

Non-instrumented extradural lumbar spine surgery under low-dose acetylsalicylic acid: a comparative risk analysis study

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Received: 13 November 2014/Revised: 29 January 2015/Accepted: 4 March 2015/Published online: 11 March 2015
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Abstract

Purpose Coronary artery disease (CAD) affects over one-third of adults and is the leading cause of overall mortality and morbidity. Acetylsalicylic acid (ASA) is widely used in the prevention of CAD. As the population continues to mature, the number of patients presenting for spinal surgery that are under ASA treatment is rising. Studies investigating the outcome of lumbar spine surgeries without discontinuation of ASA therapy are lacking. The purpose of this study is to evaluate the peri- and postoperative bleeding and cardiovascular complication rates of patients undergoing non-instrumented, extradural, lumbar spine surgery with or without discontinuation of low-dose ASA. **Methods** We retrospectively compared the intra- and postoperative blood loss, morbidity, mortality, blood transfusion requirements and hematologic findings in the ASA group (40 patients) and the control group (62 patients). The diagnosis in all patients was either lumbar disc herniation or spinal canal stenosis.

Results Intraoperative blood loss was 221 ml in the ASA group and 140.16 ml in the control group, showing no statistical difference ($p = 0.08$). Postoperative blood loss was 146.58 and 167.97 ml in the ASA and control groups, respectively, also without statistical difference ($p = 0.76$). In the ASA group one patient developed a postoperative epidural hematoma needing revision surgery, while in the control group no postoperative epidural hematomas were seen ($p = 0.40$). In addition, blood transfusion

requirements, hematologic findings, morbidity and mortality showed no significant difference.

Conclusion The continuation of ASA treatment in patients undergoing non-instrumented extradural lumbar spinal surgery seems to be safe and its perioperative continuation might therefore be recommended. Further studies confirming these results are needed.

Keywords Aspirin · Extradural spine surgery · Low-dose acetylsalicylic acid · Non-instrumented spinal surgery

Introduction

Acetylsalicylic acid (ASA) is a widely used drug in the primary and secondary prevention of coronary artery disease (CAD) [1, 2]. ASA irreversibly blocks the platelet cyclooxygenase enzyme system, preventing formation of thromboxane A₂ and irreversibly inhibiting platelet aggregation for the life of the affected platelet [3, 4]. Previous studies demonstrated that ASA reduces the risk of cardiovascular death or subsequent attacks in patients with previous myocardial infarction, unstable angina, stroke or transient ischemic attacks (TIA) [5, 6].

Approximately 40 % of the patients undergoing non-cardiac surgery worldwide have or are at risk of CAD, whereas about 4 % per year develop a major intraoperative cardiovascular complication, including cardiac death, non-fatal myocardial infarction and cardiac arrest [7, 8]. In-hospital mortality due to perioperative myocardial infarction is known to be 15–25 % [8–10].

Aspirin withdrawal syndrome, characterized by a rebound of primary hemostasis leading to a clinical prothrombotic state, is a feared phenomenon in the setting of acute ASA withdrawal perioperatively [9]. Low-dose ASA

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has been associated with an increased risk of perioperative bleeding, transfusion requirements and re-operation frequency [2, 6]. However, these complications did not translate into increased mortality or morbidity [2, 11]. Because of the high prevalence of CAD, and the risk of bleeding under ASA, the perioperative management of patients under ASA is a great challenge and a common clinical problem for attending surgeons.

Despite evidence of the benefit of antiplatelet therapy in patients with CAD, low-dose ASA is often discontinued before non-cardiac surgery to prevent perioperative bleeding complications [8, 11]. Results supporting this policy in non-cardiac surgery and based on prospective randomized studies are sparse. Only a few studies have examined the bleeding risk in patients undergoing spine surgery who are under treatment with ASA [12–14]. A survey of neurosurgeons showed that two-thirds of the respondents felt that aspirin was a risk factor for hemorrhagic complications associated with spinal procedures, and more than half of the interviewees reported having personal experience with such problems [3]. Yet extensive evidence supporting these statements is lacking.

The aim of this study is to compare the peri- and postoperative bleeding and cardiovascular complication rates of patients undergoing non-instrumented extradural lumbar spine surgery with and without discontinuation of low-dose ASA.

Materials and methods

Out of 859 consecutive patients undergoing non-instrumented, extradural lumbar spinal surgery from January 2010 to April 2012 at our institution, 105 patients (12.2 %) were undergoing low-dose ASA treatment (100 mg ASA orally admitted once a day). All patients received low molecular weight heparin (LMWH) in a prophylactic weight-adapted dosage [<80 kg 2500 units of LMWH, ≥ 80 kg 5000 units of LMWH] during the whole hospitalization period. Three cases were excluded from the study due to missing information. In 40 cases (39.2 %; 11 females (27.5 %)) ASA was not discontinued preoperatively (ASA group), while in the rest of the cases [$n = 62$, 60.8 %; 19 females (30.6 %)] ASA was discontinued at least 7 days preoperatively (control group). ASA therapy was continued in all patients under dual antiplatelet therapy (ASA and clopidogrel). In patients undergoing ASA treatment for secondary prevention of CAD the recommendations of a consulted cardiologist were followed, while for those treated for primary prevention of CAD ASA therapy was discontinued prior to surgery.

The diagnosis of all patients was either lumbar disc herniation ($n = 45$) or spinal canal stenosis ($n = 57$). For

lumbar disc herniation a microscopic fenestration, resectomy, foraminotomy, and sequestrectomy with or without discectomy were performed, while for spinal canal stenosis a microscopic fenestration, flavectomy, recessotomy, and foraminotomy were performed. Patients undergoing instrumented fixation such as transpedicular screw fixation, posterior lumbar interbody fusion, transforaminal lumbar interbody fusion, or disc prosthesis were excluded from this study.

The mean age in the ASA group was 70.9 years (± 9.5 years), with 17 patients (42.5 %) undergoing surgery for lumbar disc herniation and 23 (57.5 %) for spinal canal stenosis. In 25 cases (62.5 %) one segment, in 12 cases (30 %) two segments, and in 3 cases (7.5 %) three segments were operated on. The mean age in the control group was 70.8 years (± 9.5 years), with 29 patients (46.8 %) undergoing surgery for lumbar disc herniation and 33 (53.2 %) for spinal canal stenosis. In 38 cases (61.3 %) one segment, in 19 cases (30.6 %) two segments, and in 5 cases (8.1 %) three segments were operated on.

Distribution of age, sex, underlying medical disease, surgery performed, and number of operated segments in each group is shown in Table 1. The groups were well matched overall. However, the ASA group included a significantly higher number of patients with CAD, as well as patients who received treatment using a stent and therefore were under dual antiplatelet therapy (ASA and clopidogrel). In all of the cases clopidogrel was discontinued 7 days preoperatively.

The operation time, intraoperative and postoperative blood loss, pre- and postoperative hemoglobin, thrombocyte count, international normalized ratio (INR), and postoperative blood transfusion in the two groups were compared. Intraoperative blood loss was recorded in the anesthetic report and was assessed through the amount of blood collected in the suction tube at the end of surgery deducted from the amount of fluids applied into the surgical field. The postoperative blood loss was the amount of blood excreted through a drainage tube after surgery, which was removed 24 h postoperatively. A drainage tube on suction was placed within the muscle compartment in all patients. Postoperative complications, such as postoperative hematoma requiring re-operation, cardiovascular events, and surgical site infections, were also compared. The primary outcome measure was the number of postoperative hematomas requiring revision surgery, while secondary outcome measures were amount of intra- and postoperative blood loss, hematologic findings, postoperative cardiovascular events, pulmonary embolism (PE) and surgical site infections.

All statistical analyses were done using InStat GraphPad (GraphPad Software Inc., La Jolla CA, USA). Contingency tests were done using Fisher's exact test, while all other

Table 1 Patients' demographic data

Characteristics	ASA group (<i>n</i> = 40)	Control group (<i>n</i> = 62)	<i>p</i> value
Age (years)	70.9	70.8	0.78
Sex			
Male/female	29/11	43/19	0.91
Diagnosis			
LDH/stenosis	17/23	29/33	0.82
No. of segments			
1/2/3	25/12/3	38/19/5	0.99
Secondary diagnosis			
HTN	34	50	0.77
CAD	31	26	<i>0.0009</i>
Stent	21	8	<i>0.0001</i>
CABG	6	11	0.93
DM	14	22	0.96
TIA	3	6	0.98
PAOD	7	13	0.86
ICA stenosis	6	2	0.07
Atrial fibrillation	2	5	0.85
Hypercholesterolemia	24	26	0.12
Adipositas	10	10	0.40
Smoker	14	20	0.87
Other blood thinners	10	2	<i>0.003</i>
OAC	3	1	0.30
Clopidogrel	7	1	<i>0.006</i>

Italic values indicate significant results

ASA acetylsalicylic acid, LDH lumbar disc herniation, HTN hypertension, CAD coronary artery disease, CABG coronary artery bypass graft, DM diabetes mellitus, TIA transient ischemic attack, PAOD peripheral artery occlusive disease, ICA internal carotid artery, OAC oral anticoagulation

calculations were done using the unpaired *t* test (two-tailed) or the Mann–Whitney *U* test. A *p* value of <0.05 was considered significant.

Results

Operation and hospitalization time

The mean operation time in the ASA and control groups was 109 min (± 45.24 min) and 95.89 min (± 38.84 min), respectively, showing no statistical difference (*p* = 0.15). The mean hospitalization time in the ASA group was 6.3 days (± 2.12 days) and in the control group was 5.95 days (± 2.35 days), showing no statistical difference either (*p* = 0.28).

Postoperative hematoma

In the ASA group one patient (2.5 %) had a postoperative epidural hematoma leading to neurologic deficits and pain and requiring revision surgery, while in the control group no patient developed a postoperative hematoma (*p* = 0.40). In addition, one patient (2.5 %) in the ASA group developed a subcutaneous hematoma which resolved spontaneously (Table 2).

Intra- and postoperative blood loss and blood transfusion

Average estimated intraoperative blood loss was 221 ml (± 209.65 ml) in the ASA group and 140.16 ml (± 103.79 ml) in the control group, showing no statistically significant difference (*p* = 0.08). The mean postoperative blood loss in the drainage tube was 146.58 ml (± 105.11 ml) in the ASA group and 167.97 (± 137.09 ml) in the control group, showing no statistical difference (*p* = 0.76). The cumulative blood loss (intra- and postoperative) in the ASA and control groups was 373.95 ml (± 285.51 ml) and 312.71 ml (± 203.29 ml), respectively, also showing no statistical difference (*p* = 0.40).

The mean amount of blood transfused was 0.16 units [± 0.46 ; 3 cases (7.5 %) postoperatively] in the ASA group and 0.03 units [± 0.25 units; 1 case (1.6 %) postoperatively] in the control group, showing no significant difference (*p* = 0.30). In all cases the reason for postoperative blood transfusion was the development of symptoms and signs of anemia (fatigue, dyspnea, dizziness, hypotension, drop in saturation etc.) accompanied by a drop in hemoglobin postoperatively. Intraoperative blood transfusions were not necessary in either group (Table 2).

Hematologic findings

In the ASA group the mean hemoglobin level decreased from 133.08 g/l (± 16.04 g/l) preoperatively to 118.18 g/l (± 14.56 g/l) 1 day after surgery. In the control group the mean hemoglobin level decreased from 140.63 g/l (± 16.04 g/l) preoperatively to 123.59 g/l (± 16.06 g/l) 1 day after surgery. While the preoperative hemoglobin was significantly lower in the ASA group (133.08 vs. 140.63 g/l; *p* = 0.008), the postoperative hemoglobin levels showed no significant difference (118.18 vs. 123.59 g/l; *p* = 0.24). The decrease in hemoglobin showed no significant difference between the two groups [14.18 (± 11.30 g/l) in the ASA group vs. 13.36 g/l (± 7.46 g/l) in the control group; *p* = 0.70].

Preoperative INR was >1.2 in all cases except one (2.5 %): one patient in the ASA group showed an INR of 1.3. Preoperative platelet count was >100 $\times 10^9$ in all

Table 2 Summary of the results

Parameters	ASA group (<i>n</i> = 40)	Control group (<i>n</i> = 62)	<i>p</i> value
Hospitalization time (days)	6.3	5.95	0.28
Operation time (min)	109	95.89	0.15
EBL (ml)	221	140.16	0.08
PBL (ml)	146.58	167.97	0.76
CBL (ml)	373.95	312.71	0.40
Transfusion (units)	0.16	0.03	0.20
Postoperative hematoma	1	0	0.40
Cardiovascular events	1	1	1.0
Surgical site infection	0	1	1.0
Systemic infection	1	1	1.0
Overall morbidity	3	3	1.0
Mortality	0	0	1.0

ASA acetylsalicylic acid, EBL estimated blood loss, PBL postoperative blood loss, CBL cumulative blood loss

patients. There was no significant difference in preoperative INR or platelet count between the ASA and control groups (Table 3).

Morbidity and mortality

In both the ASA and the control group one patient (2.5 %) suffered from a non-ST-elevated myocardial infarction (NSTEMI), with the patient in the ASA group developing atrial fibrillation in addition. Surgical site infections did not occur in the ASA group, but one patient (2.5 %) developed a postoperative urinary tract infection which was managed with antibiotics for 5 days. In the control group surgical site infection occurred in one case (1.6 %) 1 week after surgery, requiring revision surgery. None of the patients showed clinical signs of PE. One patient (1.6 %) developed hospital-acquired pneumonia with pleural effusion, which was cured with antibiotics. The rate of cardiovascular complications and of postoperative infections in the two groups showed no statistical difference ($p = 1.0$). The mortality rate in both groups was 0 % (Table 2).

Discussion

The main findings of this preliminary study demonstrate that non-instrumented lumbar spine surgery under low-dose ASA might not negatively affect surgical outcome and complication rates.

Secondary and primary prevention of CAD with ASA

ASA is proven to be an effective agent for the primary (preventing first occurrence of disease) and secondary

(preventing recurrence of disease) prevention of acute myocardial infarction and stroke [1, 9]. Especially for the secondary prevention of CAD, multiple randomized clinical trials and meta-analyses provide strong support for the use of ASA [9, 15, 16]. A large meta-analysis of nearly 200 randomized trials demonstrated a nearly 25 % reduction in death with ASA versus placebo in patients with a history of CAD [17]. For this reason it is widely believed that patients with pre-existing CAD should take ASA indefinitely and without interruption [18]. Yet the benefit of ASA for primary prevention is less clear than for secondary prevention. An additional meta-analysis of 6 randomized primary prevention trials showed a 0.07 % per year absolute reduction in the incidence of vascular events, mainly non-fatal myocardial infarctions [15]. In general ASA in primary CAD prevention does not seem to affect cardiovascular mortality, except possibly in high-risk diabetes patients, however the benefit in secondary prevention is well known [9, 19].

Aspirin withdrawal in the perioperative period

Despite the presence of these data, many centres continue the common practice of stopping ASA therapy 7 to 10 days prior to non-instrumented lumbar spine surgery out of concern that the continuation of ASA may increase the risk of perioperative bleeding and consequently might produce neural compression [3, 14]. Although evidence is accumulating that the perceived perioperative bleeding risk does not outweigh the risk of a perioperative ischemic event, clinical practice has not changed much [9]. The current literature suggests that stopping ASA before surgery is associated with a significantly increased perioperative cardiovascular complication rate, whereas perioperative myocardial infarction has an in-hospital

Table 3 Summary of hematologic results

Parameters	ASA group (<i>n</i> = 40)	Control group (<i>n</i> = 62)	<i>p</i> value
Hb preoperatively	133.08 (±16.04)	140.63 (±14.56)	0.28
Hb postoperatively	118.18 (±20.44)	123.59 (±16.06)	0.15
Hb diff	14.18 (±11.30)	13.36 (±7.46)	0.08
Tc preoperatively	225.70 (±59.39)	230.39(±65.54)	0.76
Tc postoperatively	213.14 (±45.46)	229.95 (±65.60)	0.40
Tc diff	10.64 (±40.65)	12.71 (±48.50)	0.69
INR preoperatively	1.04 (±0.07)	1.03 (±0.05)	0.46
INR postoperatively	1.06 (±0.09)	1.04 (±0.05)	0.80

Values: mean (±SD)

ASA acetylsalicylic acid, *Hb* hemoglobin, *Tc* thrombocytes, *INR* international normalized ratio, *diff* difference between pre- and postoperatively

mortality rate of 17–21 % [10, 20, 21]. A meta-analysis by Burger et al. showed that perioperative ASA withdrawal led to cardiovascular events in 10.2 % of cases and lower limb ischemic events in 6.1 % [11]. Therefore, the authors encourage reconsideration of the routine withdrawal of ASA in the perioperative period and performance of surgery under ASA. In addition, newly developed intraoperative hemostatic agents (e.g., FlowSeal) can help reduce the risk of intra- and postoperative bleeding. However, careful intraoperative hemorrhage management with surgical standards remains the first step in all patients.

A systematic review of 50,279 patients on ASA therapy for primary and secondary prevention concluded that perioperative ASA discontinuation had grave prognostic implications, and recommended the perioperative continuation of ASA whenever possible [22].

A randomized, double-blind, placebo-controlled trial evaluating the risk of perioperative ASA withdrawal in 220 high-risk CAD patients undergoing non-cardiac surgery was conducted by Oscarsson et al. in 2010 [8]. Patients were randomized to either ASA or placebo treatment from 7 days before surgery until 3 days after surgery. Major adverse cardiac events occurred in 9 % of the placebo-treated patients and in 1.8 % of the ASA-treated patients (*p* = 0.02). A significantly lower incidence of perioperative CVA or TIA in the ASA group was also shown. The absolute risk reduction and relative risk reduction of ASA continuation were 7.2 and 80 %, respectively, with a number needed to treat of 14 patients.

A growing body of evidence supports a platelet rebound phenomenon once ASA is acutely discontinued, namely the aspirin withdrawal syndrome [9]. This rebound period is characterized by a clinical prothrombotic state due to increased thromboxane production and decreased fibrinolysis [9, 23, 24]. Studies have shown that low-dose ASA is associated with a more rapid rebound than high-dose ASA [23, 24]. In addition, the existing literature substantiates an increased risk of cardiovascular events during the acute

aspirin withdrawal period [9]. Therefore many authors, experts, and society guidelines advise clinicians against perioperative ASA cessation whenever possible [9].

In our study perioperative cardiovascular events did not differ significantly between the two groups. Yet, although the groups showed similar co-morbidities, the control group had a significantly lower number of patients with a history of CAD, fewer patients treated with coronary stents, and fewer patients undergoing dual antiplatelet therapy. As a result, most patients at higher risk of developing cardiovascular complications were in the ASA group, and received adequate preventive treatment. This might explain the similar rate of cardiovascular complications in the groups. Therefore the main conclusion drawn from our results is that the groups have an equal risk of hemorrhage.

Surgical and perioperative bleeding risk related to ASA continuation in spinal surgery

To date, the evidence indicates that the temporary withdrawal of ASA should only be considered for procedures in which the risk of bleeding exceeds the risk of major adverse cardiovascular events. This group of procedures is believed to be intracranial, spinal canal, post-chamber eye, middle ear, and prostate surgeries [3, 9]. It is however important to note that this information is based on observational and retrospective data and the true risk of perioperative bleeding complications while ASA is continued remains ambiguous. Burger et al. showed in a meta-analysis that although ASA increased the rate of bleeding complications by a factor of 1.5, its continuation did not increase the severity of bleeding complications except in intracranial surgery and transurethral prostatectomy [11]. Oscarsson et al. showed in their randomized, double-blind placebo-controlled trial that patients undergoing non-cardiac surgery without discontinuing ASA show no significant difference in the amount of intra- and postoperative bleeding, administered crystalloids, packed red blood cells,

or plasma transfusion compared to patients treated with placebo [8].

Studies evaluating bleeding complications in spinal surgery are sparse. Korinth et al. conducted a survey of German neurosurgeons which evaluated their practice in patients treated with ASA undergoing elective spinal surgery [3]. Two-thirds of the respondents felt that ASA was a risk factor for bleeding complications, while more than half reported having personally witnessed such complications. The majority of the respondents therefore discontinue ASA therapy an average of 7 days prior to elective spinal surgery. The authors conclude that ASA should be discontinued 7 days prior to spinal surgery, yet the risk of discontinuation has to be measured in each patient individually. However, due to the observational nature of the study and the fact that the type of surgery (e.g., instrumented vs. non-instrumented, intra- vs. extradural) is not specified and differentiated, recommendations must be made carefully.

Nuttall et al. evaluated predictors of blood transfusion after spine surgery, while multiple regression analysis demonstrated that perioperative ASA use was not associated with increased blood loss [13].

In contrast, in their retrospective study of patients undergoing spinal fusion surgery, Kang et al. showed that postoperative blood drainage was significantly higher in patients who had taken prophylactic ASA, even after discontinuation of aspirin 7 days before surgery, compared to those with no ASA treatment [12]. All other measured parameters, such as operation time, intraoperative blood loss, amount of blood transfusion, hematologic findings, complications, and clinical outcome showed no significant difference. However, this study has some major limitations such as the small sample size, the fact that prior ASA users have significantly more preoperative comorbidities, and the fact that other medications for cardiovascular diseases were not taken into account, even though they might cause compound hemorrhage.

Recently, Park et al. conducted a retrospective comparison of the bleeding risk of patients undergoing 1- or 2-level lumbar spinal fusion surgery; patients discontinuing ASA >7 or 3–7 days preoperatively were compared to patients without prior ASA treatment (control group) [14]. The results showed that if ASA was discontinued >7 days prior to surgery, there was no statistically significant difference in bleeding complications and blood loss compared to the control group. Yet once ASA was discontinued 3–7 to days prior to surgery, the amount of drained blood and the duration of indwelling of the drainage catheter was significantly higher than in the control group.

To our knowledge, studies comparing peri- and postoperative blood loss and bleeding complications in patients undergoing non-instrumented extradural lumbar spinal

surgery with or without discontinuation of ASA therapy do not exist. Because of the extent of skin incision and the extensive preparation of muscle and bones for lumbar spinal fusion surgery, the amount of blood loss is profoundly higher than in patients undergoing lumbar spinal surgery without instrumentation. For this reason, this study hypothesized, that with patients surgically treated for extradural spine disorders, such as lumbar disc herniation or spinal canal stenosis, where the skin incision is small, preparation of muscles and bones is atraumatic, and blood loss is minimal, thus it would be safe to continue ASA therapy perioperatively.

Our results support this assumption and show no statistical difference in primary or secondary outcome measures. Based on our results, we believe that in patients undergoing non-instrumented extradural spine surgery, the continuation of ASA treatment seems to be safe and might not lead to higher morbidity, mortality, or transfusion rates, or longer operation and hospitalization times. Therefore the perioperative continuation of ASA therapy, especially for the secondary prevention of CAD, should be strongly considered.

Study limitations

This is a retrospective study and subject to all the limitations of data collection inherent in such studies. Cardiovascular or other postoperative complications were based on retrospective review of medical records, while the subclinical presence of adverse events was not looked for. Yet, all adverse events which were clinically significant or led to a reoperation were concluded in the analysis.

The ASA group included significantly more patients with a history of CAD and patients treated for these disorders using coronary stents, while other characteristics of the groups were well matched. Consequently, the patients in the ASA group were more often under preoperative dual anti-platelet therapy (ASA and clopidogrel). The indication to continue ASA therapy perioperatively was often based on the patients' co-morbidities, and since the risk of cardiovascular events in the perioperative period is profoundly high in patients who have a history of CAD, or who are treated with dual antiplatelet therapy due to coronary stenting, they will ultimately be operated on under ASA treatment. For this reason this selection bias is almost unavoidable. Still, even though the ASA group contained significantly more patients with a history of CAD and under dual platelet therapy, which should lead to higher complication rates, more blood loss and higher transfusion rates, there was no significant difference in primary and secondary measures. In addition in all patients with dual antiplatelet therapy clopidogrel was discontinued at least seven days prior to surgery, therefore its effect on bleeding during the perioperative period was minimized.

Hemoglobin values 1 day postoperatively might be unreliable due to ongoing rebalancing of intra- and extravascular fluids, fluid management during and after surgery, and might be influenced by individual factors such as cardiac and renal function. Late hemoglobin (>5 days postoperatively) might be of more value, however due to the retrospective setting of the study late hemoglobin was not available for comparison.

This study includes a rather small sample size and might be underpowered. However, this is the first study evaluating the effect of ASA on the outcome of non-instrumented spine surgery, and was conducted as a basis for further prospective studies analyzing the effect of perioperative ASA treatment in spinal surgery. Such studies are important due to the fact that CAD affects more than one-third of adults and is by far the leading cause of overall mortality and morbidity. As the population continues to mature, the number of patients presenting for spinal surgery under ASA treatment for CAD is rising [3, 9].

Conclusions

Our data suggests that in patients undergoing spinal surgery for lumbar disc herniation or lumbar spinal canal stenosis, continuation of ASA treatment is safe and does not increase hemorrhage rate or morbidity. Further randomized controlled studies are needed to confirm these results.

Conflict of interest The authors have no disclosures and no conflict of interest.

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