



Research article

Threshold hemoglobin level for delayed cerebral ischemia: A single-center retrospective analysis

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ABSTRACT

Background: Delayed cerebral ischemia (DCI) occurs in approximately 20%–30 % of patients with subarachnoid hemorrhage (SAH). This is the most common complication of SAH and has a high mortality rate. In the present study, we investigated the relationship between hemoglobin (Hb) values and DCI and aimed to determine a cutoff Hb value to be used as a predictor of DCI.

Methods: A total of 259 patients who were followed up for aneurysmal SAH at the Neurosurgery Clinic of Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital were included in our study. The patients were categorized into three groups according to Hb levels, low: <10 g/dl, moderate:10–13 g/dl, and high: >13 g/dl, and the relationship between Hb value and DCI and clinical outcomes was examined. Further, the cutoff Hb value for predicting DCI was determined by receiver operating characteristics (ROC) curve analysis.

Results: Statistical analyses revealed that patients with low Hb levels of <10 g/dl had a higher frequency of DCI than those with Hb levels of <10.75 g/dl. In addition, pairwise analyses based on the determined cutoff value revealed that patients with Hb levels <10.75 g/dl experienced DCI more frequently.

Conclusion: This study aimed to determine the utility of Hb levels as a predictor of DCI by examining its risk factors. The cutoff Hb level determined here is an important predictive factor for DCI, and the results provide promising evidence in term of early detection of DCI.

1. Introduction

Subarachnoid hemorrhage (SAH) refers to the extravasation of blood into the subarachnoid space. The most common nontraumatic cause of SAH is spontaneous SAH. More than 80 % of cases of spontaneous SAH occur because of aneurysm rupture [1], and approximately 10 % are cases of nonaneurysmal perimesencephalic SAH. SAH accounts for approximately 5 % of stroke cases [2]. Although SAH mortality has decreased from 50 % to 35 % in recent years, it remains an important medical complication that contributes to mortality and morbidity [3]. Further, 10%–25 % of SAH patients die before reaching the hospital. Only approximately one-third are discharged with permanent sequelae requiring postillness care, and only 30 % are able to return to their previous life[4]. Although it constitutes a small proportion of stroke cases, SAH is an important disease that impacts society because occurs in younger population compared to patients with conventional stroke and it has a high mortality and morbidity rate [4]. This makes it critical for

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Abbreviations

aSAH	aneurysmal subarachnoid hemorrhage
CT	Computed tomography
Hb	hemoglobin
DCI	Delayed cerebral ischemia
SAH	Subarachnoid hemorrhage
WFNS	World Federation of Neurosurgical Societies

physicians to consider SAH as a possible diagnosis.

Rebleeding and delayed cerebral ischemia (DCI) are important complications that increase mortality and morbidity in patients with aneurysmal SAH (aSAH). DCI is also a significant challenge for patients recovering from early brain injury. Approximately 70 % of these patients are at risk of radiological vasospasm, and 20%–30 % of the patients are at risk of DCI between days 3 and 14 after aSAH [5]. Until recently, vasospasm was used synonymously with DCI; however, recent studies have shown that 30 % of patients with radiological vasospasm are symptomatic [6]. In addition to cerebral vascular dysfunction, other conditions, such as microthrombosis, cortical spreading depolarizations, and neuroinflammation, are associated with DCI [4]. It is highly likely that many interrelated mechanisms play a role in DCI pathophysiology. Factors such as leukocytes, blood degradation products, cytokines, oxyhemoglobin, and endothelin are still under study [4]. Preventing DCI in asymptomatic patients who have recovered from early brain injury is crucial to reduce aSAH mortality and morbidity. The ability to predict DCI will be very valuable considering its contribution to the course of the disease. In this respect, studies on clinical or molecular markers for DCI have gained impetus.

Anemia is a common complication after aSAH and has been identified as a marker of cerebral infarction, vasospasm, death, and permanent disability [7]. Hemoglobin (Hb) mediates oxygen transport to cells and is a nitric oxide (NO) carrier. NO dysfunction plays a role in cerebral vasospasm and DCI through different mechanisms. The relationship between cerebral vasospasm and Hb levels after aSAH has not been fully explored. However, as Hb is a NO and oxygen carrier, it is likely to play a role in vasospasm and DCI [8]. The guidelines on aSAH published to date have not specified a Hb cutoff value.

Therefore, the present study aimed to examine the relationship between Hb levels and DCI and to identify the Hb cutoff value for predicting DCI.

2. Material and methods

In this retrospective cohort study, data of all patients who visited the Neurosurgery Clinic of Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital between 1 January 2014, and 1 January 2022, for aneurysmal subarachnoid hemorrhage and were treated through microsurgery or endovascular means were examined. Endovascular treatment was performed for the first time at our clinic on 11 November 2017; therefore, the data of patients treated endovascularly were collected from this date onwards. Inclusion criteria were as follows: aSAH diagnosed using clinical or radiological methods, treatment and follow-up conducted at our clinic, and Hb levels recorded during hospital stay. Patients with insufficient Hb monitoring and clinical and radiological data and patients who did not present within the first 72 h were excluded from the study. All information of the patients included in our study was accessed through the Hospital Information System. The records were cross-compared by two authors. It was cross-compared with radiological imaging reports.

2.1. Demographic data

The study included 259 patients treated for aSAH using microsurgery or endovascular means at our clinic. Inclusion criteria were as follows: aSAH diagnosed using clinical or radiological methods, treatment and follow-up conducted at our clinic, and Hb levels recorded during hospital stay. Patients with insufficient Hb monitoring and clinical and radiological data were excluded from the study. The mean age of the patients was 54.5 years. Of the patients included in the study, 139 (53.7 %) were women and 120 (46.3 %) were men. Further, 9 patients were excluded because they did not present within the first 72 h, and 27 patients were excluded owing to insufficient Hb monitoring and clinical follow-up data.

2.2. Radiological data

Among the patients presenting to the outpatient clinic or emergency department, aSAH was diagnosed by evaluating clinical and radiological data. In patients with suspected SAH after clinical examination and anamnesis, computed tomography (CT) was performed. If there was strong clinical suspicion of SAH even with negative CT scan, LP was performed. If SAH was detected and thought to be aneurysmal, CT angiography was performed. For patients with suspected aneurysm or other vascular pathology, digital subtraction angiography (DSA) was planned. When an aneurysmal SAH was detected in the patient that aneurysm was suitable to be treated with endovascular treatment, treatment was applied in the same or next session. In cases where surgical treatment was required, microsurgery was conducted at the earliest, wherein the aneurysm was clipped.

2.3. Clinical evaluation

The clinical status of the patients was determined using different grading systems. Glasgow Coma Scale (GCS) as well World Federation of Neurosurgical Societies (WFNS) and Hunt and Hess scoring systems were used. For the ease of grouping patients, WFNS and Hunt and Hess scores were divided into Good and Poor groups. In both scoring systems, patients with a score of 1–3 were included in the Good group, and those with a score of 4–5 were included in the Poor group.

The day after bleeding onset when neurological decline was observed was recorded for all patients. The investigation of the causes of neurological deterioration was primarily conducted to accurately diagnose delayed cerebral ischemia (DCI). The definition of DCI was established as a condition characterized by focal neurological deficits or a decline of 2 points in the Glasgow Coma Scale (GCS) that occurs more than three days after aneurysm rupture, lasting for more than 1 h, and not attributed to any other cause based on findings from CT, MRI, or other imaging and laboratory studies. Patients were diagnosed with DCI after their epicrisis notes and radiological examinations were reviewed and other causes were excluded. The day of DCI development after aSAH as well as the time period in which surgical site infection occurred most frequently was also recorded. This analysis was conducted by dividing the time period into three groups: first 3 days, days 3–14, and days 14–21. The presence or absence of radiological vasospasm was recorded. CT angiography, MR angiography, or DSA records were reviewed and stenoses of $\geq 10\%$ were taken into consideration. The measured points and anatomical variations were double-checked by two readers. All values were measured on Radiant viewer. The evaluator made a determination regarding whether the vasospasm was due to a possible spasm or was attributable to pre-existing conditions such as developmental hypoplasia or atherosclerosis. The correlation between radiological vasospasm and DCI was analyzed.

2.4. Hb monitoring

The patients' Hb levels were monitored daily. If two or more Hb measurements were taken on the same day, the first value was considered. Data on transfusion was not always available and hence was not considered. If the course of the disease resulted in discharge or death in the first 3 days, these patients were excluded. Patients who were not followed-up for 14 days and discharged or died were evaluated based on the Hb levels measured during the respective follow-up period. Studies have shown that Hb value < 10 g/dl is associated with cerebral hypoxia [9]. The threshold hemoglobin (Hb) value for anemia in patients with aneurysmal subarachnoid hemorrhage (aSAH) has been established at 12 g/dl. In the normal population, the threshold values for anemia are determined to be 13.6 g/dl for males and 12 g/dl for females [10]. According to these data, patients are grouped according to their Hb values; The mean Hb levels were divided into three groups, < 10 g/dl, 10–13 g/dl, and > 13 g/dl, and the incidence of DCI was compared between these groups. Hb levels were analyzed based on mean values. In addition, the area under the curve of daily Hb levels was calculated and compared to the incidence of DCI. A cutoff Hb value was determined as a predictor of DCI. We also examined if there was a correlation between mean Hb levels and patients with neurologic decline and mortality.

2.5. Statistical analyses

SPSS 24.0 package program was used for statistical analyses. A p value of < 0.05 was considered statistically significant. Descriptive analyses were conducted; categorical variables were presented as numbers and percentages, whereas continuous variables were presented as mean (\pm standard deviation) and median (minimum–maximum). Chi-squared and Fisher's exact tests were used to analyze independent categorical variables. In the analysis of continuous variables, normality assumptions were evaluated with

Table 1
Patient characteristics during hospitalization.

Variable Type	N	%
Radiological vasospasm on admission		
No	90	34.7
Yes	169	65.3
Intervention type		
Surgical	202	78.0
Endovascular	56	21.6
Surgical + Endovascular	1	0.4
Neurological decline		
No	126	48.6
Yes	127	49.0
Unknown	6	2.3
Day of neurological decline		
Mean \pm SD	5.25 \pm 5.79	
Median (Min–Max)	4 (0–39)	
Late cerebral ischemia	50	39.0
Day of LCI development		
Mean \pm SD	6.88 \pm 3.39	
Median (Min–Max)	6 (0–17)	
3–14 days	47	
>14 days	3	

Kolmogorov–Smirnov and Shapiro–Wilk tests. Student's *t*-test was used to compare normally distributed variables, whereas Mann–Whitney *U* test was used to compare non-normally distributed variables (Tables 1–4). Wilcoxon signed-rank test was used to compare dependent groups. Receiver operating characteristics (ROC) analysis was performed to determine the cutoff value and calculate the area under the curve. Variables associated with DCI were also evaluated through logistic regression analysis.

The study followed STROBE guideline. The study was approved by the Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital(No:145/20 Date:August 29, 2022) and written informed consent was obtained from all study participants regarding publication of their data.

3. Results

Among all 259 patients, DCI was observed in 50 patients (19.3 %) but not in 201 patients (77.6 %). A clear diagnosis was not obtained in eight patients. On average, DCI occurred in 6.88 days. The most common period of DCI development was between days 3–14. Further, of the 259 patients included in the study, 202 (78 %) underwent surgical aneurysm clipping, 56 (21.6 %) underwent endovascular treatment, and 1 underwent both surgical and endovascular treatment. Further, 169 patients (65.3 %) had radiologic vasospasm, and DCI was observed in 43 of these patients (43/169; 25.4 %; $p < 0.001$). Of the 90 patients (90/259; 34.7 %) without radiological vasospasm, DCI was detected in 7 patients (7/90; 7.7 %). Overall, 126 (48.6 %) patients exhibited neurological decline during follow-up, and DCI was observed in 39 % of these patients. Further, 60 patients had Hb levels <10 g/dl, 156 patients had Hb levels between 10 and 13 g/dl, and 43 patients had Hb levels >13 g/dl (Table 1).

A significant relationship was found between DCI, mean Hb level, WFNS, Hunt and Hess and Fisher scores at admission, and modified Rankin scores at discharge and 6 months. No significant correlation was found between radiological vasospasm, type of intervention, and modified Rankin scores (Table 2).

Mean Hb levels were analyzed with regard to the presence or absence of DCI. Patients with lower mean Hb levels had DCI. Moreover, statistical analyses revealed that patients with Hb levels of <10 g/dl had a higher frequency of DCI than those with Hb levels of <10.75 g/dl (35 % vs. 33 %; $p < 0.002$ and $p < 0.001$, respectively). In addition, patients with Hb levels <10.75 g/dl experienced DCI more frequently (Table 3).

The relationship between Hb levels and DCI was evaluated separately in patients who underwent surgical and endovascular treatment. Similar results were observed for patients who underwent surgical treatment, whereas no statistically significant difference was found in patients who underwent endovascular treatment.

A significant relationship was found between DCI and Hb level using ROC analysis. The area under the curve was 0.680 and the cutoff value for Hb was 10.75 g/dl. This cutoff Hb value had a sensitivity of 66.0 % and a specificity of 66.2 % (Fig. 1).

4. Discussion

For many years, aSAH has been of interest for scientists from many fields working to reduce its mortality and morbidity. Objectively predicting DCI before it occurs and tailoring treatment can reduce the devastating effects of DCI. In this retrospective study, we

Table 2

Relationship between the clinical and radiological scoring of the patients, the interventions during hospitalization, Hb levels, and Modified Rankin scores at admission, discharge, and at 6 months.

Variables	Modified Rankin Score at Discharge				Modified Rankin Score at 6 months			
	0–3	4–5	Ex	p values	0–3	4–5	Ex	p values
Late cerebral ischemia								
No	132 (65.7)	30 (14.9)	39 (19.4)	<0.001	140 (69.7)	8 (4.0)	53 (26.4)	0.011
Yes	17 (34.0)	14 (28.0)	19 (38.0)		23 (46.9)	3 (6.1)	23 (46.9)	
Mean hemoglobin level								
<10.75	125 (79.6)	14 (8.9)	18 (11.5)	<0.001	129 (82.2)	3 (1.9)	25 (15.9)	<0.001
≥ 10.75	32 (31.4)	30 (29.4)	40 (39.2)		42 (41.6)	8 (7.9)	51 (50.5)	
WFNS Admission								
1–3	144 (73.1)	18 (9.1)	35 (17.8)	<0.001	149 (76.0)	3 (1.5)	44 (22.4)	<0.001
4–5	13 (21.0)	26 (41.9)	23 (37.1)		22 (35.5)	8 (12.9)	32 (51.6)	
Hunt and Hess scale Admission								
1–3	145 (71.4)	22 (10.8)	36 (17.7)	<0.001	151 (74.8)	3 (1.5)	48 (23.8)	<0.001
4–5	12 (21.4)	22 (39.3)	22 (39.3)		20 (35.7)	8 (14.3)	28 (50.0)	
FISHER Admission								
1–3	96 (81.4)	8 (6.8)	14 (11.9)	<0.001	95 (81.2)	1 (0.9)	21 (17.9)	<0.001
4	60 (42.9)	36 (25.7)	44 (31.4)		75 (53.6)	10 (7.1)	55 (39.3)	
Radiological vasospasm								
No	65 (72.2)	8 (8.9)	17 (18.9)	0.010	66 (73.3)	3 (3.3)	21 (23.3)	0.215
Yes	92 (54.4)	36 (21.3)	41 (24.3)		105 (62.5)	8 (4.8)	55 (32.7)	
Intervention type								
Surgery	126 (62.1)	38 (18.7)	39 (19.2)	0.044	137 (67.8)	9 (4.5)	56 (27.7)	0.505
Endovascular	31 (55.4)	6 (10.7)	19 (33.9)		34 (60.7)	2 (3.6)	20 (35.7)	

Mann–Whitney *U* test was used.

Table 3
Relationship between the mean hemoglobin levels during hospitalization and late cerebral ischemia in patients.

Hemoglobin	Late cerebral ischemia		p values
	No	Yes	
Mean \pm SD	11.5 \pm 1.5	10.6 \pm 1.5	<0.001 ^a
Median (Min–Max)	11.4 (8.6–15.6)	10.2 (7.9–14.5)	
<10 g/dl ^b	38 (64.4)	21 (35.6)	0.002
10–13 g/dl	126 (83.4)	25 (16.6)	
>13 g/dl	37 (90.2)	4 (9.8)	
<10.75 g/dl	67 (67.0)	33 (33.0)	<0.001
\geq 10.75 g/dl	134 (88.7)	17 (11.3)	

^a Mann–Whitney *U* test was used.

^b The marked group was found to be statistically different from the other groups.

Table 4
ROC analysis of hemoglobin levels for predicting late cerebral ischemia.

Risk Factor	EAA (95 % CI)	Hemoglobin cutoff value	p values	Sensitivity (%)	Specificity (%)
Late cerebral ischemia	0.680 (0.596–0.764)	10.75	<0.001	66.0	66.2

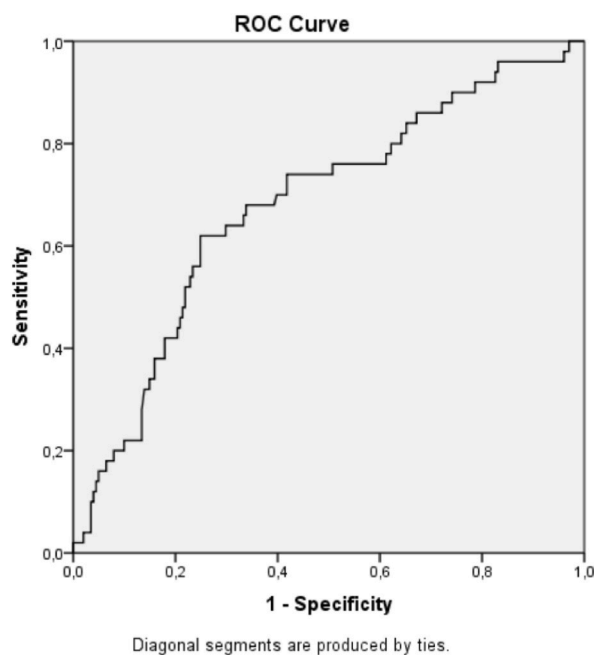


Fig. 1. ROC curve of hemoglobin mean values for the presence of delayed cerebral ischemia.

investigated whether the neurological status of aSAH patients as determined by WFNS and Hunt and Hess grading, Fisher scale scores, aneurysm treatment with endovascular or microsurgical technique, presence of radiological vasospasm, and anemia at admission were associated with DCI and mortality and morbidity. Specifically, the relationship between mean Hb levels and DCI was examined, and a cutoff value for Hb level was determined as a predictor of DCI [1–3].

The clinical conditions of the patients at the time of admission to the hospital have been considered as a risk factor for complications after aSAH and studies have been conducted on them. Many studies have shown that high WFNS, Hunt-Hess and Fisher grades are associated with poor prognosis [11,12]. In our study, when we compared WFNS, Hunt-Hess and Fisher scores with mortality and discharge mRS, we obtained statistically significant results in all groups. In all scores, lower scores were associated with lower mortality and better mRS, while higher scores were associated with higher mortality and worse mRS ($p < 0.001$).

In the literature, the incidence of radiological vasospasm in patients with SAH varies between 50 % and 67 %, whereas the incidence of DCI is 20%–30 %. The fact that DCI does not occur in the majority of patients with radiological vasospasm is associated with the pathogenesis of DCI. Etminan et al. conducted a study on 413 patients investigating radiological vasospasm, DCI, and mortality. In that study, 194 of 413 patients had moderate radiological vasospasm, and clinical deterioration occurred in 43 % of these patients. In

contrast, clinical deterioration was observed in only 14 % of the remaining 219 patients [13]. In another study of 276 patients, the rates of radiological vasospasm and DCI were similar; 60 out of 65 patients had DCI [14]. In another study [15], found that not all patients with angiographic vasospasm developed DCI. In the present study, radiological vasospasm was observed in 169 (65 %) patients, whereas DCI was observed in 50 (19.3 %) patients, both are consistent with the values in the literature. DCI was observed in 25.4 % of the patients with radiological vasospasm and in 77.7 % of the patients without radiological vasospasm. In addition, a significant correlation was found between DCI, mortality, and mRS in our study, whereas no statistically significant results were obtained with radiological vasospasm. The findings presented in our study are consistent with the those presented in the literature [5,6].

As Hb carries oxygen as well as NO, it plays an important role in the pathogenesis of DCI. The breakdown products of hemoglobin degradation and oxyhemoglobin are factors responsible for secondary brain injury. Oxyhemoglobin also acts as a scavenger of nitric oxide (NO), thereby reducing its levels. NO acts as a vasodilator, antioxidant, anticoagulant, and antithrombotic, suggesting that it plays an important role in DCI pathogenesis [16,17]. Many studies have revealed that low Hb levels are associated with poor clinical outcome. The results in the present study are consistent with that in the literature. The relationship between Hb levels and DCI, which we analyzed in three groups, indicated that the incidence of DCI increased as Hb levels decreased ($p < 0.002$). The incidence of DCI in patients with Hb levels of <10 g/dl was significantly higher compared to that in patients with Hb levels of $10\text{--}13$ g/dl and >13 g/dl. The incidence of DCI was lowest in patients with Hb levels of >13 g/dl. The low WFNS and Hunt and Hess grades at admission may be a factor in this. In a retrospective study conducted by Kramer et al. [18], 65 of 245 patients had WFNS grades of 4–5, and 180 patients had WFNS grades of 1–3. The decrease in Hb levels over time was higher in patients with higher WFNS grades compared to patients with lower WFNS grades despite transfusion. Low Hb levels were associated with poor outcomes. Further, the decrease in Hb levels within 3 days was greater in patients with poor clinical status. Hb level was significantly lower in patients with DCI (Hb levels between 9.7 and 10.8) [17]. In a retrospective study of 522 patients, Stein et al. [19] performed ROC curve analysis and determined a cutoff Hb value of 10.9 for predicting mortality. For vasospasm, the cutoff value was 10.4. The authors of the previous study noted that low Hb was associated with mortality and poor outcome. In the same study, which also evaluated patients receiving transfusions, it was determined that the need for transfusion, 30-day mortality, and poor clinical outcome were not significantly associated with transfusion that after adjusting for mean Hb levels [19]. Naidech et al. found that low mean Hb levels were associated with poor clinical outcomes (11.6 ± 1.4 vs. 10.7 ± 1.1). Mean Hb was also associated with infarction independently of radiological vasospasm. In another study, the authors showed that maintaining high Hb levels (>11 g/dl) was associated with better outcomes [20,21]. Sun et al. analyzed the data of 218 patients in their retrospective cohort study and revealed that Hunt and Hess grade, Fisher grade, and postoperative mean Hb levels were independent risk factors for DCI. The authors found a lower incidence of DCI in patients with a postoperative mean Hb level of $11\text{--}12$ g/dl [22]. In their study examining 413 patients included in the CONSCIOUS-1 study, Ayling et al. found that the incidence of DCI was high in patients with Hb < 10 g/dl along with poor clinical outcomes but it did not affect long-term mortality. In anemic patients, transfusion was associated with poor clinical outcomes but not if Hb level was >10 g/dl [23]. In a recently conducted study, 310 patients with aSAH were examined. It was found that a more sudden decrease in Hb during the hospital process, regardless of any absolute Hb value, was associated with both poor functional outcomes and an increased risk of DCI [24]. In a recent study investigating predictors of anemia, it was found that anemia is associated with prolonged hospital stay, poor clinical outcomes, and mortality [25]. One of the main objectives of the present study was to determine a cutoff value for Hb to predict DCI. In our ROC curve analysis, an Hb level of 10.75 g/dl ($p < 0.001$) was determined as the cutoff value for predicting DCI with 66 % sensitivity and 66.2 % specificity. In the present study, low Hb levels were also associated with mortality and poor neurological status. P values were <0.001 for mortality and mRS at discharge and at 6 months.

In the present study, Hb levels were also analyzed separately in terms of DCI in surgically and endovascularly treated patients. Although we wanted to contribute to the literature in this regard, we could not obtain significant results in patients that received endovascular treatment due to the low number of patients to perform statistical analysis. Nevertheless, the results in surgically treated patients were similar to the results obtained for the overall patient group. In patients treated endovascularly, the incidence of DCI was higher in patients with low Hb levels, but the difference was not statistically significant. Again, when surgical and endovascular treatment methods were compared in terms of DCI development, we could not observe any difference between these treatment modalities.

4.1. Limitations

Although the results provide evidence for a significant relationship between DCI and vasospasm through Hb levels, our study has some limitations. First of all, the study was conducted retrospectively. All patient records were kept electronically. All records were carefully reviewed by the research team and cross-comparisons were made for all data to minimize bias or subjective observation. Hb levels of the patients were recorded daily but not measured at the same time of the day. It was also not recorded whether patients received transfusions. Although the relationship between transfusion and DCI has not been clearly demonstrated in the literature, this is still one of the limitations of our study. Perfusion MRI and DSA were not performed in all patients. Although CT angiography was utilized, DSA is necessary for a more accurate assessment of vasospasm. Perfusion MRI is useful for the evaluation of delayed cerebral ischemia (DCI). Since our study is retrospective, we could not consider whether these imaging modalities were performed in order to avoid further limiting the number of patients included. Future prospective studies will address these limitations.

5. Conclusions

This study was conducted to provide more evidence to the literature on DCI and the patients hospitalized in our clinic were

evaluated according to age, gender, comorbidity, admission Glasgow Coma Scale score, admission and postoperative WFNS score, admission and postoperative Hunt–Hess score, Modified Rankin score, endovascular or surgical treatment of aneurysm, and daily Hb levels, and the effects of these factors on DCI and clinical outcomes were examined. The cutoff value identified for Hb levels can make an important contribution to the literature in terms of predicting DCI in patients with aSAH.

An Hb level of <10.75 g/dl in patients followed up after aSAH indicates DCI risk, and our results show that Hb level should be considered along with other factors in the follow-up of SAH. The results obtained in the present study make valuable contributions to the literature in this respect; however, DCI is still an important clinical condition and international and multicenter studies on prevention and treatment are warranted.

CRedit authorship contribution statement

Besnek Atakan: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Şanlı Ahmet Metin:** Writing – review & editing, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Türkoğlu Mehmet Erhan:** Supervision.

Data availability statement

The data supporting the findings of this study are available within the article and its supplementary materials. Any additional data or materials can be requested from the corresponding author.

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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.

References

- [1] R.L. Macdonald, T.A. Schweizer, Spontaneous subarachnoid haemorrhage, *Lancet* 389 (10069) (2017) 655–666, [https://doi.org/10.1016/s0140-6736\(16\)30668-7](https://doi.org/10.1016/s0140-6736(16)30668-7). PubMed PMID: 27637674.
- [2] S.N. Neifert, E.K. Chapman, M.L. Martini, W.H. Shuman, A.J. Schupper, E.K. Oermann, et al., Aneurysmal subarachnoid hemorrhage: the last decade, *Transl Stroke Res* 12 (3) (2021) 428–446, <https://doi.org/10.1007/s12975-020-00867-0>. PubMed PMID: 33078345.
- [3] P.E. Passier, J.M. Visser-Meily, M.J. van Zandvoort, M.W. Post, G.J. Rinkel, C. van Heugten, Prevalence and determinants of cognitive complaints after aneurysmal subarachnoid hemorrhage, *Cerebrovasc. Dis.* 29 (6) (2010) 557–563, <https://doi.org/10.1159/000306642>. PubMed PMID: 20375498.
- [4] J.R. Geraghty, F.D. Testai, Delayed cerebral ischemia after subarachnoid hemorrhage: beyond vasospasm and towards a multifactorial pathophysiology, *Curr Atheroscler Rep* 19 (12) (2017) 50, <https://doi.org/10.1007/s11883-017-0690-x>. PubMed PMID: 29063300.
- [5] N.W. Dorsch, M.T. King, A review of cerebral vasospasm in aneurysmal subarachnoid haemorrhage Part I: incidence and effects, *J. Clin. Neurosci.* 1 (1) (1994) 19–26, [https://doi.org/10.1016/0967-5868\(94\)90005-1](https://doi.org/10.1016/0967-5868(94)90005-1). PubMed PMID: 18638721.
- [6] C.L. Francoeur, S.A. Mayer, Management of delayed cerebral ischemia after subarachnoid hemorrhage, *Crit. Care* 20 (1) (2016) 277, <https://doi.org/10.1186/s13054-016-1447-6>. PubMed PMID: 27737684; PubMed Central PMCID: PMC5064957.
- [7] D.L. Bourke, T.C. Smith, Estimating allowable hemodilution, *Anesthesiology* 41 (6) (1974) 609–612, <https://doi.org/10.1097/0000542-197412000-00015>. PubMed PMID: 4433062.
- [8] R. Stapley, B.Y. Owusu, A. Brandon, M. Cusick, C. Rodriguez, M.B. Marques, et al., Erythrocyte storage increases rates of NO and nitrite scavenging: implications for transfusion-related toxicity, *Biochem. J.* 446 (3) (2012) 499–508, <https://doi.org/10.1042/bj20120675>. PubMed PMID: 22720637; PubMed Central PMCID: PMC3572541.
- [9] P.D. Le Roux, Anemia and transfusion after subarachnoid hemorrhage, *Neurocrit Care* 15 (2) (2011) 342–353.
- [10] N.F. Rosenberg, A. Koht, A.M. Naidech, Anemia and transfusion after aneurysmal subarachnoid hemorrhage, *J. Neurosurg. Anesthesiol.* 25 (1) (2013) 66–74.
- [11] J. Mocco, E.R. Ransom, R.J. Komotar, J.M. Schmidt, R.R. Sciacca, S.A. Mayer, et al., Preoperative prediction of long-term outcome in poor-grade aneurysmal subarachnoid hemorrhage, *Neurosurgery* 59 (3) (2006) 529–538, discussion -38.
- [12] J. de Winkel, T.Y. Cras, R. Dammers, P.J. van Doormaal, M. van der Jagt, D.W.J. Dippel, et al., Early predictors of functional outcome in poor-grade aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis, *BMC Neurol.* 22 (1) (2022) 239.
- [13] N. Ertinan, M.D. Vergouwen, R.L. Macdonald, Angiographic vasospasm versus cerebral infarction as outcome measures after aneurysmal subarachnoid hemorrhage, *Acta Neurochir. Suppl.* 115 (2013) 33–40, https://doi.org/10.1007/978-3-7091-1192-5_8. PubMed PMID: 22890640.
- [14] R. Dhar, M.N. Diringer, The burden of the systemic inflammatory response predicts vasospasm and outcome after subarachnoid hemorrhage, *Neurocrit Care* 8 (3) (2008) 404–412, <https://doi.org/10.1007/s12028-008-9054-2>. PubMed PMID: 18196475; PubMed Central PMCID: PMC2538678.
- [15] C. Dietrich, J. van Lieshout, I. Fischer, M.A. Kamp, J.F. Cornelius, A. Tortora, et al., Transcranial Doppler ultrasound, perfusion computerized tomography, and cerebral angiography identify different pathological entities and supplement each other in the diagnosis of delayed cerebral ischemia, *Acta Neurochir. Suppl.* 127 (2020) 155–160, https://doi.org/10.1007/978-3-030-04615-6_23. PubMed PMID: 31407077.
- [16] R.M. Pluta, J. Hansen-Schwartz, J. Dreier, P. Vajkoczy, R.L. Macdonald, S. Nishizawa, et al., Cerebral vasospasm following subarachnoid hemorrhage: time for a new world of thought, *Neurol. Res.* 31 (2) (2009) 151–158, <https://doi.org/10.1179/174313209x393564>. PubMed PMID: 19298755; PubMed Central PMCID: PMC2706525.
- [17] W.S. Dodd, D. Laurent, A.S. Dumont, D.M. Hasan, P.M. Jabbour, R.M. Starke, et al., Pathophysiology of delayed cerebral ischemia after subarachnoid hemorrhage: a review, *J. Am. Heart Assoc.* 10 (15) (2021 Aug 3) e021845, <https://doi.org/10.1161/JAHA.121.021845>. Epub 2021 Jul 30. PMID: 34325514; PMCID: PMC8475656.
- [18] A.H. Kramer, D.A. Zygun, T.P. Bleck, A.S. Dumont, N.F. Kassell, B. Nathan, Relationship between hemoglobin concentrations and outcomes across subgroups of patients with aneurysmal subarachnoid hemorrhage, *Neurocrit Care* 10 (2) (2009) 157–165, <https://doi.org/10.1007/s12028-008-9171-y>. PubMed PMID: 19116699.

- [19] M. Stein, L. Brokmeier, J. Herrmann, W. Scharbrodt, V. Schreiber, M. Bender, et al., Mean hemoglobin concentration after acute subarachnoid hemorrhage and the relation to outcome, mortality, vasospasm, and brain infarction, *J. Clin. Neurosci.* 22 (3) (2015) 530–534, <https://doi.org/10.1016/j.jocn.2014.08.026>. PubMed PMID: 25533213.
- [20] A.M. Naidech, J. Drescher, M.L. Ault, A. Shaibani, H.H. Batjer, M.J. Alberts, Higher hemoglobin is associated with less cerebral infarction, poor outcome, and death after subarachnoid hemorrhage, *Neurosurgery* 59 (4) (2006) 775–779, <https://doi.org/10.1227/01.Neu.0000232662.86771.A9>. PubMed PMID: 17038943.
- [21] A.M. Naidech, A. Shaibani, R.K. Garg, I.M. Duran, S.M. Liebling, S.L. Bassin, et al., Prospective, randomized trial of higher goal hemoglobin after subarachnoid hemorrhage, *Neurocrit Care* 13 (3) (2010) 313–320, <https://doi.org/10.1007/s12028-010-9424-4>. PubMed PMID: 20717750.
- [22] J. Sun, G. Tan, W. Xing, Z. He, Optimal hemoglobin concentration in patients with aneurysmal subarachnoid hemorrhage after surgical treatment to prevent symptomatic cerebral vasospasm, *Neuroreport* 26 (5) (2015) 263–266, <https://doi.org/10.1097/wnr.0000000000000340>. PubMed PMID: 25714422.
- [23] O.G. Ayling, G.M. Ibrahim, N.M. Alotaibi, P.A. Gooderham, R.L. Macdonald, Anemia after aneurysmal subarachnoid hemorrhage is associated with poor outcome and death, *Stroke* 49 (8) (2018) 1859–1865.
- [24] A.H. Shah, R. Snow, L.C. Wendell, B.B. Thompson, M.E. Reznik, K.L. Furie, et al., Association of hemoglobin trend and outcomes in aneurysmal subarachnoid hemorrhage: a single center cohort study, *J. Clin. Neurosci.* 107 (2023 Jan) 77–83, <https://doi.org/10.1016/j.jocn.2022.12.008>. Epub 2022 Dec 13. PMID: 36521368.
- [25] F. Wu, H. Chen, Z. Liu, D. Ye, X. Wang, L. Zhou, et al., Predicting postacute phase anaemia after aneurysmal subarachnoid haemorrhage: nomogram development and validation, *BMJ Open* 14 (7) (2024 Jul 18) e082799, <https://doi.org/10.1136/bmjopen-2023-082799>. PMID: 39025815; PMCID: PMC11261674.