

**Critical Illness - Related Corticosteroid Insufficiency
after Non-severe Acute Aneurysmal Subarachnoid
Haemorrhage : impact on complications and early
outcome**

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THÈSE D'EXERCICE / UNIVERSITÉ DE RENNES 1
sous le sceau de l'Université Bretagne Loire

Thèse en vue du

DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

présentée par

Baptiste OLLIVIER

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**Insuffisance corticotrope
à la phase aiguë des
hémorragies sous-
arachnoïdiennes non
graves : impact sur la
survenue de
complications et le
pronostic fonctionnel à 1
mois**

Thèse soutenue à RENNES

le 12 décembre 2018

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**Insuffisance corticotrope à la phase aiguë des
hémorragies sous-arachnoïdiennes non graves:
impact sur la survenue de complications et le
pronostic fonctionnel à 1 mois**

*Critical Illness - Related Corticosteroid Insufficiency after
Non-severe Acute Aneurysmal Subarachnoid
Haemorrhage: Impact on complications and early
outcome*

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Abstract

Introduction: Aneurysmal subarachnoid haemorrhage (ASAH) is a life threatening condition that may be aggravated by hormonal disturbances such as critical illness-related corticosteroid insufficiency (CIRCI). Our study aimed to assess the incidence of CIRCI in acute non-severe SAH and seek a connection with the occurrence of complications and functional outcome.

Materials and methods: Patients with non-severe SAH (WFNS grade ≤ 3) were included. Hormonal assays were collected in the first 48 hours: baseline and stimulated cortisol (after 250 μg of Synacthene®) and ACTH. CIRCI was defined by a random total cortisol of < 100 ng/ml or a Δ cortisol of < 90 ng/ml. Patients were followed for 30 days with identification of complications: vasospasm, delayed cerebral ischemia, rebleeding, seizure, hydrocephalus and infection. After 30 days, Glasgow outcome scale (GOS), modified Rankin scale (mRS) and the Short Form-12 (SF-12) were assessed by phone conversation.

Results: 52 patients were included from June 2013 to March 2016. The incidence of CIRCI was 17.3% in the acute phase. The overall complications incidence was 78% in the CIRCI patients versus 44% in the none CIRCI patients but there was no correlation between CIRCI and the occurrence of complications except infections. CIRCI was not statistically associated with a less favourable outcome.

Conclusion: The present results support earlier findings that CIRCI occurs frequently after ASAH. Furthermore, we have demonstrated that CIRCI was not associated with a higher rate of complication neither less favorable outcome at 1 month.

Introduction

Aneurysmal subarachnoid haemorrhage (ASAH) occurs with an incidence of 9 per 100000 per year (1), especially in young women. Although the mortality rate has decreased over time, the outcome is still poor and more than half of the patients remains disabled (2,3). The impact on cognitive functions and physical ability is important with major social and economic costs. Outcome is largely determined by the severity of the initial haemorrhage. However, complications occurring days after the ASAH also contribute to the morbidity.

The close anatomical proximity between the usual aneurysm sites and the hypothalamus and pituitary axis has led to speculation into whether pituitary dysfunctions have an impact on outcome after ASAH (4). Indeed, previous studies have reported endocrine abnormalities indicating pituitary dysfunction after ASAH but their results are conflicting (5–11). These studies described different degrees of hypopituitarism including isolated or combined with thyrotroph, corticotroph, gonadotroph or growth hormone deficiencies. The onset of these dysfunctions remains also unclear. Therefore, it is difficult to define a unique typical profile of hypopituitarism following ASAH. More recent studies have demonstrated that corticotroph insufficiency is a common complication after ASAH (12–19). However, no univocal conclusion about the physiopathology has been proposed so far. The results of these recent studies are however heterogeneous due to methodologic discrepancies, i.e. most of them including severe traumatic brain injuries and high grade ASAH. Moreover, hormonal analyses were not standardized and were performed at variable times.

Amongst overall ASAH, non-severe ASAH have better outcome with fewer sequelae but are still associated with a risk of complications between 35 to 50% (20,21). Available data on the incidence of pituitary dysfunction after non-severe ASAH and its potential consequences on the outcome remain scarce. One could hypothesize that preventing and / or treating a potential disorder of the pituitary axis could help further improvement the outcome after non-severe ASAH.

Therefore, the main objectives of this study were to investigate the incidence of hypocortisolism during the acute phase after non-severe ASAH and to assess its consequences on complications and outcome.

Methods

Patients

The local ethics committee (EudraCT number 2012-A01386-37) and the French National Agency for Health Products (n°2013-A01386-37 / 130239B-22 26/02/2013) approved the study. Patients were included after written informed consent was obtained from them or a next-of-kin. Patients with non-severe aneurysmal SAH treated at the Neurosurgical ICU of the University Hospital in Rennes were recruited from June 2013 to March 2016.

According to our institution policy, patients with ASAH hospitalized in this unit are older than 15 year-old and show a good-grade ASAH defined by a WFNS (World Federation of Neurosurgical Society) (22) grade 1, 2 or 3 and a Glasgow Coma Scale (GCS) higher than 13.

Treatment and Monitoring

According to our institution policy, prevention of delayed cerebral ischemia is achieved in all patients with oral nimodipine during 21 days. Fluid and electrolyte balance is monitored and significant hyponatremia (<131 mmol/L) is treated (23). Measurements of blood flow velocities in the middle cerebral and anterior cerebral arteries using transcranial doppler are performed every 48 hours to screen for vasospasm. Hydrocephalus is treated by external ventricular drainage, continuing oral nimodipine in case of vasospasm, maintenance of euvolemia, induction of hypertension and endovascular therapy including in-situ vasodilators and mechanical angioplasty. Delayed cerebral ischemia was defined as the onset of a neurological deficit or decrease in the level of consciousness (drop in Glasgow Coma Scale > 2 points) not attributable to other causes (24).

Data collection

We collected the following clinical and biological data at admission: sex, age, WFNS grade, Hunt and Hess score (25), risk factors for cerebral aneurysm (smoking, hypertension history), haemoglobin, the transcranial doppler (TCD) measurements and the conclusions of the initial CT scan and/or angiography including Fisher scale grade (26). The decision of therapeutic strategy for aneurysmal exclusion was decided after a multidisciplinary discussion between neuroradiologists and neurosurgeons and also noted. The following complications during hospitalization were recorded:

vasospasm defined by middle cerebral artery flow velocities ≥ 120 cm/sec on TCD, rebleeding defined by modification of the initial CT scan, hydrocephalus diagnosed on CT scan, seizure defined by partial crisis or generalized seizure identified by the medical team, and sepsis defined by the association of fever (higher than 38.3°C) and a bacterial isolation in microbiological samples. Finally, intensive care unit (ICU) length of stay, hospital length of stay and time to discharge for rehabilitation were noted. Patients were followed for 30 days after hospital discharge.

Assessment of endocrine function

Endocrine evaluation in the acute stage included blood samples drawn in the morning (8:00 am). We measured plasma levels of cortisol T0 and adrenocorticotrophic hormone (ACTH). Blood samples for cortisol and ACTH analyses were collected within 48 hours of admission at 8:00 am, immediately after a stimulation test (intravenous administration of 250 μg of corticotrophin hormone (Synacthène®, ALFASIGMA, France)) was performed. A second blood sample for cortisol T1 analysis was collected one hour later (9:00 am). Unfortunately, there has been a temporary shortage of Synacthène® in France from December 2014 to February 2015 explaining the prolonged period of inclusion of the study (June 2013 to March 2016).

The diagnosis of adrenal insufficiency commonly called Critical Illness - Related Corticosteroid Insufficiency (CIRCI) was based on international consensus statements: a random total cortisol of $<100\text{ng/mL}$ or a variation of total serum cortisol of $<90\text{ng/mL}$ after stimulation test ($\Delta\text{cortisol}$) (27,28) (figure 1).

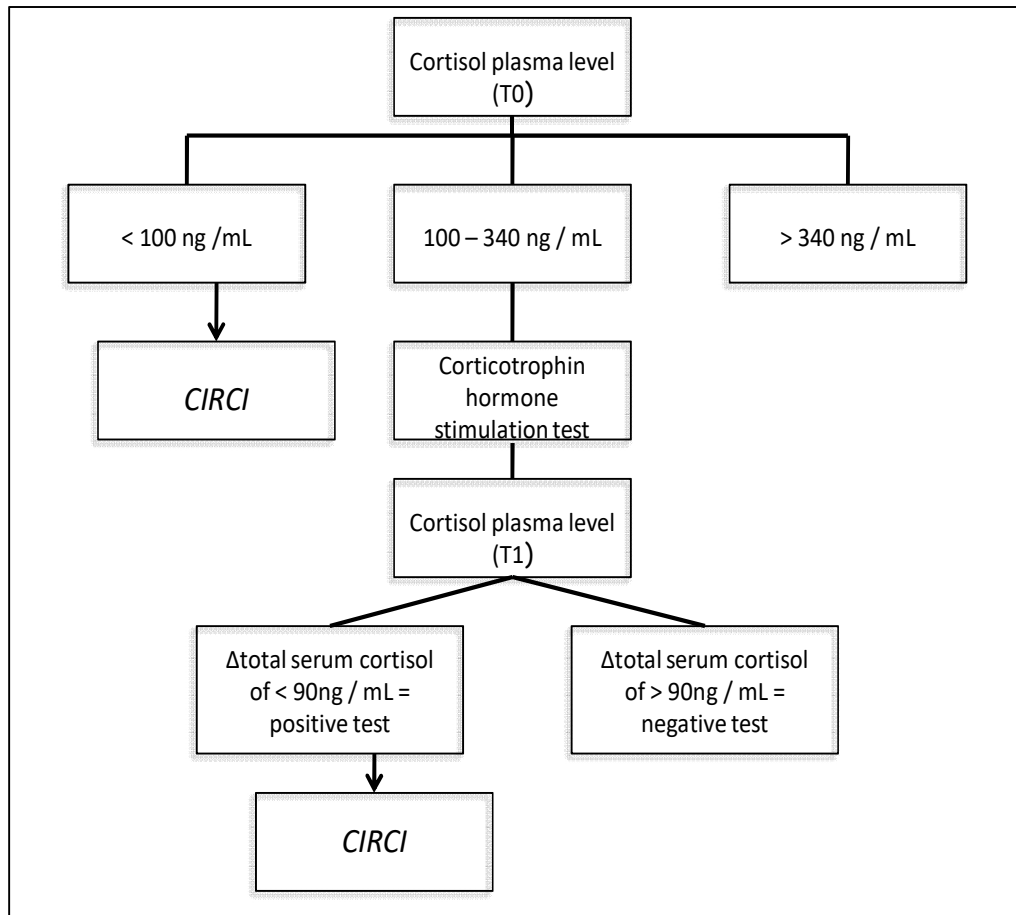


Figure 1. Hormonal assessment protocol

Abbreviation: CIRCI, Critical Illness - Related Corticosteroid Insufficiency

Clinical Outcome:

Neurological outcome was assessed using the Glasgow Outcome Scale (GOS) (29) and the modified Rankin Scale (mRS) (30) at the follow-up visit 1 month after discharge. A favorable outcome was defined as GOS of 4 to 5 or mRS of 1 to 2 and a poor outcome as GOS of 1 to 3 or mRS of 3 to 5. The functional outcome was assessed by the 12- Item Short Form Health Survey SF-12) during a phone conversation a month after discharge (31). The evaluation was performed by 2 investigators blind of the endocrine data.

Statistical Analysis:

Because earlier studies had included 30 to 40 patients with a 37.5% to 55% prevalence of pituitary dysfunction (5,6,10), a cohort of 50 patients was estimated sufficient to answer to the objectives. The data are presented as mean +/- standard deviation (SD) for the continuous variables, categorical variables are summarised as frequencies and percentages. Categorical data were compared using Fisher test. Between-group comparisons of normally distributed continuous data were analysed using Student test. Logistic regression analyses were conducted to study the association between CIRCI, complications and outcome (GOS, mRS, SF-12). Statistical significance was reached when p-value<0.05.

All statistical analyses were performed by using SAS software version 9.4 ® (SAS Institute, Cary, NC, USA).

Results*Study population*

Between June 2013 to March 2016, 134 patients were admitted to Neurosurgical ICU with a diagnosis of non-severe SAH secondary to ruptured aneurysm. As shown on the flow-chart (figure 2), out of the 62 patients initially assessed, 5 were excluded: 3 for previous use of corticosteroids and 2 patients declined participation leaving 57 to be tested in the acute stage. At follow-up, 1 month after discharge, 2 patients were excluded due to lack of complete hormone data and 3 were lost after 2 attempts to contact them, leaving 52 patients eligible for follow-up examinations.

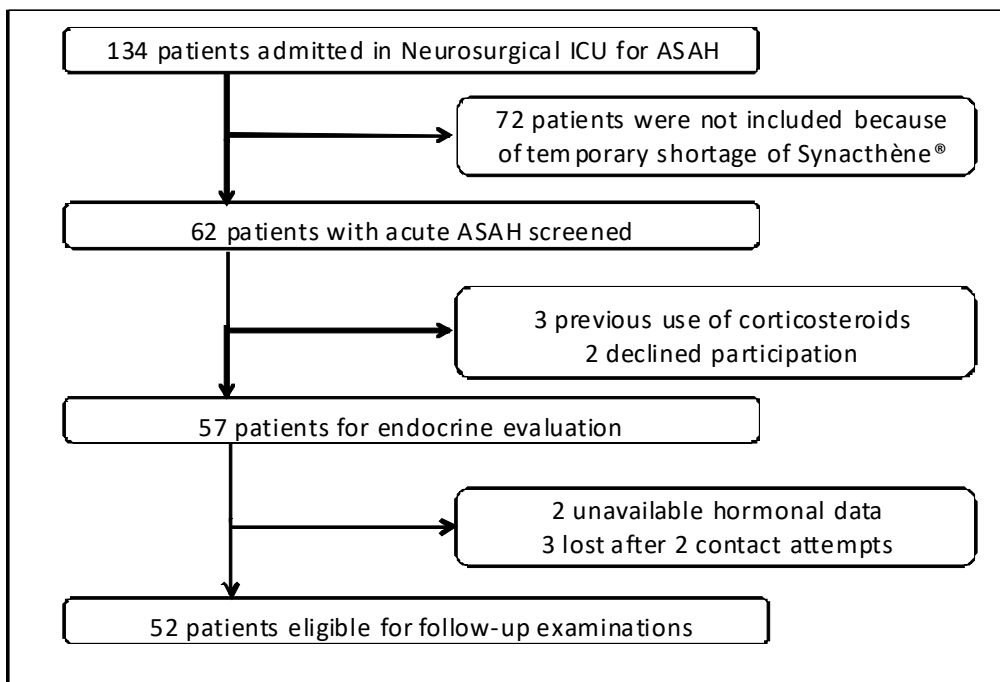


Figure 2. Flowchart

Abbreviations: ICU, intensive care unit; ASAH, aneurysmal subarachnoid haemorrhage

The baseline characteristics of the population are summarized in Table 1. The mean age was 55 +/- 12.8 years, most of the patients were female (75%). Chronic high blood pressure and active smoking were present in respectively 29% and 54 % of the patients. The mean length of stay in ICU was 17.7 +/- 8.1 days, six patients were transferred in surgical ICU due to severe neurological deterioration. Baseline characteristics were similar between groups, the rate of hypertensive patients was higher in CIRCI group (56% versus 23%) but this difference was not statistically significant ($p= 0.09$).

	Global (n=52)	CIRCI (n=9)	None CIRCI (n=43)
Age (years)	55 +/- 13	59 +/- 15	54 +/- 12
Men / Women	13 (25%) / 39 (75%)	2 (22%) / 7 (78%)	11 (26%) / 32 (74%)
ASA score (%) [I/II/III]	28 (54%) / 19 (36%) / 5 (10%)	4 (45%) / 3 (33%) / 2 (22%)	24 (56%) / 16 (37%) / 3 (7%)
Chronic hypertension	15 (29%)	5 (56%)	10 (23%)
Active smoking	28 (54%)	4 (45%)	24 (56%)
ICU length of stay (days)	17.7 +/- 8	18.8 +/- 13	17.5 +/- 7

Table 1. Baseline characteristics of patients

Abbreviations: CIRCI, Critical Illness - Related Corticosteroid Insufficiency; ICU, Intensive Care Unit; ASA, American Society of Anesthesiologists

Data are presented as median +/- SD or n(%)

According to the results shown in Table 2, 77% of the patients presented with a GCS of 15 at admission and 75% of them had a Hunt and Hess scale score equal to 2 or less. The aneurysm location was on the anterior communicating artery aneurysm in 46% of the cases and most of the patients (96%) were treated by endovascular coiling.

	Global (n=52)	CIRCI (n=9)	None CIRCI (n=43)
Initial GCS			
15	40 (77%)	6 (67%)	34 (79%)
14	10 (19%)	3 (33%)	7 (16%)
13	2 (4%)	0 (0%)	2 (5%)
Clinical severity assessment (WFNS)			
1	35 (67%)	6 (67%)	29 (67%)
2	15 (29%)	3 (33%)	12 (28%)
3	2 (4%)	0 (0%)	2 (5%)
Fisher grade			
1	10 (19%)	3 (33%)	7 (16%)
2	2 (4%)	0 (0%)	2 (5%)
3	23 (44%)	2 (22%)	21 (49%)
4	17 (33%)	4 (45%)	13 (30%)
Aneurysm localisation			
Internal carotid artery	11 (21%)	0 (0%)	11 (26%)
Anterior communicating artery	24 (46%)	6 (67%)	18 (42%)
Middle cerebral artery	12 (23%)	1 (11%)	11 (26%)
Basilar tip	1 (2%)	0 (0%)	1 (2%)
Posterior inferior cerebellar artery	2 (4%)	1 (11%)	1 (2%)
Others	2 (4%)	1 (11%)	1 (2%)
Treatment modality			
Microsurgery (clipping)	2 (4%)	1 (11%)	1 (2%)
Endovascular (coiling)	50 (96%)	8 (89%)	42 (98%)

Table 2. Clinical and radiologic characteristics of ASAH

Abbreviations : GCS, Glasgow Coma Scale; WFNS, World Federation of Neurological Surgeons; ASAH, aneurysmal subarachnoid haemorrhage

Data are presented as n (%)

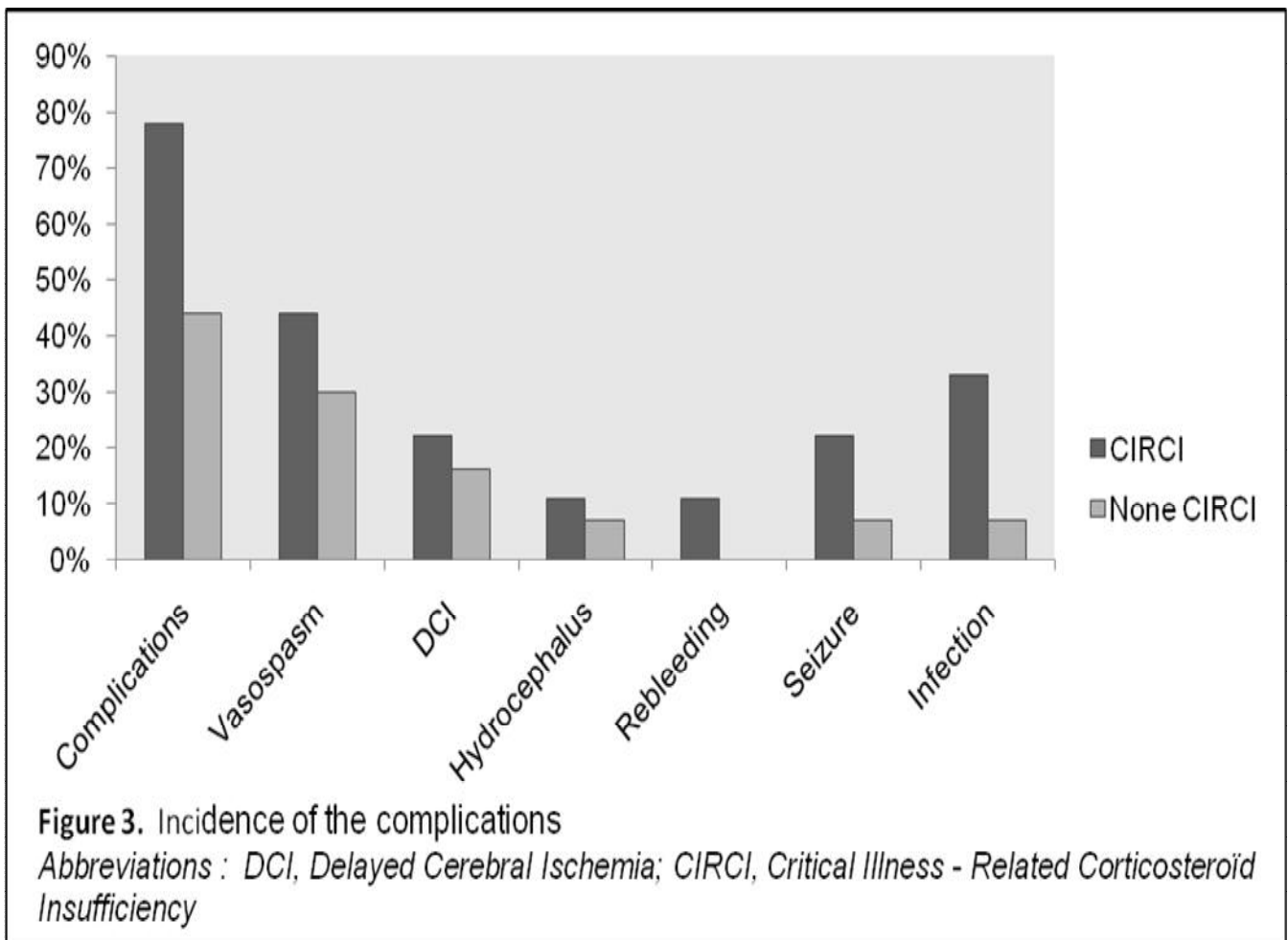
Endocrinologic analysis

The incidence of Critical Illness - Related Corticosteroid Insufficiency (CIRCI) after non-severe aneurysmal SAH was 17.3% (9 patients) in the acute phase. Indeed, the total cortisol T0 was lower than 100 ng/mL in 9 patients and the Δ cortisol after the stimulation test T1 was >90 ng/mL for all of these patients, suggesting a hypothalamic-pituitary disorder.

Complications

The overall complications incidence was 78% in the CIRCI patients versus 44% in the non-CIRCI patients, however, the difference was not statistically significant ($p = 0.14$). No significant differences were noted for each complication (new bleeding, DCI, vasospasm, hydrocephalus, seizure, infection) even concerning infectious complication (33% versus 7%, $p = 0.057$).

According to the results shown in figure 3, the most common complication was vasospasm (33%), which can lead to delayed cerebral ischemia (17%).



Outcomes

Among the 52 patients evaluated 1 month after discharge, 9 patients (18%) had a poor outcome when assessed with the Glasgow Outcome Scale (GOS 1-3) but only 7 patients (14%) when the modified Rankin Scale definition (mRS 3-5) was used. In the CIRCI group, 3 patients (33%) had a poor outcome when assessed with the GOS and 2 patients (23%) when assessed with mRS (Table 3). Concerning the assessment by the 12-Item Short Form Health Survey (SF-12), the mean PCS (Physical health Composite Scale score) component was 35.9 +/- 9 in the CIRCI group versus 37.9 +/- 8 in the none-CIRCI group. The mean MCS (Mental health Composite Scale score) component was 39.9 +/- 14 in the CIRCI group versus 38.9 +/- 9 in the none-CIRCI group. No significant differences were noted between the groups.

	Global (n=52)	CIRCI (n=9)	none CIRCI (n=43)
Glasgow Outcome Scale (GOS)			
1	0 (0%)	0 (0%)	0 (0%)
2	2 (4%)	1 (11%)	1 (2%)
3	7 (14%)	2 (22%)	5 (12%)
4	23 (44%)	4 (45%)	19 (44%)
5	20 (38%)	2 (22%)	18 (42%)
Modified Rankin Scale (mRS)			
1	22 (42%)	3 (33%)	19 (44%)
2	23 (44%)	4 (44%)	19 (44%)
3	2 (4%)	0 (0%)	2 (5%)
4	2 (4%)	0 (0%)	2 (5%)
5	3 (6%)	2 (23%)	1 (2%)

Table 3. Outcome at 1 month in 52 patients

Abbreviations : GOS, Glasgow Outcome Scale; mRS, modified Rankin Scale

Data are presented as n (%)

Logistic regression

Logistic regression was performed to explore the correlation between the occurrence of CIRCI, development of complications and outcome at 1 month (table 4). Concerning complications, the CIRCI was not associated with a higher rate of complication, except for infections (OR 6.67, IC95[1.08 ; 40.98], $p = 0.041$).

The neurological outcome (GOS, mRS) evaluated at one month after discharge was not correlated with the pre-existence of the CIRCI. Hypocortisolism at follow-up was also not associated with lower mental and physical health composite scores.

	N	Odds Ratio [95% confidence interval]	p value
Overall complications	52	4.42 [0.82 ; 23.78]	0.083
Vasospasm	52	1.85 [0.43 ; 8.01]	0.413
Delayed cerebral ischemia	52	1.47 [0.25 ; 8.61]	0.669
Rebleeding	52	15.53 [0.16 ; 1544.53]	0.243
Seizure	52	3.81 [0.54 ; 27.08]	0.181
Hydrocephalus	52	1.67 [0.15 ; 18.14]	0.675
Infection	52	6.67 [1.08 ; 40.98]	0.041
GOS 1-2-3		—	1.000
GOS 4-5	52	0.32 [0.06 ; 1.66]	0.176
mRS 3-4-5		—	1.000
mRS 1-2	52	0.46 [0.07 ; 2.86]	0.406
SF-12 (MCS)	52	1.01 [0.94 ; 1.08]	0.774
SF-12 (PCS)	52	0.97 [0.88 ; 1.06]	0.438

Table 4. Logistic regression model for CIRCI, complications and outcomes

Abbreviations: GOS, Glasgow Outcome Scale; mRS, modified Rankin Scale; SF-12, short form 12 items; MCS, mental health composite score; PCS, physical health composite score

Discussion

In this cohort of non-severe ASAH patients, the incidence of CIRCI evaluated according to international recommendations was 17.3%. We did not find any statistically significant difference for complications and outcome when comparing patients with or without CIRCI.

The patients included in our study presented similar demographic characteristics than those included in previous studies on ASAH (32–36) i.e. a majority of female patients in the 50-55 years age category with a predominance of hypertension (29%) and smoking habits (54%). Nevertheless, we did not collect the prevalence of diabetes mellitus and hypercholesterolemia which are often reported in studies but not considered as a risk factors of ASAH (37).

The overall complications rate observed in our study was 50%. No previous study has reported the incidence of overall complications. However, we found a similar incidence of seizure (10%) after ASAH than Choi et al (38). Our results concerning rebleeding (2%), hydrocephalus (8%), vasospasm (33%) and delayed cerebral ischemia (17%) contrast with the most recent studies (24,38–42) as we observed much lower rates. Indeed, Solenski et al (42) reported frequency rates of symptomatic vasospasm and rebleeding of 46% and 7% respectively.

Despite these complications, the outcome of our cohort was good with 86% of mRS 1-2 or 82% of GOS 4-5 at 1 month. This is a higher incidence than reported in most studies in which poor outcome has often been predominantly described. In a meta-analysis (43), the proportion of patients who regain independence for activities of daily life (mRS 0-2) varied between 36% and 55% 1-6 months after ASAH. These differences concerning incidence of complications and outcome can be explained by the design of our study in which we have exclusively included non-severe ASAH.

Our hypothesis was that the occurrence of the CIRCI was associated with an higher rate of complications and a less favorable outcome as described in recent studies on severe ASAH and TBI (5,12,13,44). However, we did not find any statistically significant difference between patients with or without CIRCI. Studies that showed a link between CIRCI and complications after ASAH included a mixed population of severe and non-severe ASAH. Very few studies have focused on non-severe

ASAH. One could hypothesize that the fatigue describe after the non-severe ASAH could be associated with pituitary dysfunctions (31) and therefore maybe treatable. In support of this theory low basal cortisol levels and severe deficiency of growth hormone have been found to be associated with major fatigue and weakness described by patients after SAH (45). Nevertheless, the meta-analysis including 20 studies (17) reported no statistical association between pituitary dysfunction and patients' outcome but again, it presented a wide heterogeneity in methodological tools, time of hormonal assessment and grade of ASAH.

In our study, we did not find any significant difference between patients with or without CIRCI but the results could suggest that patients with CIRCI are at high risk of complications (78% versus 44%). Furthermore, the limited number of patients combined with the low incidence of CIRCI may have resulted in a reduced power of the statistical analysis. Indeed, a posteriori power analysis revealed that 32 patients per group would be necessary to show a significant difference. According to our results, the rate of infections is higher in the CIRCI group (33% versus 7% $p = 0.057$). These results are not similar to recent studies. Indeed, Abulhasan et al reported an incidence of 16% (46). Moreover, the CIRCI was identified as a risk factor of infection (OR 6.67 IC95 [1.08 ; 40.98] $p = 0.041$) but the physiopathology remains unclear. The relationship between adrenocortical function and immunity is a complex one, however, physiologic amount of cortisol is necessary for the development and maintenance of normal immunity (47). It could be inferred that a cortisol deficiency would have a negative impact on the immune system, enhancing the risk of infection. In a recent review on the CIRCI (48), the dysfunction of the hypothalamic–pituitary–adrenal (HPA) axis during critical illness seems to be correlated to the degree of elevation in inflammatory cytokines and it is known that persistent elevation of cytokines is associated with higher disease severity and hospital mortality.

Despite, some suggestions on the contribution of the partially impaired pituitary capacity on chronic fatigue, the etiology of the longstanding fatigue following ASAH remains unclear.

The choice of the tools used to assess functional outcome after ASAH and TBI (traumatic brain injury) can be challenged. Indeed, the Glasgow Outcome Scale (GOS) is a validated and widely used instrument. Since the GOS is reduced only to the dimensions of neurological integrity and physical independence, one can suggest that the full range of psychological function is not assessed. This is why the use of a second score, i.e the modified Rankin Scale (mRS) could be useful. However, the

mRS has its own limits. It was originally design to categorize outcomes after ischemic stroke and when applied to ASAH (49), half the patients can have a post-ASAH mRS of zero while experiencing significant cognitive impairment when evaluated neuropsychologically (50). Within these patients with a mRS of zero, one in three are unable to return to work and one in six has a mood disorder 12 months after ASAH (51). The fact that neurological status and physical integrity alone do not sufficiently assess the overall state of patients after aneurysmal subarachnoid haemorrhage motivated us to use specific scores focusing on quality of life and reintegration, the Short Form-12. This scale was developed from the Short From-36 (SF-36), which is widely used and recommended by the American Agency of Health Care Policy and Research to explore rehabilitation and quality of life after stroke. There is a strong correlation between SF-12 and SF-36 (52).

Our study presents some limitations; the prolonged inclusion period is due to a temporary national shortage of Synacthène®. The hormonal assessment was performed on an unique blood sample within 48 hours after admission, whereas Aimaretti et al collected blood samples every day for the following 15 days and reported 42% of hypocortisolism (53). Also, repeated hormonal analyses could have improved the screening of CIRCI. Concerning the assessment of the outcome, the SF-12 is a powerful instrument but recently in 2018, a new scale was developed, the Subarachnoid Haemorrhage Outcome Tool (SAHOT) (54), the first subarachnoid haemorrhage-specific scientifically robust outcome measure. We could hypothesize that the use of this new tool would have certainly provide more sensibility in our assessment.

Conclusion

The present results support earlier findings that CIRCI occurs frequently after ASAH. Furthermore, we have demonstrated that CIRCI was not associated with a higher rate of complication neither less favorable outcome at 1 month. We can suggest that another study using the SAHOT for assessment of neuropsychological impairment could show different results.

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LISTE DES ABREVIATIONS

ACTH	Adrenocorticotropique Hormone
ASA	American Society of Anesthesiologists
ASAH	Aneurysmal Subarachnoid Haemorrhage
CIRCI	Critical Illness-Related Corticosteroid Insufficiency
DCI	Delayed Cerebral Ischemia
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
ICU	Intensive Care Unit
MCS	Mental health Composite Scale score
mRS	modified Rankin Score
PCS	Physical health Composite Scale score
SF-12	12-items Short Form Survey
SAHOT	Subarachnoid Haemorrhage Outcome Tool
TCD	Transcranial Doppler
WFNS	World Federation of Neurosurgical Societies

ANNEXES

Echelle de Glasgow

Ouverture des yeux	Réponse verbale	Réponse motrice
1-nulle	1-nulle	1-nulle
2-à la douleur	2-incompréhensible	2-extension stéréotypée
3-au bruit	3-inappropriée	3-fléxion stéréotypée
4-spontanée	4-confuse	4-évitement
	5-normale	5-orientée
		6-aux ordres

Classification de la WFNS

Grade	Score de Glasgow	Déficit moteur
I	15	Absent
II	13-14	Absent
III	13-14	Présent
IV	7-12	Présent ou absent
V	3-6	Présent ou absent

Classification de Hunt et Hess

Grade	Description clinique
0	Anévrysme non rompu
1	Asymptomatique ou céphalée minime
2	Céphalée modérée à sévère, raideur de nuque
3	Somnolence, confusion, déficit focal minime
4	Coma léger, déficit focal, troubles végétatifs
5	Coma profond, moribond

Glasgow Outcome Scale

5	Bonne récupération (pas de séquelle ou séquelles mineures)
4	Incapacité modérée (séquelles mais indépendant)
3	Incapacité sévère (conscient mais dépendant)
2	Etat végétatif
1	Décès

Score de Rankin modifié

0	Aucun symptôme
1	Pas d'incapacité en dehors des symptômes: activités et autonomie conservées
2	Handicap faible: incapacité d'assurer les activités habituelles mais autonomie
3	Handicap modéré: besoin d'aide mais marche possible sans assistance
4	Handicap modérément sévère: marche et gestes quotidiens impossibles sans aides
5	Handicap majeur: alitement permanent, soins de nursing permanents

QUESTIONNAIRE DE QUALITE DE VIE : SF-12

1. Dans l'ensemble, pensez-vous que votre santé est :

- 1 Excellente 2 Très bonne 3 Bonne 4 Médiocre 5 Mauvaise

2. En raison de votre état de santé actuel, êtes-vous limité pour :

- des efforts physiques modérés (déplacer une table, passer l'aspirateur, jouer aux boules...)
?

1 Oui, beaucoup limité 2 Oui, un peu limité 3 Non, pas du tout limité
- monter plusieurs étages par l'escalier?

1 Oui, beaucoup limité 2 Oui, un peu limité 3 Non, pas du tout limité

3. Au cours de ces 4 dernières semaines, et en raison de votre état physique :

- avez-vous accompli moins de choses que vous auriez souhaité ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais
- avez-vous été limité pour faire certaines choses ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais

4. Au cours de ces 4 dernières semaines, et en raison de votre état émotionnel (comme vous sentir triste, nerveux ou déprimé) :

- avez-vous accompli moins de choses que vous auriez souhaité ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais
- avez-vous eu des difficultés à faire ce que vous aviez à faire avec autant de soin et d'attention que d'habitude ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais

5. Au cours de ces 4 dernières semaines, dans quelle mesure vos douleurs physiques vous ont -elles limité dans votre travail ou vos activités domestiques ?

- 1 Pas du tout 2 Un petit peu 3 Moyennement 4 Beaucoup 5 Enormément

6. Les questions qui suivent portent sur comment vous vous êtes senti au cours de ces 4 dernières semaines. Pour chaque question, indiquez la réponse qui vous semble la plus appropriée.

- y a-t-il eu des moments où vous vous êtes senti calme et détendu ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais
- y a-t-il eu des moments où vous vous êtes senti débordant d'énergie ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais
- y a-t-il eu des moments où vous vous êtes senti triste et abattu ?

1 Toujours 2 La plupart du temps 3 Souvent 4 Parfois 5 Jamais

7. Au cours de ces 4 dernières semaines, y a-t-il eu des moments où votre état de santé physique ou émotionnel vous a gêné dans votre vie sociale et vos relations avec les autres, votre famille, vos amis, vos connaissances ?

- 1 Toujours 2 La plupart du du temps 3 Souvent 4 Parfois 5 Jamais

OLLIVIER Baptiste - Insuffisance corticotrope à la phase aiguë des hémorragies sous-arachnoïdiennes non graves: impact sur la survenue de complications et le pronostic fonctionnel à 1 mois

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Introduction : Les hémorragies sous arachnoïdiennes (HSA) sont des situations de stress aigu pouvant être aggravées par des perturbations hormonales comme l'insuffisance corticotrope, avec un impact possible sur le pronostic. Notre travail avait pour objectif d'évaluer l'incidence de celle-ci à la phase aiguë des HSA non graves et de rechercher un lien avec la survenue de complications et le devenir fonctionnel.

Matériels et méthodes: Les HSA non graves (grade WFNS ≤ 3) sur rupture d'anévrisme endocrânien étaient incluses. Les dosages hormonaux réalisés dans les 48 premières heures étaient : cortisolémie plasmatique, ACTH plasmatique et test au Synacthène® (250 microg). L'insuffisance corticotrope était définie par une cortisolémie plasmatique < 100 ng/ml et/ou un test au Synacthène® négatif (delta cortisol < 90 ng/ml). Les patients étaient suivis sur 30 jours avec recensement des complications : vasospasme, ischémie cérébrale retardée, resaignement, épilepsie, hydrocéphalie et infection. A J30, le Glasgow outcomescale (GOS), le score de Rankin modifié (mRS) et le Short Form-12 (SF-12) étaient calculés.

Résultats: 52 patients ont été inclus de juin 2013 à mars 2016. L'incidence de l'insuffisance corticotrope (CIRCI) est de 17.3% à la phase aiguë. Le taux de complications était de 78% dans le groupe CIRCI contre 44% dans le groupe non CIRCI sans corrélation statistique entre l'état de CIRCI et la survenue de complications, excepté en ce qui concerne les infections. L'insuffisance corticotrope n'était pas statistiquement associée à un pronostic fonctionnel plus défavorable à 1 mois.

Conclusion : L'insuffisance corticotrope est fréquente à la phase aiguë d'une HSA non grave mais elle n'est pas associée à un taux de complications supérieur ni à un pronostic fonctionnel plus défavorable à 1 mois.

Critical Illness - Related Corticosteroid Insufficiency after Non-severe Acute Aneurysmal Subarachnoid Haemorrhage: Impact on complications and early outcome

Introduction: Aneurysmal subarachnoid haemorrhage (ASAH) is a life threatening condition that may be aggravated by hormonal disturbances such as critical illness-related corticosteroid insufficiency (CIRCI). Our study aimed to assess the incidence of CIRCI in acute non-severe SAH and seek a connection with the occurrence of complications and functional outcome.

Methods: Patients with non-severe SAH (WFNS grade ≤ 3) were included. Hormonal assays were collected in the first 48 hours: baseline and stimulated cortisol (after 250 μ g of Synacthene®) and ACTH. CIRCI was defined by a random total cortisol of < 100 ng/ml or a Δ cortisol of < 90 ng/ml. Patients were followed for 30 days with identification of complications: vasospasm, delayed cerebral ischemia, rebleeding, seizure, hydrocephalus and infection. After 30 days, Glasgow outcome scale (GOS), modified Rankin scale (mRS) and the Short Form-12 (SF-12) were assessed by phone conversation.

Results: 52 patients were included from June 2013 to March 2016. The incidence of CIRCI was 17.3% in the acute phase. The overall complications incidence was 78% in the CIRCI patients versus 44% in the none CIRCI patients but there was no correlation between CIRCI and the occurrence of complications except infections. CIRCI was not statistically associated with a less favourable outcome.

Conclusion: The present results support earlier findings that CIRCI occurs frequently after ASAH. Furthermore, we have demonstrated that CIRCI was not associated with a higher rate of complication neither less favorable outcome at 1 month.

Rubrique de classement: Anesthésie - Réanimation / Epidémiologie

Mots-clés: hémorragie sous-arachnoïdienne / insuffisance corticotrope / complications / pronostic fonctionnel

Key words: non severe aneurysmal subarachnoid haemorrhage / critical illness-related corticosteroid insufficiency / complications / outcome

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