Is physical activity a trigger factor for subarachnoid hemorrhage?

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IS PHYSICAL ACTIVITY A TRIGGER FACTOR FOR SUBARACHNOID HEMORRHAGE?

L'ACTIVITÉ PHYSIQUE : UNE CIRCONSTANCE DE SURVENUE DE L'HÉMORRAGIE SOUS-ARACHNOIDIENNE ?

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List of abbreviations:

CT: Computerized Tomography

DSA: Digital Subtraction Angiography

ICA: Intracranial aneurysm

MESH: Medical Subject Headings

MET: Metabolic Equivalent of Test

RR: Relative Risk

SAH: Sub-Arachnoid Hemorrhage

ABSTRACT

Introduction Subarachnoid hemorrhage (SAH) is a serious pathology, associated with 43% mortality and significant disability. In the absence of relevant guidelines, some teams advocate that patients harboring an unruptured intracranial aneurysm (ICA) abstain from all sports activity, as a prophylactic precaution. The aim of the present study was to evaluate the impact of physical activity as a risk factor for SAH, through a review of the literature.

Method A systematic literature review was performed for the period 2000 to 2020 in accordance with the PRISMA guidelines. Prospective and retrospective articles reporting more than 50 patients whose physical activity was associated with onset of SAH were included. The main end-point was prevalence of SAH occurring after physical activity. For comparison purposes, the prevalences of other circumstances were calculated to establish a range of frequency.

Results Physical activity appeared to be quite rarely associated with onset of SAH, with a prevalence of 3%, compared to 30% at rest, 7.3% in association with defecation and 4.5% in association with sexual activity.

Age under 60 years, male gender (M/F ratio 1.38) and smoking (67.1%) were associated with onset of SAH during physical activity.

Conclusion Physical activity appears to be a rare trigger factor for SAH. These results are in contrast to the idea that physical activity should, as a precaution, be avoided in patients with unruptured ICA. There is at present no scientific evidence of an association with aneurysmal SAH.

Keywords: Subarachnoid hemorrhage, Unruptured intracranial aneurysm, physical activity, sport.

RESUME

Introduction L'hémorragie sous-arachnoïdienne (HSA) est une maladie grave responsable de 43 % de mortalité et d'un handicap important. Devant l'absence de recommandation, le principe de précaution a conduit certains soignants à déconseiller la pratique sportive chez les patients présentant un anévrisme intracrânien. L'objectif de ce travail était d'évaluer la responsabilité de l'activité physique comme circonstance de la survenue d'une HSA en se basant sur une revue de la littérature.

Méthode Une revue systématique de la littérature selon les critères PRISMA a été réalisée de 2000 à 2020. Des articles prospectifs ou rétrospectifs de plus de 50 patients dont l'activité physique était une circonstance d'hémorragie sous-arachnoïdienne ont été inclus. Le critère de jugement principal était la prévalence de l'HSA survenant après une activité physique. À des fins de comparaison, les prévalences des autres circonstances ont été calculées pour établir un rang de fréquence.

Résultats L'activité physique semble être une circonstance rare dans la survenue de l'HSA avec une prévalence de 3% par rapport au repos (30%), à la défécation (7,3%) ou aux rapports sexuels (4,5%).

Les patients de moins de 60 ans (67 %), les hommes (ratio H/F de 1,38) et les fumeurs (67,1 %) semblaient plus susceptibles d'être victimes d'une HSA lors de la pratique d'une activité physique.

Conclusion

L'activité physique semble être une circonstance rare d'HSA. Ces résultats vont à l'encontre du principe de précaution chez les patients atteints d'un anévrisme intracrânien non rompu, car il n'existe actuellement aucune preuve scientifique d'association de l'activité physique avec l'HSA anévrismale.

Mots clés : Hémorragie sous-arachnoïdienne, Anévrisme cérébral non rompu, activité physique, sport.

1. INTRODUCTION

Subarachnoid hemorrhage (SAH) is a serious disease associated to a 43% of mortality [1] and a capability to go back to previous professional activity in only a third of survivors [2]. Defecation and sexual activity account for 5.3 to 14% of the circumstances in which SAH occurs [3–5]. Venous hypertension due to Valsalva maneuvers is a suggested mechanism for the sudden variation of pressure gradient between intrasaccular and cisternal space responsible for aneurysmal rupture [6,7]. For this reason, the influence of physical activity in favoring aneurysmal rupture has been advocated, by consequence, various teams have suggested, as a prophylactic measure, [8] the abstention of sports in patients known and followed-up for unruptured intracranial aneurysms (IC) [9]. On the other hand, physical activity is clearly associated to a significant reduction of mortality incidence in cardiovascular diseases [10]; such a discrepancy compel us to explore the implication of such alleged danger and its eventual real role in patients with unruptured intracranial aneurysms through a literature review.

2. METHOD

2.1.Search strategy

A systematic review of the literature was performed in accordance to the PRISMA statement[11]. Database queries included PubMed, Medline and Cochrane. The search timeframe included studies from January 2000 to December 2020. A comprehensive search string for keyword and MESH terms related to "subarachnoid hemorrhage" and "physical activity" were used in the search.

2.1.1. Inclusion criteria

To be included in the systematic review, studies should be 1) written in English, 2) be prospective or retrospective, 3) reporting more than 50 patients presenting clear clinical SAH syndrome (as sudden headache, loss of consciousness, nausea/vomiting and evidence of hemorrhage on CT scan or lumbar puncture with or without identification of aneurysms on the imaging), and finally 4) any identified physical activity as one of the circumstances of SAH.

2.1.2. Exclusion criteria

After eliminating double articles, all studies written in other language and published prior to the year 2000, we proceeded to exclude, during the review, all studies in which: 1) patient raw data were not available therefore not analyzable, 2) in which the SAH criteria were not met, 3) physical activity was not analyzed as a factor related to SAH and finally 4) case and autopsy reports respectively.

2.2.Data extraction and analysis

Studies were firstly screened by title and abstract, and included studies were then screened by full text for final inclusion. All authors performed the screening and data extraction for all studies. Features recorded for each study included study design, year of publication, number of patients, inclusion criteria, the circumstances of occurrence of SAHs in absolute number of patients (physical and sexual activity, defecation, non-physical activity), the characteristics of the physical activity performed (kind of sport, degree of intensity) and patients demographic characteristics (sex, age, cardiovascular risk factors, aneurysm features).

2.3. Outcome

Prevalence of SAH occurring after physical activity (within 2 hours) was the primary end-point. Prevalence of SAH occurring after other circumstances (sexual activity, defecation or

non-physical activity as lying down, sleeping/resting or sitting down, watching TV, chatting, reading) were calculated too in order to establish a frequency range.

Secondary end-point included:

- the characteristics of the physical activity performed: type of sport (leisure sport, extreme sport, competitive sport), proportion of moderate to intense sport: Metabolic Equivalent of Task (MET) > 6 (score indicating the degree of intensity and energy burning during a given physical activity) [12]) and the reported relative risk of presenting a SAH after a sport activity (statistical calculation valued during retrospective analytical studies).

- aneurysmal characteristics: proportion of aneurysmal SAH (objectively determined by an Angio CT or a DSA), location of the aneurysm, aneurysmal size (<5 mm).

- patients' demographic characteristics: age (under 60 years), gender (man/woman ratio), cardiovascular risk factors (presence of high blood pressure, sedentary lifestyle or smoking).

2.4. Statistical analysis

The primary end-point was the prevalence rate of SAH after physical activity defined as the number of cases divided by the total number of study selected and analyzed (expressed as a percentage). Prevalence of SAH occurring after other circumstances was also calculated in order to establish a frequency range. Secondary end-points were the characteristics of

physical activity, aneurysmal and demographic features extracted as categorical variables for case patients (physical activity) and control patients (other circumstance). When a variable was not available in a study, the analysis was performed using only the available data. Confidence interval and p-value concerning the relative risks reported in retrospective studies, were extracted and reported.

3.RESULTS

After removing duplicates, our systematic review identified 14 articles (see also Figure 1); among the latter, 7 were excluded as sports activity was not analyzed as a triggering circumstance [13–19] and 1 being an autopsy report [20]. The remaining 6 were included and analyzed [4,5,21–24] among these 2 articles were from the same team and analyzing the same patients cohort leaving in this way only 5 studies for the final analysis.

3.1. Prevalence of SAH after physical activity

The prevalence of SAH after physical activity was globally estimated to 3% (range from 1,2 % to 4,4%) among 1720 patients whose circumstances were clearly identified. (see also table 1). It is a matter of fact that physical activity is associated very little to the occurrence of

SAH that instead occurs mostly at rest (lying down or sitting) in 30% of patients, defecation and sexual activity were also associated in 7,3% and 4,5% respectively (see also Table 1).

No specific sport was more frequently associated to SAH. The analysis of 3 crossover cases studies [4,21,22] reported a relative risk of SAH occurrence during moderate to intense physical activity ranging from 2.4 (95% CI:1.4-4.2) [22] to 15 (95% CI: 4,3 to 52,2)[4] (see also table 1).

3.2. Patients characteristics of physical activity SAH related

Our demographic analysis identified a 67% proportion of patients under 60 years of age in the "physical activity" SAH related group in contrast with other circumstances in which such a proportion accounted for only 42%. Man gender was predominantly associated to "sports activity" SAH group with a M/W ratio of 1.38, in contrast to the other circumstances in which womens were predominantly represented with a M/W ratio of 0.58). According to cardiovascular risk factors, smoking was present in 67.1% of patient compared to the control group accounting for 30.3%. Concerning to sedentary lifestyle and high blood pressure, the two populations appeared similar. In regards of aneurysm features (location and size), no enough information was available to draw any clear conclusion.

4.DISCUSSION

From our study we found that physical activity constitutes a rare circumstance related to SAH with a prevalence of 3% compared to the 30% at rest, 7,3% during defecation and 4,5% associated to sexual activity respectively.

Patients under 60 years old, men and smokers seemed to be more likely to experience a SAH while performing a physical activity. These findings are consistent with previous reports that describe a rare prevalence of SAH in relation with sports[24][5].

On the contrary, other studies have reported an increased risk of HSA after physical activity with a relative risks ranging from 2.4 (1.4-4.2)[22]to 15 (4,3-52,2) [4]. However, these studies had various limitations as follow: 1) the authors used different cutoff value for intense physical activity, 2) the majority of patients were unable to respond thus all information about circumstances and exposure were collected by family members and finally 3) sexual activity was mixed-up in the physical activity group. The suggested mechanism for this association is an activation of the sympathetic nervous system inducing an increased in heart rate, blood pressure and/or to Valsalva maneuvers during these physical efforts [4,21,22].

In a recent study, Hirasawa et al. have described an adaptative neuroprotective mechanism responsible for a vascular steal from ICA/ECA that might protect against cerebral hyperperfusion during a physiological exercice-induced hypertension[25].

Whereas endurance sports seemed to respond to these mechanisms, strength sports requiring immediate maximal power such as weightlifting, might be the limits of this neuroprotective mechanism [26].

In light of these results, restriction of physical activity in patients with unruptured intracranial aneurysms seems not justifiable. Furthermore physical activity nowadays has demonstrated to be a crucial protective factor in cardiovascular disease [10]. On the other hand, the protective role of physical activity in reducing the risk of SAH is still controversial [13–16]. Shiue et al. identified regular physical activity (defined as sports activity at least 3 times per week) as a protective factor [16] but other studies have not shown significant differences [13,15].

Study limitations.

Our literature review presents an inherent bias as few studies included also patients with non-aneurysmal SAH. In fact the mechanisms of peri-mesencephalic subarachnoid hemorrhage are based on a pathophysiology of venous or capillary rupture and thus do not respond to the same rupture factors as arterial aneurysm hemorrhage[27,28]. The inclusion of non-

aneurysmal SAH therefore constitutes a significant bias although in this review and generally in the literature, the proportion of non-aneurysmal SAH appears quite low being estimated between 13% and 15% [29].

5. CONCLUSION

From our review the physical activity appears to be a rare favoring factor in relation to SAH. These results actually are in contrast with the prophylactic measure of stopping physical activity in patients known with unruptured intracranial aneurysm, in fact up to date no scientific evidence of such a causing/favoring factor in association with aneurysmal SAH are available.

Declarations

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Conflict of interest : none.

Authors' contributions :

This is to certify that all authors have participated in the present study including its conception, writing and critical revision.

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Legends :

Table 1: Literature review of sports activity as circumstances of subarachnoid hemorrhage: demographic, aneurysmal and sports activity features in exposed patients.

Legends 1: M: male, F: female; NA: Not available; SAH: subarachnoid hemorrhage; *: a total prevalence of frequent and other circumstances could not be realized because the different studies did not use the same criteria ; **: Moderate to intense physical activity based on metabolic equivalent of Test (MET >: 6); *** Results concerning the relative risk of having SAH in patients with moderate to intense physical activity (MET>6) using a crossover model.

Figure 1: Flowchart of screened, selected and excluded articles following the PRISMA statement.

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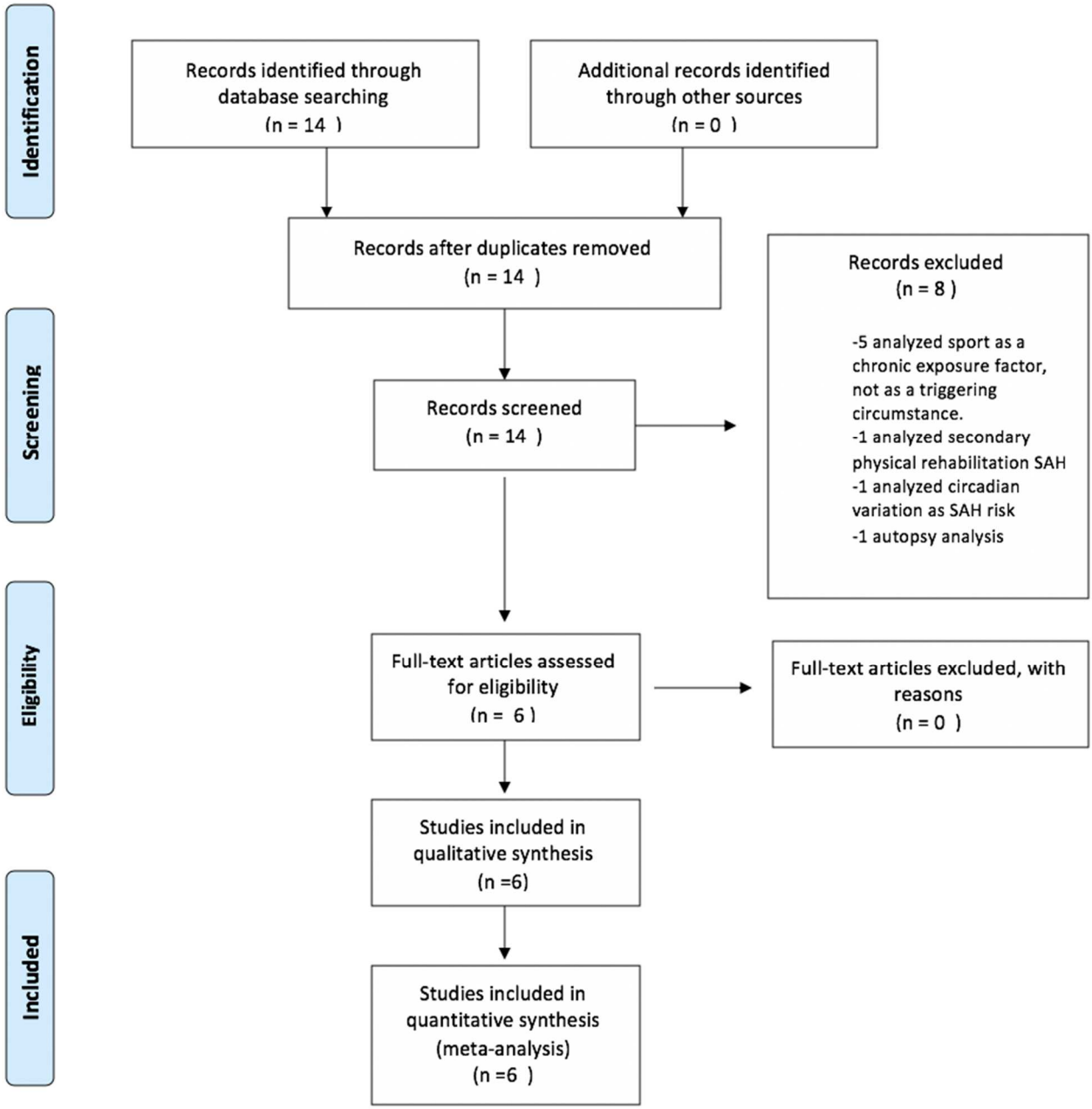
Figure 1 : PRISMA Flowchart



Authors / Date	Fann et al. 2000	Anderson et al. 2003	Matsuda et al. 2007	Vlak et al. 2011	Nanji et al. 2015	Total
Study characteristics						
Design	Analytical retrospective study	Analytical retrospective study	Observational descriptive study	Analytical retrospective study	Observational descriptive study	
Criteria for inclusion						
Activity rupture-time	< 15 minutes	< 2 hours	NA	< 1 hour	NA	
Number of patients	38	338	513	250	581	1720
Prevalence (SAH circumstances)						
Physical activity	6/38 (15,7%)	13/338 (3,8%)	14/513 (2,7%)	11/250 (4,4%)	9/581 (1,5%)	53/1720 (**3 %**)
Frequent circumstances	8/38 (21%)	193/338 (57,1%)	177/513 (34,5%)	13/250 (5,2%)	157/581 (27%)	*
Rest	NA	166/338 (49,1%)	112/513 (21,8%)	NA	157/581 (27%)	435/1442 (**30%**)
Sexual intercourse	6/38 (15,7%)	15/338 (4,4%)	NA	8/250 (3,2%)	NA	29/636 (**4,5%**)
Defecation	2/38 (5,2%)	12/338 (3,5%)	65/513 (12,6%)	5/250 (2%)	NA	84/1149 (**7,3%**)
Others circumstances	24/38 (63,1%)	142/338 (42%)	322/513 (62,7%)	226/250 (90,4%)	415/581 (71,4%)	*
Characteristics physical activity						
Leisure sports	3				7	10
Extreme sport	1	NA	NA	NA	2	3
Sport in competition	0				0	0
Moderate to high intensity	4/6 (67%)	13/13 (100%)	NA	11/11 (100%)	7/9 (78%)	35 (89%)
RR (intense activity)**	15 (4,3-52,2)	2,7 (1,6-4,6)	NA	2,4 (1,4-4,2)	NA	NA
Aneurysm characteristics						
Aneurysmal SAH	NA	51/58 (87%)	14/14 (100%)	NA	3/9 (33%)	68 (84%)
Predominant location	NA	NA	NA	NA	NA	NA
Size (< 5 mm)	NA	NA	NA	NA	NA	NA
Patient characteristics						
Age < 60 years old	NA	35/58 (60%)	11/14 (78%)	NA	8/9 (89%)	54 (67%)
Sex ratio M/F	NA	29/29 : 1	13/1 :13	NA	5/4 : 1,25	47 / 34 : 1,38
High Blood Pressure		23/ 57 (40 %)			3/9 (33%)	26 (40%)
Smoking	NA	43 / 58 (74%)	NA	NA	2/9 (22%)	45 (67,1%)
Sedentarity		14/57 (24%)			NA	14 (27%)