Acta Neurochirurgica (2019) 161:791–797
https://doi.org/10.1007/s00701-019-03846-z

ORIGINAL ARTICLE - VASCULAR NEUROSURGERY - ANEURYSM

Hemorrhagic burden in poor-grade aneurysmal subarachnoid hemorrhage: a volumetric analysis of different bleeding distributions

Pietro Panni[1,2] · Elisa Colombo[2] · Carmine Antonio Donofrio[1] · Lina Raffaella Barzaghi[1] · Luigi Albano[1] · Claudio Righi[2] · Francesco Scomazzoni[2] · Franco Simionato[2] · Pietro Mortini[1] · Andrea Falini[2] · Nicoletta Anzalone[2]

Received: 27 December 2018 / Accepted: 12 February 2019 / Published online: 21 February 2019

Abstract

Background Volumetric assessment of aneurysmal bleeding has been evaluated in few studies and emerged as a promising outcome predictor. There is a lack of studies evaluating its impact in the poor-grade population.

Methods Retrospective review of 63 consecutive poor-grade aneurysmal subarachnoid hemorrhage (aSAH) patients, defined as grade IV and V according to the World Federation of Neurological Surgeons (WFNS) classifications. Global intracranial bleeding volume was calculated with its subarachnoid, intracerebral (ICH), and intraventricular (IVH) portions by means of analytical software. Univariate and multivariate analyses were performed in order to identify independent predictors of outcome. Good outcome was defined as modified Rankin Scale (mRS) 0–2 and mortality as mRS 6. The cutoff values of bleeding volumes were derived by receiver operating curve (ROC) analysis.

Results Mean follow-up was of 12.5 (± 1.5) months. Thirty (47.7%) patients achieved good outcome, whereas 19 (30.2) patients out of 63 died. Global intracranial bleeding resulted as an independent predictor of good outcome (cutoff 24 mL). Furthermore, ICH relative percentage of global volume (10% of total) and pure SAH (64% of total) emerged respectively as independent predictors of worsened and improved outcome. Global bleeding volume (cutoff 51 mL) along with global cerebral edema showed to independently predict mortality in the examined poor-grade aSAH population.

Conclusions Volumetric assessment of aneurysmal bleeding has the potential for identifying cutoff values that independently predict outcome. Further insights into the relative importance of different bleeding volumes may be implicated in better tailoring the management of this dismal aSAH population.

Keywords Cerebral aneurysm · Poor grade · Subarachnoid hemorrhage · Volumetric · Prognosis

This article is part of the Topical Collection on *Vascular Neurosurgery - Aneurysm*

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00701-019-03846-z) contains supplementary material, which is available to authorized users.

✉ Pietro Panni
panni.pietro@hsr.it

[1] Department of Neurosurgery and Gamma Knife Radiosurgery, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Via Olgettina 60, 20132 Milan, Italy

[2] Department of Neuroradiology, Interventional Neuroradiology Division, IRCCS San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Via Olgettina 60, 20132 Milan, Italy

Introduction

The amount of intracranial bleeding caused by cerebral aneurysmal rupture has long been considered as a marker of severity of the disease and an outcome predictor [9, 22]. Effort has been devoted to evaluate the subarachnoid component as a prognosticator of delayed cerebral ischemia (DCI) and outcome. The intracerebral, intraventricular, and subdural portions have been less extensively studied and with conflicting results [1, 3, 4, 11–13, 23, 25]. Several grading scales have been introduced, the most widely applied being the Fisher's one along with its modifications, but they have been criticized due to overlapping outcomes, cumbersome scoring process partially or poor inter-rater agreement, and difficult application in clinical routine practice [4, 9–11, 15–17]. Recently, the automatic or semi-automatic evaluation of intracranial bleeding has been the subject of a few studies which sought to determine its relationship primarily with DCI occurrence and, less frequently, with outcome [2, 10, 18, 21, 24]. Even considering software-based differences in the adopted segmentation protocol, the amount of intracranial bleeding present on the initial CT scan was found to be an accurate predictor of both DCI occurrence and outcome with different reported cutoff values. Nevertheless, the relative importance of bleeding distribution has not been consistently evaluated with studies combining cisternal and intraventricular bleeding and other specifically addressing cisternal distribution [10, 18]. Besides, none of the reported studies specifically examined the prognostic importance of intracranial bleeding volume location in the poor-grade aneurysmal subarachnoid hemorrhage population. The volumetric evaluation of intracranial bleeding in the poor-grade aSAH population may potentially identify outcome predictors of great interest, notably considering the reported historical trend of improved outcomes in modern series addressing this fragile aSAH subpopulation [8, 19, 27, 29].

Material and methods

Participant's selection and data collection

Among all aSAH patients admitted to our Department between January 2014 and January 2016 and prospectively included in our database, data concerning 63 consecutive patients with poor-grade aSAH were retrospectively reviewed. Treatment algorithm followed the previously reported guidelines [6]. Patients' outcome was assessed and scored according to the mRS scale by a neurosurgeon blinded to clinical data. Patients' data management was conducted in accordance with the Declaration of Helsinki as revised in Edinburgh in October 2000. Informed consent was obtained from the patient or nearest relative.

Study variables

Poor-grade aSAHs were recorded according to WFNS classification: the worst pre-treatment GCS score and clinical status were used for WFNS grading. For each patient, data concerning baseline and demographic features, clinical course, evolution, and clinical outcome were recorded. Loss of consciousness was defined as any sudden, abnormal alteration of responsiveness to sensory stimuli at symptom onset before patient intubation. It has been further classified as any loss of consciousness irrespectively of its duration or as persistent (patient unconscious at time of intubation), as previously reported [26]. Global cerebral edema has been defined on the admission plain CT scan as complete or near-complete effacement of the hemispheric sulci and basal cisterns, and bilateral and extensive disruption of the hemispheric gray–white matter junction at the level of the centrum semiovale [5, 14, 22]. Trained personnel of the neurosurgical department unaware of the results of the present study assessed the modified Rankin Scale (mRS) at last follow-up, during face-to-face interviews or via telephone conversations with the patient, their relatives, or their general practitioner. Good outcome was defined as mRS scores from 0 to 2 and mortality as mRS 6. The objective of the present analysis focused on baseline variables looking for admission clinico-radiological independent outcome predictors in the poor-grade aSAH population.

Volumetric evaluation of intracranial hemorrhagic burden

Whole-brain non-contrast-enhanced CT scans were performed within 24 h since ictus for all patients. CT axial slices were obtained for the selected patients on admission, then retrieved from the institution's digital archive system and stored as DICOM files. Software-based semi-automatic segmentation and volumetric quantification were carried out by two independent neurororadiologists, using OsiriX MD (Osirix MD 9.0®, Pixmeo, Swiss). Both authors were blinded on the clinical features of the patients, their outcomes, and each other's work. The determination of blood volume according to the Region of Interest (ROI) methodology was based on a tissue-specific threshold interval between 40 and 90 Hounsfield Unit, in order to avoid bone-related artifacts in anatomically challenging regions like the skull base, and the manual outline of areas of blood on each CT slice. The pixels with a similar density in the neighboring areas were automatically connected by the software. Hemorrhage volumes were computed for the intraparenchymal, the intraventricular, and the cisternal region, to be combined to have the total bleeding volume. All volumes were calculated in milliliters obtained by multiplying slice thickness by the hemorrhage area. Maximum time spent to segment all ROI volumes in an individual case did not exceed 15 min. Figure 1 shows examples of volumetric evaluation of intracranial aneurysmal bleeding.

Statistical analysis

Quantitative variables are expressed as means (± standard deviation) or medians, and categorical variables are expressed as numbers (percentage). Normality of distributions was assessed using histograms. Primary outcomes of the present study were good outcome (mRS 0–2) and mortality (mRS 6) at last follow-up. Bivariate comparisons between patient groups were made using the Chi-square test or Fisher exact test for categorical variables and Student's t test or Mann–Whitney U test for quantitative variables as appropriate. Inter-rater reliability was assessed by intra-class correlation

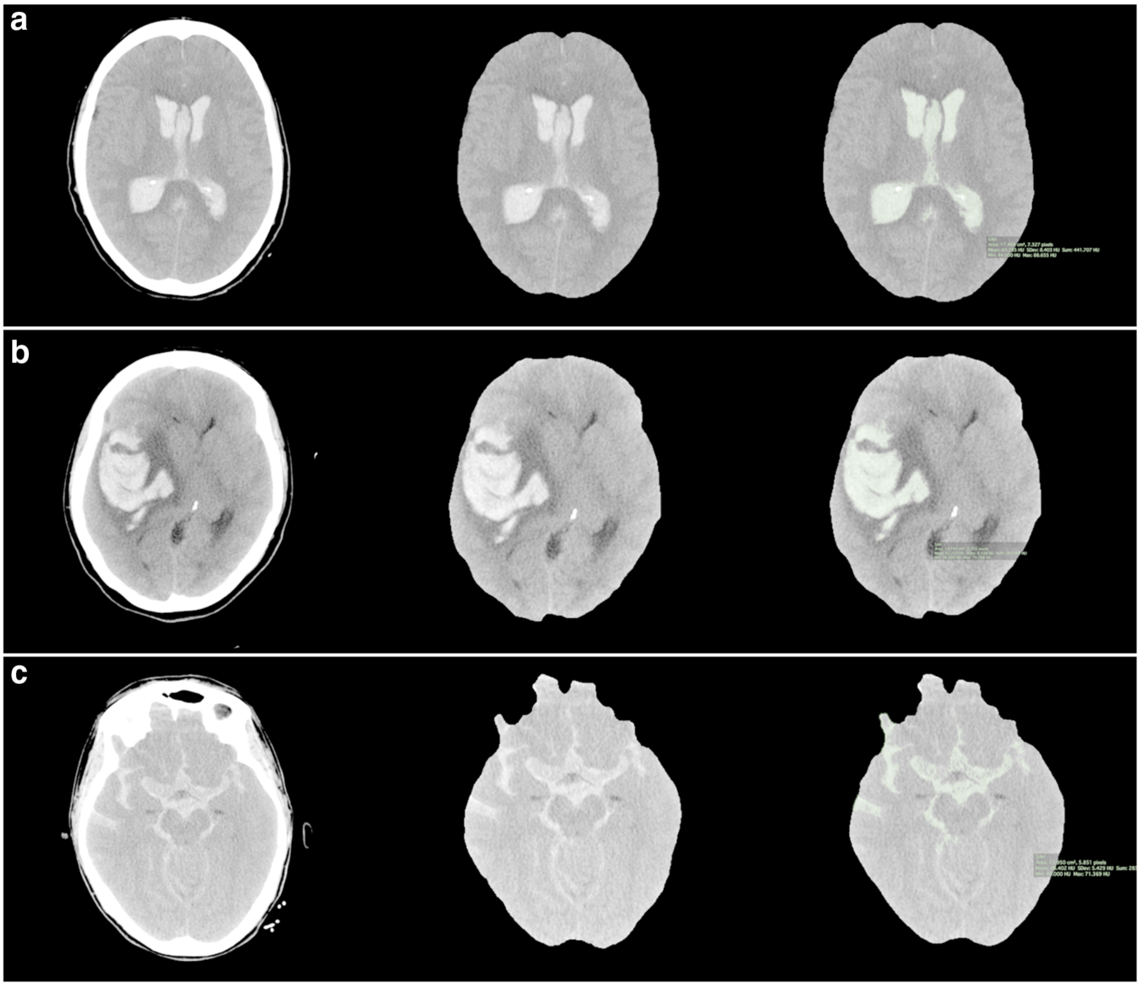

Fig. 1 Examples of CT-segmentation in a case of packed intraventricular hemorrhage (**a**) secondary to ACoA aneurysm rupture, predominant ICH after MCA aneurysm rupture (**b**), and predominant diffuse thick cisternal hemorrhage in a case of ruptured ICA blister aneurysm (**c**). From right to left: admission CT scan, bone removal, hemorrhage semi-automatic segmentation

coefficient (ICC) analysis using an absolute agreement definition reporting ICC value, 95% confidence interval, and related p value. Global volume of intracranial bleeding was considered as a scale continuous variable, while volumes of intracerebral, intraventricular, or cisternal bleeding were reported as both absolute volumetric values and relative percentages of the global. ROCs were obtained for each of the aforementioned bleeding volume variables in order to define prognostically associated cutoff values in the studied population corresponding to the Youden index of each corresponding curve. Factors significantly associated with outcome at last follow-up ($p < 0.05$) in univariable analysis were entered into binary logistic regression multivariable analysis model for dichotomized outcome (mRS 0–2 vs 3–6). Results of multivariable modeling were expressed as p for significance, odds ratio (OR), and 95% confidence interval (CI) after adjustment for covariates. The results of the binary logistic regression model were subjected to Hosmer-Lemeshow Test in order to evaluate the proportional odds assumption of the model. Positive results were considered for p values lower than 0.05. Outcome-predicted probabilities derived from binary logistic regression analysis were plotted into ROC in order to detect its sensitivity and specificity in the studied population and are graphically available as Supplementary Material Figure 3 and 4. Statistical analysis was performed with SPSS software (IBM Corporation, Released 2011, SPSS Statistics for Macintosh, Version 20.0, Armonk, NY).

Results

Sixty-three consecutive poor-grade aSAH patients were managed at our institution in the study period. Twenty-eight patients (44.4%) were classified as WFNS/HH grade IV and 35 (55.6%) as WFNS/HH grade V. Fisher grade 3 bleeding was detected in 11 (17.5%) and grade 4 in 52 (82.5%) cases, respectively. Forty-three (68.3%) patients underwent endovascular treatment, while the remaining 20 (31.7%) were subjected to surgical clipping. Global cerebral edema was detected in 9 cases (14.3%). DCI affected 15 patients (24.2%). At last follow-up (mean ± standard error, 12.5 ± 1.5 months; range, 1–45 months), 30 patients (47.6%) achieved a good outcome (mRS 0–2), while the remaining 33 (52.4%) were in poor conditions (mRS 3–6). The mortality rate was 30.2%. Median global volume of intracranial bleeding resulted to 32.7 mL (IQR 23.5–51.0 mL); median global volume of ICH, IVH, and cisternal bleeding were 19.12 mL (IQR 6.1–31.4 mL), 32.9 mL (IQR 11.6–41.0 mL), and 22.7 mL (IQR 9.9–32.3 mL), respectively. Inter-observer agreement resulted good (ICC 0.906, 95% C.I. 0.77–0.96, $p < 0.001$). Table 1 shows the results of univariable analysis of admission clinico-radiological factors associated with long-term outcome. ROC-derived cutoff value of intracranial global bleeding volume associated with outcome resulted 24 mL ($p < 0.001$). Cutoff values of ICH, IVH, and pure SAH bleeding expressed as relative percentages of the global volume with p values for association with outcome were 10% ($p < 0.001$), 11% ($p = 0.020$), and 64% ($p < 0.001$) respectively. ROC curves for global volume and relative percentage of cisternal bleeding are reported as Supplemental Figure 1 in the Supplementary Material. Table 1 shows also the results of binary logistic regression multivariable analysis after adjusting for covariates of independent outcome predictors. Higher volumes of global bleeding (adjusted OR 0.198; 95% CI 0.045–0.863, $p = 0.031$) and female sex (adjusted OR 0.043; 95% CI 0.005–0.349, $p = 0.005$) were independently associated with long-term poor outcome, while higher relative percentages of global volume represented by cisternal bleeding resulted independently associated with good outcome (adjusted OR 7.85; 95% CI 1.5–41.3, $p = 0.015$). Hosmer-Lemeshow test for the aforementioned model is 1.00. Table 2 shows the results of univariable analysis of admission clinico-radiological factors associated with mortality. Considering reported intracranial bleeding sizes, only global volume resulted statistically associated with increased mortality ($p = 0.002$). ROC-derived cutoff values of intracranial global bleeding volume associated with increased mortality rate resulted 51 mL ($p = 0.003$). Intracerebral, intraventricular, and cisternal bleeding expressed as relative percentages of the global volume with p values for association with increased mortality rate were 45% ($p = 0.184$), 62% ($p = 0.114$), and 25% ($p = 0.030$), respectively. Higher volumes of intracranial bleeding (cutoff 51 mL, OR 8.19, 95% CI 2.01–33.25, $p = 0.003$) and the presence on admission CT scan of global cerebral edema (OR 7.41, 95% CI 1.39–39.52, $p = 0.019$) resulted independent predictors of mortality (Table 2). The Hosmer-Lemeshow test for the aforementioned model is 0.819. Scatter plot showing predicted probabilities of mRS 0–2 according to global volume and relative percentage of cisternal bleeding (panel a) and mortality according to admission global volume and global cerebral edema (panel b) is reported as Fig. 1.

Discussion

There is currently a lack of formal guidelines on the management of poor-grade aSAH, forcing the need to define quantifiable and reproducible factors impacting on outcome. Most

Table 1 Univariable analysis and multivariable binary logistic regression analysis of baseline factors associated with outcome at last follow-up

	Univariable analysis			Multivariable analysis	
Variables	mRS 0–2, no. (%)	mRS 3–6, no. (%)	*p* value	OR (95% CI)	*p* value
Age	55.4 ± 2.06	60.2 ± 1.8	0.080	N.I.	–
Sex (M/F)	14/15 (48.3/51.7)	8/26 (23.5/76.5)	0.037	0.043 (0.005–0.349)	0.005
Fisher (3/4)	7/22 (24.1/75.9)	4/30 (11.8/88.2)	0.170	N.I.	–
WFNS (4/5)	20/9 (69/31)	8/26 (23.5/76.5)	< 0.001	NS	–
LOC global	15/14 (51.7/48.3)	25/6 (80.6/19.4)	0.017	NS	–
LOC persistent	7/22 (24.1/75.9)	17/14 (54.8/45.2)	0.015	NS	–
Global cerebral edema (Y/N)	2/27 (6.9/93.1)	7/27 (20.6/79.4)	0.160	N.I.	–
Acute DSA spasm (Y/N)	2/27 (6.9/93.1)	6/28 (17.6/82.4)	0.270	N.I.	–
Acute hydrocephalus (Y/N)	25/4 (86.2/13.8)	29/5 (85.3/14.7)	1.000	N.I.	–
Global volume (cutoff 24 mL)	26.2 (18.04–38.6)	34.5 (28.9–55.4)	< 0.001	0.198 (0.045–0.863)	0.031
Cisternal bleeding 64%*	26/2 (92.9/7.1)	16/17 (48.5/51.5)	< 0.001	7.85 (1.5–41.3)	0.015
ICH bleeding 10%*	2/27 (6.9/93.1)	17/17 (50/50)	< 0.001	N.S.	N.S.
IVH bleeding 11%*	3/26 (10.3/89.7)	12/22 (35.3/64.7)	0.022	NS	–

DSA digital subtraction angiography, *ICH* intracerebral hemorrhage, *IVH* intraventricular hemorrhage, *LOC* loss of consciousness, *mRS* modified Rankin Scale, *NS* not significant, *NI* not included in the multivariable analysis, *WFNS* world federation of neurosurgical society

*Values expressed as percentages of global volume

Table 2 Univariable analysis and multivariable binary logistic regression analysis of baseline factors associated with mortality

Variables	Univariable analysis			Multivariable analysis	
	mRS 0–5, no. (%)	mRS 6, no. (%)	*p* value	OR (95% CI)	*p* value
Age	56.1 ± 11	61.6 ± 9.5	0.050	NS	–
Sex (M/F)	26/18 (59.1/40.9)	15/4 (78.9/21.1)	0.108	N.I.	–
Fisher (4/3)	34/10 (77.3/22.7)	18/1 (94.7/5.3)	0.150	N.I.	–
WFNS (5/4)	21/23 (47.7/52.3)	14/5 (73.7/26.3)	0.051	NS	–
LOC global	26/18 (59.1/40.9)	14/2 (87.5/12.5)	0.035	NS	–
LOC persistent	18/26 (40.9/59.1)	6/10 (37.5/62.5)	0.527	N.I.	–
Global cerebral edema (Y/N)	3/41 (6.8/93.2)	6/13 (31.6/68.4)	0.017	7.41 (1.39–39.52)	0.019
Acute DSA spasm (Y/N)	4/40 (9.1/90.9)	4/15 (21.1/78.9)	0.229	N.I.	–
Acute hydrocephalus (Y/N)	37/7 (84.1/15.9)	17/2 (89.5/10.5)	0.711	N.I.	–
Global volume (51 mL)	5/38 (11.6/88.4)	9/9 (50/50)	0.002	8.19 (2.01–33.25)	0.003
Cisternal bleeding 25%*	38/5 (88.4/11.6)	11/7 (61.1/38.9)	0.030	NS	–
ICH bleeding 45%*	3/41 (6.8/93.2)	4/14 (21.1/78.9)	0.184	N.I.	–
IVH bleeding 62%*	4/40 (9.1/90.9)	5/14 (26.3/73.7)	0.114	NS	–

DSA digital subtraction angiography, *ICH* intracerebral hemorrhage, *IVH* intraventricular hemorrhage, *LOC* loss of consciousness, *NS* not significant, *NI* not included in the multivariable analysis, *WFNS* world federation of neurological surgeons

*Values expressed as percentages of global volume

importantly, these factors should be modifiable and an easy target for patients' management and outcome improval. Global bleeding burden resulted as an independent predictor of both clinical outcome and mortality in poor-grade aSAH. Worth noting, it emerged independently from admission-related (e.g., WFNS grade) or treatment (e.g., endovascular treatment or surgical clipping) variables. Significantly, different bleeding distributions do play a key role as outcome predictors. A higher proportion of cisternal bleeding, which implies a lower proportion of ICH or IVH bleeding, showed to be independently associated with improved outcome in this fragile subset of aSAH patients. Furthermore, global bleeding burden along with global cerebral edema, which is a clear representation of early brain injury on the admission CT scan, emerged as independent mortality predictors. Interestingly, even though reported average global intracranial bleeding

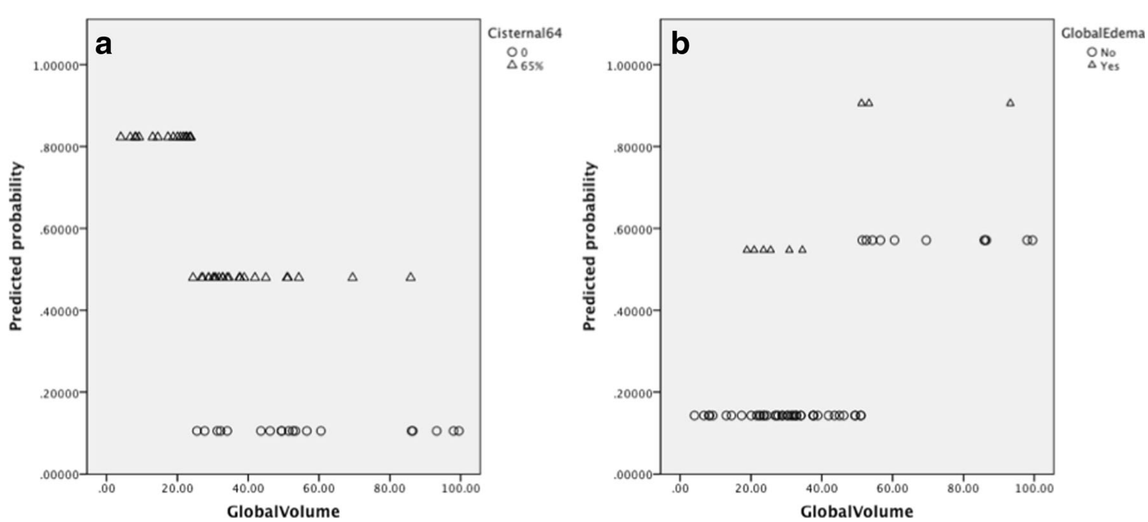

Fig. 2 **a** Scatter plot of multivariable binary logistic regression analysis derived predicted probabilities of achieving a good outcome (mRS 0–2) according to global volume of intracranial bleeding (*X*-axis) and derived cutoff values of relative percentages of cisternal bleeding 64%. As shown by the interpolation quadratic curve, for a given intracranial bleeding volume, a relatively higher proportion of subarachnoidal bleeding (≥ 65%, triangles) is associated with a significantly higher chance of good outcome. **b** Scatter plot of derived predicted probabilities of mortality according to global volume of intracranial bleeding and global cerebral edema. As shown by the interpolation quadratic curves, for a given intracranial bleeding volume, the presence of global cerebral edema on the admission CT scan is associated with higher probabilities of mortality

volumes had higher values in our study as compared with the ones reported by Lagares et al. [21] and Ko et al. [18], likely reflecting the increased bleeding volume characterizing the poor-grade aSAH context as compared with WFNS grades 1–3 [22], we found nonetheless a cutoff of intracranial bleeding volume of 24 mL as an independent outcome predictor in the studied population, which is consistent with the 20-mL cutoff reported by Lagares et al. in their analysis [21]. To the best of our knowledge, this is the first study evaluating the volumetric importance of different bleeding compartments in the poor-grade aSAH population: for a given volume, the absence of IVH or ICH bleeding (i.e., higher relative percentages of cisternal bleeding distribution) seemed to be independently associated with improved outcome (Fig. 2, panel A). Of note, the whole reported population has been scanned within the first 24 h since bleeding. This is in contrast with what previously described in volumetric studies that considered the whole clinical grading distribution, further highlighting the peculiarity of poor-grade aSAH [10, 18, 21, 24]. Even though the relative impact of ICH and/or IVH bleeding in aSAH context is still debated in literature, especially in the context of the poor-grade population, it is reasonable to consider that for a given global volume (24 mL), an intra-axial damage (e.g., ICH) could more severely affect clinical outcome than a predominant cisternal one [1, 3, 4, 11–13, 23, 25]. Interestingly, according to the results of our study, we found that the importance of different bleeding compartments matters up to a certain threshold of global bleeding, above which it does not add any prognostic information. Global bleeding volume (cutoff 51 mL) and global cerebral edema on the admission CT scan independently predicted mortality in the studied poor-grade population (Table 2, Fig. 2b), the best one to evaluate an impact on mortality among aSAH patients. Our results are consistent with previously reported data, being initial hemorrhagic ictus, global cerebral edema, and loss of consciousness key features of the so-called early brain injury phase in aSAH [5]. Global cerebral edema, when dichotomizing the outcome as mRS 0–2 versus mRS 3–6, did not emerge as an independent outcome predictor, possibly because of the small number of patients included. Nevertheless, global cerebral edema was strongly associated with high mortality (OR 7.41, 95% CI 1.39–39.52). Actually, even though global cerebral edema was associated with loss of consciousness on univariate analysis ($p = 0.043$), neither bleeding volumes nor any of their derived cutoff values resulted statistically associated with global cerebral edema ($p > 0.05$). Even though a significant proportion of our patients (57.1%) presented with IVH, in line with previous data that suggest a higher percentage of IVH and severity in the poor-grade population, it did not result as an independent outcome predictor in the studied poor-grade population on multivariate analysis [7]. Besides glial response and ischemia, emerging evidence relates acute intracranial bleeding in SAH to both focal and widespread axonal injury, highlighting similarities with traumatic brain injury [20, 28]. The role of the ventricular space as a potential buffer protecting against barotrauma has been suggested [28]. Female sex emerged as an independent predictor of worsened outcome according to our multivariate analysis. Notwithstanding previous reports [30], this association is explained by the large predominance of female patients (65.1%) in our population and the fact that women more often were affected by ruptured middle cerebral artery (MCA) aneurysms with large associated ICH, plus they were more frequently grade V on admission. The role of potential collinearity cannot be conclusively ruled out even by applying multivariate analysis. Side of ICH did not emerge as significantly impacting outcome or mortality in the studied population. This is consistent with the aforementioned thesis implying that global volume plays a more significant role than other bleeding-related variables even though the limited number of included patients with ICH could theoretically represent a source of bias.

This study is limited by its single-center and retrospective nature.

All considered, the aforementioned results can have a direct implication in the operative management of this fragile subset of patients. Aggressive CSF-diversion, intrathecal lytic therapy, surgical clot evacuation can be tailored on the basis of volumetrically derived prognostic cutoff values of bleeding volumes (ICH, IVH, or purely cisternal). Future studies are eagerly awaited in order to further establish volumetrically derived cutoff values of bleeding compartments with prognostic significance.

Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study or nearest relative.

References

1. Adams HP Jr, Kassell NF, Torner JC, Haley EC Jr (1987) Predicting cerebral ischemia after aneurysmal subarachnoid hemorrhage: influences of clinical condition, CT results, and antifibrinolytic therapy. A report of the cooperative aneurysm study. Neurology 37: 1586–1591
2. Boers AM, Zijlstra IA, Gathier CS, van den Berg R, Slump CH, Marquering HA, Majoie CB (2014) Automatic quantification of subarachnoid hemorrhage on noncontrast CT. AJNR Am J Neuroradiol 35:2279–2286
3. Bruder M, Schuss P, Berkefeld J, Wagner M, Vatter H, Seifert V, Guresir E (2014) Subarachnoid hemorrhage and intracerebral hematoma caused by aneurysms of the anterior circulation: influence of hematoma localization on outcome. Neurosurg Rev 37:653–659
4. Claassen J, Bernardini GL, Kreiter K, Bates J, Du YE, Copeland D, Connolly ES, Mayer SA (2001) Effect of cisternal and ventricular blood on risk of delayed cerebral ischemia after subarachnoid hemorrhage: the Fisher scale revisited. Stroke 32:2012–2020
5. Claassen J, Carhuapoma JR, Kreiter KT, Du EY, Connolly ES, Mayer SA (2002) Global cerebral edema after subarachnoid hemorrhage: frequency, predictors, and impact on outcome. Stroke 33:1225–1232
6. Connolly ES Jr, Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, Hoh BL, Kirkness CJ, Naidech AM, Ogilvy CS, Patel AB, Thompson BG, Vespa P, American Heart Association Stroke C, Council on Cardiovascular R, Intervention, Council on Cardiovascular N, Council on Cardiovascular S, Anesthesia, Council on Clinical C (2012) Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 43:1711–1737
7. Darkwah Oppong M, Gembruch O, Herten A, Frantsev R, Chihi M, Dammann P, El Hindy N, Forsting M, Sure U, Jabbarli R (2018) Intraventricular hemorrhage caused by subarachnoid hemorrhage: does the severity matter? World Neurosurg 111:e693–e702
8. de Oliveira Manoel AL, Mansur A, Silva GS, Germans MR, Jaja BN, Kouzmina E, Marotta TR, Abrahamson S, Schweizer TA, Spears J, Macdonald RL (2016) Functional outcome after poor-grade subarachnoid hemorrhage: a single-center study and systematic literature review. Neurocrit Care 25:338–350
9. Fisher CM, Kistler JP, Davis JM (1980) Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery 6:1–9
10. Friedman JA, Goerss SJ, Meyer FB, Piepgras DG, Pichelmann MA, McIver JI, Toussaint LG 3rd, McClelland RL, Nichols DA, Atkinson JL, Wijdicks EF (2002) Volumetric quantification of Fisher grade 3 aneurysmal subarachnoid hemorrhage: a novel method to predict symptomatic vasospasm on admission computerized tomography scans. J Neurosurg 97:401–407
11. Frontera JA, Claassen J, Schmidt JM, Wartenberg KE, Temes R, Connolly ES Jr, MacDonald RL, Mayer SA (2006) Prediction of symptomatic vasospasm after subarachnoid hemorrhage: the modified fisher scale. Neurosurgery 59:21–27 discussion 21–27
12. Guresir E, Beck J, Vatter H, Setzer M, Gerlach R, Seifert V, Raabe A (2008) Subarachnoid hemorrhage and intracerebral hematoma: incidence, prognostic factors, and outcome. Neurosurgery 63: 1088–1093 discussion 1093–1084
13. Heiskanen O, Poranen A, Kuurne T, Valtonen S, Kaste M (1988) Acute surgery for intracerebral haematomas caused by rupture of an intracranial arterial aneurysm. A prospective randomized study. Acta Neurochir 90:81–83
14. Helbok R, Ko SB, Schmidt JM, Kurtz P, Fernandez L, Choi HA, Connolly ES, Lee K, Badjatia N, Mayer SA, Claassen J (2011) Global cerebral edema and brain metabolism after subarachnoid hemorrhage. Stroke 42:1534–1539
15. Hijdra A, Brouwers PJ, Vermeulen M, van Gijn J (1990) Grading the amount of blood on computed tomograms after subarachnoid hemorrhage. Stroke 21:1156–1161
16. Ibrahim GM, Weidauer S, Macdonald RL (2011) Interobserver variability in the interpretation of computed tomography following aneurysmal subarachnoid hemorrhage. J Neurosurg 115:1191–1196
17. Klimo P Jr, Schmidt RH (2006) Computed tomography grading schemes used to predict cerebral vasospasm after aneurysmal subarachnoid hemorrhage: a historical review. Neurosurg Focus 21:E5
18. Ko SB, Choi HA, Carpenter AM, Helbok R, Schmidt JM, Badjatia N, Claassen J, Connolly ES, Mayer SA, Lee K (2011) Quantitative analysis of hemorrhage volume for predicting delayed cerebral ischemia after subarachnoid hemorrhage. Stroke 42:669–674
19. Konczalla J, Seifert V, Beck J, Guresir E, Vatter H, Raabe A, Marquardt G (2018) Outcome after Hunt and Hess grade V subarachnoid hemorrhage: a comparison of pre-coiling era (1980–1995) versus post-ISAT era (2005–2014). J Neurosurg 128:100–110
20. Kummer TT, Magnoni S, MacDonald CL, Dikranian K, Milner E, Sorrell J, Conte V, Benetatos JJ, Zipfel GJ, Brody DL (2015) Experimental subarachnoid haemorrhage results in multifocal axonal injury. Brain 138:2608–2618
21. Lagares A, Jimenez-Roldan L, Gomez PA, Munarriz PM, Castano-Leon AM, Cepeda S, Alen JF (2015) Prognostic value of the amount of bleeding after aneurysmal subarachnoid hemorrhage: a quantitative volumetric study. Neurosurgery 77:898–907 discussion 907
22. Rosen DS, Amidei C, Tolentino J, Reilly C, Macdonald RL (2007) Subarachnoid clot volume correlates with age, neurological grade, and blood pressure. Neurosurgery 60:259–266 discussion 266–257
23. Rosengart AJ, Schultheiss KE, Tolentino J, Macdonald RL (2007) Prognostic factors for outcome in patients with aneurysmal subarachnoid hemorrhage. Stroke 38:2315–2321
24. Sato T, Sasaki T, Sakuma J, Watanabe T, Ichikawa M, Ito E, Matsumoto Y, Ando H, Saito K, Kikori K, Yusa T, Suzuki K, Watanabe Y, Taira S, Sato M (2011) Quantification of subarachnoid hemorrhage by three-dimensional computed tomography: correlation between hematoma volume and symptomatic vasospasm. Neurol Med Chir (Tokyo) 51:187–194
25. Schuss P, Hadjiathanasiou A, Borger V, Wispel C, Vatter H, Guresir E (2016) Poor-grade aneurysmal subarachnoid hemorrhage: factors influencing functional outcome—a single-center series. World Neurosurg 85:125–129
26. Suwatcharangkoon S, Meyers E, Falo C, Schmidt JM, Agarwal S, Claassen J, Mayer SA (2016) Loss of consciousness at onset of subarachnoid hemorrhage as an important marker of early brain injury. JAMA Neurol 73:28–35
27. Wostrack M, Sandow N, Vajkoczy P, Schatlo B, Bijlenga P, Schaller K, Kehl V, Harmening K, Ringel F, Ryang YM, Friedrich B, Stoffel M, Meyer B (2013) Subarachnoid haemorrhage WFNS grade V: is maximal treatment worthwhile? Acta Neurochir 155:579–586
28. Wu Y, Peng J, Pang J, Sun X, Jiang Y (2017) Potential mechanisms of white matter injury in the acute phase of experimental subarachnoid haemorrhage. Brain 140:e36
29. Zhao B, Rabinstein A, Murad MH, Lanzino G, Panni P, Brinjikji W (2017) Surgical and endovascular treatment of poor-grade aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. J Neurosurg Sci 61:403–415
30. Zhao B, Yang H, Zheng K, Li Z, Xiong Y, Tan X, Zhong M, Group AS (2017) Preoperative and postoperative predictors of long-term outcome after endovascular treatment of poor-grade aneurysmal subarachnoid hemorrhage. J Neurosurg 126:1764–1771