood product administration, or coagulopathy. This problem can be eliminated by withdrawal of a sufficient quantity of blood that had been discarded before a sample is drawn.

The results of this present study agree with some previous studies. Akıncı et al.[9] reported that it is clinically wise to repeat coagulation studies from a separate venipuncture site when samples drawn from an arterial cannula show abnormal results, even when 10 ml of blood have been discarded. In Laxson and Titler's review,[10] this value was six times that of the dead space volume. Haynes et al.[11] suggested that a

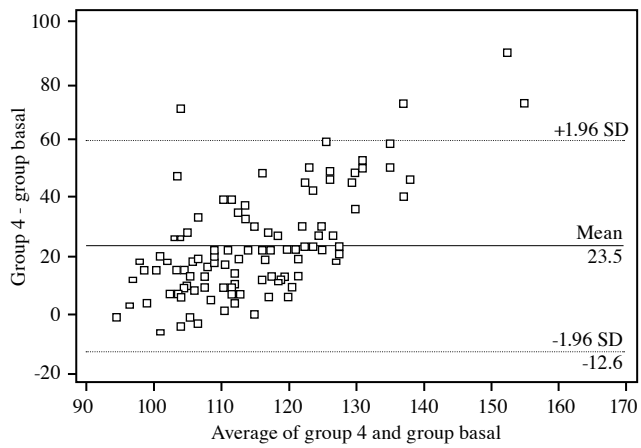

Figure 2. Differences between basal activated clotting time and after 4 ml discard volume activated clotting time. Horizontal lines represent the bias and the limits of agreement. SD: Standard deviation.

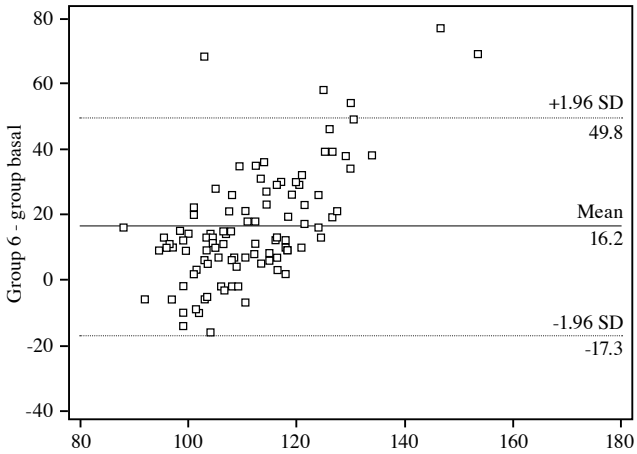

Figure 3. Differences between basal activated clotting time and after 6 ml discard volume activated clotting time. Horizontal lines represent the bias and the limits of agreement. SD: Standard deviation.

separate venipuncture should be used when obtaining blood for coagulation studies, even after withdrawing 5 ml (eight times the dead space volume) of blood from the arterial line before the measurement. We also suggest that a minimum of 6 ml (5.5 times dead space volume) of blood should be withdrawn initially from the arterial line for coagulation studies.

Contrary to our results, Heap et al.[12] reported that blood samples from arterial lines provide valid activated partial thromboplastin times (APTTs) with a discard volume of 4.5 ml (5.6 times dead space volume). Even though Reinhardt et al.[13] found no significant differences in test results between heparin concentrations of 1, 2 or 4 IU/ml, this may be due to the heparin concentrations in the flush solutions. For our study, 2 IU/ml was used, but 1 IU/ml was used by Heap et al.[12]

Heparin type may be another factor which affects the results. There may be functional differences between porcine and beef heparin since they are structurally different molecules.[14,15] We used porcine heparin (Laboratoires PANPHARMA, S.A, Luitré, France), but it is not known which type of heparin was used in the previously mentioned studies.

Repeated manipulation of the three-way tap when sampling with a syringe, as done in our study, could be a factor as it might allow heparin in the flush solution to enter the tap and contaminate the test sample. Heap et al.[12] avoided this unnecessary manipulation for APTT and TT by using the Vacutainer system.

In conclusion, even though what were previously thought to be adequate volumes of blood may be discarded in the procedure for sampling from arterial cannulae, some heparin may still contaminate this blood sample, resulting in a significant likelihood of prolongation of the ACT. It is clinically wise to use a venous line when obtaining blood for the ACT measurement. If there is no alternative other than the arterial line for obtaining blood samples for the ACT, a minimum of 6 ml (5.5 times dead space) of blood should be withdrawn initially.

Declaration of conflicting interests

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