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## To continue or discontinue aspirin? The risk of perioperative complications

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### ABSTRACT

Acetylsalicylic acid (aspirin) is a noncompetitive irreversible antagonist of the enzyme cyclooxygenase 1 (COX1). This drug is commonly used in prevention of cardiovascular and cerebrovascular events due to inhibition of platelet function. Because of the risk of surgical hemorrhage it is recommended to cessation aspirin intake couple days before the surgical intervention. However, discontinuation of aspirin treatment may results in increased risk of thrombotic events and perioperative complications. Antithrombotic Trialist's Collaboration proved that low dose of aspirin intake before surgery reduces the risk of nonfatal myocardial infarction by 33%, vascular events by 17% and nonfatal stroke by 25%. However, some studies showed the increased risk of perioperative bleeding in patients continuing aspirin treatment. The position of experts is not unambiguous and there have been doubts about the necessity of discontinuation or continuation this drug before surgery.

## ABSTRAKT

Kwas acetylosalicylowy (aspiryna) należy do grupy niekompetycyjnych, nieodwracalnych antagonistów enzymu cyklooksigenazy 1. Lek ten jest powszechnie używany w zapobieganiu incydom sercowo-naczyniowym oraz mózgowo-naczyniowym ze względu na swoje przeciwplatekowe działanie. Z powodu ryzyka krwotoku chirurgicznego zaleca się zaprzestanie przyjmowania aspiryny na kilka dni przed planowanym zabiegiem chirurgicznym. Jednak przerwanie leczenia kwasem acetylosalicylowym może zwiększać ryzyko powstawania zakrzepów i powikłań okołoperacyjnych. Antitrombotic Trialist's Collaboration udowodniło, że niska dawka kwasu acetylosalicylowego przyjmowana przed operacją zmniejsza ryzyko niezakończonego zgonem zawału mięśnia sercowego o prawie jedną trzecią, zdarzeń naczyniowych o 17% i udaru nieinwazyjnego o jedną czwartą. Jednak niektóre badania wykazały zwiększone ryzyko okołoperacyjnego krwawienia u pacjentów kontynuujących leczenie kwasem acetylosalicylowym. Stanowisko ekspertów nie jest jednoznaczne i pojawiły się wątpliwości co do konieczności przerwania lub kontynuacji tego leku przed planowaną operacją.

Słowa kluczowe: kwas acetylosalicylowy, aspiryna, powikłania

## INTRODUCTION

Aspirin (acetylsalicylic acid) belongs to the group of substances classified as non-steroidal anti-inflammatory drugs [1]. This drug owes its activity to noncompetitive irreversible antagonist of the enzyme cyclooxygenase 1 (COX1) that inhibits the synthesis of prostaglandins and thromboxane A<sub>2</sub> from arachidonic acid (AA) [2]. This makes aspirin commonly known as analgesic, antipyretic and anti-inflammatory drug [3]. It has a different effect depending on the dose. Dosages greater than 500 mg should be used to obtain analgesic effects. In smaller doses (75-150mg) acetylsalicylic acid also influences the functioning of the plates, demonstrating the platelet's antiaggregative properties [4]. Additionally it is used for decades in patients with cardiovascular and cerebrovascular events. Aspirin has been applied in prevention of myocardial infarction or stroke. The position of the experts clearly confirms the positive effect of aspirin using. Low-dose aspirin has been proven to reduce the risk of non-fatal myocardial infarction by 33% and non-fatal stroke by 25% [5]. Every 4 patients undergoing non-cardiac surgery are at risk of coronary artery disease (CAD) [5]. 15-25% of perioperative mortality is due to myocardial infarction [5, 6]. Preoperative use of aspirin due to the risk of surgical hemorrhage is often stopped couple days prior to surgical intervention [5, 7]. However, discontinuation of treatment in chronically acetylsalicylic acid intake patients can lead to increased risk of thrombotic events due to decreased fibrinolysis, increased platelet adhesion and aggregation [6]. Researches show that in chronic low-dose acetylsalicylic acid users, sudden withdrawal of aspirin can be fatal. Discontinuation of aspirin treatment increases the risk of cardiovascular disorders by 30% [8]. Despite the danger of aspirin discontinuation, currently, it is recommended to stop aspirin intake before many planned surgical procedures because of the increased risk of perioperative bleeding [6]. The optimum aspirin cessation date is highly debatable as well as the perioperative complication resulting from continuation of aspirin intake.

## **ASPIRIN CONTINUATION VS. DISCONTINUATION BEFORE NON-CARDIAC SURGERY**

It is estimated that over 100 million patients undergoes non-cardiac operations each year [5]. Studies show that up to 4 in 10 patients have coronary heart disease or are at risk group. [5]. Perioperative myocardial infarction (PMI) is very important predictor of patient's morbidity associated with surgery, which is responsible for 15-25% inhospital deaths [5, 6, 9].

Some medical studies have shown the negative effect of preoperative withdrawal of aspirin in patients on a longterm admission [5, 6, 8]. It has been proven that in patients who are constantly taking acetylcysteic acid, discontinuation of treatment increases the risk of cardiovascular disorders by 30% [7, 8].

In a randomized trial, Oscarsson et al. randomly assigned patients into the group taking placebo 7 days before surgery and the study group taking 75mg dose of aspirin. It should be emphasized that each patient had at least one cardiac risk factor. The study showed a positive effect of taking aspirin before non-cardiac operations in reduction the risk of major adverse cardiac events (MACE), stroke and transient ischemic attack (TIA). MACE during the first 30 days after surgery were observed in 1.8% patients receiving low dose of aspirin and in 9% of patients in the placebo group. TIA or stroke were reported more often in patients discontinuing aspirin treatment (9%) compared to patients who had continued aspirin treatment (2,7%). Moreover, there is a report presenting severe bleeding after transurethral prostatectomy in patients taking aspirin compared to patients who stopped aspirin taking. In other types of non-cardiac operations, no difference in bleeding between the two groups of patients was noted [5].

According to the study published in the Annals of Surgery there is no need to aspirin withdrawal before most planned surgery in patients using it for cardiovascular events prevention. The exception is ophthalmic, intracranial and transurethral surgeries. In patients undergoing this kind of operations it is recommended to stop aspirin intake before, because the risk of intra- and postoperative bleeding outweighs potential benefits [6]. However, a case-control study did not show a relationship between preoperative aspirin intake and an increased risk of bleeding while rhegmatogenous retinal detachment surgery [10].

In contrast to the previous researches, the next study showed no positive benefits of preoperative aspirin continuation. The study did not show statistical differences in perioperative complications between patients continuing aspirin intake and patients who stopped aspirin intake. Both groups of patients were characterized by a similar number of deaths (aspirin group 1.3% vs. placebo 1.2%,  $p=0,78$ ), myocardial infarction (6.2% vs. 6.3%,  $p=0,85$ ) and stroke (0.3% vs. 0.4%,  $p = 0.62$ ). However, a greater risk of perioperative bleeding were reported in patients continuing aspirin treatment (4,6%) compared to patients who had discontinued aspirin treatment (3,8%) [11].

## **ASPIRIN CONTINUATION VS. DISCONTINUATION IN CARDIAC SURGERY**

Cardiovascular disease is the leading cause of death worldwide [12]. Most patients with coronary artery disease receive aspirin to prevent thrombotic disorders [13]. It is very important to know how to take care of such patients before planned surgical procedures, taking into account the risk of thrombotic complications and dangerous bleeding.

According to the study published in the Journal of Cardiac Surgery patients who had continued aspirin treatment at any dose before coronary artery bypass grafting (CABG) had reduced risk of postoperative acute kidney injury (AKI) by 32 % and had reduced risk of death. Additionally, in patients who received aspirin at a dose lower than 160 mg, a 21% drop in the incidence of myocardial infarction was observed. Continuation of low-dose aspirin intake was associated with an increased risk of bleeding, but did not lead to increased frequency of reoperation and blood transfusion [13].

In another study we can see the same conclusions, that aspirin reduces the risk of AKI, myocardial infarction and perioperative mortality. It is suggested to not interrupt this drug in patients undergoing cardiac surgery [14]

The complications in both examined groups in the next study were comparable. No difference in perioperative MI, cerebrovascular accidents (CVAs), mortality was observed between patients. The study group was characterized by increased blood loss [15]. Scientists suggest that a dose of aspirin less than 100mg has little effect on the risk of bleeding and the same proposal we can see in the other research [15, 16]. In low dose aspirin group patient's (<100 mg/day) had decreased morbidity rate and no increased risk of bleeding was present [16]. Myles et al. did not show statistical differences between patients continuing aspirin therapy and those who stopped receiving this drug. Among patients undergoing coronary artery surgery, those who had continued aspirin treatment before surgery were not having neither a lower risk of death and thrombotic complications nor a bigger risk of blood lose than those with placebo [17].

## CONCLUSIONS

Some studies proved that in many surgical procedures, the risk of perioperative bleeding in patients continuing aspirin treatment is minimal compared to high risk of thromboembolic events associated with aspirin withdrawal. Continuation of aspirin intake resulted in reduction of the risk of postoperative complication, e.g. nonfatal myocardial infarction, cerebrovascular and cardiovascular event [5, 6, 13, 14]. However, some studies show no benefits of continuing aspirin and increased risk of bleeding [11, 15, 16, 17]. The results of the research are considered from different time of applying aspirin, various doses of aspirin and different types of operations. In patients undergoing intracranial, intramedullary, ansurethral surgeries and tonsillectomy it is recommended to stop aspirin intake before surgery to prevent patients from intra- and postoperative bleeding [6, 10, 18]. In cardiac surgery it is recommended to continue aspirin intake, but small dosage (<100mg/day) are preferred due to the lower risk of bleeding [13, 14, 16]. The presented scientific studies are not able to clearly answer the question whether aspirin should be discontinued or may be continued before the planned surgery. Opinions of scientists are divided. There are no specific guidelines on the use of aspirin prior to surgery. It seems that the decision about the need to discontinue aspirin prior to planned surgery should be made individually based on the patient's condition, type of surgery, dose of the drug being taken, risk factors for haemorrhagic or thrombotic complications. The most important thing is that the potential benefits of the decision taken outweigh the existing risk. More research is needed in the future.

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