

## Original Article

## Treatment of aneurysmal subarachnoid hemorrhage and unruptured intracranial aneurysms by neurosurgeons in Colombia: A survey

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### Abstract

**Background:** Trends in management of aneurysmal subarachnoid hemorrhage and unruptured intracranial aneurysms among neurosurgeons is very variable and had not been previously described in any Latin American country. This study was conducted to determine the preferences of Colombian neurosurgeons in pharmacologic, surgical, and endovascular management of patients with aneurysmal subarachnoid hemorrhage and unruptured intracranial aneurysms.

**Methods:** A survey-based descriptive study was performed in a sample of members from the Colombian Association of Neurosurgery. Questions about pharmacologic, surgical, and endovascular management of aneurysmal subarachnoid hemorrhage and unruptured intracranial aneurysm were carried out. We calculated the mean and the standard deviation of the results obtained from the continuous variables. The results of the categorical variables are presented as percentages.

**Results:** The preference of medication with poor clinical evidence, such as magnesium sulfate, aspirin, statins, and anti-fibrinolytics was lower than 10%. The use of intravenous nimodipine and systemic glucocorticoids was as high as 31%. The availability of endovascular therapy was 69%. The indication for treatment of patients with unruptured intracranial aneurysms that required intervention was less than 13.8%. In patients with ruptured or unruptured intracranial aneurysms, coiling was the preferred method for exclusion.

**Conclusions:** Reported compliance of evidence-based clinical guidelines was similar to that described in developed countries, and even better. However, there is little agreement in treating patients with unruptured intracranial aneurysms. For other issues, the conducts reported by Colombian neurosurgeons are in accordance with the current guidelines.

**Key Words:** Intracranial aneurysms, national survey, subarachnoid hemorrhage

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## INTRODUCTION

Several consensus have published their guidelines for diagnosis and management of aneurysmal subarachnoid hemorrhage (SAH) and unruptured intracranial aneurysms.<sup>[2,6]</sup> Still, in many situations, the physician-indicated therapies are found to be different from evidence-based recommendations.<sup>[11,13]</sup> Causes of these inconsistencies have not been established, but we believe these could be due to information access, variable continued medical education, neurosurgeon's training and experience, resources on each location, and others.

Intensive care management of aneurysmal SAH is variable among neurosurgeons, and the use of drugs such as nimodipine, aspirin, steroids, statins, magnesium sulfate, mannitol, hypertonic saline solution, anti-fibrinolytics, and "triple H therapy" is not always in conformity with current guidelines.<sup>[7,11,13,16]</sup>

Additionally, the selection of a method for aneurysm exclusion is also controversial. The increasing availability of endovascular coiling and its proven effectiveness have lead to a vertiginous increase in its popularity, although some troubles have been reported such as a high rate of recanalization. Because of the latter, there is still controversy about which is the best method for aneurysmal exclusion.<sup>[1,5,9]</sup>

The aim of the present study is to describe the current perceptions of Colombian neurosurgeons about their practice in the management of aneurysmal SAH and unruptured intra-cranial aneurysms.

## MATERIALS AND METHODS

One hundred surveys were sent to a sample of members from the Colombian Association of Neurosurgery by e-mail, and also were distributed in the III International Symposium of Vascular Neurosurgery and Endovascular Therapy (June 2010, Cartagena de Indias, Colombia). The sample corresponds to 21% of affiliates of the Colombian Association of Neurosurgery at the time of study. This is the only neurosurgical organization in this country.

The questions in the survey were formulated to determine if there is any preference within pharmacological and invasive management. We also investigated how frequently they performed each type of treatment.

The survey includes the following items:

- Demographic characteristics
- Training and experience in management of intracranial aneurysms.
- Frequency in the use of drugs to treat SAH (oral nimodipine, intravenous nimodipine, aspirin, glucocorticoids, statins, magnesium sulfate, mannitol,

hypertonic saline, and anti-fibrinolytic).

- Use of controversial treatments (systemic steroids, prophylactic anticonvulsant therapy, and triple H).
- Preference of treatment to exclude aneurysms according to location and status (ruptured or unruptured).

The statistical analysis was done with SPSS (Statistical Package for the Social Sciences) version 17.0 (SPSS, Inc., Chicago, IL, USA). The categorical variables were presented as percentages. To report continuous data, mean and standard deviation (SD) were calculated. To assess differences between categorical variables, Fisher's exact test was used. A *P*-value <0.05 was considered statistically significant.

## RESULTS

One hundred surveys were sent and 62 were received. Four incomplete responses were discarded and 58 were analyzed. The mean age of respondents was 43.4 years (SD  $\pm$  7.4, range: 30 to 60) and 96.6% were male.

The average length of experience was  $9.9 \pm 7.1$  years (range: 0 to 30). Forty one (81%) were trained in Colombia and 36.2% reported a formal additional training in a neurosurgical specialty. Of them, 20.7% have trained in cerebrovascular surgery and 13.8% in neurological endovascular therapy. Another 2.9% reported other specialties (spine surgery, functional and stereotactic, pain, neuro-intensive care and radiosurgery).

The average number of patients treated per year by each neurosurgeon was  $27.9 \pm 14.3$ . General neurosurgeons reported a mean of  $27.3 \pm 11.3$  patients treated per year, cerebrovascular trained  $34 \pm 21.9$  patients per year and endovascular trained  $21.8 \pm 11.7$  patients per year. There were no statistically significant differences in number of patients treated per year between groups (*P* = 0.2).

### Medical treatment

About the treatment with systemic steroids, 3.4% believed that it improves survival, 3.4% believed that it increases overall mortality, 10.3% believed that it improves neurological outcomes, 31% believed that it alleviates headache, and 51.7% believed that they don't have clinical effects in patients with aneurysmal SAH.

Thirteen percent do not use prophylactic anticonvulsant therapy. Other groups include use for less than three days (19%), three to five days (5.2%), five to seven days (48.3%), and until the day after aneurysm exclusion (13.8%). None reported using prophylaxis indefinitely in all patients with poor SAH grade (Hunt-Hess IV or V).

"Triple H" therapy is used as prophylaxis by 10.3% and as a therapeutic measure by 89.7%, only when vasospasm has been suspected or confirmed.

Thirty-four percent of which report to use “Triple H” therapy do it before the aneurysm has been occluded and 65.5% after such. Hypertension, hemodilution, and hypervolemia are considered harmful by 13.8%, 17.2%, and 24.1%, respectively.

Table 1 denotes the patterns of use of medications for medical management of aneurysmal SAH by Colombian neurosurgeons [Table 1].

**Occlusion of ruptured intracranial aneurysms**

Sixty-nine percent reported having availability of endovascular therapy. In patients with low severity SAH (Hunt and Hess I, II and III), 69% reported to indicate the occlusion procedure within the first 72 hours, 17.2% between 4 and 14 days, and 13.8% after the first 14 days of bleeding. In patients with poor-grade SAH (Hunt and Hess IV and V), 48.3% indicate occlusion within the first 72 hours, 10.3% between 4 and 14 days, and 41% after the first 14 days.

Ninety percent reported that the recommended mode

of occlusion varies according to the characteristics of each particular case. Microsurgical clipping was routinely indicated by 6.9%; and 3.4% reported always to prefer endovascular therapy. Fifty-two percent recommend endovascular therapy in less than 50% of cases, and 17.2% in more than 75%.

**Treatment of unruptured intracranial aneurysms**

In the Table 2 are shown the trends to treat or not treat unruptured intracranial aneurysms under different clinical scenarios [Table 2]. When treatment was indicated, endovascular therapy was preferred over microsurgical clipping by 56.9%, but this difference was not statistically significant ( $P= 0.29$ ) [Table 3].

**DISCUSSION**

This survey shows perceptions of Colombian neurosurgeons about their practice in treatment of SAH and unruptured intracranial aneurysms.

We found that the use of pharmacological treatments with good clinical evidence is similar to that described in developed countries. The use of oral nimodipine is very common, possibly as a result of a meta-analysis published that provides strong evidence in improving the prognosis for patients with ischemic complications.<sup>[3]</sup> In this study, the reported “routine use” is the highest when compared with a 78 to 91% informed in previous studies from Europe and North America.<sup>[17,18]</sup> Another survey in 100 neurosurgical departments from Germany showed that 30% of them do not use it routinely.<sup>[13]</sup> It was also found that 37.9% of the respondents use the intravenous route for administration of nimodipine in some clinical circumstances, although several studies have shown that it is expensive, ineffective, and potentially harmful. Other studies have reported its use as frequent as 81.8% of cases.<sup>[11]</sup> Although more than half of the respondents recognized that glucocorticoids in patients with SAH have no clinical effect, nearly 40% reported using them

**Table 1: Patterns of use of medications for medical management of aneurysmal subarachnoid hemorrhage**

Medication	Routinely	Usually	Rarely	Never
Oral nimodipin	54 (93.1)	2 (3.4)	2 (3.4)	0
Intravenous nimodipin	12 (20.7)	10 (17.2)	26 (44.8)	10 (17.2)
Aspirin	4 (6.9)	6 (10.3)	0	48 (82.8)
Glucocorticoids	4 (6.9)	18 (31)	16 (27.6)	20 (34.5)
Statins	6 (10)	14 (24.1)	10 (17.2)	28 (48.3)
Magnesium sulphate	2 (3.4)	4 (6.9)	14 (24.1)	38 (65.5)
Mannitol	2 (3.4)	10 (17.2)	40 (69)	6 (10.3)
Hypertonic saline	12 (20.7)	32 (55.2)	8 (13.8)	6 (10.3)
Anti-fibrinolytics (Tranexamic acid or tirilazad)	2 (3.4)	4 (6.9)	18 (31)	34 (58.6)

Figures in parentheses are in percentage

**Table 2: Preferred occlusion strategies based on aneurysm location**

Condition	Routinely	Usually	Rarely	Never
Anterior circulation				
Microsurgical clipping	2 (3.4)	24 (41.4)	19 (32.8)	13 (22.4)
Endovascular therapy	7 (12.1)	17 (29.3)	24 (41.4)	10 (17.2)
Posterior circulation				
Microsurgical clipping	8 (13.8)	14 (24.1)	16 (27.6)	20 (34.5)
Endovascular therapy	20 (34.5)	15 (25.9)	12 (20.7)	11 (19)

Figures in parentheses are in percentage

**Table 3: Preferred occlusion strategies based on patient’s age, symptoms and aneurysm size**

Condition	Routinely	Usually	Rarely	Never
Unruptured, but symptomatic	2 (3.4)	4 (6.9)	14 (24.1)	38 (65.5)
Asymptomatic and smaller than 5 mm	0	14 (24.1)	30 (51.7)	14 (24.1)
Patient younger than 60 years old with aneurysm greater than 5 mm	0	2 (3.4)	18 (31)	38 (65.5)
Patient older than 70 years old with aneurysm greater than 10 mm	0	8 (13.8)	18 (31)	32 (55.2)

Figures in parentheses are in percentage

frequently or routinely. The ineffectiveness of this group of drugs has been demonstrated in multiple clinical trials and a meta-analysis.<sup>[4]</sup> It seems to be a global problem since this finding is similar to what is described in Germany (35%) but lower than that reported in two studies conducted in Europe (78% and 78.5%).<sup>[11,13]</sup>

In the early 90's, statins emerged as a therapeutic option in patients with SAH, and a subsequent publication of a meta-analysis that showed a lower mortality, incidence of vasospasm and delayed ischemic deficits lead to its popularization.<sup>[15]</sup> However, another more updated meta-analysis found no benefit, so current guidelines do not recommend it.<sup>[7,16,20]</sup> In this study, 34.1% reported using it as usual or routinely. This frequency of use of statins is the highest compared with previous surveys, reflecting the effect of these outdated publications.<sup>[11]</sup> The beneficial effects of magnesium sulfate infusion also have not been proven with certainty, so its use has been poorly implemented.<sup>[18,21]</sup> In this survey, 10.3% reported using it as usual or routinely which is consistent with previous studies (6 to 19.4%).<sup>[11,13,18]</sup> Studies with anti-fibrinolytics have found a reduction in the incidence of re-bleeding by 40%; but this is offset by a high rate of cerebral ischemia and poor neurological outcome.<sup>[12]</sup> Therefore, this can explain why about 90% of the participants of this study do not use it which is in accordance to current recommendations.<sup>[2]</sup>

Seizures are feared due to the risk of re-bleeding during each episode. Therefore, prophylactic anti-convulsants have been recommended for SAH, usually for periods not exceeding seven days.<sup>[2]</sup> No participant responded using anticonvulsant prophylaxis indefinitely, 30% do not use it within the first week of bleeding, and 70% use it only within the first seven days after the exclusion of the aneurysm. Studies have shown that prolonged anticonvulsant prophylaxis is associated with worse functional and cognitive outcomes, so the tendency is to use them for shorter periods and only be considered for long-term administration in patients with previous seizures, parenchymal hematomas, strokes or aneurysms of the middle cerebral artery.<sup>[8]</sup> Increasing availability in Colombia of other drugs with better security profile as Levetiracetam could change the current patterns of prophylactic anticonvulsants as happened in other countries.<sup>[14,18,22]</sup>

There is consensus of the usefulness of "triple H" therapy as a reasonable approach for the treatment of symptomatic vasospasm. However, its implementation as a prophylactic measure has been formally contraindicated.<sup>[2]</sup> Therefore, most neurosurgeons (89.7%) opt for it only when vasospasm has been clinically suspected or confirmed. Although mechanistically the induction of hypervolemic hemodilution may seem beneficial, it has been shown to be potentially harmful which was informed by 24.1% of the participants.<sup>[19]</sup>

The reported availability of a service of endovascular therapy was 69%, slightly lower than in developed countries of Europe and North America (83%).<sup>[17]</sup> However, we observed that in most cases, the modality for aneurysms occlusion is selected based on the particular characteristics of each patient suggesting that availability of coiling is not an important issue.

The selection between microsurgical clipping and coiling is variable among Colombian neurosurgeons. In patients with anterior circulation aneurysms, 41.4% selected coiling as a first treatment option or a frequent practice which is consistent with the international trend toward an increase in its use after publication of the International Subarachnoid Aneurysm Trial (ISAT).<sup>[10]</sup> Two surveys conducted in Europe before the publication of long-term follow-up results of ISAT and the American Heart Association Guidelines showed a preference for coiling from 22 to 37% which increased to 70% after these publications.<sup>[17]</sup> Also, for treatment of posterior circulation aneurysms, most Colombian neurosurgeons prefer coiling.

A low rate of treatment of symptomatic patients with unruptured aneurysms, patients younger than 60 years with aneurysms greater than 5 millimeters, and patients over 70 years with aneurysms greater than 10 millimeters was detected. Taking into account the probability of SAH in patients with unruptured aneurysms, clinical trials support the treatment of all patients with the aforementioned characteristics.<sup>[6]</sup> In patients at low surgical risk, it has been suggested microsurgical clipping over endovascular route. However, this was preferred by only 43.1% of the respondents.

## LIMITATIONS

This survey assessed the perception of the participating neurosurgeons about their daily practice in treating SAH and unruptured aneurysms. However, this will not provide certainty about what is the treatment received by patients in the clinical setting.

By design, this study is susceptible to recall bias in which participants cannot remember precisely when asked for numerical variables (e.g., patient-years ratios). Response biases are common in surveys, and in this case, there may be attempts to conceal outdated practices or those without scientific evidence.

The high similitude of treatment preferences with current evidence-based clinical guidelines could be explained by the conduction of this survey after publication of the American guidelines in 2009 and regional guidelines in 2010.<sup>[2,16]</sup> It can cause results more consistent with recommendations than those found in previous surveys.

## CONCLUSION

This survey allowed the description of the patterns in treatment of aneurysmal SAH and unruptured intracranial aneurysms among neurosurgeons in Colombia.

Compliance of evidence-based clinical guidelines was similar to that described in developed countries and even better in some topics. The use of medications with poor clinical evidence such as magnesium sulfate, aspirin, statins, and anti-fibrinolytics was low. On the other hand, we found a rate of use of intravenous nimodipine and glucocorticoids similar and even lower than those seen in previous studies from other countries. It should be enacted there disuse based on studies that have shown that these drugs are ineffective or potentially harmful.

The indication for treatment of patients with unruptured aneurysms was low even in those with clinical characteristics and size of the aneurysm itself requiring occlusion.

It was noted a trend towards increased use of coiling for treatment of both ruptured and unruptured aneurysms which could be related to the widespread of controversial clinical trials that have shown the benefits of this approach over microsurgical clipping.

In the management of unruptured intracranial aneurysms, we found little agreement with current recommendations. For others issues, the conducts in management of aneurysmal SAH and unruptured intracranial aneurysms by Colombian neurosurgeons are consistent with those in developed countries and adequately supported by the current recommendations.

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## Commentary

This interesting manuscript well describes the tendencies among neurosurgeons in Colombia, in relation with the treatment of aneurysmal subarachnoid hemorrhage (SAH) and unruptured intracranial aneurysms.

As the authors note, the compliance to evidence-based clinical guidelines was similar to that described in developed countries. The use of medications with poor clinical evidence such as magnesium sulfate, aspirin,

statins and anti-fibrinolytics was low. On the other hand, they found a rate of use of intravenous nimodipine and glucocorticoids similar and even lower than seen in previous studies from other countries. It should be highlighted that the disuse probably was based on studies that have shown that these drugs are ineffective or potentially harmful.

A trend was observed towards increased use of coiling for treatment of both ruptured and unruptured aneurysms, which could be related to the widespread availability of clinical trials that have shown the benefits of this approach over microsurgical clipping.

However, the first concept that must be eradicated and that unfortunately is spreading not only among the community of Latin American neurosurgeons, but also at the level of intensive care physicians, neurologists and general practitioners, is that when you have a case of a patient with a SAH, they ask for “angiography with possible endovascular treatment”. This concept is not correct. Treatment should never be ordered without seeing that vascular malformation facing the specialist. Hence, the importance of who decides and treat the patient (either conventional surgery or endovascular surgery) is a neurosurgeon. In their training, those who are engaged in vascular disease, should be prepared with endovascular and surgical training. It is the only way in which the same expert can decide which treatment is right for each aneurysm. This does not always mean the same specialist deepen both techniques. However, integration into the same team of neurosurgeons who can discuss on the same “language” is ideal.<sup>[2,3,4,8]</sup>

Another important concept is that after the first publication of the ISAT,<sup>[6]</sup> the authors of this very discussed clinical trial<sup>[1]</sup> have adopted a less aggressive tendency, and more modest and conservative in his later publications, so that they accepted that the endovascular procedure is more expensive, which should be taken into account in our Latin American countries, requires more angiographic controls, and the percentages of rebleeding and re-treatments are greater than the conventional microsurgery.<sup>[5,7]</sup>

Finally, the advances of microsurgery in recent years in countries with high numbers of patients, such as Mexico, Brazil, Peru, Argentina, and Chile, has increased, so there is an increasingly more common and practiced concept of Integrated Management of the Disease SAH, which provides only the surgery with cisternal washing of the blood clots around the arteries at the brain base, use of the fenestration of the lamina terminalis, use of cisternal drains or ventricular drainage for post-operative monitoring of ICP, intracerebral hematomas immediate evacuation, and not just content with stopping the



**Figure 1: Integrated Management of the Disease Subarachnoid Hemorrhage (from the Course “Key Hole Microsurgery assisted by Endoscopy”, under the direction of Prof. Axel Perneczky, Mainz, Germany, 2005)**

bleeding site using a clip on the neck of the aneurysm, or filling the aneurysm with coils. The disease is the SAH and the ruptured aneurysm is just the cause [Figure 1].

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