

## Continuation of medically necessary platelet aggregation inhibitors - acetylsalicylic acid and clopidogrel - during surgery for spinal degenerative disorders: Results in 100 patients

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### Abstract

**Background:** Patients undergoing spinal surgery while under anticoagulation therapy are at risk of developing bleeding complications, even though lower incidences have been reported for joint arthroplasty surgery. There is a gap in the medical literature examining the incidence of postoperative spinal bleeding in patients who were under anticoagulation medication at the time of surgery.

**Methods:** We prospectively followed a consecutive cohort of 100 patients (58 male, 42 female) undergoing spinal surgery. The average patient age was 48.7 years and the minimum follow up time was 12 months. Diagnosis was lumbar spinal stenosis in 20, herniated lumbar discs in 63, degenerative cervical disc disease in 3, and cervical disc herniation in 14 cases. In our study, platelet aggregation inhibitors (clopidogrel and/or acetylsalicylic acid) were given for the treatment of cardiovascular and cerebrovascular thrombotic events, to reduce risk of stroke in patients who have had transient ischemia of the brain or acute coronary syndrome, and as secondary prevention of atherosclerotic events (fatal or nonfatal myocardial infarction (MI). A cessation of anticoagulants (acetylsalicylic acid or clopidogrel) in our patients in the peri- and postoperative period was contraindicated.

**Results:** Sixty-three patients were on both clopidogrel and acetylsalicylic acid and 37 on acetylsalicylic acid only. None of the patients suffered any postoperative bleeding complication. Three patients suffered postoperative wound dehiscence and one patient had an infection that required reoperation.

**Conclusion:** The question of whether preoperative platelet aggregation inhibitors must be stopped before elective spinal surgery has never been answered in the literature. In our prospective series, we have found no increase in the risk of postoperative spinal bleeding with the use of clopidogrel or acetylsalicylic acid. This finding suggests that spine surgery can be done without stopping anticoagulation. Lacking specific guidelines, each patient should be treated on an individual basis, and the potential benefits of anticoagulation should be compared with the potential risks (risk–benefit ratio).

**Key Words:** Acetylsalicylic acid, clopidogrel, spinal surgery

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## INTRODUCTION

Platelet aggregation inhibitors are indicated for primary and secondary prevention of myocardial infarction (MI), stable and unstable angina including coronary artery disease (CAD), arterial thromboembolism prophylaxis for patients with prosthetic heart valves in combination with warfarin, secondary prevention of stroke/transient ischemic attack (TIA), and acute treatment of stroke in patients not eligible for thrombolysis.<sup>[1]</sup> The perioperative anticoagulant management of such patients is challenging because interruption of anticoagulation therapy may increase the risk of embolic stroke, which can be fatal or associated with major disability in 70% of patients.<sup>[16]</sup> In managing the perioperative anticoagulation of patients, one approach is to stop the platelet aggregation inhibitors approximately 5 days before surgery and to administer bridging anticoagulation with intravenous heparin or low-molecular-weight heparin (LMWH) before and after surgery when the international normalized ratio (INR) is sub-therapeutic.<sup>[7]</sup> This approach aims to minimize the time patients are not therapeutically anticoagulated and the risk for thromboembolism. Another approach is to continue the platelet aggregation inhibitors during the perioperative period, thereby mitigating the risk for thromboembolism. Although minor procedures, such as dental extractions, can be safely carried out in anticoagulated patients, the safety of this approach in patients is not established for spinal surgical procedures.<sup>[23]</sup>

Based upon the customary rate of platelet production, approximately 5-6 days are required after cessation of ASA to replace approximately 50% of the circulating platelets (10%/24 h). Because the ASA effect on individual platelets is complete, it cannot be reversed.<sup>[8]</sup> Data from neurosurgical spine patients are sparse,<sup>[17,18]</sup> describing spontaneous hematoma associated with anticoagulant therapy in patients with spinal meningioma<sup>[22]</sup> or without.<sup>[6,9,14]</sup> However, aspirin has been identified as an important risk factor in the development of postoperative hematoma following intracranial surgery<sup>[10,15]</sup> in emergencies.<sup>[20]</sup> The purpose of the present study is to report on the incidence of bleeding complications and neurological deficits following spinal surgery and to present the management rationale in our institution.

## MATERIALS AND METHODS

### Cohort of 100 consecutive patients undergoing spinal surgery

A consecutive cohort of 100 patients underwent spinal surgery by a single surgeon in Iran over a 24-month period; procedures included 28 cervical, 48 lumbar, and 24 thoracic/thoracolumbar operations. Operations included 44 decompressions versus 56 decompressions/fusions.

Operative diagnoses included: spinal stenosis (35 patients), acute fractures/postramatic deformities (18 patients), degenerative disc disease (12 patients), herniated lumbar discs (26 patients), isthmic spondylolisthesis (5 patients), degenerative scoliosis/stenosis (4 patients), but no spinal cord injuries. The average patient age was 48.7 years (range 23-94 years), and were followed up for a minimum of 12 postoperative months.

### Antiplatelet agents and low molecular weight heparin prophylaxis

Sixty-three patients were on both clopidogrel and ASA, and 37 on acetylsalicylic acid only. Alternating compressive stockings were immediately worn by all patients postoperatively. Enoxoparin, a LMWH, was administered once daily, 20 mg starting from the eighth postoperative hour, and was utilized until the patient was mobilized and discharged.

Variables studied in all patients included: the duration of surgery and comorbid factors expressed according to an available index from the literature [Table 1].<sup>[4]</sup>

## RESULTS

No postoperative hemorrhages resulting in paralysis but four wound-related complications. No bleedings complications with/without neurological deficits occurred

**Table 1: Patient characteristics and procedures (N=100)**

Patient characteristics		No. (%)	
Total number		100	
Parameters	Duration of surgery (min)	Co-morbidity index <sup>[4]</sup>	Approach
Type of surgery			
Decompressive procedure (lumbar)			
Decompression and instrumented fusion	184	2	Posterior 9 (9)
Lumbar discectomies	60	0	Posterior 26 (26)
Combined anterior/posterior procedures	400	4	Anterior and posterior 41 (41)
Decompressive procedure (cervical)			
Laminectomy	45	1	Posterior 7 (7)
Laminoplasty	62	1	Posterior 11 (11)
Ventral fusion with Cage implantation	93	1	Anterior 6 (6)
Gender	Female		42 (42)
	Male		58 (58)
Age (years)	Median: 48.7 Range: (23-94)		

in this 100-patient cohort. However, three patients did develop postoperative wound dehiscence within 10 days after surgery and another patient had an infection that required re-operation 2 weeks after surgery.

### **Duration of surgery, incidence of pulmonary embolism, but no postoperative hemorrhages resulting in paralysis due to anticoagulation**

In 22 out of 41 cases, the duration of surgery exceeded the average (265 min) of the combined anterior/posterior fusion subgroup but remained within one standard deviation (78 min). The comorbidity index was higher than average in 13 patients (1.9) of the decompression and fusion subgroups. The overall incidence of pulmonary embolism was 1.8%. The incidence of pulmonary embolism was highest (3.9%) in combined procedures. In this 100-patient group, most of whom who suffered from shortness of breath, no deaths occurred due to symptomatic pulmonary embolism (PE). Clinical suspicion of PE was confirmed using Spiral computed tomography (CT). None of the PE patients suffered any bleeding complication as a result of the introduction of full anticoagulation. Only six patients suffered postoperative subcutaneous hematomas, which did not require any evacuation. None of these six patients developed neurological symptoms or signs, but instead presented with a tense wound and increasing pain.

### **Increased risk of postoperative bleeding in patients undergoing cervical laminectomy or circumferential spine surgery**

Both combined anterior/posterior procedures and cervical laminectomies were associated with an increased risk of postoperative bleeding for patients taking platelet aggregation inhibitors immediately prior to the surgery (e.g. not stopped ahead of time). Patients undergoing posterior procedures alone appeared to suffer fewer instance of postoperative bleeding, but these results were not statistically significant ( $P = 0.325$ ). Notably, surgical drains were used in all of the operated patients.

## **DISCUSSION**

ASA elevates the risk of a hemorrhagic complication during surgery by 50%, but does not increase operative mortality.<sup>[2]</sup> The current guideline of the European Society of Cardiology (ESC) recommends that ASA for secondary prevention should not be discontinued perioperatively in all surgeries.<sup>[21]</sup> Nonetheless, for intracranial, intraspinal, and intraocular procedures, even small hemorrhages can cause significant morbidity, so that temporarily discontinuing ASA would seem to be necessary. ASA should be stopped, therefore, a minimum of 7 days before surgery to be sure that no antiaggregatory effect persists.<sup>[2]</sup>

### **Clopidogrel with acetylsalicylic acid (ASA)**

Clopidogrel is routinely used in conjunction with aspirin to treat acute coronary system (ACS) and postpercutaneous coronary intervention (PCI) stenting. Clopidogrel appears to be slightly more effective as an antiplatelet drug than ASA (e.g. in patients at risk of ischemic events).<sup>[3]</sup>

#### **Should Antiplatelet Aggregants be Stopped Prior to Elective Spine Surgery?**

Should preoperative platelet aggregation inhibitors be stopped before elective spinal surgery; the literature never adequately answered this question. Moreover, because of the proximity of neural structures and an incalculable risk for neurological deficits, it is almost impossible to find an answer by means of a prospective randomized study. In the present study, surgery was necessary in all the patients and could not be delayed/postponed. Yet, without stopping either clopidogrel/ASA versus ASA alone, no patients sustained a postoperative hematoma resulting in paralysis, and only six sustained postoperative subcutaneous hematomas, which did not require evacuation (e.g. tense wound and increasing pain).

If an operation cannot be postponed and must be performed during the critical period, it is recommended that dual inhibition of platelet aggregation be continued perioperatively.<sup>[21]</sup> If this is unacceptable from the surgical point of view, platelet aggregation inhibitors should be stopped 7 days before surgery.<sup>[12]</sup> In spinal surgery, more so than any other surgical specialty, there exists a fine line between risk reduction for primary prevention of cardiovascular disease (CVD)/cerebral ischemia and the potentially catastrophic implications for anticoagulation therapy-induced bleeding.

### **Remaining knowledge gaps**

Glottzbecker *et al.* concluded that a robust, scientific study in spinal surgery regarding the risk/benefit ratio and postoperative bleeding is still lacking.<sup>[11]</sup> Even spontaneous spinal epidural hematomas without<sup>[5]</sup> and with<sup>[22]</sup> concomitant pathologies such as a spinal meningioma have been described. Up to 25-70% of patients with spontaneous spinal epidural hematoma (SSEH) have a history of anticoagulant treatment.<sup>[19]</sup> Nevertheless, most of the results are debatable, and have rarely led to clear recommendations/guidelines regarding the continuation/discontinuation of antiplatelet aggregants. Considering that the whole population is becoming older, more require spinal surgery and are taking platelet aggregation inhibitors for primary/secondary prevention of cardiovascular/cerebrovascular disease,<sup>[13]</sup> every surgeon performing spinal operations will be confronted with the issue as to whether to continue/discontinue antiplatelet therapies.

Therefore, the risks of discontinuing/continuing platelet aggregation inhibitors have to be weighed in each patient. This study attempts to answer the question of whether platelet aggregation inhibitors should be discontinued during spine surgery.

## CONCLUSION

Spinal operations vary tremendously in terms of complexity, length of time under anesthetic, levels of decompression and fusion, surgical approach (anterior/posterior/combined approaches), and the type of the pathology being treated. The question of whether the preoperative platelet aggregation inhibitors must be stopped before elective spinal surgery has never been answered in the literature. For clopidogrel, which was more recently introduced in cardiovascular therapy, no data exist. In our prospective series, we have found no increase in the risk of postoperative spinal bleeding with the use of clopidogrel or acetylsalicylic acid. This finding suggests that spine surgery can be done without stopping anticoagulation. Lacking specific guidelines, each patient should be treated on an individual basis, and the potential benefits of anticoagulation should be compared with the potential risks (risk-benefit ratio).

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