Review article

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Aspirin in Patients Undergoing Neurosurgery: A long time controversy

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Aspirin is frequently used to prevent ischemic episodes, either directly or indirectly. Long-term aspirin therapy can increase intraoperative blood loss and have an impact on blood clot development during surgery. This is particularly crucial for neurosurgery and other high-risk surgeries. There is currently no clinical evidence to support the European Society of Cardiology (ESC) recommendation that aspirin should be discontinued at least one week before neurosurgical intervention. In addition to summarizing current clinical data on bleeding risk associated with chronic aspirin therapy in neurosurgical patients, including brain tumour surgery, cerebrovascular procedures, and spinal surgery, this narrative review presents evidence that casts doubt on the need for aspirin interruption in neurosurgical patients. It also discusses options for monitoring the effect of aspirin and the clinical implications of these methods.

Key words: *brain tumour; cerebrovascular surgery; spinal surgery; aspirin; neurosurgery; postoperative complications; bleeding risk*

Introduction

Due to its well-known ability to reduce platelet aggregation, aspirin (acetylsalicylic acid, ASA) is frequently used for either primary or secondary prevention of ischemic events [1]. Long-term aspirin therapy can also increase intraoperative blood loss and impact blood clot formation during surgery [2]. Because even mild haemostatic problems can result in serious postoperative consequences, such as acute cerebral bleeding, this is particularly significant for high-risk surgeries, including neurosurgery [3]. Historically, expert consensus—rather than clinical evidence—has determined recommendations for discontinuation of aspirin therapy before neurosurgical procedures [4]. The 2022 ESC guidelines continue to recommend stopping aspirin therapy at least 7 days before surgeries in patients with a high peri-operative bleeding risk (e.g., undergoing complex brain surgeries, spinal surgery or certain neurosurgical operations), have repeatedly reiterated this recommendation over the years [5]. Clinical evidence gathered from observational studies in patients who have had spinal and brain surgery, however, does not support the idea that preoperative long-term aspirin therapy increases the risk of postoperative haemorrhage. Instead, there is growing evidence of its benefits in mitigating postoperative thromboembolic events [6, 7].

Current clinical data on bleeding risk associated with chronic aspirin therapy in neurosurgical patients, including brain tumour surgery, cerebrovascular procedures, and spinal surgery, are summarized in this narrative review along with evidence that casts doubt on the need for aspirin interruption in neurosurgical patients. It also discusses options for monitoring the effects of aspirin and the clinical implications of these methods.

Antiplatelet effect of aspirin

Aspirin's antiplatelet effect is achieved by suppressing the synthesis of thromboxane A2 (TXA2) after blocking the activity of cyclooxygenase (COX) within platelets [8]. Aspirin efficiently inhibits this method of platelet activation, and thromboxane A2 is a key player in the amplification of platelet aggregation [9]. Aspirin's antiplatelet effect has several clinically significant features, including its enhanced efficacy at low doses (75–325 mg/d). This effect is due to the lack of concurrent inhibition of prostacyclin in endothelial cells and irreversible COX inhibition, which distinguishes aspirin from other nonsteroidal anti-inflammatory drugs (NSAIDs). The duration of the antiplatelet effect of medications like ibuprofen, ketorolac, etc. correlates with the elimination time because they reversibly compete with the arachidonic acid substrate at the COX active site. Because aspirin irreversibly acetylates platelet COX, its antiplatelet action lasts for several days following a single dose [10]. After a single aspirin intake, the ability to produce TXA2 can only be restored with the generation of new platelets, which are regenerated by around 10% per day. Adenosine diphosphate, collagen, and thrombin are examples of non-TXA2-dependent activators of platelet aggregation that can circumvent the aspirin-dependent mechanism and produce effective coagulation. It makes aspirin a relatively weak antiplatelet agent because it only partially inhibits platelets [8]. Furthermore, up to 25% of patients may not respond to standard aspirin treatment [11].

Aspirin antiplatelet effect assessment

Increased bleeding time is the direct clinical effect of aspirin absorption on primary hemostasis [12]. Major attempts have been made in recent decades to

establish alternative and trustworthy assessments of the antiplatelet effect of aspirin due to the major challenges in standardizing this sort of test. In evaluating the aspirin effect, each of these suggested approaches showed considerable variation and a weak association with one another [13, 14]. More significantly, no trustworthy clinical evidence of any of these tests' predictive validity or association with clinically meaningful outcomes has been found to date [15]. It is important to note, that aspirin-associated hypocoagulation cannot be shown by non-specific viscoelastic tests such as thromboelastography or rotational thromboelastometry, which were created for an integrated evaluation of blood clot formation. This behaviour can also be viewed as the main risk factor for the formation of dense clots in the presence of aspirin [16].

Impact of aspirin on bleeding risk in non-neurosurgical patients

There is limited clinical evidence regarding the continuation or discontinuation of aspirin in surgical patients. However, interactions between aspirin, NSAIDs, and perioperative anticoagulants have raised concerns about the design and outcomes of related clinical trials. [17]. According to current guidelines on perioperative bleeding, "aspirin should not be withdrawn peri-operatively unless the risk of bleeding exceeds the thrombotic risk from withholding the drug," [18]. However, as previously said, neurosurgical patients require a distinct and individualized approach to care.

In Brain surgery and aspirin related studies, Rahman et al. [7] concluded that brain tumour surgeries were not associated with an increased haemorrhagic risk with patients who used low-dose aspirin before surgery. McGaul [19], mentioned perioperative aspirin related complications may increase risk in dental surgery but the results of this study cannot directly correlate with neurosurgical procedures outcome. Another case report by Kulikov et al. [20] identified that aspirin was not associated with increased bleeding risk. Another study found that haemorrhagic risk was the same in aspirin or non- aspirin groups [21]. Tonchev N, et al. [22], explained that "In patients with a high cardiovascular and cerebrovascular risk, low-dose ASA can be safely sustained after brain tumour surgery, and its perioperative use has not been linked to an increased rate of haemorrhagic complications after pituitary adenoma surgery". While Ma Y et al. [23] explained that antiplatelet therapy did not increase the risk of haemorrhage and improved outcomes after vascular revascularization procedures. Bianconi et al. [24] described intracranial haemorrhage after intracranial aneurysm clipping was more frequent in those patients who were using antiplatelet therapy. Dasenbrock et al. [25] explained in their study that the use of aspirin was not associated with an increased risk of postoperative haemorrhage in vascular surgery patients. Florez et al. [26] also presented the same finding and clearly explained that aspirin didn't increase the chance of bleeding in the intraoperative or preoperative period.

In spinal surgery patients, Zhang et al. [6] stated that there was no difference in perioperative complications between aspirin continuation and discontinuation. Similarly, Zian et al. [29] and Suk-Bong et al. [30] found that continued aspirin administration did not have an increased risk for bleeding. Meta-analysis ASA (Aspirin)-continuing group ASA-discontinuing group. Cuellar et al. [27] compared three groups—patients who never used aspirin, those who discontinued aspirin preoperatively, and those who continued aspirin therapy—and observed no differences in perioperative complications or clinical outcomes. In another study, Ju et al. [28] concluded that there was no association between low-dose ASA continuations with increased blood loss.

Balancing the risk

The clinical data presented reflect a lack of trustworthy evidence about clinical decision-making regarding the continuation or cessation of aspirin use during the perioperative phase in patients slated for elective neurosurgery procedures.

During surgery, the coagulation process gets triggered, (also known as blood clotting mechanism) which is a crucial mechanism that stops bleeding from incision site or dissection area automatically. The formation of a clot is created by various mechanisms including platelets, plasma proteins and various factors. Due to the involvement of various players in coagulation process, strength of aspirin's anticoagulation effect is unclear.

Variability in clinical practice is caused by inconsistent clinical data [31, 32]. Furthermore, there is inconsistency among the standards on this matter.

Guidelines on perioperative bleeding management from the European Society of Anaesthesiology and Intensive Care, for example, state that "intracranial surgery can be safely performed in the presence of low-dose aspirin." However, if aspirin withdrawal before surgery is taken into consideration, the time from the last medication intake to the intervention is three days. Nonetheless, a longer gap (5 – 7 days) can be taken into consideration for invasive treatments that have a high risk of bleeding [18]. Compared to the ambiguous ESC recommendations recommendation of at least 7 days of withdrawal, this period is substantially shorter [1].

A framework for such decision-making is not precisely defined. However, it is essential that multidisciplinary consultation among neurosurgeons, anaesthesiologists, cardiologists informs the choice to continue or discontinue taking aspirin in a given situation. It may include the estimated risk of blood loss consequences from prolonged bleeding, the risk of postoperative ischemia complications due to aspirin cessation, and the risk of delaying surgery. Non-specific variables including preoperative anaemia, renal dysfunction, chronic liver illness, metabolic disorders, etc., should also be considered when assessing a person's risk of bleeding [18]. Before having surgery, such defects should be fixed, if at all feasible.

It should be considered that the antiplatelet effect of aspirin may exacerbate high estimated blood loss. This is especially crucial in situations when neoplasms—tissues with aberrant vascular wall structure—will require surgical manipulation inside the tissues. For spinal and cerebrovascular surgery, this risk is generally lower.

However, in patients with high cardiac risk (history of myocardial infarction, coronary stenting, unstable angina, etc., which are among the most common indications for chronic aspirin use), the risk of thrombotic complications may exceed the risk of bleeding. In some situations, continuing aspirin therapy might yield better outcomes.

Additionally, treating patients who may suffer major repercussions from a delay in surgical intervention is often necessary in neurosurgical practice (e.g., seizures in patients with intracranial masses, increasing neurologic loss brought on by the mass effect and intracranial haemorrhage from a brain lesion, etc.). The risk-benefit ratio of stopping aspirin in these situations is still unknown. The ESC's suggestion to stop aspirin may understate the dangers and consequences of delaying surgery.

Conclusion

The discontinuation of aspirin before neurosurgical procedures remains a contentious clinical issue. Neurosurgical patients exhibit a wide range of bleeding risks during surgery, necessitating individualized risk assessments.

However, present neurosurgical treatment protocol, for the all preoperative patients, aspirin cessation is currently advised and followed. These protocols encourage doctors to make the same therapeutic choices regardless. Future research should focus on developing evidence-based guidelines to support logical and individualized clinical decision-making in this area.

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Conflict of interest

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References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Čelutkienė J, Chioncel O, Cleland JGF, Coats AJS, Crespo-Leiro MG, Farmakis D, Gilard M, Heymans S, Hoes AW, Jaarsma T, Jankowska EA, Lainscak M, Lam CSP, Lyon AR, McMurray JJV, Mebazaa A, Mindham R, Muneretto C, Francesco Piepoli M, Price S, Rosano GMC, Ruschitzka F, Kathrine Skibelund A; ESC Scientific Document Group. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021 Sep 21;42(36):3599-3726. doi: 10.1093/eurheartj/ehab368
2. Gerstein NS, Albrechtsen CL, Mercado N, Cigarroa JE, Schulman PM. A Comprehensive Update on Aspirin Management During Noncardiac Surgery. Anesth Analg. 2020 Oct;131(4):1111-1123. doi: 10.1213/ANE.0000000000005064
3. Solheim O, Jakola AS, Gulati S, Johannesen TB. Incidence and causes of perioperative mortality after primary surgery for intracranial tumors: a national, population-based study. J Neurosurg. 2012 Apr;116(4):825-34. doi: 10.3171/2011.12.JNS11339
4. Korinth MC. Low-dose aspirin before intracranial surgery--results of a survey among neurosurgeons in Germany. Acta Neurochir (Wien). 2006 Nov;148(11):1189-96; discussion 1196. doi: 10.1007/s00701-006-0868-4
5. Mehilli J, Halvorsen S. The '10 commandments' for the 2022 European Society of Cardiology guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. Eur Heart J. 2023 Feb 1;44(5):336-337. doi: 10.1093/eurheartj/ehac703
6. Zhang C, Wang G, Liu X, Li Y, Sun J. Safety of continuing aspirin therapy during spinal surgery: A systematic review and meta-analysis. Medicine (Baltimore). 2017 Nov;96(46):e8603. doi: 10.1097/MD.0000000000008603
7. Rahman M, Donnangelo LL, Neal D, Mogali K, Decker M, Ahmed MM. Effects of Perioperative Acetyl Salicylic Acid on Clinical Outcomes in Patients Undergoing Craniotomy for Brain Tumor. World Neurosurg. 2015 Jul;84(1):41-7. doi: 10.1016/j.wneu.2015.02.016
8. Kwok CS, Loke YK. Critical Overview on the Benefits and Harms of Aspirin. Pharmaceuticals (Basel). 2010 May 14;3(5):1491-1506. doi: 10.3390/ph3051491
9. Rucker D, Dhamoon AS. Physiology, Thromboxane A2. 2022 Sep 12. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–.
10. Tsoupras A, Gkika DA, Siadimas I, Christodoulopoulos I, Efthymiopoulos P, Kyzas GZ. The Multifaceted Effects of Non-Steroidal and Non-Opioid Anti-Inflammatory and Analgesic Drugs on Platelets: Current Knowledge, Limitations, and Future Perspectives. Pharmaceuticals (Basel). 2024 May 14;17(5):627. doi: 10.3390/ph17050627
11. Roman-Gonzalez A, Naranjo CA, Cardona-Maya WD, Vallejo D, Garcia F, Franco C, Alvarez L, Tobón LI, López MI, Rua C, Bedoya G, Cadavid Á, Torres JD. Frequency of Aspirin Resistance in Ischemic Stroke Patients and Healthy Controls from Colombia. Stroke Res Treat. 2021 May 21;2021:9924710. doi: 10.1155/2021/9924710
12. Matsuoka T, Kobayashi K, Lefor AK, Sasaki J, Shinozaki H. Antithrombotic drugs do not increase intraoperative blood loss in emergency gastrointestinal surgery: a single-institution propensity score analysis. World J Emerg Surg. 2019 Dec 30;14:63. doi: 10.1186/s13017-019-0284-8
13. Snoep JD, Hovens MM, Eikenboom JC, van der Bom JG, Huisman MV. Association of laboratory-defined aspirin resistance with a higher risk of recurrent cardiovascular events: a systematic review and meta-analysis. Arch Intern Med. 2007 Aug 13-27;167(15):1593-9. doi: 10.1001/archinte.167.15.1593
14. Aradi D, Storey RF, Komócsi A, Trenk D, Gulba D, Kiss RG, Husted S, Bonello L, Sibbing D, Collet JP, Huber K; Working Group on Thrombosis of the European Society of Cardiology. Expert position paper on the role of platelet function testing in patients undergoing percutaneous coronary intervention. Eur Heart J. 2014 Jan;35(4):209-15. doi: 10.1093/eurheartj/eht375
15. Favaloro EJ. Clinical utility of closure times using the platelet function analyzer-100/200. Am J Hematol. 2017 Apr;92(4):398-404. doi: 10.1002/ajh.24620
16. Tiscia GL, De Laurenzo A, Cappucci F, Favuzzi G, Chinni E, Vaira P, Ostuni A, Margaglione M, Grandone E. Thromboelastography parameters in Italian pregnant women: do antithrombotic drugs change reference values? J Investig Med. 2020 Apr;68(4):902-905. doi: 10.1136/jim-2019-001261
17. Shah S, Urtecho M, Firwana M, Nayfeh T, Hasan B, Nanaa A, Saadi S, Flynn DN, Abd-Rabu R, Seisa MO, Rajjoub NS, Hassett LC, Spyropoulos AC, Douketis JD, Murad MH. Perioperative Management of Antiplatelet Therapy: A Systematic Review and Meta-analysis. Mayo Clin Proc Innov Qual Outcomes. 2022 Oct 21;6(6):564-573. doi: 10.1016/j.mayocpiqo.2022.09.006
18. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, Fries D, Görlinger K, Haas T, Imberger G, Jacob M, Lancé M, Llau J, Mallett S, Meier J, Rahe-Meyer N, Samama CM, Smith A, Solomon C, Van der Linden P, Wikkelsø AJ, Wouters P, Wyffels P. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol. 2013 Jun;30(6):270-382. doi: 10.1097/EJA.0b013e32835f4d5b
19. McGaul T. Postoperative bleeding caused by aspirin. J Dent. 1978 Sep;6(3):207-9. doi: 10.1016/0300-5712(78)90243-9
20. Kulikov A, Gruenbaum SE, Quinones-Hinojosa A, Pugnaloni PP, Lubnin A, Bilotta F. Preoperative Risk Assessment Before Elective Craniotomy: Are Aspirin, Arrhythmias, Deep Venous Thromboses, and Hyperglycemia Contraindications

to Surgery? World Neurosurg. 2024 Jun;186:68-77. doi: 10.1016/j.wneu.2024.03.018
21. Rychen J, Weiger VF, Halbeisen FS, Ebel F, Ullmann M, Mariani L, Guzman R, Soleman J. Perioperative continuation or ultra-early resumption of antithrombotics in elective neurosurgical cranial procedures. Neurosurg Focus. 2023 Oct;55(4):E6. doi: 10.3171/2023.7.FOCUS23357
22. Tonchev N, Pinchuk A, Dumitru CA, Stein KP, Neyazi B, Sandalcioglu IE, Rashidi A. Postoperative Hemorrhage and Venous Thromboembolism in Patients with Pituitary Adenomas Under Acetylsalicylic Acid. J Clin Med. 2024 Nov 21;13(23):7020. doi: 10.3390/jcm13237020
23. Ma Y, Wang T, Wang H, Amin-Hanjani S, Tong X, Wang J, Tong Z, Kuai D, Cai Y, Ren J, Wang D, Duan L, Maimaitili A, Hang C, Yu J, Bai X, Powers WJ, Derdeyn CP, Wu Y, Ling F, Gu Y, Jiao L; CMOSS Investigators. Extracranial-Intracranial Bypass and Risk of Stroke and Death in Patients With Symptomatic Artery Occlusion: The CMOSS Randomized Clinical Trial. JAMA. 2023 Aug 22;330(8):704-714. doi: 10.1001/jama.2023.13390
24. Bianconi A, Ceraudo M, Nico E, Minardi M, Allevi M, Prior A, Garbossa D, Zona G, Fiaschi P. To use or not to use antithrombotics in unruptured cerebrovascular malformations? A systematic review focusing on this clinical and surgical dilemma. Neurosurg Focus. 2023 Oct;55(4):E14. doi: 10.3171/2023.7.FOCUS23117
25. Dasenbrock HH, Yan SC, Gross BA, Guttieres D, Gormley WB, Frerichs KU, Ali Aziz-Sultan M, Du R. The impact of aspirin and anticoagulant usage on outcomes after aneurysmal subarachnoid hemorrhage: a Nationwide Inpatient Sample analysis. J Neurosurg. 2017 Feb;126(2):537-547. doi: 10.3171/2015.12.JNS151107
26. Florez WA, García-Ballestas E, Maeda F, Joaquim A, Pavlov O, Moscote-Salazar LR, Tsimpas A, Martinez-Perez R. Relationship between aspirin use and subarachnoid hemorrhage: A systematic Review and meta-analysis. Clin Neurol Neurosurg. 2021 Jan;200:106320. doi: 10.1016/j.clineuro.2020.106320
27. Cuellar JM, Petrizzo A, Vaswani R, Goldstein JA, Bendo JA. Does aspirin administration increase perioperative morbidity in patients with cardiac stents undergoing spinal surgery? Spine (Phila Pa 1976). 2015 May 1;40(9):629-35. doi: 10.1097/BRS.0000000000000695
28. Ju H, Hart RA. Hidden blood loss in anterior lumbar interbody fusion (ALIF) surgery. Orthop Traumatol Surg Res. 2016 Feb;102(1):67-70. doi: 10.1016/j.otsr.2015.10.003
29. Zian A, Overdevest GM, Schutte PJ, Klok FA, Steyerberg EW, Moojen WA, van der Gaag NA. Aspin: neurosurgical aspirin intervention prognostic study - perioperative continuation versus discontinuation of aspirin in lumbar spinal surgery, a randomized controlled, noninferiority trial. Trials. 2024 Feb 29;25(1):156. doi: 10.1186/s13063-024-07945-w
30. Kang SB, Cho KJ, Moon KH, Jung JH, Jung SJ. Does low-dose aspirin increase blood loss after spinal fusion surgery? Spine J. 2011 Apr;11(4):303-7. doi: 10.1016/j.spinee.2011.02.006
31. Li M, Yang S, Liu Q, Guo R, Wu J, Cao Y, Wang S. Evaluating the safety of early surgery for ruptured intracranial aneurysms in patients with long-term aspirin use: a propensity score matching study. Chin Neurosurg J. 2020 Nov 30;6(1):37. doi: 10.1186/s41016-020-00216-y
32. Fiaschi P, Iaccarino C, Stefini R, Prior E, Prior A, Zona G. Clinical practice for antiplatelet and anticoagulant therapy in neurosurgery: data from an Italian survey and summary of current recommendations - part I, antiplatelet therapy. Neurosurg Rev. 2021 Feb;44(1):485-493. doi: 10.1007/s10143-019-01229-7