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Predictors of good outcome in good grade subarachnoid hemorrhage

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THÈSE D'EXERCICE / UNIVERSITÉ DE RENNES 1

Thèse en vue du
DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Présentée par

Amandine LE GALL

Née le 20/04/1987

Intitulé de la thèse :

Facteurs prédictifs de bon pronostic après hémorragie sous-arachnoïdienne non grave.

Predictors of good outcome in good grade subarachnoid hemorrhage

**Thèse soutenue à RENNES
le 3 octobre 2016**

devant le jury composé de :

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Liste des abréviations

GOS: Glasgow outcome scale

SAH: subarachnoid hemorrhage

ICU: Intensive care unit

GCS: Glasgow Coma Scale

CSF: cerebral spinal fluid

BMI: body mass index

WFNS: World Federation of Neurologic Surgeons

DCI: delayed cerebral ischemia

Résumé:

Introduction : La prise en charge des hémorragies sous-arachnoïdiennes (HSA) a beaucoup évolué ces dernières années avec une mortalité moindre mais une morbidité qui reste élevée. Dans la littérature, on retrouve essentiellement des données sur les facteurs prédictifs de pronostic péjoratif dans des études où sont incluses des HSA tout grade de gravité confondu. Il existe peu d'information sur les HSA non graves. Le but de cette étude était de déterminer les facteurs prédictifs de bon pronostic dans cette sous-population de patient, en vue d'adapter leur prise en charge.

Méthode : Cette analyse rétrospective concernait les patients admis aux soins intensifs de neurochirurgie au CHU de Rennes en 2012 pour HSA avec un score WFNS (World Federation of Neurologic Surgeons) compris entre 1 et 3. L'étude portait sur les facteurs prédictifs de complications habituelles des HSA : vasospasme, resaignement, et hydrocéphalie ; et sur le bon pronostic fonctionnel à un an. Il était défini par un score de la Glasgow Outcome Scale ≥ 5 . L'analyse statistique comportait une analyse univariée puis une régression logistique multivariée avec un seuil de significativité à 0.05.

Résultats: 92 patients ont été inclus. Parmi eux, 34 ont présenté une complication: 30 vasospasmes sur le doppler transcrânien (32.6%), 16 vasospasmes symptomatiques (17.4%), 5 resaignements (5.4%), 15 hydrocéphalies (16.3%), 9 (9.7%) convulsions et 7 (7.6%) sepsis. Le vasospasme était significativement associé aux scores WFNS ($p < 0.0001$) et Fisher ($p = 0.0296$) à l'admission, au resaignement ($p = 0.0374$), à la température maximale de la première semaine ($p = 0.0031$). L'hydrocéphalie était associée à un score WFNS élevé à l'admission. Un bon pronostic était constaté pour 57 (72%) patients. En analyse multivariée, l'absence de vasospasme sur le doppler transcrânien (OR = 6.38 [1.57; 25.84], $p = 0.0094$) et l'absence de crise convulsive (OR = 9.99 [1.19 ; 83.63], $p = 0.0337$) étaient associées à un bon pronostic fonctionnel à un an (GOS ≥ 5).

Conclusion: Les patients souffrant d'HSA non graves avaient un bon pronostic fonctionnel dans notre étude. L'existence d'un vasospasme sur le doppler transcrânien et la crise convulsive étaient significativement associées à un mauvais pronostic fonctionnel à un an. La question d'un monitoring et d'une réanimation agressive en cas de vasospasme au doppler transcrânien mais asymptomatique par ailleurs mérite ainsi d'être posée.

Abstract:

Background: The management of Subarachnoid hemorrhage (SAH) has improved in recent years with lower mortality but morbidity remains high. Several studies have focused on predictors of poor outcome in all grades SAH. Information about good grade SAH is scarce. The aim of this study was to determine predictors of good outcome after good grade SAH to potentially modify their management.

Methods: We conducted a retrospective analysis of all patients admitted in neurosurgical ICU in 2012 for SAH with WFNS (World Federation of Neurologic Surgeons) score between 1 and 3. We focused on predictor of SAH complications: vasospasm, rebleeding and hydrocephalus, and 1-year functional outcome. A good outcome was defined by Glasgow Outcome Scale ≥ 5 at 1-year. Univariate analysis of possible risk factors was performed with subsequent multivariate logistic regression analysis. A *P* value < 0.05 was considered significant.

Results: Within the 92 patients included, 34 presented a complication during hospitalization: 30 (32.6 %) transcranial Doppler vasospasm, 16 (17.4%) symptomatic vasospasm, 5 (5.4%) rebleeding, 15 (16.3%) hydrocephalus, 9 (9.7%) seizures and 7 (7.6%) sepsis. Vasospasm was correlated to WFNS ($p < 0.0001$) and Fisher grade ($p = 0.0296$) at admission, rebleeding ($p = 0.0374$), higher temperature during the first week ($p = 0.0031$). Hydrocephalus was associated with higher WFNS grade at admission. An excellent outcome was found in 57 (72%) patients. In multivariate analyses, no transcranial Doppler vasospasm (OR = 6.38 [1.57; 25.84], $p = 0.0094$) and no seizure (OR = 9.99 [1.19; 83.63], $p = 0.0337$) were associated with a good functional outcome at 1 year (GOS ≥ 5).

Conclusion: In our study, patients with good grade SAH had a good functional outcome. Only vasospasm on transcranial Doppler and seizure were associated with poor outcome. The question of intensive monitoring and resuscitation in patients presenting a vasospasm on transcranial Doppler without any clinical symptoms still needs to be assessed.

Introduction

Non-traumatic subarachnoid hemorrhage (SAH) is associated with a significant morbidity and mortality worldwide [1]. The incidence varies from regions to regions from 2 to 16 cases for 100 000 inhabitants, but it is probably underestimated [2]. It is affecting young people with a mean age of diagnosis of 55 years. The mortality in the acute phase is about 50 % among which 15 % before hospital admission [3]. A third of the survivors present a poor outcome with dependence in their everyday life activities [4]. The management of aneurysmal SAH is highly standardized in the acute phase for diagnosis, treatment of aneurysm and common complications: vasospasm, rebleeding, hydrocephalus [5]. However, these treatments do not protect survivors from intellectual and/or functional disabilities. Forty-percent of them cannot go back to their professional activity [6]. Various predictors of poor outcome after a SAH have been identified: age, world federation of neurologic surgeons (WFNS) score on admission, size of the aneurysm and its location in the posterior cerebral circulation, intra-ventricular hemorrhage, intra-cerebral hematoma, hypertension at admission, history of hypertension, symptomatic vasospasm, cerebral ischemia, over 38 ° C temperature on the 8th day [7; 8; 9]. Predictive factors for excellent outcome have also been described : good clinical condition after resuscitation, absence of intra-cerebral hemorrhage on presentation, no evidence of infarction on brain imaging, and absence of blood transfusion during hospitalization. However, these studies included different grades of gravity. Less is known about the outcome and the predictive factors of patients with a good-grade SAH at admission [10]. Indeed, these patients with a Glasgow Coma Scale (GCS) higher than 14 are usually hospitalized for 10 to 15 days in neurosurgical ICU [11]. We questioned this long hospitalization and hypothesized that the determination of predictive factors of outcome in good-grade SAH would allow a shorter length stay. Therefore, the aim of this single center retrospective study was to determine predictors of excellent outcome in good-grade SAH.

Materials and Methods:

Patients

From January, 1st 2012 to December, 31st 2012, all patients hospitalized in the Neurosurgical Intensive Care Unit Hospital of Rennes Teaching Hospital after the diagnosis of non-traumatic SAH were retrospectively included. According to our institution policy, patients with SAH hospitalized in this unit are older than 15 years with a good-grade SAH defined by a WFNS grade 1, 2 or 3 and a Glasgow Coma Scale (GCS) higher than 14. The files of these patients were retrospectively studied. The local ethics committee waived informed consent as it was a non-interventional study (number 14.47).

The diagnosis of SAH was brought through cranial CT scan or lumbar puncture. The anatomical study of aneurysms was mostly made by angioCT or digital subtraction angiography in difficult cases.

Data collection

We collected the following clinical and biological data at admission: sex, age, body mass index (BMI), WFNS grade, diabetes, dyslipidemia, risk factors for cerebral aneurysm (smoking, alcoholism, hypertension history), hemoglobin, the transcranial doppler (TD) measures and the conclusions of the initial CT scan and/or angiography. The therapeutic strategy for aneurysmal exclusion decided after multidisciplinary discussion between neuroradiologists and neurosurgeons was also noted.

The following complications during hospitalization were recorded: vasospasm defined by middle cerebral artery flow velocities ≥ 120 cm/sec on TD, rebleeding defined by modification of the initial CT scan, hydrocephalus diagnosed on CT scan, seizure defined by partial crisis or generalized tonic clonic seizure objectified by the medical team, and sepsis defined by the association of fever (higher than 38.3°C) and a bacterial identification.

According to our institution policy, hydrocephalus was treated by external ventricular drainage, vasospasm with oral nimodipine, maintenance of euvolemia, induction of hypertension and endovascular therapy with vasodilators and angioplasty balloons. Finally, intensive care unit (ICU) length of stay, total hospital stay and time to discharge for rehabilitation were noted

Main outcome

The main outcome was the functional outcome at one year assessed with the Glasgow outcome scale (GOS) and the recovery of previous employment. Patients admitted in neurosurgery intensive care for good grade SAH had little or no disability at admission. Aim of treatment is to maintain physical and intellectual condition of patient. So we defined an excellent outcome as patients with $GOS \geq 5$. Assessment of this score is part of the routine care of neurosurgeons and/or neuroradiologists during the systematic consultation one year after the initial treatment.

Statistical analysis

Patient characteristics were described using mean \pm standard deviation and quartile for continuous variables and as frequency for categorical variables. Univariate analysis was performed using the parametric Student test or nonparametric Wilcoxon for quantitative variables. For qualitative variables, the groups were compared with parametric tests of χ^2 or nonparametric test of Fisher. Analysis was carried out by the software SAS version 9.4. Variables associated with P values ≤ 0.2 were used in the final multivariate model. A multivariable logistic regression model was used to test the predictive power of these the risk factors on symptomatic vasospasm and good outcome. If a variable was missing, it was not included in the analysis. P values < 0.05 were considered statistically significant.

Results

In 2012, 92 patients were hospitalized for SAH in neurosurgical ICU in our institution.

Patient's characteristics are shown Table 1. As only non-severe patient are hospitalized in this unit, the majority of SAH were classified WFNS I and II and all patients had a GCS superior or equal to 14.

Neurological complications

Among the 92 patients, 34 presented a complication during hospitalization: 30 (32.6 %) TD vasospasm, 16 (17.4%) symptomatic vasospasm, 5 (5.4%) rebleeding, 15 (16.3%) hydrocephalus, 9 (10%) seizure and 7 (8%) sepsis.

Vasospasm

Aneurysm located on the anterior and middle cerebral arteries, WFNS and Fisher grade at admission were significantly associated with the risk of TD vasospasm (Table 2). When we compared with patients with no TD vasospasm, patients had a higher maximum temperature ($38.45 \pm 0.91^{\circ}\text{C}$ versus $37.94 \pm 0.66^{\circ}\text{C}$, $p = 0.0031$). Rebleeding was significantly associated with diagnosis of TD vasospasm (4 cases versus 1, $p = 0.0374$). The length of stay in ICU (10.3 days versus 8.1, $p=0.1236$) and in the hospital were not prolonged (19.6 days versus 16.3 days, $p = 0.1597$) in these patients. The diagnosis of TD vasospasm was not associated with a significant difference in terms of recovery of professional activity at one year.

Patients with symptomatic vasospasm ($n=16$) had a higher maximum temperature during the first week ($38.78 \pm 0.69^{\circ}\text{C}$ versus $37.97 \pm 0.73^{\circ}\text{C}$, $p = 0.0003$), and more frequent rebleeding (4 patients versus 1, $p = 0.002$) than patients without symptomatic vasospasm. There was no significant association between symptomatic vasospasm and hydrocephalus. In case of symptomatic vasospasm, the length of stay in the hospital was longer (23.6 days vs 16 days, $p = 0.0008$) and patients were more likely to need rehabilitation after hospitalization ($p =$

0.03). The diagnosis of symptomatic vasospasm was associated with a poorer recovery of professional activity at one year ($p = 0.0465$) (Table 2).

Rebleeding

Only 5 patients presented rebleeding during hospitalization. The event was too rare to reach statistical significance. Aneurysms were located on the anterior communicating artery, the basilar artery and the carotid artery with WFNS score 1 or 2 and Fisher 4. The length of stay in the ICU (13.8 ± 7.3 vs 9 ± 6.1 days) and the total length of stay (20 ± 11.3 vs 17.3 ± 10.1 days) were prolonged when compare with patients without rebleeding but no statistically significant. At one year, none of these 5 patients was back to his/her previous employment.

Hydrocephalus

The existence of hydrocephalus was statistically correlated with a higher WFNS score at admission ($p=0.0067$). Fisher score at admission were not significantly different in patient with or without hydrocephalus. Clinically, they had a higher maximal temperature during the first week ($38.7 \pm 0.9^{\circ}\text{C}$ versus $38 \pm 0.7^{\circ}\text{C}$, $p=0.0032$) compared with patients without hydrocephalus. The length stay in the ICU (13.8 ± 8.6 days vs 7.8 ± 5.4 days, $p = 0.01$) and total duration of hospitalization (22.5 ± 9 vs 16.6 ± 10.1 , $p = 0.009$) were significantly prolonged.

Main Outcome

In our cohort, the majority of patients had a good outcome. 57(72%) patients had a GOS ≥ 5 at 1-year. The evaluation of GOS was not possible for 13 patients. They did not come for the follow-up visit 1 year after the SAH.

Localization of aneurysm had no impact on outcome, even for posterior circulation. Length of stay in the ICU was shorter when GOS ≥ 5 (7.4 ± 4.8 versus 13.4 ± 7.1 days, $p=0.0003$).

The hospital stay was also shorter for the group of patients with a good outcome (15.5 ± 6 days versus 23.8 ± 15.9 , $p=0.0017$). In the group of patients with an excellent outcome, 28 out of 50 patients (56%) were able to go back to their previous activity compare with 1(2%) patient in the group of patients with $GOS < 5$ (Table 3).

Multivariable analysis

In multivariable analysis, the variables included in the model were sex, age, history hypertension , active smoking, localization aneurysm on the middle cerebral, WFNS, Fisher, TD vasospasm, symptomatic vasospasm, seizures, rebleeding, sepsis, treatment by vasoactives drugs, rehabilitation, maximal systolic blood pressure, minimal saturation during and maximal temperature during the first week, ICU and total hospital stay. Finally, predictive factors significantly associated with excellent outcome were no occurrence of seizure (OR = 9.99 [1.19; 83.63], $p = 0.0337$) and no TD vasospasm (OR = 6.38 [1.57; 25.84], $p = 0.0094$) after SAH (Table 4).

Discussion:

In our study, the functional outcome of patients with subarachnoid hemorrhage WFNS 1 to 3 was notably good. The majority (72%) had a GOS \geq 5 at 1-year. Absence of TD vasospasm and seizure were predictive of a good outcome at 1-year.

Most studies focused on poor outcome of poor grade SAH. Historic series of patients undergoing surgical treatment [8] showed that risk factors for unfavorable outcome at 3 months were multiple and included the use of anticonvulsant drugs, symptomatic vasospasm, increased age, worse admission WFNS grade, greater SAH clot thickness on admission CT scan, posterior circulation and larger aneurysm, intraventricular hemorrhage, intracerebral hemorrhage, admission systolic hypertension, history of hypertension, SAH and myocardial infarction, fever 8 days after SAH, cerebral ischemia. Literature on good outcome of good grade SAH is scarce. Recently, Pegoli and al [10] studied predictive factors of excellent outcome after SAH. In their cohort of 381 patients with all grade of gravity, 63.3% of the patients presented an excellent outcome assessed with Rankin scale score at last follow-up within 1 year of the SAH. In comparison with our results, 81% of the patients with a good clinical grade (WFNS Grade I–III) at admission achieved an excellent outcome. In multivariable analyses, they found excellent functional outcome was very likely in patients who were in good clinical condition after neurological resuscitation, did not have an intraparenchymal hematoma on the first CT scan, did not develop brain infarctions from delayed ischemia, and did not receive a blood transfusion during the hospital stay. However, they did not consider TD vasospasm but only symptomatic vasospasm.

TD vasospasm being a risk factor for poor outcome after good grade SAH, we further studied risk factor for TD vasospasm in our cohort. Predictive factors of TD vasospasm were localization of aneurysm on the anterior and middle cerebral arteries, Fisher and WFNS grade, the highest maximal temperature during the first week, and rebleeding. Literature refers mostly to symptomatic vasospasm [12, 13]. Qureshi and al tried to develop a strategy

to identify patients at risk for symptomatic vasospasm after SAH [12]. Out of 283 patients in their cohort, 93 (33%) developed symptomatic vasospasm. They identified four independent predictors of symptomatic vasospasm: thickness of subarachnoid clot on computed tomographic scan; early rise in middle cerebral artery mean flow velocity, defined as a value ≥ 110 cm/sec recorded on or before post-SAH day 5, Glasgow Coma Scale score < 14 ; and location of aneurysm on anterior cerebral or internal carotid artery aneurysm. They proposed a scoring system (symptomatic vasospasm risk index) to stratify patient's risk of symptomatic vasospasm and help to select patients who require closer observation in ICU. Their hypothesis was that patients with important risk according to their score system could benefit of prophylactic treatments to reduce the incidence of symptomatic vasospasm. This risk index has not been validated. However, it requires a close TD monitoring for the first 5 days. In 2016, Tetsuji Inagaw collected risk factors for cerebral vasospasm following SAH. He concluded that severe SAH on CT at admission was the most reliable risk factor for cerebral vasospasm after SAH [14]. Finally, no single risk factor or model can accurately predict symptomatic vasospasm [15]. The strongest risk factor for development of vasospasm appears to be WFNS grade at admission, amount of cisternal and intraventricular blood on CT [13].

Cerebral vasospasm is noted on angiography in as many as 30 to 70% of patients following SAH and 50% on transcranial Doppler (TD) ultrasonography [16]. In their systematic review and meta-analysis, Kumar and al [17] showed that vasospasm diagnosed on TD can predict delayed cerebral ischemia (DCI). The study demonstrated that TD was able to predict the subsequent development of symptomatic vasospasm and make a positive contribution to the diagnosis of vasospasm in 72% of patients. In 2014 the consensus conference on multimodality monitoring in neurocritical care, the Neurocritical Care Society and the European Society of Intensive Care Medicine recommend TD monitoring to predict angiographic vasospasm after aneurysmal SAH and suggest that trends of TD can help

predict delayed ischemic neurological deficits associated to vasospasm after aneurysmal SAH [18].

However, the benefit of such monitoring is not clearly demonstrated [19]. Indeed, mortality and morbidity of patients after TD or angiographic vasospasm, is not well known [20]. Results of studies are contradictory. Consequently, the management of asymptomatic vasospasm is not clearly codified. Some begin treatment as soon as velocities are increased on transcranial Doppler; others may treat angiographic vasospasm in asymptomatic patients, while some require a neurological deterioration to institute aggressive measures [21, 22].

In literature, treatment of angiographic vasospasm did not improve necessarily functional outcome and it is unclear whether asymptomatic vasospasm detected by noninvasive testing like transcranial Doppler, affects outcome [20]. For Oliveira Manoel and al, angiographic vasospasm, in the absence of DCI, should not be treated. In case of a new focal deficit or a decrease in level of consciousness, not explained by other causes, physicians should begin aggressive treatment. Their first step is the fluid challenge or euvolemia. In the absence of response, they proposed the use of vasopressors [23]. In a prospective study including 580 patients, Frontera and al identified symptomatic vasospasm, DCI, angiographic spasm, and TD vasospasm. DCI and symptomatic vasospasm were associated with cognitive impairment, and poor quality of life. Only DCI was independently associated with severe disability or death (modified Rankin score 4 – 6) at 3-months. Angiographic and TD vasospasm were not associated with poor outcome [24]. On the other hand, some studies showed that the occurrence of angiographic vasospasm was associated with poor outcome. The gravity of sequelae was proportional to the severity of vasospasm [25; 26]. More studies are clearly needed to assess this common situation in clinical practice.

Our study has several limitations: a single-center retrospective cohort. The evaluation of GOS was retrospective according to the consultation data collected. We have chosen GOS score for its simplicity for retrospective collect, and its previous use in the literature [27]. It is easy to use but it is associated with a certain lack of sensitivity. Indeed patient often report fatigability, cognitive disorders like poor concentration, memory disorders that are not

accurately measured by the GOS score [28]. These disorders are probably underestimated [29, 30], which could explain the discrepancy between the proportion of patients with a GOS score rather good and the low rate of recovery of previous activity (58%).

Conclusion:

In our study, patients with good grade SAH had generally a good functional outcome. TD vasospasm and seizure are the two most important predictors of good outcome in our cohort. Therefore, detection of patients at risk is not simple. Consequently it is necessary to maintain the same monitoring and management during the period at risk of vasospasm for this subgroup of good grade SAH at admission. The question of aggressive management of TD asymptomatic vasospasm remains.

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TITRE DE LA THESE d'EXERCICE

(Ce document sera à insérer dans les thèses définitives)

Titre : Facteurs prédictifs de bon pronostic après hémorragie sous-arachnoïdienne non grave.

Rennes, le

Le Directeur de thèse

Rennes, le

Le Président de jury

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Table 1: Characteristics of patients. Data are presented as numbers (%) for qualitative variables and mean \pm SD for quantitative variables. Data are missing (5 Fisher grade) for 5 patients. 8 patients had 2 localizations of aneurysms and 5 cases of perimesencephalic subarachnoid hemorrhage. ICU: intensive care unit, WFNS: World Federation of Neurological Surgeons, GOS : glasgow outcome scale.

| | Overall cohort (n = 92) |
|---------------------------------------------------------|-------------------------|
| Sex (female): | 57 (62) |
| Age (years) | 49 \pm 13 |
| Body mass index | 25 \pm 5 |
| Hypertension history | 29 (32) |
| Active smoking | 53 (58) |
| Dyslipidemia | 17 (19) |
| Alcoholism | 3 (3) |
| Time between first symptoms and diagnosis (days) | 2.2 \pm 4.3 |
| Seizure | 9 (10) |
| Hemoglobin at admission | 13.8 \pm 1.4 |
| Aneurysm localization: | |
| - anterior communicating artery | 29 (32) |
| - anterior cerebral artery | 7 (8) |
| - Middle cerebral artery | 24 (26) |
| - Posterior cerebral artery | 1 (1) |
| - Basilar artery | 7 (8) |
| - Superior cerebellar artery | 4 (4) |
| - Internal carotid artery | 23 (25) |
| WFNS : | |
| 1 | 80 (87) |
| 2 | 10 (11) |
| 3 | 2 (2) |
| Fisher score : | |
| 1 | 17 (20) |
| 2 | 21 (24) |
| 3 | 22 (25) |
| 4 | 27 (31) |
| Sepsis | 7(8) |
| Aneurysm treatment: | |
| Clipping | 8 (9) |
| Coiling procedure | 79 (86) |
| Length of stay ICU (days) | 8.8 \pm 6.3 |
| Length of stay hospital (days) | 17.5 \pm 10.1 |
| Outcome: | |
| GOS: 1: Death | 5 (6) |
| 2: Persistent vegetative state | 0 |
| 3: Severe disability | 3 (4) |
| 4: Moderate disability | 14 (18) |
| 5: Low disability | 57 (72) |

Table 2: Association of baseline and hospital variables with vasospasm on transcranial Doppler (TD) and symptomatic vasospasm. Data are presented as numbers (%) for qualitative variables and mean \pm SD for quantitative variables. *: $p < 0.05$. WFNS: World Federation of Neurological surgeons, SAH: subarachnoid hemorrhage, BMI: body mass index, MBP: mean blood pressure.

| | TD Vasospasm (n=30) | No TD Vasospasm (n=62) | Symptomatic vasospasm (n=16) | No symptomatic vasospasm (n=76) |
|---------------------------------------------------------|------------------------|------------------------------|------------------------------------|---------------------------------------|
| WFNS: | | | | |
| 1 | 20 | 60 (96) | 12 (75) | 68 (90) |
| 2 | 9 (30) | 1 (2) | 3 (19) | 7 (9) |
| 3 | 1 (3) | 1 (2) | 1 (6) | 1 (1) |
| | | | | |
| Fisher: | | | | |
| 1 | 1 (3) | 16 (28) | 1 (6) | 16 (22) |
| 2 | 7 (23) | 14 (25) | 2 (13) | 19 (27) |
| 3 | 11 (37) | 11 (19) | 5 (31) | 17 (24) |
| 4 | 11 (37) | 16 (28) | 8 (50) | 19 (27) |
| | | | | |
| Age (years) | 47 \pm 13 | 50 \pm 14 | 51 \pm 10 | 49 \pm 14 |
| Sex: Male/Female | 12 (40)/18 (60) | 23 (37)/39 (63) | 5 (31)/11 (69) | 30 (39)/46 (61) |
| BMI | 24.8 \pm 4.2 | 24.6 \pm 5 | 25.5 \pm 4.8 | 24.5 \pm 4.7 |
| Diabetes | 0 (0) | 1 (2) | 0 (0) | 1 (1) |
| Dyslipidemia | 4 (13) | 13 (21) | 3 (19) | 14 (18) |
| History hypertension | 9 (30) | 20 (32) | 6 (38) | 23 (30) |
| Active smoking | 16 (53) | 37 (60) | 8 (50) | 45 (59) |
| Alcoholism | 2 (7) | 1 (2) | 1 (6) | 2 (3) |
| Aneurysm treatment : | | | | |
| Clipping | 5 (17) | 3 (5) | 3 (19) | 5 (7) |
| Coiling procedure | 25 (83) | 54 (88) | 13 (81) | 66 (87) |
| Seizure | 4 (13) | 5 (8) | 2 (13) | 7 (9) |
| Hemoglobin at admission | 13.8 \pm 1.5 | 13.8 \pm 1.5 | 13.9 \pm 1.8 | 13.8 \pm 1.3 |
| Time between first symptoms and diagnosis (days) | 2 \pm 3.9 | 2.3 \pm 4.5 | 2.1 \pm 3.8 | 2.2 \pm 4.4 |
| Lowest MBP (mmHg) the 1st week: | 81.6 \pm 7.8* | 76.7 \pm 9.5 | 83.8 \pm 8.1 * | 77.1 \pm 9.1 |
| Highest MBP (mmHg) the first week: | 115.9 \pm 17.3 | 116.0 \pm 17.3 | 119.8 \pm 14 | 115.2 \pm 17.8 |
| Treatment by vasopressor: | 10 (33%)* | 9 (15%) | 6 (37%) | 13 (17%) |

Table 3: Predictive factors of good outcome. Data are presented as numbers (%) for qualitative variables and mean \pm SD for quantitative variables, * $p \leq 0.05$, MBP: mean blood pressure.

| | GOS < 5 (n = 22) | GOS \geq 5 (n = 57) | |
|--------------------------------------------------|--------------------------------|---------------------------------------------|----------------|
| Sex : male/female | 3 (14)/ 19 (86) | 27 (47)*/30 (53)* | |
| Age (years) | 56 \pm 15 | 47 \pm 12* | |
| Hypertension history | 11 (50) | 13 (24)* | |
| Dyslipidemia | 5 (23) | 8 (14) | |
| Alcoholism | 1(5) | 1(2) | |
| Active smoking | 9 (41) | 35 (61) | |
| Treatment aneurysm : | | | |
| Clipping | 4 (18) | 3 (5) | |
| Coiling procedure | 18 (82) | 51 (95) | |
| WFNS | | | |
| 1 | 16 (73) | 52 (91) | |
| 2 | 5 (23) | 4 (7) | |
| 3 | 1 (5) | 1 (2) | |
| Fisher | | | |
| 1 | 1 (5) | 12 (23) | * } p = 0.0061 |
| 2 | 1 (5) | 16 (30) | |
| 3 | 8 (38) | 12 (23) | |
| 4 | 11 (52) | 13 (24) | |
| Lowest MBP (mmHg) the 1st week | 79.6 \pm 9.8 | 77.4 \pm 8.7 | |
| Highest MBP (mmHg) the first week | 114.7 \pm 13.9 | 115.2 \pm 16.4 | |
| Maximum temperature the 1st week | 38.7 \pm 0.7 | 37.9 \pm 0.7* | |
| Vasospasm on transcranial Doppler : | | | |
| no | 8 (36) | 42 (74)* | |
| yes | 14 (64) | 15 (26)* | |
| Clinical Vasospasm : | | | |
| no | 12 (55) | 51 (90)* | |
| yes | 10 (45) | 6 (11)* | |
| Seizure | 4 (18) | 2(4)* | |
| Hydrocephalus | 5 (23) | 6 (11) | |
| Rebleeding | 5 (23) | 0* | |
| Sepsis | 4 (18) | 2 (4)* | |
| Treatment by vasopressor : | | | |
| no | 13 (59) | 49 (86) * | |
| yes | 9 (41) | 8 (14)* | |

Table 4: Multivariate analyses showing independent associations with outcome (GOS < 5).

Data are presented as odds ratios [95% CI]. CI: confidence interval; TD: transcranial Doppler,

ICU: intensive care unit.

| <i>Variables</i> | <i>n</i> | <i>OR [95% CI]</i> | <i>P value</i> |
|---------------------|----------|---------------------|----------------|
| TD Vasospasm | 30 | 6.38 [1.57 ; 25.84] | 0.0094 |
| Seizure | 9 | 9.99 [1.19 ; 83.63] | 0.0337 |

Annexes:

Glasgow outcome scale (GOS) of functional status:

| GOS score | Functional status | |
|-----------|-----------------------------|------------------------------------------------------------------------------------------|
| 5 | GOOD RECOVERY | Resumption of normal life; there may be a minor neurologic and/or psychological deficits |
| 4 | MODERATE DISABILITY | Able to work in a sheltered environment |
| 3 | SEVERE DISABILITY | Dependent for daily support by reason of mental or physical disability or both |
| 2 | PERSISTENT VEGETATIVE STATE | Patient exhibits no obvious cortical function. |
| 1 | DEATH | |

WFNS: Scale for grading patients with a subarachnoid haemorrhage.

| Grade | GCS | Motor deficit |
|-------|-------|---------------|
| I | 15 | - |
| II | 14-13 | - |
| III | 14-13 | + |
| IV | 12-7 | +/- |
| V | 6-3 | +/- |

Modified Fisher scale:

| Grade | Criteria |
|----------------|---------------------------------------|
| grade 0 | no SAH or IVH |
| grade 1 | focal or diffuse, thin SAH, no IVH |
| grade 2 | focal or diffuse, thin SAH, with IVH |
| grade 3 | focal or diffuse, thick SAH, no IVH |
| grade 4 | focal or diffuse, thick SAH, with IVH |

SAH: subarachnoid hemorrhage

IVH: intraventricular hemorrhage

41 feuilles - Thèse : Médecine.

Résumé français

Introduction : La prise en charge des hémorragies sous-arachnoïdiennes (HSA) a beaucoup évolué ces dernières années avec une mortalité moindre mais une morbidité qui reste élevée. Dans la littérature, on retrouve essentiellement des données sur les facteurs prédictifs de pronostic péjoratif dans des études où sont incluses des HSA tout grade de gravité confondu. Il existe peu d'information sur les HSA non graves. Le but de cette étude était de déterminer les facteurs prédictifs de bon pronostic dans cette sous-population de patient, en vue d'adapter leur prise en charge.

Méthode : Cette analyse rétrospective concernait les patients admis aux soins intensifs de neurochirurgie au CHU de Rennes en 2012 pour HSA avec un score WFNS (World Federation of Neurologic Surgeons) compris entre 1 et 3. L'étude portait sur les facteurs prédictifs de complications habituelles des HSA : vasospasme, resaignement, et hydrocéphalie ; et sur le bon pronostic fonctionnel à un an. Il était défini par un score de la Glasgow Outcome Scale ≥ 5 . L'analyse statistique comportait une analyse univariée puis une régression logistique multivariée avec un seuil de significativité à 0.05.

Résultats: 92 patients ont été inclus. Parmi eux, 34 ont présenté une complication: 30 vasospasmes sur le doppler transcrânien (32.6%), 16 vasospasmes symptomatiques (17.4%), 5 resaignements (5.4%), 15 hydrocéphalies (16.3%), 9 (9.7%) convulsions et 7 (7.6%) sepsis. Le vasospasme était significativement associé aux scores WFNS ($p < 0.0001$) et Fisher ($p = 0.0296$) à l'admission, au resaignement ($p = 0.0374$), à la température maximale de la première semaine ($p = 0.0031$). L'hydrocéphalie était associée à un score WFNS élevé à l'admission. Un bon pronostic était constaté pour 57 (72%) patients. En analyse multivariée, l'absence de vasospasme sur le doppler transcrânien (OR = 6.38 [1.57; 25.84], $p = 0.0094$) et l'absence de crise convulsive (OR = 9.99 [1.19 ; 83.63], $p = 0.0337$) étaient associées à un bon pronostic fonctionnel à un an (GOS ≥ 5).

Conclusion: Les patients souffrant d'HSA non graves avaient un bon pronostic fonctionnel dans notre étude. L'existence d'un vasospasme sur le doppler transcrânien et la crise convulsive étaient significativement associées à un mauvais pronostic fonctionnel à un an. La question d'un monitoring et d'une réanimation agressive en cas de vasospasme au doppler transcrânien mais asymptomatique par ailleurs mérite ainsi d'être posée.

Rubrique de classement : Réanimation, Neurochirurgie, Radiologie

Mots-clés : Hémorragie sous-arachnoïdienne, Pronostic, Vasospasme, Facteurs prédictifs

Mots-clés anglais MeSH : Subarachnoid Hemorrhage, Vasospasm, Outcome, Prediction

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