

Coagulation tests and their association with postoperative blood loss after cardiac surgery with cardiopulmonary bypass

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Background. Platelet count (PLT), activated partial thromboplastin time (APTT), prothrombin time (PT) and fibrinogen are standard coagulation tests used for patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).

Materials and methods. 83 adult cardiac surgery patients were enrolled into a prospective study. Blood samples for APTT, PT, PLT, fibrinogen were collected preoperatively (T0), on admission to the intensive care unit (T1), 6 and 24 hours postoperatively (T6, T24). 24-hour postoperative blood loss (24h-PBL) was registered.

Results. The highest APTT mean value was 47 ± 13 sec at T6, increasing from the baseline by 37%. The lowest mean value of PLT was $140 \pm 47 \times 10^9/L$ at T24, decreasing from the baseline by 32.5%. PT and fibrinogen mean values at all time points were within the normal range. Correlation with 24h-PBL was shown by T0 and T6 fibrinogen ($r = -0.5$, $r = -0.4$, $P < 0.0001$) and T6 and T24 PLT count ($r = -0.25$; $P = 0.02$, $r = -0.3$; $P = 0.01$).

Conclusions. Marked changes of coagulation tests from standard values after CPB were shown by APTT and PLT. PLT and fibrinogen may have the possible predictive value for greater 24h-PBL.

Key words: APTT, PT, PLT, fibrinogen, cardiac surgery

BACKGROUND

Bleeding continues to be the first cause for early mediastinal re-exploration and is associated with

worse outcomes (1, 2). Commonly, the coagulation profile is estimated by standard laboratory tests: platelet count (PLT), activated partial thromboplastin time (APTT), prothrombin time (PT) and fibrinogen level. **The purpose** was to evaluate changes of laboratory coagulation tests and their correlation with 24-hour postoperative blood loss (24h-PBL) in patients after cardiac surgery with cardiopulmonary bypass (CPB).

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MATERIALS AND METHODS

The study protocol and the informed consent form were approved by the Ethics Committee of Pauls Stradins Clinical University Hospital.

Patients

83 adult patients (pts), who did not receive perioperatively antifibrinolytic treatment, undergoing cardiac surgery by the use of CPB were enrolled in this prospective observational study. Inclusion criteria were age >18 years, first-time coronary artery bypass grafting (CABG) and/or valve replacement under CPB, EuroSCORE < 10%, coagulation tests within normal ranges at baseline and no anti-coagulants, antiaggregants or non-steroidal anti-inflammatory drugs for at least the last 5 days prior to surgery, in order to disclose drug-induced platelet dysfunction. The last dose of low-molecular-weight heparin (LMWH) was administered in the evening 12 h before the surgery. Exclusion criteria were emergency and redo operations, preoperative hemostatic disorders with a history of hemorrhagic events or coagulopathy and severe renal and/or hepatic dysfunctions.

Perioperative management

All pts underwent similar general anesthesia using fentanyl, etomidate and cisatracurium for induction. Anesthesia was maintained with sevoflurane and supplemented during CPB with fentanyl, propofol and cisatracurium. Before the start of CPB heparin was administered in a dose of 300 to 400 units/kg initially, followed by 5 000 to 10 000 units to maintain an activated coagulation time (ACT) above 480 sec during CPB. After separation from CPB, protamine (1 mg per 100 units of heparin) was administered initially, followed by additional doses until ACT returned to the baseline, or <130 s.

Data collection and analyses

The demographic variables, type of surgery and surgical parameters of each pt were registered. PT, APTT, fibrinogen level and PLT count were measured by standard laboratory methods. For analysis blood samples were obtained at the baseline (day before the surgery – T0), on admission at the intensive care unit (T1), 6 h (T6) and 24 h after surgery (T24). Blood loss was recorded as mL of chest tube drainage (CTD) 24 h postoperatively.

Statistical analysis

Statistical Package for the Social Sciences (SPSS® 18.0) was used.

RESULTS

Clinical course. 83 adult cardiac surgical pts were considered for inclusion (Table 1).

APTT. The preoperative APTT values of all pts were >26 sec; 27 pts had APTT \geq 36 sec compared with the normal value. At T1 25 pts had higher or equal APTT values than the normal value. At T6 mean APTT increased for about 37% from the baseline, when 57 pts had APTT values \geq 36 sec, with mean 47 ± 13 sec. At T24 mean APTT was 38 ± 7 sec, still 51 pts had \geq APTT compared with the normal (Table 2). 24h-PBL did not statistically differ between pts with normal and higher APTT values at different time points, and APTT did not show any correlation with 24h-PBL.

PT. Most of the pts preoperatively had PT within the normal range; PT < 70% was only in 7 pts. At T1 a tendency to have higher PT values was observed, but at T6 and at T24 PT returned to the baseline (Table 2) There were no any correlation between PT and 24h-PBL.

Table 1. Characteristics of patients undergoing cardiac surgery with CPB

Characteristic	Total n = 83
Demographic data	
Age, years	65 \pm 11
Male sex, n, %	42 (51%)
EuroSCORE, %	4.8 \pm 1.8
BSA, m ² (Mosteller)	1.9 \pm 0.2
EF, %	56 \pm 8
Type of surgery, n, %	
Coronary, n, %	34 (41%)
Valve, n, %	31 (37%)
Mixed, n, %	18 (22%)
Surgical parameters	
CPB duration, min	105 \pm 40
Aorta occlusion time, min	66 \pm 27
Reperfusion time, min	34 \pm 15
Heparin, dose, ml	7.6 \pm 1.4
Protamine dose, mg	302 \pm 66
Temperature on CPB, °C	35.3 \pm 0.4

Data are reported as mean \pm SD or number (%).

BSA – body surface area, EF – ejection fraction,

CPB – cardiopulmonary bypass, n – number of patients.

Table 2. Laboratory coagulation tests (APTT, PT, PLT, fibrinogen) mean values at different time points of the perioperative period in patients undergoing cardiac surgery with CPB

Coagulation tests	T0	T1	T6	T24
APTT, sec	34.4 ± 6.9	34 ± 4.8	47 ± 13	38 ± 7
PT, %	89 ± 14	90 ± 12	87 ± 12	88 ± 12
PLT ($\times 10^9/L$)	216 ± 58	144 ± 47	146 ± 49	140 ± 47
Fibrinogen, g/L	4.1 ± 1.3	3.2 ± 1.05	3.5 ± 0.9	4 ± 0.9

Data are reported as mean ± SD.

APTT – activated partial thromboplastin time, PT – prothrombin time, PLT – platelet count, T0 – day before the surgery, T1 – day on admission at intensive care unit, T6 – six hours after surgery, T24 – twenty-four hours after surgery.

PLT. Mean PLT at T0 was $216 \pm 58 \times 10^9/L$ and 9 pts had PLT count $< 150 \times 10^9/L$, but they did not have greater bleeding tendency after surgery. An obvious tendency to decrease PLT count was seen during the first 24 h after surgery. At T1 PLT count of 50 pts and at T6 of 49 pts decreased under the normal level. The lowest PLT count was at T24 decreasing about 35.2% of the baseline and 51 pts had lower values than the normal value (Table 2). At T6 and at T24, a statistically significant difference ($P = 0.03$; $P = 0.01$) in 24h-PBL between the pts with normal and low PLT count was detected (Fig. 1). Correlation was observed between T24 PLT and

T24 blood loss ($r = -0.3$; $P = 0.01$) and between T6 PLT and T24 blood loss ($r = -0.25$; $P = 0.02$).

Fibrinogen. The preoperative fibrinogen level of all pts was within the normal range with a mean value of 4.1 ± 1.3 g/L. It decreased by 22% from the baseline at T1, when 4 pts had fibrinogen < 1.8 g/L. Normal fibrinogen level was reached already after 6 h for all pts and it also continued to raise 24 h after the surgery (Table 2). Fibrinogen showed a strong negative correlation with 24h-PBL: fibrinogen at T6 with 24h-PBL ($r = -0.4$; $P < 0.0001$) and preoperative (T0) fibrinogen with 24h-PBL ($r = -0.5$; $P < 0.0001$) (Fig. 2).

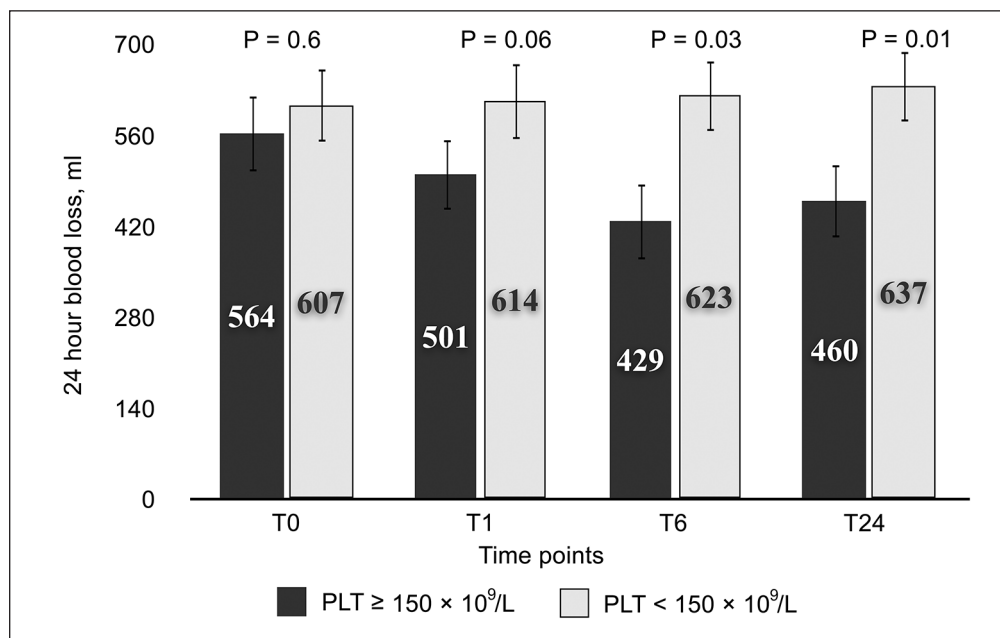


Fig. 1. Differences in 24-hour postoperative blood loss between the patients with PLT count \geq or $< 150 \times 10^9/L$

Differences between 24-hour postoperative blood loss in patients with platelet count (PLT) more or equal $150 \times 10^9/L$ and in patients with less than $150 \times 10^9/L$ in different time points: T0 – baseline, T1 – admission in intensive care unit, T6 – six hours after surgery, T24 – twenty-four hours after surgery. Significant difference ($P < 0.05$) appears at T6 and at T24. Data presented as mean ± SD

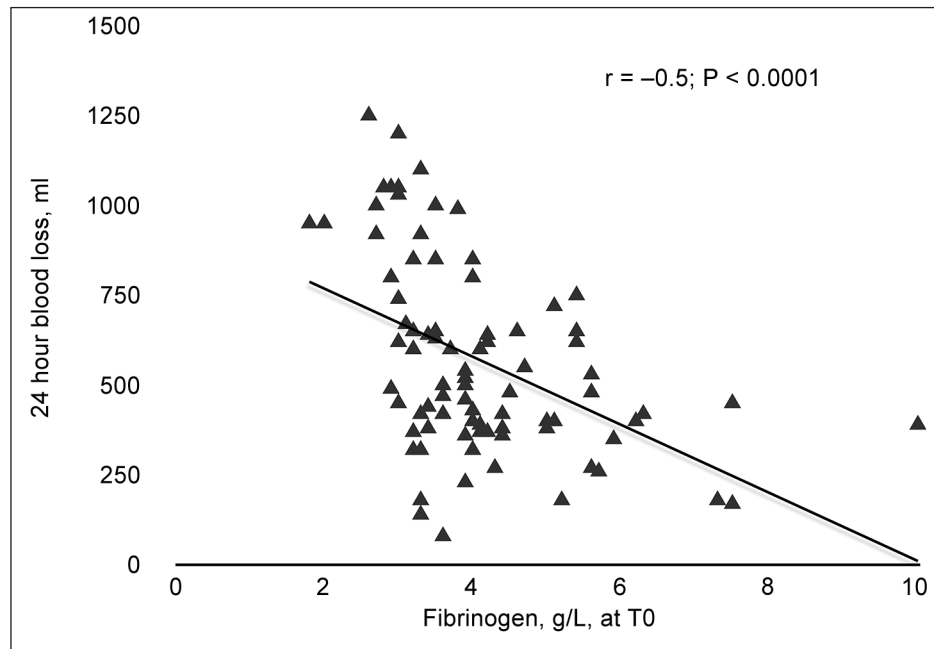


Fig. 2. Scattergram of 24-hour postoperative blood loss versus preoperative plasma fibrinogen levels

Relationships between preoperative (T0) plasma fibrinogen levels and blood loss in 24 hours of patients subjected to cardiac surgery employing cardiopulmonary bypass

DISCUSSION

In this study, the changes of the laboratory coagulation tests and their association with 24h-PBL after the CPB surgery were investigated. It seems that preoperative *APTT* values were most likely affected by the use of LMWH because 27 pts at T0 had higher or equal than normal *APTT* values and 21 pts of them were taking LMWH (12 h before surgery). In literature there are data indicating that LMWH stopped more than 8 h before the surgery does not affect the bleeding volume after the surgery (3). We also found that 24h-PBL did not differ between pts with higher or normal preoperative *APTT*. After the surgery at T6 higher than normal *APTT* values were in 69% ($n = 57$) of pts, but at T24 in 61% ($n = 51$) of pts. That could be explained by “heparin rebound phenomena”. In this state ACT measurements should be done and additional protamine should be given, if necessary. Phenomena of “heparin rebound” usually occur in 1–8 h after heparin neutralization with protamine (4). Higher *APTT* values after the surgery could be explained by hemodilution and reduction of the coagulation factors by 50% (5, 6).

Despite the fact that more than a half of pts after the surgery had higher than normal *APTT* values at T6 and at T24, we did not find any *APTT* association with 24h-PBL. *PT* showed the smallest changes after CPB and did not correlate with 24h-PBL. Preoperatively, only 7 pts had *PT* lower than normal, and those pts did not show greater bleeding tendency after the surgery. After CPB, nobody had lower than normal *PT* levels. We did not find any correlation between *PT* and 24h-PBL. *PLT* showed a convincing tendency to decrease after CPB. At T24 more than a half of pts had reduced *PLT* count by 32.5%. We speculate that the main reasons could be hemodilution and consumption of *PLT* during CPB, when their count is known to decrease by about 30–50% (7). *PLT* typically remains depressed for 7–10 days postoperatively after the cardiac surgery with CPB (2, 8) and it is one of the factors influencing the volume of postoperative blood loss (9). Our results show similar findings, suggesting that *PLT* count may affect the volume of 24h-PBL. *Fibrinogen* plays a fundamental role in maintaining hemostasis, serving both as the precursor of fibrin and a mediator of platelet aggregation (10). In the present study, fi-

brinogen levels decreased at T1 from the baseline by 22%, which is likely due to fibrin consumption during CPB (2). Lower fibrinogen levels correlated with greater postoperative blood loss and the highest correlation was found between preoperative (T0) fibrinogen and 24h-PBL. Our findings coincide with other investigations as well showing that reduced fibrinogen levels are associated with increased bleeding (11) and mortality (12) after the surgery.

CONCLUSIONS

The marked changes of APTT and PLT after the cardiac surgery with CPB could be explained by the effect of CPB on the hemostasis system. The highest predictive value for greater blood loss was shown by PLT and fibrinogen.

ACKNOWLEDGMENTS

The study was supported by Grant 2009/0147/1DP/1.1.2.1.2/09/IPIA/VIAA/009 from the European Social Fund.

Received 21 June 2012

Accepted 1 August 2012

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KREŠĖJIMO TYRIMAI IR JŪ RYŠYS SU POOPERACINIŲ KRAUJO NETEKIMU PO ŠIRDIES OPERACIJOS SU DIRBTINE KRAUJO APYTAKA

Santrauka

Įvadas. Trombocitų skaičiaus (PLT), aktyvuoto dalinio tromboplastino laiko (ADTL), protrombino laiko (PT) ir fibrinogeno tyrimai yra standartiniai krešėjimo tyrimai, skiriami pacientams, kuriems atliekamos širdies operacijos su dirbtine kraujo apytaka (DKA).

Tyrimo medžiaga ir metodai. Į prospektyvinę studiją buvo įtraukti 83 suaugusieji širdies operacijų pacientai. ADTL, PT, PLT ir fibrinogeno kraujo mėginiai buvo paimti prieš operaciją (T0), guldant į intensyvios terapijos skyrių (T1), praėjus 6 ir 24 valandoms po operacijos (T6, T24). Užregistruotas 24 valandų pooperacinis kraujo netekimas (24h-PKN).

Rezultatai. Didžiausia vidutinė ADTL reikšmė – 47 ± 13 sek., už bazinę didesnė 37 %, nustatyta T6 periodu. Mažiausia vidutinė PLT reikšmė – $140 \pm 47 \times 10^9/L$, mažesnė už bazinę 32,5 %, buvo T24 periodu. PT ir fibrinogeno vidutinės reikšmės visais laiko periodais išliko normos ribose. Su 24h-PKN koreliavo T0 ir T6 fibrinogenas ($r = -0,5$; $r = -0,4$; $P < 0,0001$), T6 ir T24 trombocitų skaičius ($r = -0,25$; $P = 0,02$; $r = -0,3$; $P = 0,01$).

Išvados. Iš standartinių krešėjimo tyrimų, be DKA, ryškiais pokyčiais pasižymėjo ADTL ir PLT. Teigiamą prognostinę vertę didesniai 24h-PKN gali turėti PLT ir fibrinogenas.

Raktažodžiai: APTT, PT, PLT, fibrinogenas, širdies operacija