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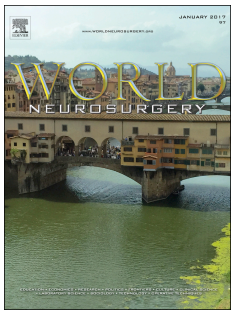

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PII: S1878-8750(20)30605-7

DOI: https://doi.org/10.1016/j.wneu.2020.03.134

Reference: WNEU 14593

To appear in: *World Neurosurgery*

Received Date: 8 February 2020

Revised Date: 20 March 2020

Accepted Date: 22 March 2020

Please cite this article as: Kamenova M, Lutz K, Schaedelin S, Fandino J, Mariani L, Soleman J, Subperiosteal versus Subdural Drain after Burr-hole Drainage under blood thinners: a Subanalysis of the cSDH-Drain RCT, *World Neurosurgery* (2020), doi: https://doi.org/10.1016/j.wneu.2020.03.134.

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Disclosure of Funding: This study was funded by the Research Foundation Kantonsspital Aarau. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Conflicts of interest: none

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Abstract

The chronic subdural hematoma (cSDH)-Drain trial compared recurrence rates and clinical outcome associated with the use of subperiosteal drain (SPD) and subdural drain (SDD) after burr-hole drainage for cSDH. This subgroup analysis aimed to determine, whether one drain type is preferable for patients treated with platelet inhibitors (PI) or anticoagulants (AC).

This subanalysis included 133 patients treated with PI/AC of the 220 patients from the preceding cSDH-Drain trial. For these patients the association between the drain type used and recurrence rates, mortality, as well as clinical outcome at 6 weeks and 12 months follow-up were analyzed using a logistic regression analysis model. Additionally, recurrence rates, clinical outcome, and mortality were assessed for each PI or AC type separately.

The insertion of SPD was associated with 7.35% recurrence rates compared to 13.85 % with SDD in patients treated with PI or AC (OR 0.41, 95% CI 0.06 – 2.65, p=0.36). Outcome measurements and mortality did not differ significantly between both groups at 6 weeks and 12 months follow up. In addition, there was no statistically significant association between drain type and recurrence rate or mortality when comparing data for each PI or AC type. At 24 hours after surgery, significantly more patients under phenprocoumon and natrium-dalteparin had a GCS between 13 and 15 in the SDD group compared to the SPD group (p=0.006), while at 6 weeks follow up significantly more patients in the SDD group treated with ASA had a good mRS (p=0.01). At 12 months no significant difference in outcome measurements was seen for all PI and AC types

In patients treated with PI or AC, the insertion of SPD after burr-hole drainage of cSDH showed comparable recurrence, mortality, and long term outcome rates when compared to SDD.

Key words: chronic subdural hematoma, subperiosteal drain, subdural drain, burr-hole drainage, platelet inhibitors, anticoagulants

Introduction

Chronic subdural hematoma (cSDH) represents, with an incidence of 1.7-13.1 per 100,000 inhabitants per year, one of the most common neurosurgical conditions especially among the elderly population[1,2,3,4,5]. In patients with neurological symptoms, burr-hole drainage and drain insertion is the most common treatment modality[6]. The insertion of a drain was shown to be associated with lower recurrence and mortality rates at 6 months[2]. We recently published the results of a randomized controlled trial (cSDH-Drain Trial) comparing the use of subperiosteal drain (SPD) and subdural drain (SDD) after burr hole drainage of cSDH[7]. When compared to SDD, SPD led to similar recurrence rates, while the rate of infections and iatrogenic brain injuries was significantly reduced[7]. The ideal treatment modality for patients with cSDH under platelet aggregation inhibitors (PI) or anticoagulants (AC) remains unclear[8,9]. Since SPD is not positioned in direct contact to cortical structures, bridging veins, or hematoma membranes, it might be favourable to SDD, especially in this group of patients who seemingly suffer a higher risk for bleeding and recurrence. On the other hand, SDD which is placed directly within the hematoma cavity, might lead to lower recurrence rates in this group of patients, who are potentially prone to more recurrence rates. We therefore performed a post-hoc subanalysis of this sub-group of patients, comparing recurrence rates and outcome depending on the type of drain used.

Methods

This is a subanalysis of the preceding cSDH-Drain trial[7]. The detailed study design, methodology and results have been presented recently[10,7] In brief, the cSDH-Drain trial was a two-centre, prospective, randomized trial including 220 patients with symptomatic cSDH requiring surgical evacuation. After burr-hole drainage, patients were randomly assigned to receive either a subdural drain (SDD-group) or a subperiosteal drain (SPD-group). The primary endpoint was symptomatic recurrence requiring a reoperation within 12 months. Secondary outcomes included clinical and radiological outcome, morbidity and mortality rates, and length of stay. Follow up time for all patients was 12 months postoperatively. Of 262 screened patients, 220 were randomized to receive either SPD or SDD. All patients were included in the

final analysis (120 SPD and 100 SDD, for further details please refer to Soleman et al. Figure 2)[7]. Recurrence rate was lower in the SPD group (8.33%, 95% confidence interval [CI] 4.28-14.72) than in the SDD group (12.00%, 95% CI 6.66-19.73), with the treatment difference (3.67%, 95% CI -12.6-5.3) not meeting predefined noninferiority criteria[7] . The SPD group showed significantly lower rates of surgical infections (p = 0.04) and iatrogenic morbidity through drain placement (p = 0.02). Length of stay and mortality rates were comparable in both groups.

Similarly to the initial study, for this subanalysis recurrence was defined as cSDH diagnosed on CT or MRI on the same side as the initial operation, with new or progressing clinical symptoms requiring surgical treatment. Indications for blood thinners are described in Supplementary Table 1. As defined in the main study protocol[10], AC medication was reversed preoperatively using Vitamin-K substitution (e.g. Konakion) and/or coagulant-factors (e.g. beriplex) aiming for an international normalized ratio (INR) of <1.3. In case of DOACS and PI medication, the decision whether reversal medication should be applied was left for the treating surgeon, since standard reversal treatment was not defined within the protocol of the main trial. Due to the lack of supporting data, reversal treatment using tranexanic-acid (e.g. cyclocaprone), minirin, platelet transfusion, and/or Vitamin-K substitution is rarely used at our institutions. Resumption of AC/PI medication was defined within the main study protocol. AC was resumed no earlier than six weeks postoperatively. PI medication was resumed no earlier than two weeks postoperatively, while in cases of PI treatment as a primary prophylaxis, postoperative discontinuation of up to six weeks was tolerated.

Compliance with ethical standards

Informed consent: Written informed consent of the patient or the next-of-kin (in comatose or incompetent patients) was obtained by a member of the neurosurgical staff prior to randomization.

Conflict of Interest: None.

Disclosure of Funding: This study was funded by the Research Foundation Kantonsspital Aarau. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The

corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

Ethical approval: The trial was done and analyzed according to the STROBE guidelines. The study protocol was approved by the local ethics committees (Ethikkommission Nordwest- und Zentralschweiz, Switzerland)

Statistical analysis

The associations between recurrence rates, mortality (corrected for the patients age), and the drain type inserted were analysed using a logistic regression model. Clinical outcome, including Glasgow Coma Scale (GCS), modified Rankin scale (mRS), Glasgow Outcome Scale (GOS), and Markwalder Score (MWS) at 24 hours, 6 weeks and 12 months after surgery for the two drain types were compared and analysed using the chi square test. For analysis, the outcome scores were dichotomized as follows: GCS 13-15 and <13, mRS ≤ 3 and >3, GOS >3 and ≤3, and MWS ≥1 and <1. The risk for recurrence or mortality in patient with a specific PI or AC (acetylsalicylic acid (ASA; Aspirn Cardio®, Bayer Schweiz AG), natrium-dalteparin (Fragmin®, Pfizer PFE Switzerland GmbH) and phenprocoumonum (Marcoumar®, MEDA Pharma GmbH), clopidogrel, different oral anticoagulants (DOAC; including: acenocumarol (Sintrom®, Medius AG), rivaroxaban (Xarelto®, Bayer Schweiz AG), fondaparinux (Arixtra®, Aspen Pharma Schweiz GmbH), apixaban (Eliquis®, Bristol-Myers Squibb SA)) were compared to patients without PI or AC using a multivariate logistic model. Finally, the interaction between the type of drain inserted and recurrence rate for each PI/AC type was analyzed using a likelihood ratio test comparing the model with interaction and the model without interaction. Patients treated with two concurrent PI/ACs (e.g. ASA and phenprocoumonum) were included for the analysis in the more “aggressive” PI or AC group type. ASA was assessed as the least aggressive, since its effect on perioperative bleeding and recurrence was estimated the lowest, followed by clopidogrel, prasugrel, phenprocoumonum, and natrium-dalteparin. A p-value <0.05 was considered significant. All statistical analyses were done using R (Comprehensive R Archive Network (CRAN), R Foundation for Statistical Computing, Vienna, Austria, Version

3.2.2). The analyses were performed on the per protocol analysis set as defined for the main trial analysis.

Results

Among the 220 study participants recruited between April 15, 2013, and December 9, 2015, 133 patients (60.5%) were treated with PI or AC. Of these, 65 (48.9%) patients received an SDD, while 68 (51.1%) patients received an SPD, respectively. Baseline subgroup characteristics are presented in Table 1, while distribution of drain type and PI/AC types are shown in Table 2.

Recurrence rates and Mortality

The insertion of SPD was associated with 7.35% recurrence rates compared to 13.85 % with SDD in patients treated with PI or AC, however this difference was not statistically significant (OR 0.41, 95% CI 0.06 – 2.65, p=0.36) (Table 3). For patients treated with PI or AC, mortality rate did not differ significantly between the SDD and SPD group (9.2%, n=6 vs. 11.7%, n=8, OR 3.01, 95% CI 0.45 - 22.08, p=0.26). Causes for death in the SDD group were one intracerebral bleeding under DOAC, one stroke under clopidogrel, one natural death under Vitamin K antagonists, one empyema under clopidogrel, one cancer death under ASA. Causes for death in the SPD group were one multiple organ failure under DOAC, one leucemia death under Vitamin K antagonists, one postoperative intracranial bleeding under ASA, one multiple organ failure under ASA, one natural death under ASA, one cardiac failure under Aspirin, one natural death under DOAC and one death of unknown cause under ASA and Vitamin K antagonists. Older patients showed generally higher mortality rates (p=0.01); nevertheless after correcting for age, the drain type did not influence significantly mortality rates (Table 3). The logistic model showed similar recurrence rates (Table 4) and higher mortality rates in patients treated with DOAC (OR 4.21 CI [0.98-16.48], p=0.04) compared to patients without PI or AC (Table 5). The likelihood ratio test showed no interaction between the type of drain inserted and type of PI/AC for recurrence of cSDH (p=0.20) and mortality at 12 months (p=0.81).

Clinical outcome

Generally, when patients were under PI or AC, at 24hours, 6 weeks and 12 months follow-up, GCS, mRS and GOS did not differ significantly between the two

groups (Table 6). After comparing outcome for each PI or AC type separately, at 24 hours after surgery, significantly more patients under phenprocoumonum and natrium-dalteparin had a GCS between 13 and 15 in the SDD group compared to the SPD group (p=0.006), while at 6 weeks follow up significantly more patients in the SDD group treated with ASA had a good mRS (p=0.01) (Table 6). At 12 months no significant difference in outcome measurements was seen for all PI and AC types.

Discussion

To date, the cSDH-Drain trial is the largest randomized study comparing recurrence rates of surgically drained cSDH after the insertion of SPD or SDD. In daily neurosurgical practice, we are often confronted with cSDH patients treated with PI and/or AC; therefore, it is not surprising that 60.5% of our study participants received PI or AC. With this subanalysis, we intended to evaluate an additional aspect that might influence the treatment of cSDH in a subgroup of patients, where to date no guidelines exist and the literature is sparse. According to our results, in patients treated with PI or AC undergoing burr hole drainage of cSDH, recurrence rates were lower in the SPD group compared to the SDD group; however significance was not seen. Similarly, at 12 months follow up, no statistically significant association between mortality rates and the inserted drain type were seen. Patients treated with DOAC showed a strong association with mortality, while the drain type in DOAC patients did not influence mortality rates. For all PI or AC types no statistically significant association between the drain type inserted and recurrence or mortality rates was apparent. Patients from the SDD group who were under phenprocoumonum/natrium-dalteparin or acetylsalicylic acid showed significantly higher rates of good GCS at 24 hours, and good mRS at 6 weeks follow up. Otherwise, outcome measurements did not differ significantly between both groups.

Recurrence rates

Similar to the recurrence rates within the main study, in the subgroup of patients treated with PI or AC, SPD was associated with lower recurrence rates compared to SDD, although significance was not reached. This might be explained by the fact that the SPD insertion technique is associated with less subdural manipulation. Therefore, the risk of injuring bridging veins or cortical vessels, which

might predispose acute or chronic rebleeds, is smaller. A few studies compared recurrence rates in patients undergoing burr hole drainage for cSDH who received PI[8,9] or oral anticoagulants[11]; however none of them investigated the association with the inserted drain type[12,13]. According to the literature, when evaluating recurrence rates of cSDH after SPD insertion compared to SDD insertion, most authors emphasize comparable recurrence rates with both drainage types[5,14,15,16,17,18,19,20] or in some cases lower recurrence rates with SPD[16]. Therefore, it is not surprising that patients who might have a higher bleeding risk, due to PI or AC therapy, would also benefit from a less invasive drain insertion technique.

Clinical outcome and mortality

To our knowledge, there are no studies focusing on the outcome and mortality in patients undergoing burr hole drainage, who are under PI or AC, depending on the inserted drain type. At 24 hours, 6 weeks, and 12 months follow up, clinical outcome was overall comparable in both groups. No difference was seen between the groups in mortality rates at 12 months either. These findings are in accordance with the results of our main trial, where clinical outcome and mortality did not differ between the SPD and SDD group. Interestingly, 24 hours after surgery significantly more patients under phenprocoumonum/ natrium-dalteparin treatment achieved a GCS of 13-15 in the SDD group compared to the SPD group, while at 6 weeks follow up significantly more patients in the SDD group treated with ASA showed higher mRS scores. Comparing our results to external data and interpreting them is difficult, as the current study is the first one to investigate specifically this question. Previous reports describe lower mortality, less complications, and significantly better mRS at 6 months after insertion of SPD compared to SDD[5,18]. However, within these studies the intake of blood thinners was not specifically assessed. Our results might have been skewed by the rather small sample size of the medication-subgroups. Therefore, trials with larger cohorts are definitely needed to confirm our findings. Lastly, even though some differences between the two drain groups for the short term clinical outcome for some PI/AC medications were found, the long-term clinical follow up could not detect these differences in clinical outcome between the drain groups anymore.

Recurrence rates and mortality according to the type of blood thinner

No statistically significant association between drainage type and different types of PI or AC for recurrence and mortality was found. However, we observed generally a higher mortality in patients treated with DOAC compared to patients without anticoagulation, irrespective of the drainage type. Since the patients were not randomly assigned to their medical treatment, this comparison is most likely confounded. Probably, patients treated with DOAC were in general sicker, and therefore mortality rates were higher in this group of patients.

Limitations

Although this subanalysis is based on a large, randomized controlled trial, some limitations exist. First, the main study was not initially designed to test the associations between drain types and PI/IC, so that the conclusions of this post-hoc subanalysis might not be statistically confirmatory. Exact data on the perioperative discontinuation or postoperative resumption time of PI or AC was not available. In addition, reversal treatment for PI and DOACS (e.g. cyclocapron, minirin, platelet transfusion etc.), was based on the decision of the treating surgeon and not collected or documented in a systematic manner. However, the protocol of the main study defined discontinuation margins for both. Finally, the dose of the applied PI or AC was not assessed, which might have skewed our results as well. Strengths of this study are the highly relevant subset of data, presented from the largest RCT analysing recurrence rate and outcome after surgical drainage of cSDH and insertion of SPD compared to SDD. To date, this is the first study analysing which drain type seems to be more suitable for patients undergoing burr hole drainage of cSDH treated with PI or AC.

Conclusion

In patients treated with PI and/or AC, the insertion of SPD after burr-hole drainage of cSDH showed comparable recurrence, mortality, and long term outcome rates when compared to SDD. These findings, in conjunction with the initial findings of the cSDH-Drain trial, might suggest that the insertion of SPD may be warranted also in patients treated with PI or AC.

Conflict of interest:

On behalf of all authors, the corresponding author states that there is no conflict of financial and non-financial interests.

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Author Contribution statement

MK contributed to design of the study, interpreted data, wrote the manuscript

KL contributed to data collection

SS performed statistical analyses

JF and **LM** provided critical feedback at various stages of the study, approved the final version of the manuscript

JS contributed to design and conduct of the study, analyzed and interpreted data, approved the final version of the manuscript.

Variable	SDD (n=64)	SPD (n=68)	P value
Age (mean ± SD)	80.1 (±7.3)	77.9 (±9.7)	0.02
Sex (male) n (%)	47 (73.4)	46 (67.6)	1
Comorbidities n (%)			
• COPD	0	4 (5.9)	0.38
• Dementia	8 (12.5)	6 (8.8)	0.26
• Liver cirrhosis	0	1 (1.5)	0.59
• Obesity	2 (3.1)	3 (4.4)	0.46
• AF	20 (31.2)	23 (33.8)	0.84
• Smoking	2 (3.1)	3 (4.4)	0.92
• Drug abuse	0	0	1
• Alkohol abusus	5 (7.8)	0	0.14
• CAD	6 (9.4)	4 (5.9)	0.53
• Stroke	10 (15.6)	13 (19.1)	0.75
• PE	2 (3.1)	5 (7.4)	0.73
• DVT	2 (3.1)	6 (8.8)	0.30
Symptoms			
• Coma n (%)	3 (4.6)	2 (2.9)	0.52
• Incontinence n (%)	2 (3.1)	1 (1.5)	0.85
• Sensory deficit n (%)	3 (4.6)	5 (7.4)	0.63
• others n (%)	0	1 (1.5)	0.87
Outcome meassurments preop			
• GCS median (mean [IQR])	14 [14; 15]	15 [14; 15]	0.29
• mRS (1-3) n (%)	49 (76.6)	47 (69.1)	0.39
• GOS (4-5) n (%)	45 (70.3)	45 (66.2)	1
• Markwalder score (0-1) n (%)	19 (29.7)	22 (32.8)	0.77
Hematoma characteristics			
• Midline shift (mean ± SD)	8.3 (±5.3)	6.8 (±4.5)	0.10

• Hemorrhage width mm (mean ± SD)	21.4 (±6.3)	18.3 (±5.9)	
- right (mean ± SD)	19.8 (±5.6)	18.3 (±6.8)	0.44
- left (mean ± SD)	21.7 (±7.2)	17.9 (±5.5)	0.01
• Bilateral hemorrhage n (%)	14 (21.9)	15 (22.1)	1.0

Table 1. Baseline characteristics of each drain type

SDD: subdural drain; SPD: subperiosteal drain; n: number; AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease; PE: pulmonary embolism; DVT: deep vein thrombosis; GCS: Glasgow Coma Scale; mRS: modified Rankin scale; GOS: Glasgow Outcome Score

Type of PI/AC	SDD (n=65)	SPD (n=68)
Acetylsalicylic acid	22 (33.8)	27 (40)
Natrium-dalteparin	1 (1.5)	2 (2.9)
Phenprocoumonum	21 (32.3)	20 (29.4)
Clopidogrel	4 (6.2)	4 (5.9)
DOAC	7 (10.8)	8 (11.8)
Acetylsalicylic acid and natrium-dalteparin	1 (1.5)	0
Acetylsalicylic acid and phenprocoumonum	2 (3.1)	3 (4.4)
Acetylsalicylic acid and clopidogrel	5 (7.7)	4 (4.9)
Acetylsalicylic acid and prasugrel	1 (1.5)	0

Table 2. Distribution of drainage type and PI/AC

PI: platelet inhibitors; AC: anticoagulants; SDD: subdural drain; SPD: subperiosteal drain; n: number; DOAC: different anticoagulants¨

All values: n (%)

Term	Variables	OR [95% CI]	p-value
Estimated association between **recurrence rates, drain type and use of PI/AC**	SPD (vs. SDD)	0.41[0.06; 2.65]	0.36
Estimated association between **mortality, drain type and use of PI/AC**	SPD (vs. SDD)	3.01 [0.45; 22.08]	0.26
Estimated association between **mortality, drain type and use of PI/AC corrected for age**	PI or AC/age	1.19 [0.47;1.16]	0.73

Table 3. Associations between recurrence rates, mortality and PI/AC according to the drain type

PI: platelet inhibitors; AC: anticoagulants; SDD: subdural drain; SPD: subperiosteal drain CI: confidence interval; OR: odds ratio

Type of PI/AC	Logistic model (PI/AC type compared to no PI/AC)	
	OR (95% CI)	p-value
Acetylsalicylic acid/ clopidogrel/prasugrel	1.36 (0.47-3.89)	0.56
Phenprocoumonum/natrium-dalteparin	0.87 (0.22-2.92)	0.83
DOAC	1.54 (0.22-7.03)	0.61

Table 4. Distribution of recurrence rates at 12 months according to PI or AC type and drain type (logistic model analysis)

PI: platelet inhibitor; AC: anticoagulants; DOAC: other anticoagulants; SPD: subperiosteal drain; SDD: subdural drain; n: number
*patients with concurrent acetylsalicylic acid treatment included in these groups (Phenprocoumonum/natrium-dalteparin group: 3 patients with SPD and 3 patients with SDD; Clopidogrel/prasugrel group: 4 patients with SPD and 6 patients with SDD)
bold: significant

PI/AC type	Logistic model (PI/AC type compared to no PI/AC)	
	OR (95% CI)	p-value
Acetylsalicylic acid/ clopidogrel/prasugrel	1.57 (0.53-4.71)	0.41
Phenprocoumonum/natrium-dalteparin	0.74 (0.15-2.80)	0.67
DOAC	4.21 (1.06-16.73)	**0.04**

Table 5. Distribution of mortality rates at 12 months according to PI or AC type and drain type (logistic model analysis).

PI: platelet inhibitor; AC: anticoagulants; DOAC: other anticoagulants; SPD: subperiosteal drain; SDD: subdural drain; n: number;
*patients with concurrent acetylsalicylic acid treatment included in these groups (Phenprocoumonum/natrium-dalteparin group: 3 patients with SPD and 3 patients with SDD; Clopidogrel/prasugrel group: 4 patients with SPD and 6 patients with SDD)
bold: significant

	All PI/AC			Acetylsalicylic acid			Phenprocoumonum/natrium-dalteparin*			Clopidogrel/prasugrel*			DOAC		
F/U time	SPD	SDD	p-value	SPD	SDD	p-value	SPD	SDD	p-value	SPD	SDD	p-value	SPD	SDD	p-value
GCS (13-15)															
24h	56 (82.3)	59 (92.2)	0.12	20 (74.1)	20 (90.9)	0.16	21 (84.0)	25 (100)	**0.006**	8 (100)	10 (100)	1	7 (87.5)	4 (57.1)	0.28
6w	62 (96.9)	55 (94.8)	0.66	23 (95.6)	19 (100)	1	24 (100)	24 (96.0)	1	7 (87.5)	8 (100)	1	8 (100)	4 (66.7)	0.16
12m	54 (98.2)	51 (100)	1	21 (95.5)	18 (100)	1	21 (100)	20 (100)	1	7 (100)	8 (100)	1	5 (100)	5 (100)	1
mRS (≤3)															
24h	49 (72.6)	53 (82.8)	0.15	17 (63.0)	16 (72.7)	0.55	20 (80.0)	23 (92.0)	0.42	8 (100)	10 (100)	1	4 (50.0)	4 (57.1)	1
6w	53 (82.8)	55 (94.8)	0.05	17 (70.8)	19 (100)	0.01	22 (91.7)	24 (96.0)	0.61	8 (100)	8 (100)	1	6 (75.0)	4 (66.7)	1
12m	46 (83.4)	47 (92.2)	0.24	18 (81.8)	16 (88.9)	0.67	16 (76.2)	19 (95.0)	0.18	7 (100)	7 (87.5)	1	5 (100)	5 (100)	1
GOS (>3)															
24h	54 (79.4)	55 (85.9)	0.37	24 (88.9)	17 (77.3)	0.44	19 (76.0)	24 (96.0)	0.09	7 (87.5)	10 (100)	0.44	4 (50.0)	4 (57.1)	1
6w	50 (78.1)	51 (87.9)	0.23	15 (62.5)	18 (94.7)	0.03	22 (91.7)	24 (96.0)	0.61	7 (87.5)	7 (87.5)	1	6 (75.0)	2 (33.3)	0.28
12m	46 (83.4)	45 (88.2)	0.58	16 (72.7)	15 (83.3)	0.48	20 (95.2)	19 (95.0)	1	6 (85.7)	7 (87.5)	1	5 (100)	4 (80.0)	1
Markwalder score (≥1)															

24h	43 (63.2)	45 (70.3)	0.46	12 (44.4)	13 (59.1)	0.4	19 (76.0)	21 (84.0)	0.73	8 (100)	7 (70.0)	0.22	4 (50.0)	4 (57.1)	1
6w	54 (84.4)	49 (84.5)	1	18 (75.0)	18 (94.7)	0.11	22 (91.7)	23 (92.0)	1	7 (87.5)	5 (62.5)	0.57	7 (87.5)	3 (50.0)	0.24
12m	48 (87.3)	45 (88.2)	1	18 (81.8)	15 (83.3)	1	20 (95.2)	19 (95.0)	1	6 (85.7)	7 (87.5)	1	4 (80.0)	4 (80.0)	1
							Total (n)							
24h	68	64		27	22		25	25		8	10		8	7	
6w	64	58		24	19		24	25		8	8		8	6	
12m	55	51		22	18		21	20		7	8		5	5	

Table 6. Distribution of outcome measurements for PI/AC type and type of drain inserted

F/U: follow up; PI: platelet inhibitor; AC: anticoagulants; DOAC: other anticoagulants; SPD: subperiosteal drain; SDD: subdural drain; n: number; h: hours; w: weeks; m: months; GCS: Glasgow Coma Scale; GOS: Glasgow Outcome Scale; mRS: modified Rankin Scale
*patients with concurrent acetylsalicylic acid treatment included in these groups (Phenprocoumonum/natrium-dalteparin group: 3 patients with SPD and 3 patients with SDD; Clopidogrel/prasugrel group: 4 patients with SPD and 6 patients with SDD)
Bold: significant
Values: n (%)

	SDD (n=64)	SPD (n=68)
Acetylsalicylic acid/ clopidogrel/prasugrel n (%)		
• Primary prophylaxis	9 (12.5)	10 (14.7)
• CAD	9 (14.1)	9 (13.2)
• CVI	4 (6.3)	5 (7.4)
• Carotid stenosis	2 (3.1)	1 (1.5)
• unknown	1 (3.1)	2 (2.9)
• AF	1 (1.6)	
• Polycythaemia vera		1 (1.5)
• Vascular dementia		1 (1.5)
• TIA		2 (2.9)
• PAOD	1 (3.1)	
Acetylsalicylic acid/ + clopidogrel/prasugrel n (%)		
• PAOD	1 (1.6)	
• CAD	2 (3.1)	2 (2.9)
• TEA	1 (1.6)	
• CVI	1 (1.6)	
• Coiling of an intracranial aneurysm		1 (1.5)
Acetylsalicylic acid/ + Phenprocoumonum n (%)		
• CAD	1 (1.6)	1 (1.5)
• Jugular vein thrombosis	1 (1.6)	
• CVI		1 (1.5)
• AF		1 (1.5)
• unknown	1 (1.6)	
Phenprocoumonum/natrium-dalteparin n (%)		
• AF	13 (20.3)	15 (22)
• Faktor V Leiden mutation	1 (1.6)	
• PE	3 (4.7)	3 (4.4)
• Sinus vein thrombosis	1 (1.6)	

• unknown	1 (1.6)	
• CAD	3 (4.7)	
• Bone fracture		1 (1.5)
• DVT		3 (4.4)
• Pulmonary hypertension		1 (1.5)
DOAC n (%)		
• AF	5 (7.8)	5 (7.4)
• uknown	1 (1.6)	1 (1.5)
• DVT		1 (1.5)
• Bone fracture	1 (1.6)	1 (1.5)

Supplementary Table 1 Indications for blood thinners

SDD: subdural drain; SPD: subperiosteal drain; n: number; AF: atrial fibrillation; COPD: chronic obstructive pulmonary disease; CVI: cerebral vascular infarction; CAD: coronary artery disease; PE: pulmonary embolism; DVT: deep vein thrombosis; PAOD: peripheral arterial occlusive disease; TEA: carotid thromboendarterectomy

Abbreviations list

AC	Anticoagulants
ASA	Acetylsalicylic Acid
CAD	Coronary Artery Disease
cSDH	Chronic subdural hematoma
CVI	Cerebrovascular Disease
d	days
DVT	Deep Vein Thrombosis
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Score
mRS	modified Rankin Scale
min	minutes
n	number
DOAC	Different Oral Anticoagulation
OR time	Operation time
PBC	Packed Blood Cells
PI	Platelet Inhibitors
SDD	Subdural Drain
SPD	Subperiosteal drain
STEMI	ST-segment Elevation Myocardial Infarction
TIA	Transient Ischemic Attack
y	years

Credit Author Statement

Maria Kamenova, M.D. contributed to design of the study, interpreted data, wrote the manuscript nceptualization, Writing- Original Draft, Investigation

Katharina Lutz, M.D. contributed to data collection

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