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Activation of the coagulation system during coronary artery bypass grafting: Comparison between on-pump and off-pump techniques

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Objective: The activation of the coagulation and fibrinolytic systems and platelet function in patients undergoing coronary artery bypass surgery on-pump or off-pump techniques was compared.

Methods: Thirty-two patients were randomly assigned to on-pump or off-pump coronary artery bypass grafting. Heparin was given at the same dose. Activation of the coagulation and fibrinolytic systems was evaluated by measurement of several markers. Platelet function was evaluated by in vitro bleeding time test. Blood samples were collected at 7 different times, up to postoperative day 6.

Results: Overall tissue factor production was similar in the two groups. Thrombin formation was more elevated in the on-pump group ($P < .001$), particularly during the operation; prothrombin fragment 1.2 discharge values were higher than the preoperative ones ($P = .002$). Levels of tissue-plasminogen activator showed no difference between the groups ($P = .1$). D-dimers release was higher in the on-pump group ($P = .0002$). In vitro bleeding time was longer in the on-pump group ($P < .0001$), particularly in the first 24 hours; it was not prolonged in the off-pump group. In both groups, regardless of aspirin treatment, discharge in vitro bleeding times were lower than the preoperative ones ($P < .01$).

Conclusion: Although the extrinsic coagulation pathway is similarly activated, thrombin formation is more pronounced in patients having on-pump bypass grafting. Patients subjected to off-pump bypass grafting have normally functioning platelets and a weak activation of the fibrinolytic system. At discharge, both groups have preserved platelet function and increased thrombin formation. Further studies with angiographic evaluation are needed to establish a correlation between coagulation parameters, platelet function, and graft patency.

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Off-pump coronary artery bypass grafting (OPCAB) is frequently used to perform coronary artery bypass grafting (CABG). The advantages and disadvantages of this technique in comparison with the standard operation performed with the arrested heart and cardiopulmonary bypass (CPB) are becoming clearer. Most of the studies involving the general population[1,2] have shown that a significant reduction of postoperative bleeding and blood product transfusion is observed after OPCAB compared with on-pump operations. Moreover, subgroup analysis of patients with a higher rate of comorbidities (older age, renal failure, diabetes, previous stroke, calcific aorta) showed that the OPCAB technique might reduce operative mortality and morbidity.[3,4]

Coagulation disorders and consequent perioperative bleeding represent one of the most frequent complications of on-pump surgery. Excessive bleeding, blood product transfusion, and chest reopening for bleeding are widely known risk factors for

Abbreviations and Acronyms

ANOVA = analysis of variance
CABG = coronary artery bypass grafting
CPB = cardiopulmonary bypass
ELISA = enzyme-linked immunosorbent assay
OPCAB = off-pump CABG
PAI-1 = plasminogen activator inhibitor-1
PF = prothrombin fragment
POD = postoperative day
TF = tissue factor

adverse events after on-pump surgery.[5] Consequently, several strategies (technical, pharmacologic) aimed to reduce the risk of excessive bleeding have been adopted during on-pump surgery. Such strategies have also been suggested for patients undergoing OPCAB,[6] although this technique, due to the absence of CPB, may result in a different coagulative state.

So far few studies have analyzed the coagulation and fibrinolytic systems during and after OPCAB in comparison with on-pump operations.[7-9] A recent editorial[10] hypothesized that OPCAB patients may have a higher risk of early graft failure because of the reduced activation of the fibrinolytic system associated with an enhanced activation of the inflammatory and coagulation systems.

The aim of the present study is to evaluate the difference in the activation of coagulation and fibrinolytic systems and platelet function in patients undergoing OPCAB operations or standard on-pump CABG.

Methods

The local ethics committee approved the study protocol. After informed consent, 32 consecutive patients requiring elective CABG, considered suitable for both on-pump and OPCAB procedures, were enrolled in the study. The patients were assigned in a randomized fashion to the on-pump group or the OPCAB group.

The following exclusion criteria have been applied:

Preoperative: Known pre-existing hemolytic or coagulative disorders; oral or intravenous anticoagulant treatment; all kinds of antiplatelet treatment taken within 5 days before the operation.

Intraoperative: Intolerance from a hemodynamic point of view to the lifting of the heart and the exposure necessary to perform OPCAB; patients with coronary arteries surgically inaccessible (intramyocardial) for a beating heart operation; patients in whom a complete revascularization was not achievable with OPCAB (in these cases, patients have been converted to receive on-pump CABG and have been excluded from the study).

Perioperative Management

After premedication with lorazepam, anaesthesia was induced with a combination of fentanyl, midazolam, and sodium thiopenthal and maintained with proprofol. Antifibrinolytic drugs were not administered. Heparin was given at the same dose (300 U/kg) in both groups. Intraoperative heparin monitoring was performed by standard activated clotting time (Hemochron 8; ITC, a subsidiary of Thoratec Corporation, Pleasanton, Calif). Additional heparin bolus (5000 U) was given if the activated clotting time was below 400 seconds in the on-pump group and below 300 seconds in the OPCAB group. In both groups protamine was administered to reverse heparin (1 mg of protamine/100 IU of heparin). In the on-pump group CPB was established with a 2-stage venous cannula and aortic return. Moderate hypothermia (34°C) was maintained during the operation. Cardiac arrest was induced and maintained with antegrade cold blood cardioplegia. Cardiotomy suction was used in all patients of the on-pump group. Cell saving devices were not used. A heart stabilizer (Octopus; Medtronic Inc, Minneapolis, Minn) has been used in all OPCAB operations and intracoronary shunts have been used in 87% of these cases to allow bloodless anastomoses.

All patients were admitted postoperatively in the intensive care unit and extubated when hemodynamically stable, fully rewarmed, awake, without surgical bleeding, and with optimal blood gases. Postoperatively, patients received aspirin (100 mg orally or intravenously) and low molecular weight heparin (nadroparin 2850 U Anti-Xa, subcutaneously) starting 12 hours after the end of the operation in the absence of significant mediastinal bleeding. Low molecular weight heparin administration was discontinued on postoperative day 5.

Assays

Specific assays were performed to assess the activation of coagulation and fibrinolytic systems between the two groups. Blood samples were centrifuged for 15 minutes at 3500 rpm and frozen at −80°C until assayed. Plasma was assayed by monoclonal antibodies sandwich enzyme-linked immunosorbent assay (ELISA) technique.

Activation of the coagulation system was evaluated by use of the prothrombin fragment 1.2 (PF-1.2) (Enzygnost F1+2 Micro; Dade Behring Marburg GmbH, Marburg, Germany), tissue factor (TF) (IMUBIND Tissue Factor ELISA; American Diagnostica GmbH, Pfungstadt, Germany), and fibrinogen (Biopool Fibrinogen Assay Kit, Biopool International, Ventura, Calif) measurements. Activation of the fibrinolytic system was evaluated by measuring tissue plasminogen activator (IMUBIND tPA ELISA; American Diagnostica GmbH, Pfungstadt, Germany), plasminogen activator inhibitor-1 (PAI-1) (IMUBIND Plasma PAI-1 ELISA; American Diagnostica GmbH, Pfungstadt, Germany), and D-dimers (ACL 9000, IL Instrumentation Laboratory, Arcore (MI), Italy).

Platelet function was evaluated by the platelet function analyzer (PFA-100; Sysmex UK Ltd, Milton Keynes, United Kingdom), a device designed to simulate platelet-dependent hemostasis in whole blood in vitro.[11] The system consists of a cartridge in which a membrane and an aperture are coated with collagen/adenosine-5′-diphosphate. Anticoagulated whole blood is aspirated through a capillary under steady high shear rates. The presence of the platelet agonist and the high shear rates result in a platelet plug that gradually occludes the aperture. The time required for full occlusion of the aperture is defined closure time (range: 71-118 seconds). PFA-100 measuring was done 15 minutes after blood sampling.

TABLE 1. Intraoperative characteristics and postoperative outcome

	On-pump group (16 patients)	OPCAB group (15 patients)	*P* value
Operation time (min)	303.8 ± 88.1	289 ± 38.8	NS
Heparinization time (min)	159.6 ± 40.4	121.6 ± 35.7	.009
Heparin dose	4.6 ± 0.6	4.0 ± 0.5	.009
CPB (min)	107 ± 21.2		
Aortic crossclamping (min)	64.9 ± 19.3		
CABG (No.)	3.25 ± 0.86	2.7 ± 0.8	NS
IABP use	0	0	
ICU stay (d)	1.62 ± 1.5	1.53 ± 1.06	NS
ARF (creatinine >2.5 mg/dL)	1 (6.25%)	0	NS
AF	2 (12.5%)	4 (26.6%)	NS
Total blood loss (mL)	861.2 ± 340.3	933.7 ± 382.6	NS
Mediastinal blood loss (mL)	508.1 ± 246.1	539 ± 221.2	NS
Pleuritic blood loss (mL)	353.1 ± 201.3	394.6 ± 239.5	NS
Total blood product transfusion (units)	2.1 ± 2.7	1.3 ± 1.2	NS
PRC transfusion (unit)	2.1 ± 2.7	1.3 ± 1.2	NS
Hgb, g/dL value at POD 6	9.3 ± 2.34	10.9 ± 1.35	.02
Mortality rate	1 (6.25%)	0	NS

OPCAB, Off-pump coronary artery bypass; *CPB,* cardiopulmonary bypass; *CABG,* coronary artery bypass grafting; *IABP,* intra-aortic balloon pump; *ICU,* intensive care unit; *ARF,* acute renal failure; *AF,* atrial fibrillation; *PRC,* packed red cells; *Hgb,* hemoglobin; *POD,* postoperative day; *NS,* not significant.

Hematocrit (HKT), hemoglobin, and platelet count were measured at all sample times.

All ELISA assays were doubled tested, and the mean value was used for analysis. Results were corrected for hemodilution according to the formula: (corrected assay)Tx = (assay)Tx × (HKT)T0/(HKT)Tx.

Sample Times

Blood samples were collected at 7 different times, before, during and after the operation: T0: during induction before the beginning of the operation; T1: 45 minutes after heparin administration; T2: 15 minutes after protamine administration; T3: 3 hours after the end of the operation; T4: first postoperative day (POD); T5: fourth POD; T6: sixth POD. Samples for firbrinogen were not performed at T1 and T2.

Statistical Analysis

On the basis of preliminary data obtained with PFA-100, the trial was designed to enroll 30 patients to demonstrate a 50% reduction of in vitro bleeding time and coagulation markers after the operation in the OPCAB group compared with the on-pump group (alpha = .05, power = 0.8). Results of the measured coagulation parameters showed a nonnormal distribution. Logarithmic conversion of data was carried out to apply repeated-measures analysis of variance (ANOVA) for overall comparison between the groups and the Student *t* test to compare measured outcomes at each sample time. The Wilcoxon test was applied to compare preoperative values (T0) with postoperative values (T6) within each group. Categorical variables are presented as absolute numbers and percentages were compared using the Fisher exact test. Statistical analyses were performed using the Stat-View Statistical Software Package (SAS Institute Inc, Cary, NC) and Number Cruncher Statistical System (NCSS, Kaysville, Utah).

Results

One patient of the OPCAB group did not tolerate the lifting of the heart; he was converted to on-pump treatment and consequently was excluded from the study.

Preoperative patient characteristics were similar in the two study groups: age, gender, ejection fraction, cardiovascular risk factors, and body mass index were equally represented in the groups. The operation length and the number of grafts performed (3.25 vs 2.7) were slightly greater in the on-pump group without a statistically significant difference. However, duration of heparinization was significantly longer in the on-pump group (Table 1). No differences in clinical outcomes were observed between on-pump and OPCAB patients (Table 1). Postoperative blood loss and blood product transfusion were also comparable, but hemoglobin values measured on POD 6 were higher in the OPCAB group.

TF serum levels (Figure 1, *A*) were comparable between the two groups (2-way ANOVA for repeated measures: $P = .11$ corrected for hemodilution; $P = .54$ not corrected for hemodilution). TF levels measured before discharge were above the levels measured preoperatively ($P < .001$ in both groups). Serum levels of PF-1.2 (Figure 1, *B*) were significantly higher in the on-pump group particularly during and immediately after CPB (2-way ANOVA for repeated measures: $P < .0001$ corrected and not corrected for hemodilution; Table 2). In both groups, PF-1.2 tends to rise in the postoperative period: PF-1.2 levels measured at T6 were significantly higher than those measured at T0 ($P = .002$ in both groups). Fibrinogen levels (Table 2) did not

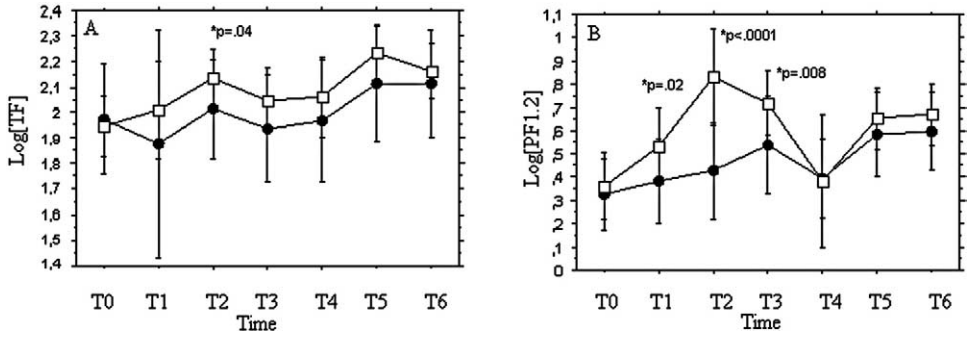

Figure 1. A, Tissue factor *(TF)* values after log transformation and correction for hemodilution in 7 observation times. B, Prothrombin fragments 1.2 *(PF 1.2)* values after log transformation and correction for hemodilution in 7 observation times. *Open squares,* On-pump group; *filled circles,* OPCAB group. Significant *P* values obtained with the *t* test are reported.

differ between the groups ($P = .5$). Discharge values of fibrinogen were higher than preoperatively ($P = .001$ and .006 for on-pump and OPCAB groups, respectively). Levels of T-PA (Figure 2, *A*) showed no difference between the groups (2-way ANOVA for repeated measures: $P = .07$ corrected for hemodilution; $P = .36$ not corrected for hemodilution). At discharge in both groups, tissue plasminogen activator levels were comparable with those obtained

TABLE 2. Coagulation and fibrinolytic markers after correction for hemodilution and platelet function measured at 7 different sample times with *P* values

	T0	T1	T2	T3	T4	T5	T6
TF (pg/mL)							
On	91.92 ± 11.58	112.36 ± 34.84	141.31 ± 7.28	115.93 ± 39.61	121.83 ± 97.32	175.82 ± 100.11	149.32 ± 55.76
Off	105.24 ± 23.7	101.05 ± 29.78	113.01 ± 29.3	96.07 ± 23.42	106.18 ± 57.72	147.57 ± 70.53	143.12 ± 43.81
P	.66	.28	.04	.09	.23	.06	.42
PF-1.2 (nmol/L)							
On	2.43 ± 0.61	3.17 ± 0.72	8.09 ± 1.66	5.51 ± 0.8	2.83 ± 0.05	4.37 ± 0.72	4.75 ± 0.84
Off	2.06 ± 0.47	2.4 ± 0.13	2.46 ± 0.63	3.35 ± 1.25	2.7 ± 1.58	4.08 ± 0.86	4.19 ± 1.45
P	.49	.021	<.00001	.008	.92	.26	.22
TPA (ng/mL)							
On	18.36 ± 24.2	40.65 ± 49.44	26.62 ± 19.84	25.17 ± 10.26	16.45 ± 8.63	17.86 ± 10.25	14.93 ± 7.9
Off	10.73 ± 9.39	11.76 ± 7.16	17.02 ± 8.79	19.79 ± 12.28	15.75 ± 9.87	12.54 ± 8.75	14.79 ± 8.85
P	0.94	.26	.21	.60	.66	.85	.77
PAI (ng/mL)							
On	18.06 ± 10.68	26.78 ± 11.68	69.48 ± 29.45	93.03 ± 76.7	63.28 ± 77.99	40.28 ± 2.37	33.47 ± 18.16
Off	21.15 ± 8.15	31.47 ± 2.86	37.41 ± 4.97	75.41 ± 13.82	59.51 ± 87.38	35.7 ± 14.18	34.32 ± 11.43
P	.85	.81	.002	.24	.83	.71	.94
D-dimer (ng/mL)							
On	193.71 ± 79.9	531.94 ± 1292.38	1692.95 ± 1445.1	1199.86 ± 499.35	536.81 ± 357.31	422.84 ± 324.71	609.18 ± 328.61
Off	249.2 ± 4.95	268.25 ± 110.42	250.07 ± 50.09	386.72 ± 493.7	400.45 ± 283.4	441.83 ± 257.13	777.76 ± 512.88
P	.87	.42	.01	.08	.49	.82	.91
PFA-100 (s)							
On	89.33 ± 27.14	189.09 ± 82.65	154.7 ± 77.31	119.2 ± 79.38	75.14 ± 22.38	70.85 ± 10.17	63.15 ± 8.86
Off	91.2 ± 15.64	93.92 ± 37.88	78.85 ± 14.65	68 ± 18.17	92.79 ± 19.77	62.69 ± 14.56	61.07 ± 6.87
P	.61	.003	.0003	.01	.23	.08	.53
Fibrinogen (mg/dL)							
On	424 ± 105.2			380.2 ± 109.8	568 ± 182.9	752.1 ± 164.4	695.4 ± 155.3
Off	439.8 ± 135.3			421.9 ± 134.2	521 ± 196.3	688.4 ± 149.8	667.1 ± 162.2
P	.84			.43	.44	.28	.61

TF, Tissue factor; *PF,* prothrombin fragment; *TPA,* tissue plasminogen factor; *PAI,* plasminogen activator inhibitor; *PFA-100,* platelet function analyzer-100.

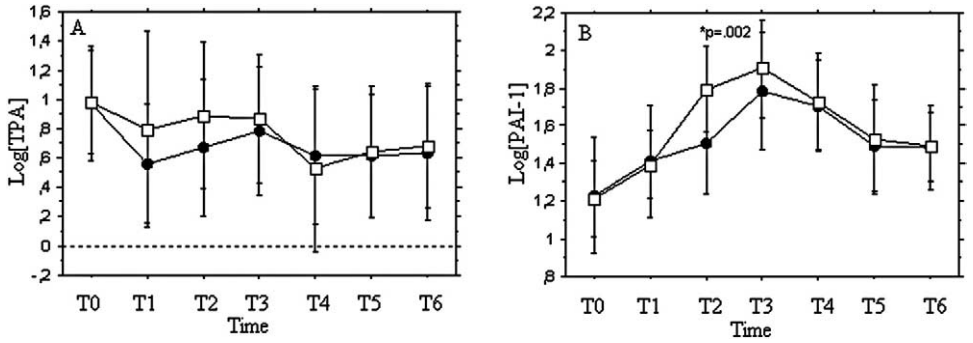

Figure 2. A, Tissue plasminogen activator *(TPA)* values after log transformation and correction for hemodilution in 7 observation times. B, Plasminogen activator inhibitor-1 *(PAI-1)* values after log transformation and correction for hemodilution in 7 observation times. *Open squares,* On-pump group; *filled circles,* OPCAB group. Significant *P* values obtained with the *t* test are reported.

preoperatively. Perioperative PAI-1 levels (Figure 2, *B*) were higher in the on-pump group (2-way ANOVA for repeated measures: $P = .03$ corrected and not corrected for hemodilution); they rose consistently also in the OPCAB group 3 hours and 24 hours after the end of the operation. At discharge, PAI-1 levels were significantly higher than preoperatively ($P = .001$ and .002 in the on-pump and OPCAB groups, respectively). There was an increase of D-dimers soon after the beginning of the operation in both groups (Figure 3, *A*), but the overall release of D-dimers was significantly more pronounced in the on-pump group (2-way ANOVA for repeated measures: $P < .0001$ corrected and not corrected for hemodilution). D-dimers levels remained elevated throughout the study period; at T6 they were significantly higher than at T0 ($P = .01$ and .02 in the on-pump and OPCAB groups, respectively).

PFA-100 analysis demonstrated significantly longer closure times for the on-pump patients ($P < .0001$), particularly at T1, T2, and T3 (Figure 3, *B*). PFA-100 closure time was not prolonged at all in the OPCAB group during heparinization. Regardless of aspirin treatment, discharge values (T6) of PFA-100 were lower than the preoperative ones ($P = .007$ and .001 in the on-pump and OPCAB groups, respectively).

Discussion

CABG performed with CPB is a safe operation that achieves excellent short- and long-term results. Currently, CPB is associated with a number of adverse effects that may have a negative impact on an aging CABG population. Consequently, OPCAB has been developed to avoid the use of CPB and maintain a more physiologic coagulation and inflammatory state. Previous studies have shown that this hypothesis is only partially true. Gu and colleagues[12] demonstrated that the inflammatory response is reduced but not abolished in patients undergoing OPCAB operations. The

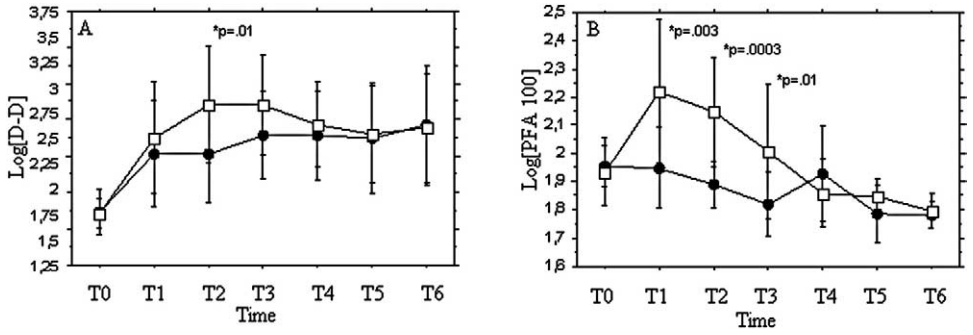

Figure 3. A, D-dimer *(D-D)* values after log transformation and correction for hemodilution in 7 observation times. B, Platelet function evaluated by the platelet function analyser-100 *(PFA-100)* after log transformation in 7 observation times. Two-way ANOVA for repeated measures: *P* <.0001. *Open squares,* On-pump group; *filled circles,* OPCAB group. Significant *P* values obtained with the *t* test are reported.

same group prospectively studied 22 patients with single-vessel disease who underwent OPCAB either through a median sternotomy or with minimally invasive thoracotomy: markers of activated coagulation system were detected 24 hours after the operation.[7]

Other studies have consequently compared the activation of the coagulation system in patients undergoing CABG with or without CPB. Englberger and colleagues[8] analyzed 27 patients assigned in a randomized fashion to undergo myocardial revascularization either with the off-pump technique (9 patients) or with CPB (16 patients). Plasma levels of fibrin monomer, thrombin-antithrombin complex, and D-dimer were significantly higher in the on-pump group immediately after surgery, whereas they were similar 18 hours postoperatively. Their study is limited by the short period of observation: 18 hours after the end of the operation. Lo and colleagues[9] evaluated 40 patients undergoing coronary surgery with or without CPB. Blood samples were drawn up to 96 hours after the end of the operation. PF-1.2 and D-dimer levels were significantly higher in the on-pump group at the end of the operation and 2 hours later; in OPCAB patients, PF-1.2 levels significantly increased 2 hours after the operation and peaked on POD day 4. In both groups, plasma concentrations of von Willebrand factor increased from the first POD compared with baseline and peaked at POD 4.

Our study adds some new insights to the results of the previously published reports.

The role of the extrinsic coagulation pathway and TF in the post-CPB coagulation state has been well documented.[13] We compared, for the first time, TF production with and without CPB. We found no significant difference in TF production between on-pump and OPCAB patients, meaning that surgical trauma, even in the absence of CPB and cardiotomy suction, leads to the activation of the extrinsic pathway. In both groups, TF levels rise in the postoperative phase, probably as a result of a systemic inflammatory state rather than as a response to a topical prothrombotic stimulus. This is confirmed by the similar perioperative trend of fibrinogen, a widely known inflammatory marker. Fibrinogen is the substrate for the fibrin production, participates in platelet aggregation, and acts as acute phase protein, increasing during the inflammatory responses.[14] The inflammatory and coagulation systems share a common activation pathway. The link is represented by nuclear factor κB. Nuclear factor κB, during CPB, regulates TF activation and consequent thrombin release. Nuclear factor κB regulates also the inflammatory response secondary to CPB surgery.[15]

Our study confirms that during CPB, despite heparin administration, thrombin formation is not prevented.[16] Considering the relevant perioperative difference of thrombin formation associated with similar TF values between the groups, our study suggests that the extrinsic pathway and TF should not be considered the only trigger for thrombin formation during CPB and that the intrinsic pathway also plays a role. In contrast, in OPCAB patients, administration of a heparin dose similar to the one used during CPB (300 U/Kg) eliminates the production of thrombin during the time of surgery. Future trials will clarify the optimal heparin management in patients undergoing OPCAB. We also demonstrated that in OPCAB patients there is an increase of PF-1.2 production (corresponding to TF increase) starting on POD 2 and continuing to at least POD 7. Levels are comparable with those observed in patients undergoing on-pump CABG. Patients of both groups received low molecular weight heparin postoperatively; measured procoagulant markers levels may have been affected by such treatment as it has been demonstrated in other clinical settings.[17] Nevertheless, we believe that administration of low molecular weight heparin could not alter the comparison between the groups.

The correlation between plasma activation of procoagulation markers and clinical outcome (namely graft patency) is still a matter of debate. Moor and colleagues[18] found that the percentage increase in PAI-1 activity on the first postoperative day was significantly higher in patients who subsequently were found to have vein graft occlusion at angiographic evaluation 3 months after CABG. In our study, PAI-1 levels were more elevated in the on-pump patients, although a steady increase was observed also in the OPCAB group. In both groups, peak release was observed 3 hours after the end of the operation. At the same time, tPA release was very modestly stimulated, particularly in the OPCAB patients. We also observed that fibrinolysis (D-dimer) is activated to a lesser extent in OPCAB patients. On the basis of our observation, the proposed use of antifibrinolytic agents in OPCAB patients[6] seems unjustified unless future randomized trials with angiographic control studies will prove the safety of antifibrinolytic administration with regard to graft patency.

Platelet function, as analyzed by an in vitro bleeding test, is better preserved during OPCAB surgery than during CPB. The lack of CPB and cardiotomy suction, together with the reduced formation of thrombin, may explain why platelet function is preserved in OPCAB patients. The preserved platelet function did not affect blood loss or transfusion rates in our study. These findings are in contrast to other studies that have shown a reduction of both blood loss and transfusion in off-pump patients, although our sample size is not sufficiently large to produce reliable clinical outcome data. The administration of aspirin 100 mg daily from POD 1 does not affect platelet function postoperatively. In both groups, bleeding times measured at discharge were lower than those measured preoperatively. PFA-100 has already been used to assess platelet dysfunction in patients undergoing CPB surgery[19]; it is a validated method

to assess platelet function in patients with cardiovascular disease[20] and to measure aspirin resistance in patients with coronary artery disease, showing that 35% of patients who had had acute myocardial infarction seemed to be nonresponders to long-term aspirin therapy in doses of 75 and 160 mg/day.[21] Other studies have evaluated platelet function in OPCAB patients[22,23]; nevertheless, our study provides the longest observation suggesting that dosages of aspirin 100 mg daily may be insufficient to prevent vein graft failure. We hypothesize that the activated inflammatory and coagulative state observed after cardiac operations, by increasing von Willebrand factor release[9] and platelet leukocytes aggregates, may influence platelet response to aspirin treatment; future studies should clarify whether treatment aimed to attenuate these systems may also decrease aspirin resistance.

Vein graft failure remains a major problem after CABG. Occlusion in the first weeks is secondary to thrombosis, whereas intimal hyperplasia and eventually atherosclerotic changes with superimposed thrombus formation underlie subsequent closure. Two recent randomized controlled trials[24,25] revealed that patency rate was significantly worse in patients undergone off-pump procedures compared with patients undergoing CPB. Moreover, data from a large registry demonstrate that off-pump patients have a higher rate of perioperative myocardial infarction and have a significantly worse 3-year risk-adjusted survival.[26] There are several possible explanations for the poorer graft performance in patients operated on by the off-pump technique: the poorer coronary vessel exposure, heart movement, poor coronary visualization provoked by bleeding, all render the distal anastomosis more difficult to perform and sometimes less accurate than those made with the heart arrested. The tools used during the anastomoses (intracoronary shunts, coronary occluding stitch, carbon dioxide blower) to improve visualization may all potentially damage the coronary and graft endothelium.[27] Our study shows that the coagulation state of OPCAB patients differs from that of the on-pump group only during the first 24 hours. Of particular interest is the lack of platelet dysfunction observed during this period in the OPCAB patients associated with the lack of fibrinolysis. It remains to be demonstrated whether this association should be considered a procoagulative state. After the first 24 hours, both groups continue to produce thrombin probably as a consequence of their inflammatory state rather than the intraoperative procoagulative stimulus. This is associated with an increased platelet function, as measured by a platelet function analyzer (PFA-100). The actual antiplatelet treatment is not adequate to protect the graft from early thrombosis. Our data would support the addition of more aggressive antiplatelet and antithrombotic drug regimens in both on- and off-pump patients to decrease vein graft failure. We believe this might be particularly helpful in OPCAB patients in whom less accurate distal anastomosis and coronary artery endothelial damage may occur. Further studies with angiographic evaluation are needed to establish a correlation between coagulation parameters, antiplatelet treatment, and graft patency.

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