Journal of Neurology (2019) 266:1351–1357
https://doi.org/10.1007/s00415-019-09265-5

ORIGINAL COMMUNICATION

Increased risk for subarachnoid hemorrhage in patients with sleep apnea

Sebastian Zaremba[1] · Luca Albus[1] · Patrick Schuss[2] · Hartmut Vatter[2] · Thomas Klockgether[1] · Erdem Güresir[2]

Received: 11 February 2019 / Revised: 26 February 2019 / Accepted: 26 February 2019 / Published online: 5 March 2019

Abstract

Objectives Recent retrospective studies found sleep disorders, including obstructive sleep apnea and its symptoms to occur more often in patients following aneurysmal subarachnoid hemorrhage, but studies investigating the incidence of subarachnoid hemorrhage in patients with diagnosed obstructive sleep apnea [OSA] compared to other sleep disorders are missing.

Methods To test our hypothesis that aneurysmal subarachnoid hemorrhage occurs more often in patients with OSA compared to other sleep disorders, we analyzed clinical data of 5514 patients with OSA, 4150 with other sleep disorders, and 964 patients with aneurysmal subarachnoid hemorrhage diagnosed between 01/01/2007 and 12/31/2016. As a secondary outcome, location and size of the ruptured aneurysm were calculated based on computer tomography. Incidence of SAH, as well as size and location were compared between patients with OSA and patients with other sleep disorders, diagnosed by polysomnography.

Results Aneurysmal subarachnoid hemorrhage occurred in 8.3 per 100,000 patients with sleep disorders per year. Its incidence was significantly higher in patients with obstructive sleep apnea (14.5 per 100,000 patients per year), compared to other sleep disorders (2.4 per 100,000 patients per year; RR = 6.8; $p = 0.04$). The size of the ruptured aneurysm was larger in patients with OSA (19.0 ± 5.7 mm vs. 8.5 ± 0.5 mm; $p = 0.004$).

Interpretation Aneurysmal subarachnoid hemorrhage occurs more often in patients with diagnosed OSA compared to patients with other sleep disorders, possibly due to increased aneurysm enlargement. Obstructive sleep apnea might be a yet unrecognized risk factor for aneurysmal subarachnoid hemorrhage, and sleep apnea screening should be considered in patients with intracranial aneurysm.

Keywords Subarachnoid hemorrhage · Sleep apnea · Intracranial aneurysm · Sleep disorders · Intracranial bleeding

Introduction

Aneurysmal subarachnoid hemorrhage [SAH] is associated with high morbidity and mortality of approximately 33% within the first week after occurrence [1]. Epidemiological studies from the United Kingdom and the USA have reported prevalence rates of 9.7/100,000 [1] to 14.5/100,000 person per year [2], respectively. For Germany, annual hospitalization rates between 2.8 and 7.3/100,000 have been reported [3]. Symptoms of OSA include snoring and more frequent nocturnal awakenings and have been retrospectively reported by 35% of the patients with SAH [4] and occur more often compared to controls [5]. A recent retrospective study found OSA to be present more often in patients with intracranial aneurysms compared to other neurosurgical patients, and its coincidence might be associated with unfavorable outcome in these patients, e.g., aneurysm rupture [6]. However, it is unclear if SAH occurs more often in patients with prediagnosed OSA compared to other sleep disorders. In this study, we aimed to investigate the incidence of SAH in a cohort of patients with diagnosed sleep disorders to test our hypothesis that OSA is associated with an increased risk for SAH compared to patients with other sleep disorders.

✉ Sebastian Zaremba
sebastian.zaremba@ukbonn.de

[1] Department of Neurology, University Hospital Bonn, Rheinische Friedrich-Wilhelms-University, Sigmund-Freud-Strasse 25, 53127 Bonn, Germany

[2] Department of Neurosurgery, Rheinische Friedrich-Wilhelms-University, Bonn, Germany

Methods

Study population

We examined data from all patients admitted to Bonn University Hospital, Germany between January 1st, 2007 and January 1st, 2017. The neurosurgical department of the Bonn University Hospital has a well-defined catchment area for neurovascular pathologies (e.g., ruptured and unruptured aneurysms) of approximately 1 million citizens. The three sleep laboratories in the university hospital (Departments of Neurology, Internal Medicine and Ear Nose and Throat Medicine) are the largest sleep disorders program in this area. Data were obtained from the clinical information system (ORBIS, Agfa HealthCare, Bonn, Germany) containing billing and electronic health record data from all patients treated at Bonn University Hospital. Ethics approval was waived by the local institutional review board due to the retrospective nature of the study, and patient consent was not required. We collected patient age, discharge diagnoses, length of stay and date and time of hospital admission and hospital discharge, as well as length of hospital stay (LOS).

Data acquisition

We determined the diagnosis of sleep disorder based on ICD-10 (international classification of diseases, 10th edition) diagnosis codes. In addition, the inpatient database was searched for any patient with a billing diagnosis for SAH based on ICD-10 diagnosis codes (see Fig. 1).

Patients diagnosed with sleep disorders were identified based on documented diagnosis according to the criteria defined by the American Academy of Sleep Medicine in the international classification of sleep disorders (ISCD) in the edition valid at the time of first patient admission with the diagnosis of a sleep disorder in each patient [7], or by documented polysomnographic (PSG) reports. In these cases, complete overnight PSG monitoring for two consecutive nights was required for study inclusion. PSG was performed between 22.00 and 07.00 h, including two-channel electroencephalography, electrooculography, chin electromyography (EMG), electrocardiography, thoracic and abdominal respiratory efforts measured by impedance plethysmography, body position monitored by a position sensor, oxygen saturation measured by pulsoxymetry, surface EMG of tibialis muscles and oronasal airflow recorded by thermistor. Sleep stages and arousal were determined visually in accordance to the standard criteria between January 2007 and December 2011 and according to the AASM criteria from January 2012 to December 2016. For patients with sleep disordered breathing, only periodic limb movements were accepted as comorbidity in this study, as this might be secondary to the sleep-related breathing disorder.

The medical records of all patients coded with the particular billing diagnoses were then reviewed by a member of the study team to confirm the correct diagnoses. In patients with SAH, we reviewed brain scan reports (magnetic resonance imaging/computed tomography) and discharge summaries to confirm the diagnosis. The size and location of the ruptured aneurysm was obtained. In addition, severity of SAH was classified based on documented clinical status

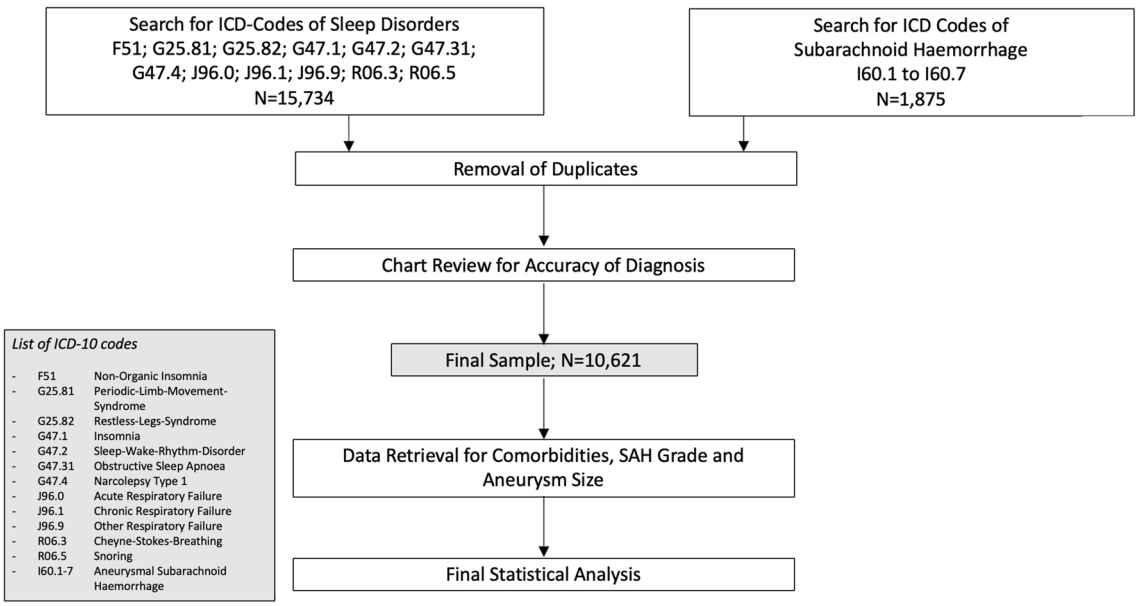

Fig. 1 Flow of data acquisition and analysis throughout the study

on hospital admission according to the classification of Hunt and Hess [HH] [8]. Based on radiology reports, the amount of intracranial hemorrhage was graded using the Fisher CT grading scale [9]. The dates of hospital admission and discharge with SAH and diagnosed sleep disorder were obtained from the electronic patient record to identify its temporal relationship.

All other filed diagnoses were obtained from the database for each patient for exploratory analysis. As height and body weight are nor routinely documented in our clinical database, we used type II diabetes and hyperlipidemia/hypercholesterinemia as surrogate markers for obesity.

Outcome measures

The primary outcome was occurrence of SAH within the 10-year study period in a patient diagnosed with a sleep disorder. We therefore identified patients who were billed for a ICD-10 diagnosis of SAH in combination with a diagnosis of a sleep disorder within the study period, or any patients carrying the diagnosis of SAH or a diagnosis of a sleep disorder on any admission to our hospital within the study period. The timespan between occurrence of SAH and sleep disorder was defined as the time between first admission with the diagnosis of sleep disorder and SAH, respectively.

As a secondary outcome, the size and location of the ruptured aneurysm were compared between patients with and without OSA.

With an exploratory intent the diagnosis of hypertension, defined as ICD-10 codes of essential hypertension, hypertensive heart disease, hypertensive chronic kidney disease, hypertensive heart and chronic kidney disease or secondary hypertension respectively.

Statistical analysis

Rates of SAH in patients with any diagnosed sleep disorders were calculated. In addition, the occurrence of SAH in patients with OSA vs. other sleep disorders was compared using the Chi-square test (likelihood ratio). With an exploratory intent, the size and location of the ruptured aneurysm were compared between SAH patients with and without OSA using the paired *T* test.

Rates of hypertension in patients with SAH with and without OSA were compared with an exploratory intent. In addition, severity of SAH (assessed by HH and Fisher grade on admission) was handled as continuous variables between SAH patients with and without OSA using paired *T* test for independent samples, and likelihood ratio (LR) test was used for categorical variables between SAH patients with and without OSA.

Statistical analysis was performed using SPSS version 24. We considered a two-tailed *P* value of less than 0.05 to be statistically significant.

To identify any confounding variables in our analysis, we designed a logistic regression model with SAH as the dependent variable and OSA, age, gender, diagnosed hypertension, smoking status, diabetes mellitus type 2 and hyperlipidemia/hypercholesterinemia as the independent variables.

Results

A total of 964 patients (38.9% male; $n=375$) with the diagnosis of SAH and 9664 patients (69.3% male; $n=6701$) diagnosed with sleep disorders were treated within the 10-year observational period. Of these patients, 5514 were diagnosed with OSA (57.1%), while 4150 were diagnosed with other sleep disorders but not suffering from OSA. The clinical characteristics of the study cohort are shown in Table 1.

Only nine patients diagnosed with sleep disorders were also diagnosed with SAH during the 10-year study period. Of these nine patients, eight suffered from OSA, while one had been diagnosed with periodic limb movement disorder (PLMD). The incidence of SAH in all patients with sleep disorders equaled 8.3 per 100,000 patients per year. The incidence for SAH was higher in patients with OSA compared to other sleep disorders, 14.5/100,000 per year vs. 2.4/100,000 per year (RR = 6.77; LR = 4.36; $p=0.04$).

If the sleep disorder was diagnosed, OSA was diagnosed prior to SAH in all but one study patient with both diagnoses (mean latency 240.50 ± 291.6 days). In the one patient with SAH prior to OSA, the latency of the diagnosis of OSA was 51 days. In addition, one patient with SAH and OSA did also carry the diagnosis of periodic limb movements during sleep and no other diagnosis of sleep disorder was filed in any of the patients with SAH.

The location of the ruptured aneurysm was documented in 808 of the 964 patients with diagnosed SAH (83.8%). In our cohort, the predominant locations were the vertebrobasilar system and the anterior communicating artery (ACoA, Table 2). The average size of the ruptured aneurysm was significantly larger in patients with OSA compared to patients without OSA (19.00 ± 5.7 mm vs. 8.1 ± 0.4 mm; $p=0.004$, 95% − 18.552 to − 3.627; Fig. 2). However, the average HH and Fisher grades did not differ significantly between patients with and without OSA (H&H 3.02 ± 0.05 vs. 3.14 ± 0.46; $p=0.80$, 95% CI − 1.187 to 0.902; Fisher 3.00 ± 0.00 vs. 2.96 ± 0.03; $p=0.90$, 95% CI − 0.697 to 0.630). In addition, the rate of diagnosed arterial hypertension did not differ significantly between groups. Hypertension was diagnosed in

Table 1 Demographics of study cohort with respect to diagnoses

	All patients	Patients with SAH	Patients with OSA	Patients with other sleep disorders (no OSA)
n	10,621	964	5514	4150
Male (*n*; %)	7070 (66.6%)	375 (38.9%)	4255 (77.1%)	2446 (58,9%)
Age (mean ± st dev)	61.0 ± 15.5	57.1 ± 14.1	59.4 ± 13.5	55.7 ± 23.1
Hypertension (*n*; %)	2914 (27.4%)	281 (29.1%)	1317 (23.9%)	1307 (31.4%)
Smoker (*n*; %)	457 (4.3%)	55 (5.7%)	240 (4.4%)	135 (3.3%)
Insomnia (*n*; %)	89 (0.8%)	0 (0.0%)	7 (0.1%)	82 (2.0%)
Hypersomnia (*n*; %)	217 (2.0%)	0 (0.0%)	28 (0.5%)	189 (4.6%)
Narcolepsy type 1 (*n*; %)	109 (1.0%)	0 (0.0%)	9 (0.2%)	100 (2.4%)
Circadian rhythm disorder (*n*; %)	22 (0.2%)	0 (0.0%)	2 (0.0%)	20 (0.5%)
Periodic limb movement syndrome (*n*; %)	261 (2.4%)	2 (0.2%)	138 (2.5%)	123 (3.0%)

SAH aneurysmal subarachnoid hemorrhage, *OSA* obstructive sleep apnea

Table 2 Localization of the ruptured aneurysm in patients with and without sleep apnea

	All patients with SAH (*N* = 964) (%)	Patients with SAH without OSA (*N* = 957) (%)	Patients with SAH and OSA (*N* = 8) (%)
Middle cerebral artery	20.9	20.9	0
Posterior cerebral artery	1.4	1.4	0
Anterior cerebral artery	1.4	1.4	0
Posterior communicating artery	10.5	10.5	0
Anterior communicating artery	30.2	30.2	50.0
Carotid artery	9.4	9.4	0
Vertebral and basilar artery	18.8	18.8	25.0
Posterior inferior cerebellar artery	2.6	2.6	0
Other	4.7	4.7	25.0
Unknown	18.8	18.8	0.0

SAH aneurysmal subarachnoid hemorrhage, *OSA* obstructive sleep apnea

33.3% of the SAH patients with additional OSA and in 29.6% of those without OSA, respectively. Smoking status was only documented as a comorbidity in 4% of the entire study population. None of the patients with SAH and OSA were a smoker, compared to 55 patients with SAH alone. We observed no significant difference in the prevalence of diabetes (13.9% vs. 11.1%; $p = 0.876$) and hyperlipidemia/hypercholesterinemia (11.1% vs. 13.2%; $p = 0.878$) in SAH patients with and without OSA. None of the other factors, i.e., age ($p = 0.700$), gender ($p = 0.252$), smoking status ($p = 0.994$), hypertension ($p = 0.995$), diabetes ($p = 0.975$), or hyperlipidemia/hypercholesterinemia ($p = 0.842$) were significant predictors of SAH in our patient population according to the binary logistic regression analysis.

Discussion

In this retrospective study, we were able to show for the first time that SAH is more common in patients with OSA compared to other sleep disorders. In our sample, the diagnosis of OSA was associated with a 6.8-fold risk for SAH compared to other sleep disorders. In addition, our data indicates that patients with OSA are more likely to have significantly larger ruptured aneurysm compared to SAH patients without OSA.

We found SAH to occur in approximately 8.3/100,000 patients with sleep disorders per year. The risk for SAH was significantly higher in patients with OSA (14.5/100,000 per year) compared to other sleep disorders.

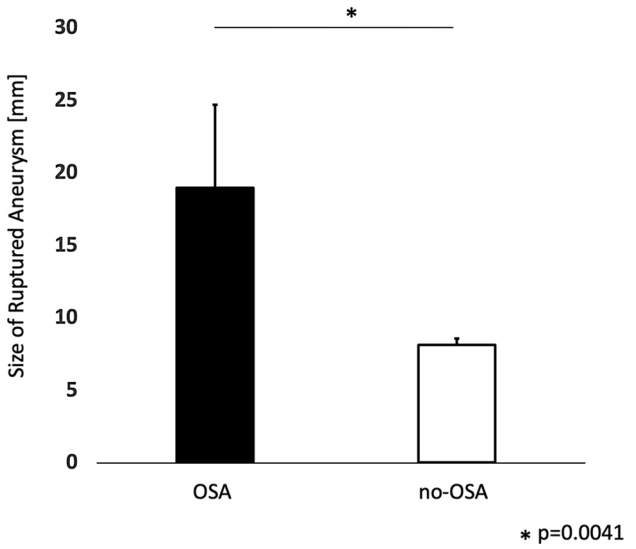

Fig. 2 Obstructive sleep apnea was associated with increased size of the ruptured intracranial aneurysm. Average size of ruptured aneurysm in millimeters (mm) for patients with aneurysmal subarachnoid hemorrhage and with obstructive sleep apnea (OSA) or without obstructive sleep apnea (no OSA)

The rate of SAH in patients with OSA doubled the rate previously reported for the general population of Germany (2.8 to 7.3/100,000) [3]. Symptoms of OSA are reported more often by patients with SAH compared to controls [5]. A recent study found increased rates of OSA in patients previously diagnosed with intracranial aneurysms and SAH [6]. OSA was diagnosed based on clinical symptoms and confirmed by polysomnography (PSG) following SAH in that study. It is not reported if any of the study patients were diagnosed with OSA prior to SAH. Given the higher rate of aneurysm rupture and poorer HH grade in the OSA group of that study, one can assume that impairment of neurological function and disability following SAH might result in increased rates of OSA in that study cohort [10]. In our study, the diagnosis of OSA based on PSG was made prior to the diagnosis of SAH in all but one patient. In the latter patient, OSA was diagnosed only 51 days following SAH (HH grade 1). Given this short time period, one might assume that OSA was already present along with occurrence of SAH in this patient. In all other patients with SAH and OSA, the sleep-related breathing disorder was diagnosed prior to SAH. We hypothesize that OSA might have been able to alter the clinical course of these patients with intracranial aneurysm prior to SAH.

The high rate of SAH in patients with OSA in our study population compared to patients with other sleep disorders might indicate that OSA is associated with an increased risk for SAH. Previously, OSA has been postulated to be associated with unfavorable outcome in patients with intracranial aneurysms including aneurysm rupture based on retrospective studies [6, 11]. Additionally, we found that the size of the ruptured aneurysm was significantly larger in SAH patients with OSA, compared to patients without OSA. Similarly, Bir et al. reported an increased rate of wide-necked aneurysms (>4 mm) in patients with OSA and postulated that OSA might favor the enlargement of the aneurysm diameter [6]. Additionally, Burns et al. found that a larger intracranial aneurysm is more likely to grow [12]. Studies in patients with aortic aneurysm found similar negative effects of OSA on the progression of aneurysm size in patients with thoracic and abdominal aortic aneurysm [13–15]. This is of critical concern, as aneurysm size has been widely accepted to be among locations the most important predictor for rupture of intracranial [16, 17] and aortic aneurysms [18]. We assume that the enlargement in aneurysm size mediated by OSA might be involved in the increased rate of SAH in patients with OSA reported here.

The known risk factors for development, enlargement and rupture of intracranial aneurysm include hypertension and low body mass index [BMI], beside smoking, alcohol consumption, age and female gender [19, 20]. As expected, most of the patients with SAH in our population were female, i.e., 61.1%, while only 30.7% of the patients with sleep disorders were female and only 22.9% in the patients with OSA, respectively. This indicates the diametral risk profile of patients with SAH vs. those with sleep disorders is similar to previous studies in these populations [21, 22]. None of the known risk factors for SAH (age, gender, smoking or hypertension) were significant predictors of SAH in our population of patients with sleep disorders, likely due to the low rate of SAH. Hypertension, particularly during sleep is often observed in OSA patients, who often present causes a diminished fall or even rise in nocturnal blood pressure [23]. Previous authors have postulated that hypertension may be involved in the linking of OSA to the increased size of intracranial aneurysm [6]. Nevertheless, the rate of diagnosed hypertension did not differ significantly between the groups of SAH patients with and without OSA in our study cohort. We might have insufficient power to detect the difference between groups given the low incidence of SAH. However, previous studies found the role of hypertension as a risk factor for aneurysm enlargement as it differs between thoracic and abdominal aneurysm, which might indicate the role of other factors beyond physical stress. For abdominal and thoracic aortic aneurysms, inflammatory processes, oxidative stress and arteriosclerosis, as well as sympathetic activation have been postulated to mediate the negative effects of OSA on aortic aneurysms [24]. In sleep apnea, periodic cessation of breathing results in intermittent hypoxia and arousal from sleep, as well as sleep fragmentation. All of these factors lead to sympathetic activation. In addition, hypoxemia causes oxidative stress, and might trigger vessel wall inflammation (see [25] for review). Together, these

factors may trigger aneurysm enlargement beyond chronic hypertension. OSA has been reported to induce systemic and local (endothelial) pro-inflammatory effects [26, 27]. Inflammatory processes have been found to play a role in the formation of some aortic aneurysms and might orchestrate the pathophysiological mechanisms involved in the genesis of aneurysms [24, 28]. Nevertheless, it is unclear if all pathophysiological mechanisms of aortic aneurysm translate to intracranial aneurysms. Future studies investigating the effect of OSA-induced sympathetic activation, oxidative stress, inflammation and physical challenge due to hypertension in patients with intracranial aneurysm are wanted.

A previous study has reported worse outcomes following SAH in patients later diagnosed with OSA [6]. OSA was associated with higher rates of diabetes mellitus, prior stroke, cardiac events, development of intracranial vasospasms and hypertension in that study. Studies in other populations of ICU patients have found OSA to be further associated with impaired respiratory outcomes. Thus, increased rates of reintubation, mechanical ventilation and respiratory complications have been reported [29]. Our data are not able to elucidate potential negative effects of OSA following SAH. However, we speculate that most of OSA found in surgical ICU patients may translate to ICU patients with SAH. Studies to further investigate potential negative effects of OSA during this critical time period following SAH are needed.

Our study is limited by the low overall number of SAH patients with sleep disorders and the low rate of diagnosed OSA in the SAH patients in our study collective. Therefore, we were not able to adjust our analysis for any confounding factors, such as age, gender, hypertension or smoking status. Given the high rate of undiagnosed OSA in the general population due to the lack of day- and night-time symptoms [30], we speculate that OSA might have been present in more than 987 patients with SAH included in our study. This might result in an even higher incidence of SAH in sleep disorders and OSA. However, it is known that the risk for SAH is increased in female patients with low BMI [20] potentially resulting in lower rates of OSA compared to the general population—risk factors for OSA include male gender and obesity [31, 32]. We were not able to calculate the BMI for our study patients, given the study design (retrospective analysis of discharge reports). However, we assume that difference in BMI would not change the conclusion of the present study, given the inverse relationship with BMI for OSA and SAH. We are further not able to draw any conclusions on the effects of cigarette smoking, a known risk factor for SAH in our cohort. Smoking status is not routinely identified as a comorbidity in most hospitals in Germany. Although, all patients diagnosed with OSA in our institution were prescribed continuous positive airway pressure (CPAP), it remains unclear based on our data, and how many of the patients were using CPAP on a regular basis. Prospective studies in patients with intracranial aneurysm using reliable diagnostic methods for OSA and confounder control are required to further investigate the occurrence rate of SAH in patients with and without OSA. Very large multicenter studies in patients with sleep disorders are needed to further elucidate the increased risk for SAH in OSA patients suggested by our data.

Due to the single center design of our study, some of the patients diagnosed with a sleep disorder at our institution might have to be treated for SAH at another hospital. We might underestimate the rate of SAH in patients with sleep disorder based on our study. However, as our hospital is the only neurosurgical referral center in the area, we assume that the vast majority of patients with SAH were treated in our hospital. Multicentric studies investigating the clinical data from neurological, neurosurgical and traumatological hospitals throughout Germany are needed to further elucidate the interaction of sleep disorders and SAH, especially given the low incidence of SAH in the general population.

We here report for the first time the incidence of subarachnoid hemorrhage in patients with sleep apnea compared to other sleep disorders and found an increased rate of SAH in patients with OSA. Aneurysm size was significantly larger in patients with SAH and OSA compared to patients with SAH alone. However, the rates of hypertension in SAH did not differ depending on OSA status, potentially pointing at alternative pathophysiological mechanism mediating negative effects of OSA on intracranial aneurysms. Our data suggests that OSA might be a yet unrecognized risk factor for SAH, and sleep apnea screening might be indicated in patients with intracranial aneurysm. Prospective studies using competitive methods to diagnose OSA are needed to confirm our finding and to investigate the role of OSA as a risk factor for SAH and the mediating mechanisms. If our findings can be confirmed in large-scale prospective multicenter studies, this might advocate for sleep apnea screening in patients with intracranial aneurysm, as increasingly recognized in patients with other cerebro- and cardiovascular disorders.

Author contributions SZ designed the study protocol, performed data acquisition, analyzed the data and wrote the first draft of the manuscript. LA helped in acquisition and analysis of the data and helped to improve the quality of the manuscript. PS contributed to the preparation of the final manuscript. HV contributed to the preparation of the final manuscript. TK contributed to the preparation of the final manuscript. EG designed the study protocol, helped in the analysis of the study data and contributed to the preparation of the final manuscript.

Compliance with ethical standards

Conflicts of interest SZ does not have any conflicts of interest. LA, PS, HV and TK do not have any conflicts of interest. EG has no conflicts of interest.

References

1. Pobereskin LH (2001) Incidence and outcome of subarachnoid haemorrhage: a retrospective population based study. J Neurol Neurosurg Psychiatry 70:340–343
2. Shea AM, Reed SD, Curtis LH et al (2007) Characteristics of nontraumatic subarachnoid hemorrhage in the United States in 2003. Neurosurgery 61:1131–1137 **(discussion 1137–1138)**
3. Walendy V, Strauss C, Rachinger J et al (2014) Treatment of aneurysmal subarachnoid haemorrhage in Germany: a nationwide analysis of the years 2005–2009. Neuroepidemiology 42:90–97
4. Schuiling WJ, Rinkel GJ, Walchenbach R et al (2005) Disorders of sleep and wake in patients after subarachnoid hemorrhage. Stroke 36:578–582
5. Alaqeel AM, Almasri SH, Alotaibi NM et al (2013) Prevalence of symptoms and risk of sleep apnea in patients with ruptured cerebral aneurysm. Neurosciences (Riyadh) 18:248–251
6. Bir SC, Nanda A, Cuellar H et al. Coexistence of obstructive sleep apnea worsens the overall outcome of intracranial aneurysm: a pioneer study. J Neurosurg 2017:1–12
7. AASM (2005) The international classification of sleep disorders: diagnostic and coding manual, 2nd edn. Westchester, IL
8. Hunt WE, Hess RM (1968) Surgical risk as related to time of intervention in the repair of intracranial aneurysms. J Neurosurg 28:14–20
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. Morrone E, Pistarini C, Cazzulani B et al (2016) Sleep apnea after posterior cerebral artery aneurysm rupture and elevated intracranial pressure: a Chiari-like syndrome. Sleep Med 21:42–44
11. Chernyshev OY, Bir SC, Maiti TK et al (2017) Changing paradigm in the management of elderly patients with intracranial aneurysms: an institutional review. J Clin Neurosci
12. Burns JD, Huston J 3rd, Layton KF et al (2009) Intracranial aneurysm enlargement on serial magnetic resonance angiography: frequency and risk factors. Stroke 40:406–411
13. Barone-Rochette G, Thony F, Boggetto-Graham L et al (2015) Aortic expansion assessed by imaging follow-up after acute aortic syndrome: effect of sleep apnea. Am J Respir Crit Care Med 192:111–114
14. Mason RH, Ruegg G, Perkins J et al (2011) Obstructive sleep apnea in patients with abdominal aortic aneurysms: highly prevalent and associated with aneurysm expansion. Am J Respir Crit Care Med 183:668–674
15. Tachikawa R, Hamada S, Azuma M et al (2014) Impact of obstructive sleep apnea on abdominal aortic diameters. Am J Cardiol 114:618–623
16. Shojima M, Morita A, Nakatomi H et al (2017) Size is the most important predictor of aneurysm rupture among multiple cerebral aneurysms: post hoc subgroup analysis of unruptured cerebral aneurysm study Japan. Neurosurgery
17. Brown RD Jr, Broderick JP (2014) Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening. Lancet Neurol 13:393–404
18. Brewster DC, Cronenwett JL, Hallett JW Jr et al (2003) Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. J Vasc Surg 37:1106–1117
19. Guresir E, Vatter H, Schuss P et al (2013) Natural history of small unruptured anterior circulation aneurysms: a prospective cohort study. Stroke 44:3027–3031
20. Francis SE, Tu J, Qian Y et al (2013) A combination of genetic, molecular and haemodynamic risk factors contributes to the formation, enlargement and rupture of brain aneurysms. J Clin Neurosci 20:912–918
21. Lindbohm JV, Kaprio J, Jousilahti P (2016) et.al. Sex, Smoking, and Risk for Subarachnoid Hemorrhage. Stroke 47:1975–1981
22. Fietze I, Laharnar N, Obst A et al (2018) Prevalence and association analysis of obstructive sleep apnea with gender and age differences—results of SHIP-trend. J Sleep Res 1:e12770 **(Epub ahead of print)**
23. Kario K (2009) Obstructive sleep apnea syndrome and hypertension: ambulatory blood pressure. Hypertens Res 32:428–432
24. Gaisl T, Bratton DJ, Kohler M (2015) The impact of obstructive sleep apnoea on the aorta. Eur Respir J 46:532–544
25. Zaremba S, Güresir E (2019) Is there a causal relationship between obstructive sleep apnea and the pathophysiology of intracranial aneurysm? Somnology. https://doi.org/10.1007/s11818-019-0191-y **(epub ahead of print)**
26. Nadeem R, Molnar J, Madbouly EM et al (2013) Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. J Clin Sleep Med 9:1003–1012
27. Jelic S, Le Jemtel TH (2008) Inflammation, oxidative stress, and the vascular endothelium in obstructive sleep apnea. Trends Cardiovasc Med 18:253–260
28. Eagleton MJ (2012) Inflammation in abdominal aortic aneurysms: cellular infiltrate and cytokine profiles. Vascular 20:278–283
29. Mokhlesi B, Hovda MD, Vekhter B et al (2013) Sleep-disordered breathing and postoperative outcomes after elective surgery: analysis of the nationwide inpatient sample. Chest 144:903–914
30. Kapur V, Strohl KP, Redline S et al (2002) Underdiagnosis of sleep apnea syndrome in U.S. communities. Sleep Breath 6:49–54
31. Senaratna CV, Perret JL, Lodge CJ et al (2017) Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev 34:70–81
32. Jordan AS, McSharry DG, Malhotra A (2014) Adult obstructive sleep apnoea. Lancet 383:736–747