gery.⁴ The authors also mentioned use of multiple variables that might or might not be clinically relevant and assigned propensity scores in the outcome models to adjust for antifibrinolytic use. I believe that such an analysis is suboptimal to propensity score matching in quantiles. Surgeons need to take a closer look and revisit the data published in this article before banning aprotinin from their practice.

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About the activation of the coagulation system during on-pump and off-pump coronary surgery and the use of antifibrinolytic drugs

To the Editor:

The results of the study by Paparella and colleagues¹ recently published in the *Journal* confirm part of the observations described in previous reports addressing the activation of coagulation and fibrinolysis in coronary surgery performed with (ONCAB) or without (OPCAB) cardiopulmonary bypass (CPB). However, some of the statements contained in their "Discussion" section deserve critical consideration. Because no difference in tissue factor (TF) "production" was observed in the 2 groups of patients while prothrombin fragment 1.2 levels were higher in patients undergoing ONCAB, the authors state that the extrinsic pathway of coagulation should not be con-

sidered the only trigger for thrombin formation during CPB. Although the intrinsic pathway might also play a role in thrombin formation during CPB, the observation of circulating levels of TF that are not significantly different does not per se demonstrate a similar activation of the extrinsic pathway of coagulation in the 2 groups of patients. TF is a transmembrane protein expressed by white blood cells under conditions of activation, and deposition of such cells in the CPB circuit has been shown before.² Therefore plasma levels of TF might not reflect the true "exposure" of TF to circulating blood. The authors state that in patients undergoing OPCAB, administration of a heparin dose similar to the one used during CPB (300 U/kg) eliminates the production of thrombin during the time of the operation. "Elimination" of thrombin production would lead to severe bleeding, which cannot obviously be the aim of heparin administration. The authors also state that platelet function, as analyzed by using an in vitro bleeding test (PFA-100), is better preserved during OPCAB surgery than during CPB and that the lack of CPB and cardiotomy suction, together with the reduced formation of thrombin, might explain why platelet function is preserved in patients undergoing OPCAB. The PFA-100 is influenced by the platelet count and the hematocrit level, which are both obviously higher in patients undergoing OPCAB, and by von Willebrand factor levels, which are known to increase postoperatively. Thus the PFA-100 can hardly be considered validated in evaluating platelet function in the setting of cardiac surgery. Despite the observation of a similar postoperative "hypercoagulable" pattern in the 2 groups of patients, the authors also emphasize that D-dimer levels are lower in patients undergoing OPCAB, advising against the use of antifibrinolytic drugs, which might increase the risk of vein graft occlusion in this surgical setting. These conclusions are in disagreement with the results previously reported by our group³ and with the clinical observations of the authors. A similar, although not negligible, 24-hour postoperative bleeding value was recorded in the 2 groups (total blood loss: ONCAB, 861.2 ± 340.3 mL; OPCAB, 933.7 ± 382.6 mL). In a pilot study carried out in patients not receiving antifibrinolytic drugs, we recorded an average total blood loss of 850 mL in patients undergoing

ONCAB and 750 mL in patients undergoing OPCAB.³ In a larger study powered to detect differences in bleeding between patients undergoing ONCAB and patients undergoing OPCAB randomized to receive tranexamic acid or placebo, the average total blood loss was 754 mL and 552 mL in patients undergoing ONCAB off or on tranexamic acid treatment and 654 and 375 mL in patients undergoing OPCAB off or on tranexamic acid treatment, respectively, with a significant reduction in bleeding for both groups in the tranexamic acid arm ($P < .006$).⁴ In both studies the difference in total bleeding observed between patients undergoing ONCAB and patients undergoing OPCAB was obviously affected by the different amount of heparin infused in the 2 groups (3 times higher in patients undergoing ONCAB). Moreover, in the same study we found that tranexamic acid administration not only significantly reduces perioperative bleeding and the need for allogeneic transfusions both in patients undergoing ONCAB and patients undergoing OPCAB but also modulates inflammation, particularly in OPCAB surgery.⁴ In view of these certain advantages of antifibrinolytic drugs and of a procoagulant postoperative state of uncertain significance,^{5,6} the advice against the use of antifibrinolytic agents is, in our opinion, at least debatable.

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Reply to the Editor:

Thank you for the invitation to respond to Dr Casati and colleagues' letter. We used an in vitro bleeding time test (Platelet Function Analyzer [PFA]-100) to evaluate platelet function perioperatively at 7 different observation times. Only one of these observations was performed during cardiopulmonary bypass with hemodiluted patients. Fibrinolytic activity can indirectly be measured, evaluating the balance between the promoter of fibrinolysis (tissue-type plasminogen activator) and its inhibitor (plasminogen activator inhibitor 1). In our study¹ we observed that tissue-type plasminogen activator levels are not increased, whereas plasminogen activator inhibitor 1 and D-dimer levels are modestly increased after off-pump coronary artery bypass (OPCAB) surgery. These data would suggest that fibrinolysis is not particularly activated during OPCAB surgery. Dr Casati states that an antifibrinolytic agent should be used in patients undergoing OPCAB surgery because he has previously demonstrated² a significant reduction of postoperative bleeding in patients undergoing OPCAB treated with tranexamic acid (25 patients) compared with patients undergoing OPCAB treated with placebo (25 patients). In their study Casati and colleagues² were not able to show a significant difference in blood product transfusion between the groups. Moreover, hemoglobin and hematocrit values reported up to 24

hours postoperatively were not influenced by tranexamic acid administration. As we remarked in our article, recent studies with angiographic control have shown a worse graft patency in patients operated on by means of the OPCAB technique compared with those undergoing the on-pump technique. Inaccurate anastomosis rather than a procoagulative state is probably the main cause of these results; nevertheless, this has not been proved. Although numerous investigators have documented profound short-term and midterm coagulative-fibrinolytic and inflammatory alterations in patients undergoing coronary artery bypass grafting surgery, there are no clinical studies that evaluated prospectively and on an appropriate number of patients the value of prothrombotic and proinflammatory markers in predicting early graft occlusion. Existing studies are small and produced conflicting results: Poston and associates³ reported that thrombelastography and whole blood aggregometry do not predict graft occlusion; however, in another study the same authors showed a reduction in platelet sensitivity to aspirin by means of both thrombelastography and aggregometry in patients with early graft failure.⁴ Karski and coworkers⁵ have recently demonstrated that tranexamic acid administration does not worsen early saphenous graft patency in patients receiving on-pump coronary artery bypass grafting. However, our results show that in the first 24 hours after the operation, patients undergoing on-pump operations and OPCAB have a different activation of the coagulation and fibrinolytic systems. Consequently, what is safe for patients undergoing on-pump operations might not be safe for those undergoing OPCAB. The reason why we operate on patients with coronary artery disease is to improve their long-term outcome while trying to minimize their perioperative risk. Considering that postoperative bleeding is not a serious complication after OPCAB surgery, we agree with Dr Casati's final remarks: "Further randomized studies, enrolling larger numbers of patients, are needed to confirm the antiinflammatory effects of TA and to rule out the potential risk of thrombotic complications."²

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A new surgical paradigm: Hybrid open and endovascular repair of the ascending aorta and aortic arch for acute type A dissection

To the Editor:

I read with interest the editorial by Dobrilovic and Elefteriades¹ reflecting on the potential future application of simultaneous hybrid endoluminal graft repair of the descending thoracic aorta after traditional open surgical repair of the ascending aorta and aortic arch for acute type A aortic dissection, as discussed in the article by Uchida and associates.²

Although the results reported by Uchida and associates² are noteworthy, stabilizing the true lumen in the descending thoracic aorta with an endoluminal graft after total aortic arch replacement may not be the final, or best, approach for acute type A aortic dissection. The current surgical paradigm is