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Utility of the aspirin and P2Y12 response assays to determine the effects of antiplatelet agents in patients with subdural hematoma undergoing neurosurgery

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Abstract
Data on the use of reactivity tests in high-risk procedures derive mainly from cardiac surgery but could also have applicability in neurosurgery. Our study aims to evaluate the safety of reactivity tests in patients with surgical indications for chronic subdural hematoma (CSDH). We conducted a case-control study to determine risk factors and outcomes (early-onset complications if they occurred <7 days; late-onset if they occurred >7 days) in patients undergoing evacuation of CSDH recruited in the 2-year period 2022-2024. Patients with a history of antiplatelet treatment and reactivity test with early negativization (patients in whom the platelet aggregation test became negative before the required suspension period for safely performing the surgical intervention) and urgent neurosurgical indication were considered cases. Patients who were not taking antiplatelet therapy were considered controls. Complications taken into consideration were cerebral acute subdural hematoma, intraparenchymal hemorrhage, and ischemic complications.
We analyzed data from 170 patients who consecutively underwent neurosurgical intervention for CSDH. We enrolled 68 cases who were on antiplatelet therapy before the procedure and showed early negativization on reactivity tests (cases) and 102 controls who were patients who had never been on antiplatelet therapy (controls). We did not observe statistically significant early-onset complications in the case group when compared to the control one (p: 0.64). Regarding late-onset complications, the incidence of total hemorrhagic events was similar in the two study groups (p: 0.14).
CSDH is an extremely common condition in the elderly population and in patients on antiplatelet drugs. This condition often requires an urgent neurosurgical intervention, and waiting for antiplatelet treatment to be ineffective could worsen the outcome. Reactivity tests could therefore be a useful and safe tool to guide the timing of neurosurgery and to reduce the hospitalization time.

Introduction

The increasing age of patients undergoing neurosurgery has led to the necessity of managing polytherapy, especially antiplatelet medications used for cardiovascular disease.[1] The increased bleeding risk related to such medications may be an independent risk factor for the development of intracranial hemorrhage in patients presenting with blunt head injury.[1,2] It is, therefore, important to ascertain the history of antiplatelet medication use, since it may affect a patient's outcome and guide clinical management.[2] An example is chronic subdural hematoma (CSDH), regarding which guidelines are not clear on the proper management of antiplatelet and anticoagulant medications.[3] CSDH is a pathological blood collection in the subdural space. It is one of the most frequent neurosurgical diseases and typically affects the elderly.[4] Neurosurgical evacuation is generally indicated for hematomas that are wider than >1 cm, with evidence of cerebral compression or with the presence of neurological symptoms, in patients susceptible to surgery.[5] Current guidelines do not adequately address the management of antithrombotic medications in patients diagnosed with CSDH, and this raises doubts about the optimal approach to mitigate the risk of spontaneous or postoperative intracranial hemorrhages while balancing thromboembolic risk.[3] In some cases, the hemorrhagic risk (progression or recurrence of bleeding) associated with continuing antiplatelet therapy outweighs the thrombotic risk associated with discontinuing the treatment.[6] In addition, among patients taking antiplatelet medication regularly, the proportion of "non-responders" - individuals who retain their platelet function even while on aspirin or clopidogrel - can range from 5.5% to 45%.[7] Platelet reactivity test has a central role in cardiac surgery in determining the optimal timing for surgery.[8-10] However, their applications could extend to other fields: for instance, in patients undergoing antiplatelet therapy who develop a CSDH requiring evacuation, these tests could help define the optimal timing for neurosurgical intervention, aiming to perform the procedure as early as possible and at the same time minimizing hemorrhagic complications. In fact, the extreme variability in individual responses to antiplatelet drugs makes these tests potentially valuable tools in surgical settings,[11-13] although considering the need for standardization of analysis methods.[14,15] In order to evaluate the possible role of reactivity tests in perioperative risk assessment, we conducted a study on the ischemic and hemorrhagic complications of patient undergoing urgent neurosurgery for CSDH evacuation; in particular, we compared patients taking antiplatelet medications with an early negativization on reactivity test to patients not taking any antiplatelet medication.

Materials and Methods

Study design and patients

We conducted a retrospective case-control study analyzing data from the 2022-2024 period in a population of patients who required urgent neurosurgical evacuation of CSDH.

We defined the cases as patients on treatment with antiplatelet drugs such as aspirin (75 mg, 100 mg, 160 mg, 300 mg) and P2Y12 receptor inhibitors (clopidogrel, ticlopidine, prasugrel, ticagrelor), who underwent platelet reactivity tests before the neurosurgical intervention and had a platelet reactivity test within the early normal limits. For platelet aggregation tests within early normal limits, we considered the normalization of the platelet reactivity test before the required discontinuation period of the antiplatelet drug (5 days for P2Y12 receptor inhibitors and 7 days for Aspirin) to safely proceed with a neurosurgical intervention, as indicated by the guidelines.[16]

We defined the controls as patients who had the same pathology and the same clinical severity and underwent surgery but had never received antiplatelet treatment before. The on-call neurosurgeon indicated neurosurgical intervention based on the clinical severity and the neurological symptoms the patient developed, irrespective of the platelet aggregation test results. A systematic review that analyzed the surgical management of CSDH in the elderly across thirteen studies found that seven recommended surgical intervention on a case-by-case basis, five recommended surgery for symptomatic patients, and one study operated on all patients with CSDH.[17-19]

Exclusion criteria of our study were: late negativization on the reactivity test considered as the normalization of the platelet reactivity test within the time limits in which the anti-aggregatory effect

pharmacologically ends after discontinuation of the drug (5 days for P2Y12 receptor inhibitors and 7 days for aspirin), patients younger than 18 years, pregnancy, presence of platelet dysfunction due to underlying comorbid conditions (Bernard-Soulier syndrome, Glanzmann thrombasthenia, Gray platelet syndrome, delta storage pool deficiency, von Willebrand disease), patients on anticoagulants (direct oral anticoagulants such as apixaban, dabigatran, rivaroxaban and edoxaban, and vitamin K anticoagulants such as warfarin, acenocoumarol and fluindione).
In our study, we focused on complications potentially influenced or caused by the effects of antiplatelet or anticoagulant drugs, such as the potential risk of cerebral ischemia, hemorrhage, and recurrence of CSDH, excluding infectious complications and seizures occurrence.[20-23]

Outcome
As a composite primary outcome, we evaluated ischemic and/or hemorrhagic complications related to urgent CSDH evacuation in patients on antiplatelet treatment who underwent platelet reactivity tests, compared to patients who had never received antiplatelet treatment. In particular, ischemic or hemorrhagic complications were classified into two main temporal categories: early-onset, occurring during hospitalization or within 7 days of the surgical procedure, and late-onset, with a latency period beyond this threshold within 30 days of the surgical procedure. The main early-onset complications analyzed were the development of an acute subdural hematoma, intraparenchymal hemorrhage, or cerebral ischaemia. For late complications at 30 days, we considered cerebral ischemia and radiological and/or clinical recurrence of CSDH with the need for reoperation. We did not consider medical complications.[5,20-26]

Data collection
For patient recruitment, we used a computerized electronic medical record (Archimed® medical software version 6.20 by B. Dannaoui, Florence, Italy). We collected data regarding the neurosurgical intervention (type of procedure and its duration), the type of subdural hematoma (unilateral or bilateral), the patient's comorbidities (presence of hypertension, diabetes mellitus, chronic kidney disease, alcohol abuse, SARS-CoV-2 infection, history of cerebral hemorrhage), hospitalization data (length of stay, the use of postoperative thromboembolic prophylaxis, initiation of anticoagulant therapy at discharge), the patient's coagulation profile (including platelet count, PT, and aPTT), renal function, and the number of days of discontinuation of antiplatelet treatment (ASA and P2Y12 receptor inhibitors) before the surgical evacuation of the subdural hematoma. We recorded early-onset hemorrhagic complications, such as acute subdural hematoma and intraparenchymal hemorrhage, and late-onset hemorrhagic complications, such as recurrence of subdural hematoma requiring reintervention, and ischemic complications. The standard approach at our center involves burr hole craniostomy, while craniotomy or mini-craniotomy are reserved for specific, less frequent cases. Postoperative cranial CT scans, conducted at least on the first or second day following surgery, were evaluated to identify complications occurring within 7 days.
A recent systematic review demonstrated that hyperdense components on computed tomography (homogeneous and mixed hyperdense density) were the strongest prognostic factor for hematoma recurrence.[25]
The study was performed following the Declaration of Helsinki and local regulations. The protocol was approved by the Ethics Committee of the University Hospital of Careggi, Florence. The authors declare they have no conflict of interest.

Platelet function testing
For all the patients analyzed, we collected blood samples and performed platelet reactivity tests, specifically TXA2-dependent platelet reactivity [aspirin reaction units (ARU)] for patients taking aspirin and P2Y12 receptor inhibitor-dependent platelet reactivity [P2Y12 reaction units (PRU)] for those on P2Y12 inhibitors. Platelet reactivity was assessed using the VerifyNow POCT system. VerifyNow® is a method used to assess the therapeutic effectiveness of antiplatelet agents by

measuring platelet aggregation in whole blood via an optical detection system based on turbidimetry.[27,28] To evaluate the effectiveness of aspirin therapy, whole blood is introduced into a cartridge containing arachidonic acid and fibrinogen-coated beads. Platelets adhere to the beads, reducing the turbidity of the blood, which is reported as ARU. Values below the cut-off indicate sensitivity to aspirin, while values above the cut-off suggest that platelets retain residual functionality despite aspirin treatment. VerifyNow can also be used to assess the efficacy of clopidogrel therapy, using ADP as a platelet agonist. The responses are reported as PRU. The cut-off values used to identify patients at higher risk of developing early and late complications following CSDH evacuation surgery were <208 PRU and <550 ARU.[27,28] Platelet reactivity on-treatment in patients was assessed using VerifyNow aspirin and P2Y12 assays (Accumetrics, San Diego, CA, USA). In brief, venous blood samples were collected from each patient just prior to discharge, while they were on a stable maintenance dose of 100 mg aspirin, 75 mg clopidogrel ± 200 mg cilostazol. The blood was anticoagulated with sodium citrate (0.109 mol/L, ratio 9:1). For patients receiving an intravenous glycoprotein IIb/IIIa inhibitor, platelet reactivity was measured at least 5 days after the percutaneous coronary intervention (PCI) procedure. The variability of these tests has been reported as <10% in previous studies and 7.5% at our institution. Several studies have highlighted a link between the VerifyNow (Accumetrics, San Diego, CA, USA) P2Y12 assay outcomes and hematocrit levels.[29-31] The observed negative correlation between the PRU value and hematocrit may reflect either a genuine *in vivo* effect of hematocrit on platelet reactivity or a potential laboratory artifact. Kakouros *et al*. suggested that this is an *in vitro* phenomenon unrelated to intrinsic changes in clopidogrel responsiveness, and that correcting for hematocrit can reliably identify patients who might benefit from alternative antiplatelet treatments.[29] Kim *et al*. showed that the hematocrit-induced alteration of the VerifyNow P2Y12 assay results is likely an *in vitro* effect, emphasizing the need to consider hematocrit when interpreting the test outcomes.[30] Furthermore, Kim *et al*. argued that the relationship between hemoglobin levels and high residual platelet reactivity while on clopidogrel may be attributable to laboratory inaccuracies.[31]

Statistical analysis

The study was carried out and reported according to the STROBE guidelines for observational studies.[32] The normality of data distribution was assessed using the Shapiro-Wilk test. Continuous variables were expressed as mean plus or minus standard deviation or as median with interquartile range, as appropriate. Categorical data were reported as counts and percentages. Categorical variables were compared using Chi-squared or Fisher's test, as appropriate. Continuous variables were compared with the Student's test or the Mann-Whitney U-test, when appropriate. Every variable associated with an outcome of the study with $p<0.10$ (entry level) was included in a multivariate binary logistic regression. Stepwise elimination was performed to finalize the independent predictors of the multivariate models. Statistical significance was reached when the p-value was <0.05 (two-tailed). Results of the multivariate analyses were expressed as odds ratios and the corresponding 95% confidence interval. Statistical analyses were performed using STATA-16/MP (StataCorp LP, College Station, TX, USA).

Results

Characteristics of patients in the two groups are reported in Table 1. There were significant differences in the patient characteristics between the two groups in terms of age and several comorbidities (Table 1). In particular, the population of cases was generally older, with a higher incidence of arterial hypertension and diabetes mellitus in the medical history.

Table 2 shows data about the neurosurgical characteristics of the hematoma and intervention. It is important to emphasize that the two populations (cases and controls) had comparable characteristics, with no statistically significant differences in terms of subdural hematoma features and surgical intervention-related characteristics.

Table 3 presents the distribution of antiplatelet agents in the two populations. The most common antiplatelet therapy in the case population was aspirin only (77.9% of the cohort). About 10% of the cohort was taking a combination of aspirin and clopidogrel, and 11.8% were taking clopidogrel only. Table 4 shows results about outcomes. No significant differences were observed between cases and controls in terms of early-onset or late-onset hemorrhagic complications.

Discussion

In our study, no statistically significant differences emerged in terms of early and late complications (both hemorrhagic and ischemic) between the group of patients with CSDH who were previously on antiplatelet therapy and had a negative early platelet reactivity test (compared to the standard suspension timing for that type of antiplatelet) at the time of neurosurgical intervention, and the group of patients who underwent the same surgical procedure but had never been on antiplatelet therapy. It is particularly noteworthy that early and late hemorrhagic complications were essentially comparable between the two groups. This could justify a targeted and reasoned use of platelet aggregation tests as a guide for neurosurgical interventions in elderly and complex patients with CSDH requiring surgical evacuation while on home antiplatelet therapy. The literature already provides evidence regarding the potential utility of platelet aggregation tests in other surgical settings. Dual antiplatelet therapy (DAPT) with aspirin and a thienopyridine is essential after PCI with stent implantation.[33] However, there is a marked heterogeneity in the platelet response to clopidogrel: in up to 30 percent of patients (called "poor responders"), standard doses of clopidogrel fail to completely inhibit adenosine diphosphate (ADP)-induced platelet aggregation.[33,34] A patient-level pooled meta-analysis of six prospective studies found that higher on-treatment platelet reactivity around the time of PCI, as measured by the VerifyNow P2Y12, was predictive of long-term cardiovascular events, including death, MI, and stent thrombosis.[33] Although most protocols are derived from the cardiac literature, DAPT is a routine practice to reduce thromboembolic events after neurovascular stent placement.[34-37] There is good evidence that loss-of-function polymorphisms are associated with reduced levels of the active clopidogrel metabolite and with reduced on-treatment inhibition of ADP-induced platelet activation. There is an increasing body of evidence that suggests that the PRU, as assessed by the VerifyNow P2Y12 assay, though sometimes limited by low platelet count or low hematocrit, is the most useful assay for predicting periprocedural hemorrhagic and thrombotic complications during flow diverter (FD) placement. The use of antiplatelet medication response testing prior to neuroendovascular procedures remains controversial within the neurointerventional community.[34-38] Although a randomized trial of elective unruptured brain aneurysm coil embolization showed fewer thromboembolic complications when antiplatelet approaches were tailored based on ARU>550 or PRU>213, such thresholds have not been widely adopted.[39,40] To reduce thromboembolic complications during neurovascular stent placement, DAPT has become standard practice over the past decade.[33] While most protocols are based on cardiac literature, significant variability exists in the platelet response to clopidogrel among patients undergoing neurointerventional procedures. Standard oral doses of clopidogrel fail to fully inhibit ADP-induced platelet aggregation in up to 30% of patients, a phenomenon known as poor response.[41] Loss-of-function polymorphisms are known to reduce the levels of the active clopidogrel metabolite and impair ADP-induced platelet inhibition.[42,43] These genetic variants do not affect the pharmacodynamics of other P2Y12 inhibitors, such as prasugrel or ticagrelor. Increasing evidence suggests that the PRU measured by the VerifyNow P2Y12 assay, though sometimes influenced by low platelet count or hematocrit, may be the most reliable test for predicting periprocedural hemorrhagic and thrombotic complications during FD placement.[44-47] Additionally, thromboelastography may help predict central nervous system ischemic and access site hemorrhagic complications.[48] A neurointerventional study of 96 patients undergoing neurovascular stenting (including carotid stents, intracranial stents for atherosclerosis and stent-assisted aneurysm coiling, and vertebral artery stents for atherosclerosis) found a 16% risk of thromboembolism in clopidogrel-resistant patients, compared to 1.6% in non-resistant patients ($p<0.01$).[49] In another study of 44 patients undergoing aneurysm flow diversion embolization with

pipeline endovascular devices, a pre-procedure PRU>240 predicted perioperative thromboembolic complications.[50,51] Unlike coronary interventions, where an upper PRU threshold typically influences treatment plans due to the primary concern of coronary thrombosis, plans for cerebral arterial interventions may be altered if PRU is <40 (indicating increased hemorrhage risk) or >240 (indicating increased thrombosis risk), though there is no consensus on precise cutoffs. PREMIER was the first prospective multicenter study to evaluate the use of FD in 141 patients with small/medium unruptured intracranial aneurysms located in the internal carotid and vertebral arteries.[52] Multiple repeat measurements of the VerifyNow assay in healthy volunteers who did not take antiplatelet drugs revealed significant intraindividual variability in PRU values, in contrast to ARU values, which remained relatively stable.[53] Some studies have examined the variability of ARU and PRU values during the periprocedural period of endovascular treatments, focusing mostly on longer-term variability, ranging from 1 week to 6 months after treatment.[54] Khanna *et al*. measured ARU and PRU values in patients after PCI at discharge and at 1 week, 1 month, 3 months, and 6 months post-discharge.[55] They reported that ARU values remained unchanged over the study period, while PRU values significantly increased at 1 month post-discharge, with no significant changes thereafter. Similarly, Tello-Montoliu *et al*. compared PRU values in PCI patients at discharge, 3 months, and 6 months, finding that PRU values were higher at 3 months compared to discharge, but no further differences were observed between 3 months and 6 months.[56] Watanabe *et al*. compared PRU values at 7 days and 30 days after transcatheter aortic valve implantation and found no significant difference (136.7±73.4 *vs*. 150.4±83.2, p=0.13).[57] Patients in their study had been on aspirin (100 mg/day for at least 7 days) and either clopidogrel (75 mg/day for at least 7 days) or had been loaded with 300 mg of clopidogrel followed by 75 mg/day before the procedure. These findings suggest that while ARU values remain stable over time, PRU values tend to stabilize after 1 week or more following the procedure. The effects of antiplatelet medication on coagulation pathways in post-traumatic intracranial hemorrhage are not well understood, but available data suggest that the use of these agents increases the risk of an unfavorable outcome, especially in cases of severe traumatic brain injury (TBI). Therefore, new assays for monitoring platelet activity may be useful in this field to predict hemorrhagic outcome and the risk for cardiac events such as life-threatening stent thrombosis if antiplatelet therapy is withdrawn. In a clinical review, Beynon *et al*. analyzed available studies on the impact of pre-injury use of antiplatelet agents in patients with TBI and interventions for identifying and counteracting antiplatelet effects in these patients. In this review, they described that the results of the studies that analyzed effects of pre-injury antiplatelet treatment are conflicting and do not allow a comprehensive characterization of antiplatelet agent effect on patient with TBI but several factors may have contributed to the discordance of the results: retrospective design, small sample sizes and the absence of the assessment of pre-injury activity through laboratory examinations.[57] Bachelani *et al.* used the specific assay 'aspirin response test' (VerifyNow, Accumetrics, San Diego, CA, USA) for identifying effects of aspirin on platelet activity after TBI. In this study, this test showed that 42% of patients with an unknown history of aspirin had signs of platelet inhibition. The authors assessed the efficacy of antiplatelet transfusion through repeating the 'aspirin response test' and failure of normalizing function was associated with a trend towards a higher risk of mortality.[58] Bansal *et al.* used VerifyNow P2Y12 for the detection of clopidogrel-induced platelet inhibition in 46 trauma patients and showed that a large percentage of patients had undetectable or low platelet inhibition despite reported use of clopidogrel. Assay information may present valuable information in the clinical setting since unnecessary interventions such as platelet transfusion or application of hemostatic drugs can be avoided.[59] Parry *et al*. analyzed data from a single-center prospective cohort study that included patients with a clinical history of TBI in which serum platelet reactivity levels were determined immediately on admission using the aspirin and P2Y12 response unit assays.[60] A sample of 317 patients was available for analysis, of which 87% had experienced mild TBI, 7% moderate, and 6% severe. Rapid measurement of platelet function indicated that as many as one-fourth of patients on antiplatelet treatment do not have platelet dysfunction, but further work to validate the utility of the ARU and PRU assays in the TBI population as a prognostic and management

tool is required. Finally, literature shows that there is no clear evidence-based consensus on how to manage patients undergoing burr-hole drainage for CSDH who are under ASA treatment. Therefore, the decision to maintain or interrupt ASA treatment is based mostly on the surgeons' preference. A randomized placebo-controlled study for this frequent question is urgently needed in order to provide class I evidence for the best possible treatment of this large group of patients.[61] Poon *et al*. described moreover the outcomes after CSDH drainage on antithrombotic drugs, either antiplatelets or anticoagulants, using data from a previous UK-based multi-center, prospective cohort study, in which outcomes included recurrence within 60 days, functional outcomes at discharge and thromboembolic events during hospital stay.[62] They observed that neither antiplatelet nor anticoagulant drugs use influenced the risk of CSDH recurrence or persistent/worse functional impairment and that delaying surgery, after cessation of antiplatelet drugs, did not affect the risk of bleeding recurrence and patients on an antithrombotic drug pre-operatively were at higher risk of thromboembolic events with no excess risk of bleeding recurrence or worse functional outcome after CSDH drainage. Same results were found by Kerttula *et al.* in the retrospective population-based cohort study about the effect of antithrombotic therapy (ATT) on the recurrence and outcome of CSDH after burr-hole craniotomy:[63] ATT did not affect CSDH recurrence. Conversely, on their data, the length of the temporary postoperative ATT discontinuation did not correlate with the rate of thromboembolic complications. In their study cohort, the ATT discontinuation was long, but the results suggest that even long-term discontinuation may be safe, regardless of the indication of ATT.

Our study has several limitations. First, it was a retrospective monocentric study with a small sample size. Due to the small sample size, correlations with PRU values could not be determined. We do not survey CYP2C19 polymorphisms, a strong predictor of clopidogrel hypo-response Finally, the absence of detailed data on surgical types (mini-craniotomy vs. burr holes) in our study could be a bias.

Despite several limitations, this study has some strengths. To our knowledge, this should be the first study that has explored this topic in the field of CSDH. Additionally, patients with CSDH are often elderly, with multiple comorbidities and on antiplatelet treatment. Having a test capable of optimizing the neurosurgical timing and estimating the hemorrhagic risk could be useful in reducing short- and medium-term complications.

Evaluating all these limitations, we recommend considering the data from our study with caution, underlining the need to conduct further studies on this topic to analyze the real usefulness of reactivity tests as neurosurgical tools in patients with CSDH.

Conclusions

Our study showed no statistically significant differences in early and late complications (both hemorrhagic and ischemic) between the group of neurosurgically treated CSDH patients on antiplatelet treatment and early negativization on reactivity tests and the group of patients who underwent the same surgical procedure but had never been on antiplatelet therapy. Despite several limitations of our study, the selective use of platelet aggregation tests, particularly in elderly or complex patients with CSDH requiring neurosurgery, may be considered. Our results should be interpreted with caution, and further studies are needed to clarify the role of platelet reactivity testing in neurosurgery.

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Table 1. Baseline characteristics of patients in intervention and control groups.

Baseline characteristics	Cases (68 pts)	Controls (102 pts)	p<0.05
Sex male	43	78	0,06
Sex female	25	24	0,06
Average age (years)	82.93	76.09	**<0.05**
Age >75 years	57	42	**<0.05**
Insulin therapy	11	8	0.09
Anticoagulant therapy	1	3	0.5
Antiplatelet therapy	68	0	
History of arterial hypertension	54	48	**<0.05**
History of diabetes mellitus	19	12	**<0.05**

pts, patients.

Table 2. Characteristics of chronic subdural hematoma and of neurosurgical interventions performed in the two study populations.

Characteristic	Cases (68 pts)	Controls (102 pts)	p<0.05
Monolateral hematoma	53	77	0.71
Bilateral hematoma	15	25	0.71
Medium length of neurosurgical intervention (minutes)	53.09 (41.3-60.43) minutes	55.31 (43.17-63.01) minutes	0.58

pts, patients.

Table 3. Distribution of antiplatelet agents in two populations.

	Cases (68 pts)	Controls (102 pts)
No agent, n (%)	0	102
Aspirin only, n (%)	53	0
Clopidogrel only, n (%)	8	0
Both agents, n (%)	7	0

pts, patients.

Table 4. Outcomes of the study.

Outcomes	Cases	Control	OR	95% CI	p<0.05
Early-onset complications (<7 days)	7	9	1.28	0.45-3.60	0.64
Acute subdural hematoma	8	7	1.31	0.45-3.76	0.61
Intraparenchymal hemorrhage	1	0			0.29
Late-onset complications (>7 days)	5	16	0.46	0.16-1.32	0.14
Cerebral ischemia	0	2			0.20
Recurrence of subdural hematoma requiring reintervention	4	3	2.19	0.47-10.09	0.30

OR, odds ratio; CI, confidence interval.