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Baseline and average platelet count can predict the outcome of patients with aneurysmal subarachnoid hemorrhage

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ABSTRACT

Background: Baseline values and the change of platelet count (PLT) during disease were reported to be associated with prognosis of patients with cancer and intensive care treatment. We aimed to evaluate the association between PLT with the course and prognosis of aneurysmal subarachnoid hemorrhage (SAH).
Methods: Admission (AdmPLT) and the 14-days mean PLT (MeanPLT) values of 763 SAH patients treated between 01/2005 and 06/2016 were recorded and, for further analysis, divided into four categories: <150, 150–260, 261–400 and > 400 × 10^9/L. Primary endpoints were cerebral infarcts in follow-up computed tomography scans, in-hospital mortality and unfavorable outcome at 6-months follow-up defined as modified Rankin scale>3. Adverse events during SAH were assessed as secondary endpoints.
Results: Higher PLT values were independently associated with lower risk of cerebral infarction (MeanPLT: aOR = 0.65 per-PLT-category-increase, $p = 0.001$), in-hospital mortality (AdmPLT: aOR = 0.64, $p = 0.017$; MeanPLT: aOR = 0.23, $p < 0.0001$) and unfavorable outcome (AdmPLT: aOR = 0.70, $p = 0.031$; MeanPLT: aOR = 0.35, $p < 0.0001$). Moreover, individuals with poorer outcome were less prone to PLT increase during SAH (mean values: -+20.3 vs + 30.5 × 10^9/L for cerebral infarction; +9.3 vs + 32.8 × 10^9/L for in-hospital mortality; +14.4 vs + 31.1 × 10^9/L for unfavorable outcome). The following adverse events during SAH were related to AdmPLT and/or MeanPLT: non-aneurysm related secondary rebleeding, intracranial hypertension requiring conservative treatment or decompressive craniectomy, sepsis and acute kidney failure.
Conclusion: Low PLT at admission and their less prominent increase during SAH were strongly linked with poor outcome of SAH. Further analysis is required to clarify the background of this association and potential therapeutic implications.

1. Introduction

The rupture of intracranial aneurysms resulting in a subarachnoid hemorrhage (SAH) is a devastating neurological disease with high morbidity and mortality,[1] with patients often suffering from severe long-term impairments.[2–4] Besides aneurysm rebleeding, delayed cerebral ischemia (DCI) caused by cerebral vasospasm has been believed for a long period to be the main factor influencing neurological outcomes after SAH.[5] In recent years, the focus has shifted from vasospasm, additionally acknowledging the effects of early brain injury (EBI), cortical spreading depolarization, oxidative stress, inflammation, and apoptosis on SAH outcome.[6] The multifactorial genesis of poor outcome patients with SAH has been extensively studied in experimental and clinical research, taking into account the effect of neuroinflammation,[7–10] blood-cell count and function,[11,12] different biomarkers[13] and coagulation.[14]

In this context, the laboratory parameters routinely measured at the onset and during SAH might present valuable markers for predicting the burden of complications and poor outcome of SAH. In particular, the baseline values and change of platelet count (PLT) are known to be prognostic factors in the treatment of oncologic and critically ill patients[43,44,45]. Moreover, PLT count, activation[15] and inflammation,[16,17] function,[18]and the occurrence of thromboembolism[19–21] have been supposed to play a critical role regarding neurological outcome

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following SAH. However, exact predictive value of PLT count at the onset and during SAH for disease prognosis remains unclear.

Therefore, this study aims to further elucidate the role of PLT and its change during the course of SAH regarding outcome and complications in a large representative cohort.

2. Material and methods

All patients treated for aneurysmatic SAH between 01/2005 and 06/2016 at a single tertiary center were included into an institutional database. Patients with available laboratory reports at admission and during the first 14 days post ictus were eligible for this study. The study was registered in the German clinical trial register (Unique identifier: DRKS00008749). The approval of the institutional ethics committee (Ethik-Kommission, Medizinische Fakultät der Universität Duisburg-Essen, Registration number: 15-6331-BO) for this study was obtained. All patients or relatives were informed and gave written consent as part of the treatment contract.

2.1. SAH management

All patients treated for suspected SAH received radiographic imaging (digital subtraction angiography (DSA) or computed tomography (CT) angiography) for identification of the bleeding source. Early aneurysm treatment (~~usually~~ within 24 h) was performed either by endovascular coiling or microsurgical clipping after interdisciplinary discussion between the neurosurgeons and ~~the~~ neurointerventionalists ~~on call.~~ Acute hydrocephalus was treated by placement of an external ventricular drainage, which was also used for continuous intracranial pressure (ICP) monitoring. Pathologically increased ICP (>20 mmHg) refractory to conservative management[22] were treated by decompressive craniectomy (DC). Follow-up head CT scans were performed within the first 24 h after aneurysm occlusion and if clinically indicated.

Standard treatment protocol included nimodipine orally for 21 days after ictus and transcranial doppler ultrasound was performed daily for the first 14 days after ictus. Patients with clinical signs of vasospasm and/or pathological transcranial ultrasound results were scheduled for DSA for verification and invasive endovascular treatment.

Laboratory routine tests were routinely carried out at admission and 3 times a week or if indicated. A few cases with significant thrombocytopenia, pseudothrombocytopenia and heparin-induced thrombocytopenia were excluded by appropriate testing.

2.2. Data management

Clinical, demographic, laboratory and radiographic data was retrospectively collected.

Clinical grading on admission was done according to the World Federation of Neurological Surgeons (WFNS) scale.[23] For analysis, the WFNS grade at admission was dichotomized in good (WFNS 1–3) and poor grades (WFNS 4–5). Radiographic severity of SAH was assessed utilizing the original Fisher scale[24] and further dichotomized in high (Fisher 3–4) and low (Fisher 1–2) radiographic severity. A clinical deterioration before treatment of the aneurysm in conjunction with new hemorrhage on CT was defined as aneurysm rebleeding. Occurrences of new focal (hemiparesis, aphasia, hemianopia, or neglect) or global (two points decrease on Glasgow Coma Scale) neurological impairment lasting for at least 1 h beginning 4 days after SAH were labeled as delayed ischemic neurologic deficit (DIND).[25]

The follow-up CT scans up to 6 weeks after SAH were reviewed by the senior author (RJ). Occurrence of new hypodensities not associated with ICH or surgical approach was defined as cerebral infarction. New intracranial bleeding on the follow-up imaging not related to aneurysm (re)rupture was defined as non-aneurysm related secondary rebleeding.

Patients with a severe systematic infection during the first 14 days following ictus were documented as "septic" if they met the criteria of the quick Sepsis-related Organ Failure Assessment (qSOFA)[26] or diagnosed with "any systemic infection" if these criteria were not yet met. Patients with acute chest pain and matching clinical criteria[27] for the acute coronary syndrome (ACS) were noted. A reduction of glomerular filtration, accompanied by increased serum levels of urea and creatinine and subsequent reduction in the volume of urine output, was defined as acute renal failure.[28] Neurological outcome was ascertained at 6 month follow-up using the modified Rankin Scale (mRS).[29] An mRS >3 was defined as unfavorable outcome.

The recorded laboratory variables included PLT and white blood cells (WBC) count. PLT count on admission (AdmPLT) and the mean values for the first 14 days of treatment (MeanPLT) were calculated. Patients were subsequently divided into four subgroups after considering boundaries for thrombocytopenia ($<150 \times 10^9$/L), thrombocythemia ($>400 \times 10^9$/L) and a mean PLT of 260×10^9/L for the cohort: Group 1 (PLT $<150 \times 10^9$/L), Group 2 (PLT 150-260 $\times 10^9$/L), Group 3 (PLT 261-400 $\times 10^9$/L), and Group 4 (PLT $>400 \times 10^9$/L). WBC count was dichotomized according to the institutional cutoff for the leukocytosis ($>11.0 \times 10^9$/L).

2.3. Study endpoints and statistical analysis

SPSS Version 23 for Windows (IBM Corp.) and Prism 9 (GraphPad Software, Inc.) were used for all statistical analyses. The significance level was set at $p \leq 0.05$. Missing data were replaced using multiple imputation.

Primary study endpoints were defined as the occurrence of cerebral infarction, in-hospital mortality, and unfavorable outcome at 6 months follow-up. Secondary endpoints included the above-mentioned ~~cerebral and non-cerebral~~ adverse events occurring during SAH.

The associations between the AdmPLT/MeanPLT values and the study endpoints were first addressed in the univariate analysis using the Chi-Square or the Fisher exact tests, as appropriate. The significant results were then tested in the final multivariate binary regression model adjusted for endpoint and PLT count relevant confounders: patients' age, sex, initial clinical and radiographic SAH severity, presence of acute hydrocephalus and WBC value (on admission or the 14-days mean value, as appropriate). Moreover, the association between the change in the PLT course (difference between MeanPLT and AdmPLT) and the primary/secondary study endpoints were also analyzed using the Student's *t*-test for normally distributed data and the Mann-Whitney-U test for non-normal distributed data.

3. Results

The final analysis included 763 consecutively admitted SAH patients with complete laboratory reports between 01/2005 and 06/2016. Mean age of the cohort was 55 years. The majority of the patients were female (65.7%). 41.8% of the patients were in initial poor clinical condition and 85.7% had a high radiographic severity of SAH (a complete overview of the baseline characteristics of the study cohort is given in Table 1).

3.1. Development of PLT count after SAH

The vast majority of the analyzed cohort (>92%) presented with AdmPLT within the reference range, with only 51 cases (6.7%) showing thrombocytopenia (Group 1: $<150 \times 10^9$/L) and nine individuals (1.2%) with initial thrombocythemia (Group 4: $>400 \times 10^9$/L). Over the course of SAH, PLT showed a mean increase of 25.5×10^9/L, ranging from a decrease of 164.9×10^9/L to an increase of 255.1×10^9/L. Accordingly, the proportion of SAH individuals with higher PLT values (Groups 3 & 4) significantly increased throughout the disease course (from 30.7% to 46.2%, $p < 0.0001$). The distribution of PLT categories on admission and during the two-weeks treatment period is shown in Table 1. Moreover, a histogram with the visualization of PLT values at the beginning of and during SAH is presented in Fig. 1.

Table 1
Baseline characteristics, complications and outcome of the final cohort.

Parameter	Count/(%*)	
Platelet count (x10^9/L):	**At admission:**	**14-days mean:**
<150	51 (6.7%)	38 (5.0%)
150–260	478 (62.6%)	372 (48.8%)
261-400	225 (29.5%)	317 (41.5%)
>400	9 (1.2%)	36 (4.7%)
Age, >55 years	346 (45.3%)	
Sex, female	501 (65.7%)	
WFNS, Grade = 4-5	319 (41.8%)	
Fisher, Grade 3-4	599 (85.7%)	
Acute hydrocephalus	541 (70.9%)	
Treatment modality, clipping	286 (39.2%)	
Aneurysm rebleeding	43 (5.6%)	
Secondary rebleeding (not aneurysm-related)	26 (3.5%)	
ICP increase requiring medical treatment	314 (41.6%)	
Decompressive craniectomy	206 (27.0%)	
Angiographic vasospasm	271 (64.5%)	
DIND	196 (30.4%)	
Systemic infections	287 (41.4%)	
Sepsis	25 (3.6%)	
Acute coronary syndrome	23 (3.4%)	
Acute kidney failure	10 (1.5%)	
Cerebral infarction in the follow-up CT	364 (48.1%)	
In-hospital mortality	133 (17.4%)	
Unfavorable outcome at 6 months	260 (36.8%)	

WFNS: World Federation of Neurosurgical Societies; ICP: intracranial pressure; DIND: Delayed ischemic Neurological Deficit. * - the percentages were calculated upon the number of the cases with known values.

3.2. Effect of different PLT count subgroups on the study endpoints

Patients' demographic characteristics and initial severity of SAH were associated with AdmPLT & MeanPLT count (Table 2). As to the study endpoints, there was an association between PLT count with different adverse events and SAH outcome in the univariate analysis, and the effect was more prominent for MeanPLT values than for AdmPLT. The higher the PLT count, the lower the risk for the following complications: not-aneurysm related secondary rebleeding (AdmPLT: odds ratio [OR] = 0.46 per-category-increase [hereinafter], $p = 0.03$; MeanPLT: OR = 0.52, $p = 0.039$), intracranial hypertension requiring conservative (AdmPLT: OR = 0.75, $p = 0.023$; MeanPLT: OR = 0.75, $p = 0.011$) or surgical (OR = 0.72, $p = 0.02$; MeanPLT: OR = 0.79, $p = 0.05$) treatment, sepsis (MeanPLT: OR = 0.29, $p < 0.0001$), acute kidney failure (AdmPLT: OR = 0.32, $p = 0.05$; MeanPLT: OR = 0.13, $p < 0.0001$), cerebral infarction (MeanPLT: OR = 0.71, $p = 0.002$), in-hospital mortality (AdmPLT: OR = 0.57, $p = 0.001$; MeanPLT: OR = 0.28, $p < 0.0001$), and unfavorable outcome at 6 months (AdmPLT: OR = 0.58, $p < 0.0001$; MeanPLT: OR = 0.45, $p < 0.0001$).

Accordingly, patients with thrombocytopenia showed the highest infarction rates (AdmPLT: 56.9%; MeanPLT: 65.8%), in-hospital mortality (AdmPLT: 43.1%; MeanPLT: 55.3%) and unfavorable neurological outcome (AdmPLT: 66%; MeanPLT: 78.4%). In contrast, the most favorable results with regard to cerebral infarction (AdmPLT: 47.1%; MeanPLT: 40.6%), in-hospital mortality (AdmPLT: 12.9%; MeanPLT: 6.9%) and 6-months outcome (AdmPLT: 28.3%; MeanPLT: 25.1%) were achieved in SAH patients with PLT count within the high normal range (261-400 × 10^9/L, Fig. 2, see also the Supplementary Table E1 with the rates of study endpoints for each PLT category). Of note, the results with regard to the complication rates in the highest PLT subgroup (Group 4, >400 × 10^9/L, SAH patients with thrombocythemia) were strongly biased due to a very small sample size (9 and 36 patients in the highest AdmPLT and MeanPLT categories respectively).

In the final multivariate analysis adjusted for relevant confounders (see the summary for multivariate analyses in Table 3, the complete data on multivariate analyses are presented in theSupplementary Table E2), PLT count showed independent associations with the following primary and secondary endpoints: non-aneurysm related secondary rebleeding (AdmPLT: adjusted OR [aOR] = 0.39, $p = 0.022$; MeanPLT: aOR = 0.49, $p = 0.040$), medical ICP treatment (MeanPLT: aOR = 0.61, $p < 0.0001$), decompressive craniectomy (AdmPLT: aOR = 0.70, $p = 0.026$; MeanPLT: aOR = 0.72, $p = 0.016$), sepsis (MeanPLT: aOR = 0.38, $p =$

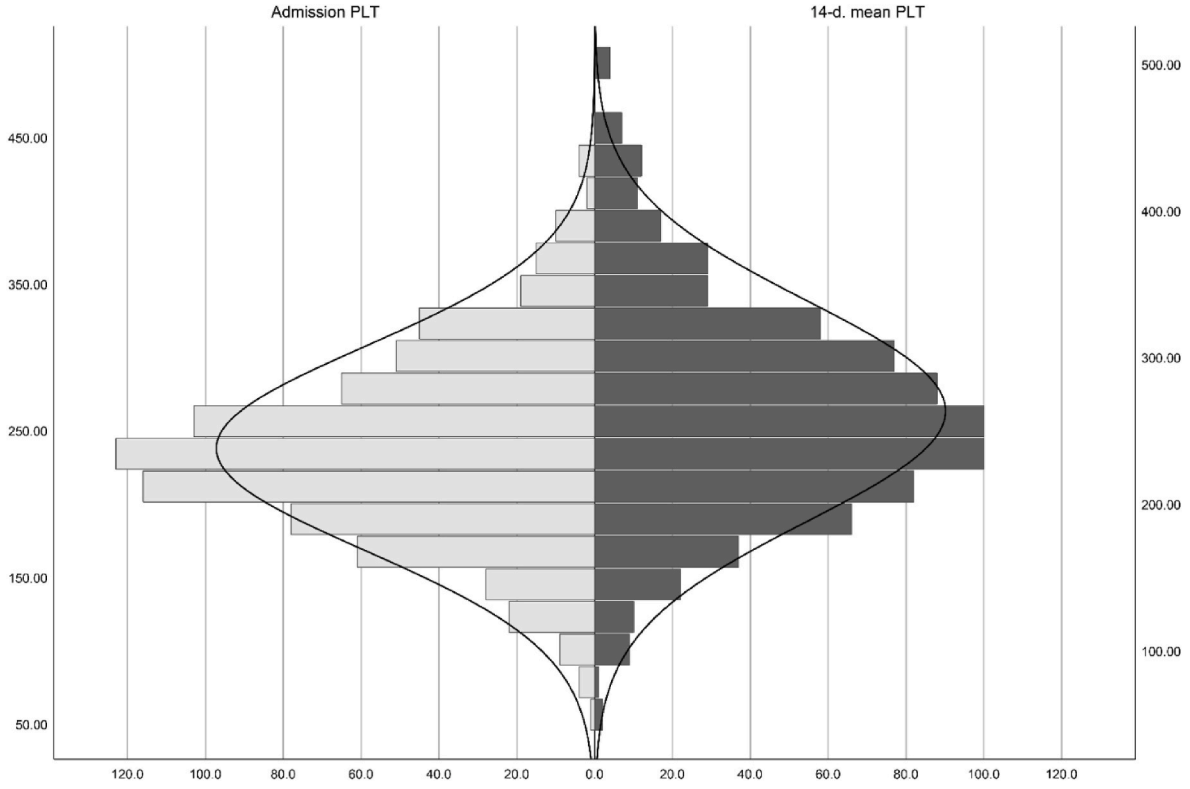

Fig. 1. distribution of baseline-population; x = n, y = PLT.

Table 2
Univariate analysis of the association between PLT count (at admission & 14-days mean value) with baseline characteristics, adverse events and outcome of SAH.

Parameter	PLT count at admission		14-days mean PLT count	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Age, >55 years	0.65 (0.50–0.83)	**0.001**	0.65 (0.52–0.81)	**<0.0001**
Sex, female	1.95 (1.49–2.56)	**<0.0001**	1.51 (1.20–1.90)	**0.001**
Fisher Grade = 3-4	0.80 (0.56–1.13)	0.207	0.90 (0.66–1.24)	0.525
WFNS = 4-5	0.67 (0.52–0.86)	**0.002**	0.76 (0.61–0.94)	**0.012**
Treatment modality (clipping)	0.84 (0.65–1.08)	0.176	1.08 (0.86–1.36)	0.490
Acute hydrocephalus	0.73 (0.56–0.95)	**0.021**	0.91 (0.72–1.15)	0.410
Aneurysm rebleeding	0.61 (0.35–1.04)	0.069	0.64 (0.40–1.03)	0.067
Secondary rebleeding (not aneurysm-related)	0.46 (0.23–0.93)	**0.030**	0.52 (0.28–0.97)	**0.039**
Decompressive craniectomy	0.72 (0.54–0.95)	**0.020**	0.79 (0.62–1.00)	**0.050**
Medical treatment of ICP increase	0.75 (0.58–0.96)	**0.023**	0.75 (0.60–0.94)	**0.011**
Angiographic presence of cerebral vasospasm	1.09 (0.76–1.55)	0.651	1.32 (0.97–1.81)	0.082
DIND occurrence	0.81 (0.60–1.08)	0.151	0.88 (0.68–1.13)	0.306
Systemic infections	0.78 (0.60–1.02)	0.072	1.01 (0.80–1.27)	0.962
Sepsis	0.51 (0.24–1.05)	0.068	0.29 (0.15–0.57)	**<0.0001**
Acute coronary syndrome	1.31 (0.65–2.65)	0.451	1.01 (0.53–1.90)	0.982
Acute kidney failure	0.32 (0.10–1.00)	**0.050**	0.13 (0.04–0.38)	**<0.0001**
Cerebral infarction	0.91 (0.71–1.16)	0.430	0.71 (0.57–0.89)	**0.002**
In-hospital mortality	0.57 (0.41–0.80)	**0.001**	0.28 (0.20–0.39)	**<0.0001**
Unfavorable outcome at 6 months	0.58 (0.44–0.76)	**<0.0001**	0.45 (0.35–0.58)	**<0.0001**

WFNS: World Federation of Neurosurgical Societies; ICP: intracranial pressure; DIND: Delayed ischemic Neurological Deficit; OR: Odds Ratio; CI: Confidence Interval.

0.008), acute renal failure (MeanPLT: aOR = 0.16, $p = 0.001$), cerebral infarction (MeanPLT: aOR = 0.65, $p = 0.001$), in-hospital mortality (AdmPLT: aOR = 0.64, $p = 0.017$; MeanPLT: aOR = 0.23, $p < 0.0001$), and unfavorable outcome (AdmPLT: aOR = 0.70, $p = 0.031$; MeanPLT: aOR = 0.36, $p < 0.0001$).

3.3. Effect of PLT count change on the study endpoints

The change in the PLT count during SAH also correlated with the risk of complications and poor outcome. The subgroup of patients deceasing during initial hospitalization had a mean decrease in PLT (-9.3×10^9/L), compared to an increase of $+32.8 \times 10^9$/L among those who survived the initial hospital stay ($p < 0.0001$). Then, SAH patients with unfavorable neurological outcome had a less prominent increase in PLT during SAH than individuals with a better outcome ($+14.4$ vs $+ 31.1 \times 10^9$/L, $p < 0.0001$). Similar results were observed with regard to cerebral infarction, with a less prominent increase in PLT in those patients who suffered from this complication ($+20.3$ vs $+ 30.5 \times 10^9$/L, $p = 0.001$, see Fig. 3). Finally, some adverse events during SAH (systemic infections, sepsis, and acute renal failure) also showed significant associations with the dynamics of PLT count during SAH (see supplementary Table E3).

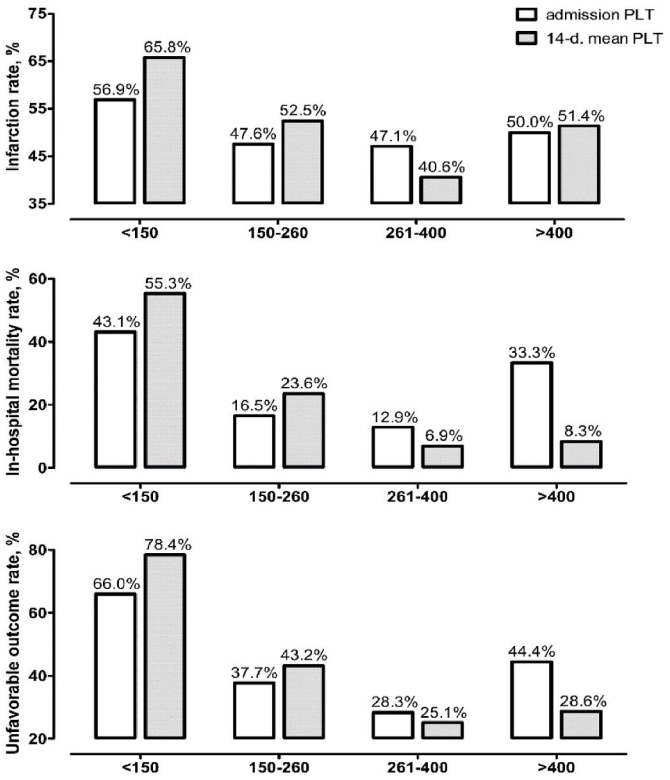

Fig. 2. rates of infarction, in-hospital mortality and unfavorable outcome for each group regarding admPLT and meanPLT.

Table 3
Multivariate analysis of the predictive value of PLT count for selected primary and secondary endpoints of the study (see also the Supplementary Table S2 in Online Supplements for the complete multivariate analysis for each of the presented endpoints).

PLT count at admission		
Parameter	*aOR (95% CI)*	*p-value*
Secondary bleeding	0.39 (0.17–0.88)	**0.022**
Decompressive craniectomy	0.70 (0.51–0.96)	**0.026**
Medical ICP treatment	0.82 (0.61–1.09)	0.166
Acute kidney failure	0.66 (0.07–5.84)	0.655
In-hospital mortality	0.64 (0.44–0.92)	**0.017**
Unfavorable outcome	0.70 (0.50–0.97)	**0.031**
14-days mean PLT count		
Parameter	*aOR (95%)*	*p-value*
Secondary bleeding	0.49 (0.25–0.97)	**0.040**
Decompressive craniectomy	0.72 (0.55–0.94)	**0.016**
Medical ICP treatment	0.61 (0.47–0.79)	**<0.0001**
Sepsis	0.38 (0.18–0.78)	**0.008**
Acute kidney failure	0.16 (0.05–0.47)	**0.001**
Cerebral infarction	0.65 (0.50–0.83)	**0.001**
In-hospital mortality	0.23 (0.16–0.34)	**<0.0001**
Unfavorable outcome	0.36 (0.26–0.50)	**<0.0001**

ICP: intracranial pressure; aOR: adjusted Odds Ratio; CI: Confidence Interval.

4. Discussion

We analyzed the correlation between baseline PLT count and its change during treatment of SAH with the neurological outcome and occurrence of complications. We found that low PLT on admission and, particularly, lower PLT values over the course of acute treatment were strongly and significantly associated to a higher risk of in-hospital mortality and cerebral infarction, leading to poor neurological outcome in patients with SAH, even when adjusted for known confounders.

As established, poor neurological outcome has been associated with

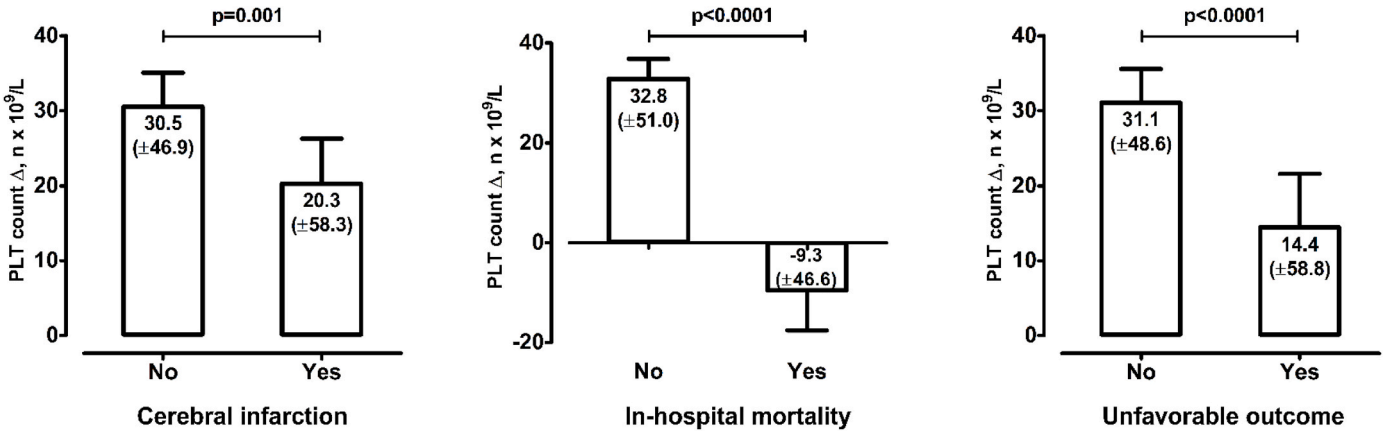

Fig. 3. Development of PLT during the course of SAH and its influence on cerebral infarction, in-hospital mortality and unfavorable outcome.

cerebral vasospasm,[4] EBI and DCI,[6,30] all intertwined and influenced by a multifactorial cascade including neuroinflammation,[7–10] blood-cell count and function,[11,12] biomarkers[13] and coagulation.[14]

Activated platelets lead to altered microvascular function in inflammatory diseases, and platelet adhesion intensifies, via contact-dependent and -independent mechanisms, the activation of vascular endothelial cells and leucocytes in inflamed microvessels[31] – for example, in spastic, post SAH cerebral vessels. This vessel alteration leads to an accumulation of activated platelets into thrombi, which may lead to embolic occlusion of microvessels,[32] as well as further modulating thrombo-inflammation through leukocyte activation throughout treatment, resulting in DCI,[33] clinically presented via DIND. This pathophysiological process partially explains our findings, when considering that persistently low PLT during treatment of SAH may be a sign of continuous and pathological high activation and consumption of thrombocytes via a feedforward mechanism, which leads to higher rates of DCI and, thus, poor neurological outcome.

The same mechanism seems to play a role in patients suffering from EBI. Animal models have shown that the formation of platelet aggregates – and as a result from this – activation and consumption of thrombocytes, which could potentially result in lower PLT at the time of admission, can occur as early as within 10 min from the beginning of SAH,[34] with evidence from autopsy studies on patients who died shortly after SAH implying that early microthromboses are a potential mechanism of EBI,[32] which explains why low PLT on admission could also lead to EBI, and thus might have predictive value regarding the occurrence of complications and poor clinical outcome.

One major player in this endovascular process is von Willebrand factor (VWF), a plasma protein present in - and responsible for activation of platelets, leading to formation of microthrombi[35] with elevated plasma levels of VWF indicating endothelial dysfunction. Contrary in function to VWF is ADAMTS13 (A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13), a protein tasked with cleaving large VWF molecules.[36] High serum levels of VWF, accompanied by low levels of ADAMTS13, result in higher rates of DCI, EBI and poor neurological outcome after SAH,[37,38] making modifying ADAMTS13 levels a possible therapeutic approach.[39]

Our data seems to reflect a pattern, which is also observable for non-SAH patients undergoing ICU treatment. It is shown that low PLT values on admission or occurrence of thrombocytopenia during treatment correlate with unfavorable outcome.[40–42] In ICU patients who beforehand underwent surgical treatment for their illness, a possible explanation for this might be a correlation between thrombocytopenia and higher rates of re-bleeding,[40] while other studies have shown thrombocytopenia to be an independent risk factor for higher rates of mortality, in part due to development of stroke (ischemic or hemorrhagic).[41] Additionally, and as previously mentioned, PLT affects not only the occurrence of thromboses, but also inflammatory, immune and wound-healing responses, atherosclerosis, angiogenesis, tumor progression, metastasis, and other diverse processes, leading to overall poor outcome.[43]

Our data shows that PLT on admission and over the course of SAH is independently associated with factors for poor SAH prognosis. Regarding the current evidence in the literature and our findings, the activation and consumption of PLT in peripheral blood probably reflects the extent of different pathophysiologic mechanisms developing after aneurysm rupture, particularly the processes of (micro-)thrombosis and neuroinflammation. In turn, these processes might contribute to the severity of EBI, DCI and DIND, thus, the risk of poor neurological outcome after SAH.

5. Limitations

The data used in this study is gathered retrospectively from available laboratory reports obtained from the aforementioned patients. Thus, other influencing factors that might correlate with PLT count and function, like mean platelet volume (MPV) or VWF could not be reproduced. Furthermore, there was no data to analyze the functional quality of thrombocytes, for example, via PFA-200 test. Also, despite the data being solid, some groups were quite small due to the distribution of PLT count across the population (as seen in Fig. 1).

6. Conclusion

Low PLT at admission and their less prominent increase during SAH were strongly linked with poor outcome of SAH. Feedback-loops between PLT, leucocytes, the vascular endothelium and neuroinflammation might lead to higher rates of complications and poor outcome, but are not fully understood yet. Further research needs to be completed to elucidate these connections and relations and to explore the possibilities of predictive qualities and therapeutical implications of these findings.

CRediT authorship contribution statement

Christoph Rieß: Writing – original draft, Project administration, Investigation. **Marvin Darkwah Oppong:** Writing – review & editing. **Thiemo-Florin Dinger:** Writing – review & editing. **Jan Rodemerk:** Writing – review & editing. **Laurèl Rauschenbach:** Writing – review & editing. **Meltem Gümüs:** Writing – review & editing. **Benedikt Frank:** Writing – review & editing. **Philipp Dammann:** Writing – review & editing. **Karsten Henning Wrede:** Writing – review & editing. **Ulrich Sure:** Validation. **Ramazan Jabbarli:** Supervision, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.wnsx.2024.100302.

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Abbreviations

ACS –: acute coronary snydrom
ADAMTS13 -: A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13
Adm –: admission
CT –: computed tomography
DC –: decompressive craniectomy
DCI –: delayed cerebral ischemia
DIND -: delayed ischemic neurologic deficit
DSA –: digital subtraction angiography
EBI -: early brain injury
ICU –: intensive care unit
ICP: intracranial pressure
MPV –: mean platelet volume
mRS –: modified Rankin scale
PLT: platelet count
qSOFA -: quick Sepsis-related Organ Failure Assessment
SAH -: Subarachnoid hemorrhage
VWF –: von Willebrand factor
WBC –: white blood cell count
WFNS -: World Federation of Neurological Surgeons scale