



## Impedance aggregometry may help in prediction of increased perioperative bleeding in cardiac surgery

### Impedantna agregometrija može pomoći u predviđanju povećanog perioperativnog krvarenja u kardiohirurgiji

To the Editor:

Preoperative risk assessment for increased perioperative bleeding is essential for surgical patients, and, especially for cardiac surgery patients. Specificity of operations on open heart, does not just reflect in complexity of surgical action and usage of extracorporeal bloodstream which disturbs the hemostasis, but also in the fact that the patients often are preoperatively treated with antiplatelet drugs<sup>1</sup>. The standard preoperative hemostasis testing, including prothrombin time (PT, INR) and activated partial thromboplastin time (aPTT), does not give us an insight into what is happening with platelets which are one of the main factors of normal hemostasis.

Impaired platelet function is rarely congenital; the most often it is acquired, commonly caused by medications such as acetylsalicylic acid (ASA) and other antiplatelet drugs. While ASA usefulness in decreasing adverse ischemic events in patients with coronary artery disease is clearly proven, there are different views about preoperative stopping of ASA and its connection with increased risk of bleeding during cardiac surgery operations<sup>2</sup>.

Preoperative ASA therapy, is forbidden 5–7 days before cardiac surgery intervention by recommendations in order to reduce the potential risks of bleeding during operation. However, without testing platelet function we cannot know whether it is disrupted or whether there is a presence of residual antithrombotic agent therapeutic effect, especially taking into account that each person individually respond to the therapy<sup>3</sup>. In this sense, impedance platelet aggregometry as the method for precise assessment of platelet function may provide valuable information on platelet function and consequently help in estimating the risk of increased bleeding and transfusion requirements. For this purpose, semi-automatic impedance aggregometer (Multiplate analyzer, Dynabyte Medical, Germany) is commonly used. It analyzes platelet function from the whole blood sample. One of the tests that is performed by this apparatus is the ASPI test which uses arachidonic acid as a substrate of platelet cyclooxygenase. When cyclooxygenase is blocked, thromboxane formation is

inhibited and, in turn, platelets activation. The ASPI test is sensitive to cyclooxygenase-blockers such as ASA.

We did not find in literature a strong recommendation for cut-off values of the ASPI test that represents moderate or high risk for increased bleeding during and after cardiac surgery operation. On the other hand, there are many recommendations for values of the ADP test which demonstrates residual antiplatelet effects of the ADP blockers such as clopidogrel<sup>4</sup>.

Some researchers suggest that aggregometry prior to cardiac surgery for detection of residual antiplatelet effect of ASA is unnecessary and that preoperative ASA increases postoperative bleeding, but this may be avoided by the use of the ASA doses < 325 mg/day<sup>3</sup>. On the other hand, some researchers suggest individual approach for each patient going to heart surgery by determining platelet aggregability and stopping ASA<sup>4,5</sup>.

Petricević et al.<sup>6</sup> in their study, which included 101 elective cardiac surgery patients, demonstrated significant negative correlation between platelet function measured with ASPI test and increased bleeding. A conclusion<sup>7</sup> of the study performed by Myles et al. was that ASA had to be stopped before cardiac surgery because of the bleeding complications. Preoperative administration of ASA is connected with higher blood loss during surgery without positive effect on graft patency in comparison with taking ASA 6h after operation. Aspirin increases postoperative blood drainage after cardiac surgery and also a need for blood transfusions<sup>8</sup>.

Recently published Guidelines on perioperative medication in adult cardiac surgery<sup>11</sup> have suggested that in patients on ASA who needed to undergo coronary artery bypass graft (CABG) surgery continuing ASA throughout the preoperative period should be considered. However, in patients who refused transfusion, who are at high risk of re-exploration for bleeding such as complex and redo operations, with severe renal insufficiency, haematological diseases and hereditary platelet function deficiency, stopping ASA at least 5 days before surgery was recommended (class IIa, level C of recommendation).

Having in mind these opposite attitudes, we wanted to establish whether preoperative platelet function testing for

the presence of residual antiplatelet effect of ASA before cardiac surgery, even after stopping ASA at least 5 days before surgery, may provide clinically important information that would be related to increase in intraoperative bleeding and consequent increase in blood transfusions. We retrospectively analyzed 60 operated on cardiac surgery patients

(double and triple by-pass grafting), who had similar demographic characteristics, the same preoperative antiplatelet therapy (they all received monotherapy with 100 mg of ASA that was ceased 5 days before operation), similar platelet count, length of extracorporeal circulation procedure, coagulation screening, etc. (Table 1).

Table 1

Basic demographic and clinical data of 60 patients enrolled in the study

Data	Group with NPF, n = 31 (51.7%)	Group with IPF n = 29 (48.3%)	p value
Gender (female / male), %	25.8 / 74.2	24.1 / 75.8	
Age (years), mean $\pm$ SD	65.1 $\pm$ 7.31	62.3 $\pm$ 7.38	> 0.05
Eritrocytes (n x 10 <sup>12</sup> /L), mean $\pm$ SD	4.46 $\pm$ 0.44	4.37 $\pm$ 0.41	> 0.05
Platelets (n x 10 <sup>9</sup> /L), mean $\pm$ SD	242.9 $\pm$ 60.83	221.7 $\pm$ 45.85	> 0.05
Received ASA (% of patients)	100	100	
ASPI test (AU min), mean $\pm$ SD	1.056 $\pm$ 229.44	416.7 $\pm$ 195.95	< .0001
TRAP test (AU min), mean $\pm$ SD	1,451.6 $\pm$ 170.47	1,348.3 $\pm$ 259.22	> 0.05
CABG II / CABG III (%)	54.8 / 45.2	51.7 / 48.3	
Perioperative blood loss (mL), mean $\pm$ SD	980.6 $\pm$ 199.86	1,527.5 $\pm$ 637.74	< .0001
Autotransfusion (mL), mean $\pm$ SD	388.3 $\pm$ 76.07	587.6 $\pm$ 210.87	< .0001
Allogeneic transfusion (mL), mean $\pm$ SD	180.6 $\pm$ 253.53	253.4 $\pm$ 294.27	> 0.05

**NPF- normal platelet function; IPF impaired platelet function; ASA - acetylsalicylic acid; AU - aggregation unit per minute; SD – standard deviation; CABG – coronary artery bypass graft.**

The platelet function testing with the ASPI test was performed in all patients. It was shown that almost 50% of the analyzed patients had impaired platelet function in the ASPI test after cancelling ASA (416.7  $\pm$  195.95 aggregation units per minute) which led to increased perioperative drainage for almost 600 mL compared to the group of patients who had unimpaired platelet function (1,527.5  $\pm$  637.74 mL v.s. 980.6  $\pm$  199.86 mL,  $p < 0.0001$ ). Also, the group with the impaired ASPI test received more autologous blood transfusions.

It was shown that preservation of platelet function and the absence of residual antiplatelet effect of acetylsalicylic acid preoperatively resulted in a significantly lower amount of intraoperative bleeding and lower amount of autologous transfusion, which is of great importance for the course and outcome of the surgery.

In conclusion, results of our study showed importance of testing platelet function with the ASPI test before operation, regardless the cessation of the ASA therapy 5 days before

elective surgery in order to avoid excessive perioperative blood loss, blood transfusions and to possibly postpone cardiac surgery.

Bearing in mind the complexity of cardiac surgery operations and possible bleeding complications, testing with impedance aggregometry before the intervention should not be ignored. Our data suggest that aggregometry may optimize the timing for surgical procedures, especially in patients who have residual antiplatelet effect.

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