

Original Article

Management of postoperative cerebral vasospasm in skull base surgeries: A systematic review of case reports and series

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ABSTRACT

Background: This study provides a comprehensive overview of the management of postoperative vasospasm after skull base surgeries. This phenomenon is rare but can be of serious sequelae.

Methods: Medline, Embase, and PubMed Central were searched, along with examining the references of the included studies. Only case reports and series that reported vasospasm following a skull base pathology were incorporated. Cases with pathologies other than skull base, subarachnoid hemorrhage, aneurysm, and reversible cerebral vasoconstriction syndrome were excluded from the study. Quantitative data were presented as mean (Standard Deviation) or median (range), accordingly, while qualitative data were presented as frequency (percentage). Chi-square test and one-way analysis of variance were used to assess for any association between the different factors and patient outcomes.

Results: We had a total of 42 cases extracted from the literature. The mean age was 40.1 (± 16.1) with approximately equal males and females (19 [45.2%] and 23 [54.8%], respectively). The time to develop vasospasm after the surgery was 7 days (± 3.7). Most of the cases were diagnosed by either angiogram or magnetic resonance angiography. Seventeen of the 42 patients had pituitary adenoma as the pathology. Anterior circulation was nearly affected in all patients. For management, most patients received pharmacological with supportive management. Twenty-three patients had an incomplete recovery as a result of vasospasm.

Conclusion: Vasospasm following skull base operations can affect males and females, and most patients in this review were middle-aged adults. The outcome of patients varies; however, most patients did not achieve a full recovery. There was no correlation between any factors and the outcome.

Keywords: Cerebral vasospasm, Skull base surgery, Skull base tumors, Systematic review, Vasospasm management, Vasospasm

INTRODUCTION

Although cerebral vasospasm is a known complication of subarachnoid hemorrhage (SAH), there have been several reports in which vasospasm has occurred following tumor resection.^[22,31] Furthermore, vasospasm that complicates an intracranial surgery carries high morbidity and

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mortality because this condition can be challenging to recognize in time for appropriate intervention. Since prospective studies and randomized clinical trials can be challenging to conduct given the limited number of cases, case reports can serve as an essential source of information.

The present study aims to provide a comprehensive overview of the management of postoperative vasospasm after skull base surgeries alongside the patients' demographic data, diagnostic methods, and the outcomes of the surgeries. Statistical analysis is conducted to determine which factors are attributed to the complete recovery.

MATERIALS AND METHODS

In this systematic review, Medline, Embase, and PubMed Central (PMC) were searched without any limitations on the date of publication. The keywords used in combinations were as follows: cerebral vasospasm, cranial vasospasm, cerebrovasospasm, brain vasospasm, postoperative, postsurgery, postoperative complication, postoperative vasospasm, removal, and resection. The included papers were supplemented by examining the references of the papers. Case reports and series that reported cerebral vasospasm following skull base surgeries were included in the study, while reports of cases other than skull base pathologies, cases with SAH, aneurysms, and reversible cerebral vasoconstriction syndrome were excluded from the study. The search was conducted in accordance with a predetermined protocol and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis. Quantitative data were presented as the mean and standard deviation or median and range, while qualitative data were presented as frequency and percentage. Chi-square test and one-way analysis of variance (ANOVA) were used to analyze for any association between the examined factors and patient outcome.

Eligibility and selection criteria

Case reports and series of skull base surgeries associated with postoperative vasospasm were the only studies included in the study, while studies that included SAH, aneurysm, and reversible cerebral vasospasm syndrome were excluded from the study. Titles and abstracts that met our prespecified criteria were reviewed by two independent investigators and in duplicate. After that, the same investigators assessed the full-text of the included studies for eligibility. In addition, the relevant information was extracted from the studies that met our inclusion criteria in a prespecified data collection sheet. A third investigator would be needed to resolve any disagreement if it was to occur.

Data synthesis and analysis

The data extracted from the included articles (author, year of publication, country, and journal), study design (case report and case series), demographics (age of subjects and sex), clinical features (presentation and time to develop vasospasm), disease features (pathology, location, and which circulation affected), diagnostics techniques (imaging such as angiogram, magnetic resonance angiography [MRA], or computed tomography angiography [CTA]), type of surgery, type of management (pharmacology, intervention, or supportive), the outcome (whether it was complete [patient neurological status has returned to its baseline immediate postoperative status], incomplete recovery [no or gradual improvement in deficit] or death), follow-up, and the outcome of the follow-up. Studies were screened based on the inclusion and exclusion criteria that were mentioned above by one group of two authors independently.

The senior author was involved in the process of reviewing and discussing the variations in the study selection and the quality of the papers. SPSS (Release 23.0.0.0, IBM, USA) was used in the process of data management as well as the analysis. Descriptive statistics were used in the formulation of a summary of baseline demographics and clinical characteristics. Categorical variables will be expressed in the form of frequency and percentages, while continuous variables will be expressed as mean and standard deviation, or median and interquartile range if not normally distributed. To determine the association between the patients characteristics and the outcomes of the post-operative vasospasm, ANOVA and Chi-square tests were used accordingly.

RESULTS

Embase, Medline, and PMC records generated 680, 208, and 152 articles, respectively. In the total of 1040 articles, 123 duplicates were excluded from the study. Title and abstract screening excluded 865 articles. Fifty-two papers were potentially relevant and underwent full-text screening, which resulted in the exclusion of 23 papers for lack of full text (10 papers), pathologies other than skull base (8), and SAH (5) [Figure 1].

The net relevant cases were 29, supplemented by reference screening relevant articles, and 11 were added manually. Twenty-nine articles reporting 42 cases are included, analyzed, and summarized in Table 1.^[1,2,5-8,12,14-18,23-26,28-30,32,33,35,36,38,42,43,46-48,3,11,13,19,20,27,37,39,41,44,45]

Presentation and diagnosis

In terms of demographics, females comprised 23 cases versus 19 males. The mean age was 40.1 (± 16.1). Regarding clinical

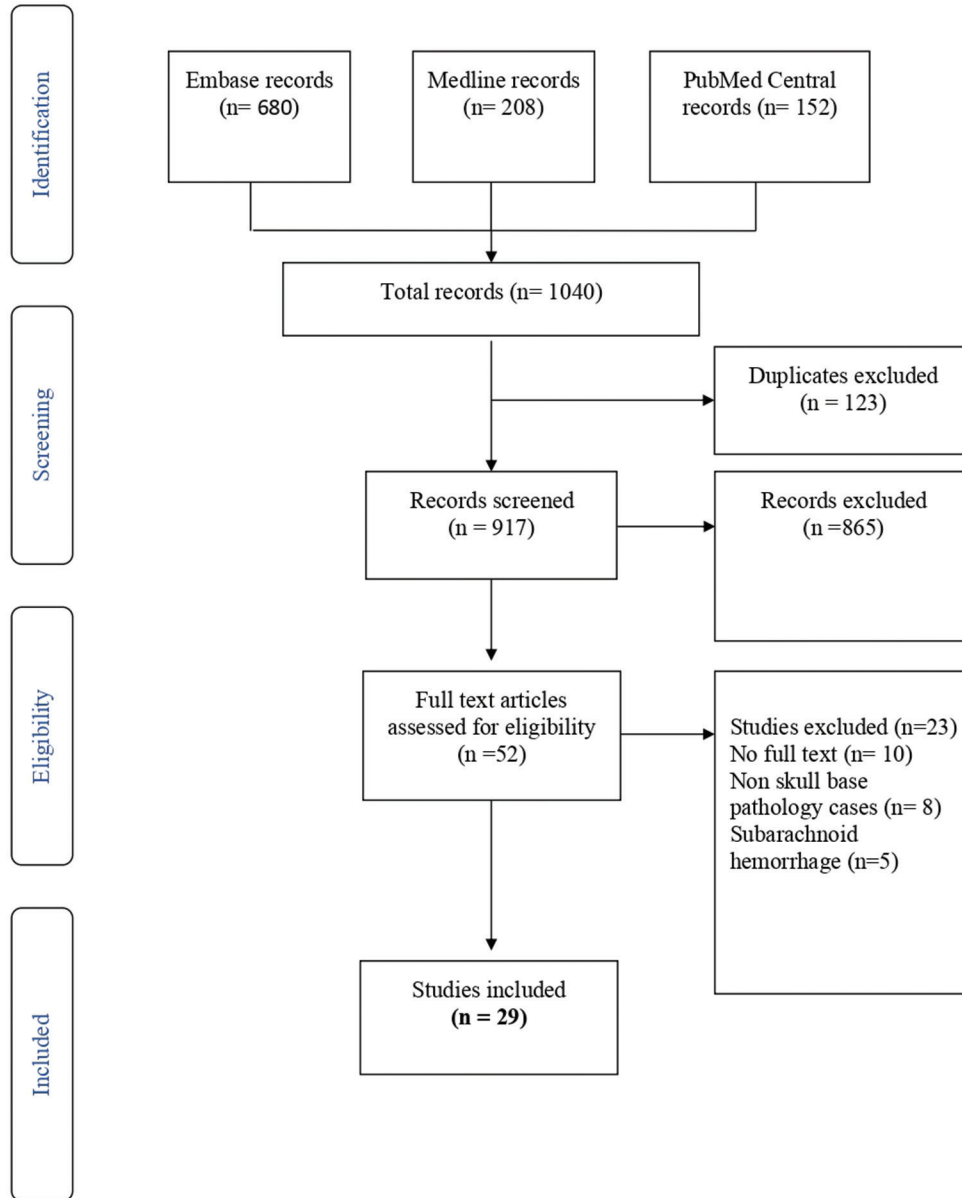


Figure 1: Preferred reporting items for systematic reviews and meta-analyses flow diagram. n: Number

presentation, visual disturbance was the most significant symptom reported in 42% of cases. Hemiparesis and mental status changes were reported in three each. The majority of cerebral vasospasm cases were diagnosed using cerebral angiography (38.1% of cases) followed by MRA in 23.8%.

Operative data

The performed operations were either endoscopic or open surgeries. Open surgeries with different approaches were reported in 24 cases (57.1%), while endoscopic surgeries comprised 16 cases (38.1%). There was one case of combined endoscopic and open surgery. The most common location of lesions was sellar/suprasellar space in 64.3%

of cases, far from the following location, the posterior fossa, which was reported in 16.7% of cases. The anterior cranial fossa was the least reported location associated with postoperative vasospasm. On the other hand, the most common pathology was pituitary adenoma, comprising of 17 (40.5%) cases followed by meningioma in 9 (21.4%) cases. Craniopharyngioma, schwannoma, and hemangioblastoma comprised 8, 3, and 2 cases, respectively.

Circulation and vasospasm time

Almost all patients had the anterior circulation affected, whether alone (85.7%) or combined (14.3%). The average time to develop vasospasm following surgeries was 7 days

Table 1: Patients characteristics and diagnosis.

Characteristics	Findings
Total patients	<i>n</i> =42
Age (SD)	40.1 (\pm 16.1)
Gender	Male (<i>n</i> =19 [45.2%]) Female (<i>n</i> =23 [54.8%])
Diagnosis method	Angiogram (<i>n</i> =16 [38.1%]) MRA (<i>n</i> =10 [23.8%]) TCD (<i>n</i> =8 [19%]) CTA (<i>n</i> =4 [9.5%]) CT (<i>n</i> =2 [4.8%]) None (<i>n</i> =1 [2.4%]) NR (<i>n</i> =1 [2%])
Pathology	Pituitary adenoma (<i>n</i> =17 [40.5%]) Meningioma (<i>n</i> =9 [21.4%]) Craniopharyngioma (<i>n</i> =8 [19%]) Schwannoma (<i>n</i> =3 [7.1%]) Hemangioblastoma (<i>n</i> =2 [4.8%]) Cavernous Angioma (<i>n</i> =1 [2.4%]) Epidermoid tumor (<i>n</i> =1 [2.4%]) Dermoid cyst (<i>n</i> =1 [2.4%])
Location of the pathology	Sellar and suprasellar (<i>n</i> =27 [64.3%]) Posterior fossa (<i>n</i> =7 [16.7%]) Middle fossa (<i>n</i> =2 [4.8%]) Anterior fossa (<i>n</i> =1 [2.4%])
Circulation is affected	Anterior (<i>n</i> =36 [85.7%]) Both (<i>n</i> =6 [14.3%])
Time to develop vasospasm (Days) (mean [SD])	7 (\pm 3.7)
SD: Standard deviation, MRA: Magnetic resonance angiography, CT: Computed tomography, CTA: Computed tomography angiography, TCD: Transcranial Doppler ultrasonography, NR: Not reported, <i>n</i> : Number	

(\pm 3.7). The earliest time to develop vasospasm was one day following a case of hemangioblastoma and a case of phenoclinoidocavernous meningioma. On the other hand, the latest period was 14 days after the epidermoid tumor and craniopharyngioma resection.

Management and outcome

In terms of management, data are summarized in Table 2. Out of the 42 patients, 19 (38.7%) received nimodipine as a pharmacological treatment option. The treatment strategy used in most cases was pharmacological and supportive management, mainly in the form of hypertensive, hyperdynamic, and hypervolemic therapy. Fourteen cases received no form of management. Nine cases (21.4%) underwent interventional management of cerebral vasospasm through angiography with intra-arterial calcium channel blockers, balloon angioplasty, or both. Patients' outcomes were divided into three possibilities: complete recovery, incomplete recovery, and death. Despite all the

Table 2: Management and outcomes.

Outcome	Findings
Total patients	<i>n</i> =42
Type of management	Pharmacological and supportive management (<i>n</i> =15 [35.7%]) Received nothing (<i>n</i> =14 [33.3%]) Supportive (<i>n</i> =4 [9.5%]) Intervention (<i>n</i> =3 [7.1%]) Intervention and pharmacological (<i>n</i> =3 [7.1%]) Supportive and intervention (<i>n</i> =2 [4.8%]) Supportive and pharmacological and intervention (<i>n</i> =1 [2.4%])
Pharmacology management	Nimodipine (<i>n</i> =15 [38.7%]) Combination (<i>n</i> =4 [9.5%]) Dexamethasone (<i>n</i> =2 [4.8%]) Milrinone (<i>n</i> =1 [2.4%]) NR (<i>n</i> =22 [43.1%])
Surgery	Open (<i>n</i> =24 [57.1%]) Endoscopic (<i>n</i> =16 [38.1%]) Combined (<i>n</i> =1 [2.4%]) NR (<i>n</i> =3 [5.9%])
Outcome	Incomplete recovery (<i>n</i> =23 [54.8%]) Complete recovery (<i>n</i> =9 [21.4%]) Death (<i>n</i> =10 [23.8%])
NR: Not reported, <i>n</i> : Number	

different treatment strategies and interventions, most of the cases, 23 (54.8%), made an incomplete recovery. Death was the outcome in 10 (23.8%) patients. Finally, only 9 patients (21.4%) made a complete recovery.

Inferential

Cross-tabulation between the outcome and the management strategy and statistical analysis showed no significant correlation between the outcome and whether the patient was managed with pharmacological and supportive, pharmacological and interventional, supportive and interventional, supportive only, interventional only, or no management at all [Table 3]. Moreover, the type of tumor pathology resulting in cerebral vasospasm development, whether pituitary adenoma, meningioma, or craniopharyngioma, was not statistically significant when correlated with the outcome. One-way ANOVA was utilized to examine the correlation between the time to develop vasospasm was associated with better or worse outcomes. However, the correlation was statistically insignificant. In addition, factors such as age, involved circulation, and type of surgery were also investigated as potential contributors to the outcome, yet they did not demonstrate any statistically significant associations.

Table 3: Association between the patient's characteristics and the outcome.

Associated factor	Outcome	P-value (ANOVA or Chi-square)
Age	Outcome	0.62
Pathology	(Complete recovery,	0.97
Time to develop vasospasm	recovery,	0.38
Type of management	Incomplete	0.64
Affected circulation	recovery, Death)	0.72
Surgery		0.56

ANOVA: Analysis of variance

Patients who had a complete recovery

A total of nine patients had a complete recovery, and their data are summarized in Table 4. Out of them, six were female. The mean age of those patients was 35.6 years (± 17.6). Cerebral angiography and MRA were the most common diagnostic modality used in this sample, four each. Only one used CTA. In terms of pathology, pituitary adenoma was the dominant one, found in 3 cases (33.3%) of those who made a complete recovery followed by craniopharyngioma and meningioma with 2 cases (22.2%) each. The sellar/suprasellar space was the location with the majority of cases, 7 (77.8%), followed by the posterior fossa, 4 (22.2%). Five of them underwent open surgeries, while four had endoscopic surgeries. The anterior circulation was affected in all of them, with two having both anterior and posterior circulations involved. The management was divided into pharmacological and supportive, no management, interventional only, and pharmacological and interventional, with 3, 3, 2, and 1 case(s), respectively.

DISCUSSION

Brain tumor surgeries can lead to several potential complications, one of which is cerebral vasospasm.^[43,34] Cerebral vasospasm is a pathological narrowing of the blood vessels in the brain, which can reduce blood flow and lead to ischemia. This can have significant implications for the patient, including decreased quality of life.^[21]

Cerebral vasospasm is a well-known complication following SAH, but it can also occur following brain tumor surgeries.^[12,40] The exact mechanisms underlying cerebral vasospasm are not well understood, but several factors are thought to contribute, including injury to the blood vessel walls, increased production of vasoactive substances, and changes in blood flow dynamics.^[21]

The incidence of cerebral vasospasm following brain tumor surgeries is not well established, but it is estimated to be exceedingly rare.^[12] Furthermore, the predisposing factors are hard to determine due to the rarity of cases. However, one of

Table 4: Characteristics of the patients who had complete recovery.

Characteristics and outcomes of patients who had a complete recovery	Findings
Total patients	$n=9$
Age (mean (SD))	35.6 (± 17.6)
Gender	Female ($n=6$ [66.7%]) Male ($n=3$ [33.3%])
Diagnosis method	MRA ($n=4$ [44.4%]) Angiogram ($n=4$ [44.4%]) CTA ($n=1$ [11.1%])
Pathology	Pituitary adenoma ($n=3$ [33.3%]) Craniopharyngioma ($n=2$ [22.2%]) Meningioma ($n=2$ [22.2%]) Schwannoma ($n=1$ [11.1%]) Hemangioblastoma ($n=1$ [11.1%])
Location of the pathology	Sellar and suprasellar ($n=7$ [77.8%]) Posterior fossa ($n=2$ [22.2%])
Affected circulation	Anterior ($n=7$ [77.8%]) Both ($n=2$ [22.2%])
Type of management	Pharmacological and supportive management ($n=3$ [33.3%]) Received nothing ($n=3$ [33.3%]) Intervention ($n=2$ [22.2%]) Intervention and pharmacological ($n=1$ [11.1%])
Pharmacology management	Combination ($n=3$ [33.3%]) Nimodipine ($n=1$ [11.1%]) Dexamethasone ($n=1$ [11.1%]) Milrinone ($n=1$ [11.1%])
Interventional management	Angiograph with CCB infusion ($n=3$ [33.3%]) Balloon angioplasty ($n=1$ [11.1%])
Surgery	Endoscopic ($n=5$ [55.6%]) Open ($n=4$ [44.4%])
Time to develop vasospasm (Days) (mean [SD])	8.5 (± 4)

SD: Standard deviation, MRA: Magnetic resonance angiography, CTA: Computed tomography angiography, n : Number

the main reasons skull base tumors are particularly prone to cause cerebral vasospasm is because they are often large. This provides a greater opportunity for manipulation of vessels during surgery, which can increase the risk of vasospasm. In addition, the epidural approach commonly used during skull base surgeries often results in a greater amount of blood in the operative field and basal cisterns compared to tumors in other areas. This can also contribute to the development of vasospasm.^[6]

The diagnosis of cerebral vasospasm is typically made using a combination of clinical examination, imaging studies, and blood flow measurements. Computed tomography and

magnetic resonance imaging are commonly used to visualize the blood vessels and assess blood flow, while transcranial Doppler ultrasound and digital subtraction angiography can be used to measure blood flow directly.^[21]

The treatment of cerebral vasospasm following brain tumor surgeries typically involves a combination of medical and interventional therapies. Medical management may include the use of calcium channel blockers, such as nimodipine, to relax the blood vessels, and improve blood flow. Hemodynamic support, such as maintaining adequate blood pressure and blood flow, may also be used to reduce the incidence and severity of vasospasm. In severe cases, interventional techniques, such as angioplasty, may be necessary to improve blood flow and alleviate vasospasm.^[4] In a study by Bejjani *et al.*, the authors presented a cerebral vasospasm case following a brain tumor resection. They highlighted the importance of maintaining a high index of suspicion for this condition in cases of delayed clinical deterioration after brain tumor surgeries, mainly when the tumor is adjacent to the basal cisterns. They concluded that early recognition and management of this condition could improve the outcome and reverse neurological deficits.^[10]

In another study by Bejjani *et al.*, they retrospectively studied patients with SAH who underwent angioplasty in their institution. One of their objectives was to attempt to determine if there was an association between study outcomes (clinical improvement, outcome at the time of discharge, and long-term outcome) and possible risk factors (patient age, patient sex, Hunt and Hess grade after SAH, interval, number of vessels undergoing angioplasty, day of surgery, and day of angioplasty). Using univariate analysis, they determined that the only significant association was between clinical improvement and interval (<24 h and >24 h) from deterioration to angioplasty. They found no statistically significant association between the other risk factors and any of the study outcome measures.^[9]

To further investigate the association between clinical improvement and interval, a multivariate approach with logistic regression was used. This approach included the additional factors (patient age, patient sex, Hunt and Hess grade at admission, day of angioplasty, and number of vessels undergoing angioplasty). The results of the multivariate analysis showed that the additional factors did not add to the association between improvement and interval. The interval remained a good predictor of patient improvement. This suggests that the interval from deterioration to angioplasty is the most important factor in determining patient outcome.^[9]

In addition, this condition can limit the effectiveness of postoperative treatment and rehabilitation, which can lead to longer recovery times and poorer outcomes. Therefore, it is important to monitor patients closely following brain surgery and to quickly identify and treat any signs of

cerebral vasospasm to minimize the risk of long-term complications.^[4] There must be vigilance in monitoring patients postoperatively for any signs of cerebral vasospasm. Early detection and treatment of this condition may help to avoid serious long-term injuries or death.^[4] In this study, the time to develop postoperative vasospasm was found to be 7 days, in which it was similar to Alotaibi *et al.* study which was 8 days.^[4] As for the circulation, the most common affected circulation was anterior circulation and most patients had complete recovery after the vasospasm. All the previous findings were consistent with a previous review done by Alotaibi *et al.* In terms of diagnosis, we found that the most reliable method for diagnosing vasospasm following tumor resection was through imaging studies such as Angiogram or MRA. We also found that the most common form of management for vasospasm following tumor resection was the administration of vasodilators such as nimodipine with supportive management such as hypertension, hypervolemia, and hemodilution. We found that there is nothing that can predict the outcome of patients who had vasospasm after tumor resection. Many of our results were similar to Alotaibi and Lanzino study; however, our study mainly focuses on the management of vasospasm after skull base surgery. The results showed that many patients who develop postoperative vasospasm will not have complete recovery despite the management and detection of the condition. Although the management is similar to SAH, there are many factors to keep in mind, one of which is injury to the affected vessel during the surgery which can disturb the response to the intra-arterial vasodilators, high sympathetic tone may also interfere with the vasodilators, and these injured vessels may also be prone to be rupture during an interventional management such as balloon angioplasty.^[4,19]

We hope that our findings will help to produce more high-quality studies that will aim to assess the best method to manage vasospasm post neurosurgery and to assess the factors that can predict the outcomes of such patients.

CONCLUSION

This systematic review provides a comprehensive overview and analysis of the management of postoperative cerebral vasospasm after brain tumor surgery. The results of this study suggest that there is no significant correlation between the outcome and the management strategy, pathology, time to develop vasospasm, age, circulation, or type of surgery. However, the data showed that the majority of cases had an incomplete recovery, with only 11 patients having a complete recovery. Cerebral vasospasm is a rare but potentially severe complication of brain tumor surgeries, and early recognition and management of this condition can improve the outcome and reverse neurological deficits. While there is no reliable way to predict the outcome of patients who develop cerebral

vasospasm following brain tumor surgeries, vigilance in monitoring patients postoperatively for any signs of cerebral vasospasm is crucial. This study provides insight into the management of postoperative vasospasm after brain tumor surgery and can help guide future research and clinical practice.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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