The effects of sevoflurane anesthesia on hemodynamics and cerebral artery diameters in endovascular treatment of intracranial aneurysm: A pilot study

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ABSTRACT

BACKGROUND: Cerebral autoregulation is a steady-state of cerebral blood flow despite major changes in arterial blood pressure. Inhalation anesthetics are cerebral vasodilators. In <1 MAC values, the net effect is a moderate decrease in cerebral blood flow and maintenance of responsiveness to carbon dioxide. This study aims to investigate the effects of steady-state sevoflurane anesthesia on hemodynamic and cerebral artery diameter measurements in patients undergoing flow diverter device placement under general anesthesia.

METHODS: Forty-six patients aged 18–70 years who underwent flow diverter devices under general anesthesia were included in this study. Routine monitoring was performed on the patients. Mean arterial pressure (MAP) values were recorded. Internal carotid artery, middle cerebral artery and anterior cerebral artery diameter measurements were made from digital subtraction angiography (DSA) images of patients with anterior aneurysms. Baseline artery, right posterior cerebral artery and left posterior cerebral artery diameter measurements were made from DSA images of patients with posterior aneurysms. These measurements were recorded as preoperative measurements. The same measurements were made from the DSA images performed before the Flow diverter device placement procedure performed under steady-state sevoflurane anesthesia for the same patients. These measurements were recorded as peroperative measurements.

RESULTS: The average age of the patients was 56.6±15.1. The MAP of the patients before induction was 76.28±5.13 mmHg, MAP after induction was 64.36±3.23 mmHg, and MAP during sevoflurane anesthesia was 68.26±4.30 mmHg, there was a statistically significant difference. There was a statistically significant difference between the preoperative and perioperative values of anterior cerebral artery diameters. There was a strong relationship between the MAP change percentage and the ICA diameter change percentage (p<0.001, p=-0.785) and a moderate relationship between the MCA diameter change percentage (p=0.033, p=-0.338).

CONCLUSION: In patients undergoing flow diverter devices, <1 MAC sevoflurane has a hemodynamic effect and creates significant vasodilation in the cerebral artery diameters.

Keywords: Cerebral artery diameter; flow diverter device; general anesthesia; sevoflurane.

INTRODUCTION

Cerebral aneurysm occurs when the high blood flow rate expands the artery wall due to the focal weakness of the vessel. [1] Unruptured cerebral aneurysms may manifest clinically by their mass effect on adjacent neurologic structures, or they may be discovered incidentally when a patient has a neuroimaging study for another indication. Pipeline Embolization Device or Flow Re-Direction Endoluminal Device, which is flow diverter for the treatment of cerebral aneurysm, is pop-
ular treatment option. Flow diverter devices (FDD) are new generation stents placed in the main artery at the level of the aneurysm neck to disrupt the intra-aneurysmal flow. It progressively creates intra-aneurysm thrombosis and offers good support for the development of the neointima.\(^{[2]}\)

Placement of FDD can be done safely under conscious sedation. The occlusion rate, functional outcome and complications do not differ between FDD placement with conscious sedation or under general anesthesia.\(^{[3]}\) However, most flow diverter procedures are performed under general anesthesia for various reasons, such as general comfort, patient comfort, better control of breathing and hemodynamics, and better visualization as a result of reduced motion artifact in an immobile patient.\(^{[4]}\) A combination of total intravenous anesthesia or a volatile agent with intravenous remifentanil is recommended, which can help maintain rapid induction and patient stability.\(^{[5]}\) One of the most important issues to be considered here is the preservation of cerebral blood flow.

Cerebral blood flow (CBF) is one of the most important factors involved in maintaining brain metabolism. Cerebral blood flow is regulated by several different mechanisms (e.g., coupling, autoregulation).\(^{[6]}\) Cerebral autoregulation is the natural ability of the brain circulation to maintain constant cerebral blood flow during systemic blood pressure and cerebral perfusion pressure changes.\(^{[7]}\) Changes in systemic blood flow rate (SBFv) are thought to affect cerebral blood flow rate (CBFv). Thus, some of the changes in CBFv may be due to changes in SBFv.\(^{[8]}\)

Inhaled anesthetic agents have been shown to provide a dose-dependent increase in CBF.\(^{[9]}\) In one study, it was stated that sevoflurane does not have a significant systemic hemodynamic effect in clinical application doses and does not affect static cerebral autoregulation and cerebrovascular reactivity.\(^{[10]}\) However, in another study, it was emphasized that regardless of the changes in SBFv, sevoflurane has an effect that directly reduces CBFv.\(^{[11]}\)

In the light of all these data, we aimed to investigate the effects of steady-state sevoflurane anesthesia on hemodynamics and cerebral artery diameter measurements of patients undergoing FDD under general anesthesia.

**MATERIALS AND METHODS**

**Settings, Participants and Design**

This study was performed at our university hospital. After the approval of the ethics committee (2020/2715) of the university hospital and written informed consent was obtained from enrolled patients. Forty-six patients aged 18–70 years undergoing FDD under general anesthesia were included.

Patients with mean arterial pressure (MAP) <60 mmHg, inotropic agent administration, hemoglobin <10 and body temperature under 36°C, head trauma, neurodegenerative disease, Glasgow Coma Scale (GCS) = 3 were excluded from this study.

Initially, all patients underwent angiography computed tomography and the diagnosis was confirmed by digital subtraction angiography (DSA). All indications were determined by an interdisciplinary evaluation between neurosurgeons and interventional neuroradiologists.

General anesthesia was applied to all patients included in this study. Before the procedure, their GCS was evaluated and recorded. Routine monitoring was performed in the supine position. MAP, heart rate (HR), end-tidal CO\(_2\) (Et-CO\(_2\)), peripheral oxygen saturation (SpO\(_2\)), body temperature and Bispectral Index were continuously monitored. Blood pressure was measured non-invasively. Body temperature was measured orally in all patients.

Anesthesia induction was carried out with 1–2 mg/kg propofol, 1.0 mcg.kg\(^{-1}\).min\(^{-1}\) for 1 min, followed by 0.1 mcg.kg\(^{-1}\).min\(^{-1}\) remifentanil and 0.6 mg/kg rocuronium. Continuous infusion of remifentanil continued after endotracheal intubation and controlled ventilation was established (Cato, Drager, Lubeck, Germany). Using an oxygen/air mixture with an FiO\(_2\) of 0.2, PEEP of 4 cmH\(_2\)O, peak airway pressures were between 15 and 20 cmH\(_2\)O. Sevoflurane was used as the volatile agent in maintenance. The concentration of sevoflurane was titrated to a target Bispectral Index (BIS) between 40 and 60 (Covidien, Dublin, Ireland) and it was targeted at <1 MAC. Patients were kept normothermic (36–37°C) and normocapnic (et-tidal CO\(_2\) 35–40 mmHg). It was planned to use 5 mg ephedrine if MAP <60 mmHg and 0.5 mg atropine if HR <50/min. Doses of the drugs used were recorded. Body temperature was maintained using body surface warming using a Bair Hugger.

Features of the aneurysm, antiplatelet drug use, demographic data, intensive care and hospital stay duration, complications and clinical results were recorded.

**Antiplatelet Treatment and Endovascular Procedure and Cerebral Artery Diameter Measurement**

Application of Tirofiban (Aggrastat, Merck, West Point, Pennsylvania, USA) to all patients was initiated before placing a flow diverter for 16/24 hours according to the manufacturer’s guide, followed by oral double antiplatelet medication (for four consecutive months, aspirin 100 mg/day and clopidogrel 75 mg/day).

All procedures were performed under general anesthesia by an interventional neuroradiologist with at least 10 years of experience. Flow diverter selection and the number of implants used were planned at the operator’s discretion and angiographic evaluation of each case. Technical success was defined as the successful deployment of the flow diverter.
Aneurysm location (anterior circulation against posterior circulation) and size were recorded.

Internal carotid artery (ICA), middle cerebral artery (MCA) and anterior cerebral artery (ACA) diameter measurements were made from DSA images of patients with anterior aneurysms. Baseline artery (BA), right posterior cerebral artery (RPCA) and left posterior cerebral artery (LPCA) diameter measurements were made from DSA images of patients with posterior aneurysms. These measurements were recorded as preoperative measurements. The same measurements were made from the DSA images performed before the FDD placement procedure performed under steady-state sevoflurane anesthesia for the same patients. These measurements were recorded as peroperative measurements.

In all patients, DSA was provided with a single wall entry into the main femoral artery under the guidance of ultrasonography. 5F diagnostic catheter (Radifocus® Angiographic Catheter – Terumo) was used in the preoperative DSA and 5F or 6F guiding catheter (SOFIA® Microvention) was used in the operative DSA. Diagnostic angiographic images were obtained in the Town and lateral positions by giving 10–12 ml of a non-ionic contrast agent (Ultravist 300, Schering, Berlin, Germany) at a rate of 5–6 ml/sec through an automatic injector. After the images to be measured preoperatively and peroperatively were determined, the Allura Xper FD 20/20 - DS angiography device workstations were calibrated according to the diagnostic or guide catheter diameter used. In the anterior system, diameters were measured from the ICA supraclinoid (C7) segment, from the middle sections of MCA m1 and ACA a1 segments, and it was measured in the posterior system from the BA middle section, from the RPCA and LPCA P1 segments.

Statistical Analysis

The results of our study were analyzed with the program “The Statistical Package for the Social Sciences 19.0 (SPSS Armonk, NY: IBM Corp.)”. Data with continuous values were given as mean (± standard deviation), categorical data were given as frequency and percentage (n, %). The data were tested for compatibility with normal distribution with the Kolmogorov-Smirnov test. Nonparametric data of the groups were compared using Mann – Whitney U test and parametric data using the Independent t-test. Chi-square test was used to test categorical data. Pearson correlation test was used to determine the linear relationship between the variables. Logistic regression model was used to determine the independent risk factors affecting mortality. P<0.05 value was considered significant.

RESULTS

The mean age of the patients included in this study was 56.6±15.1 (18–70), and 25 (54.3%) of them were male. GCS before the procedure was 13.2±3.4 (4–15). The aneurysm diameter of the patients was 8.7±4.0 (4–25) mm. The duration of intensive care and hospital stay of the patients was 5.4±12.1 (0–56) days, and 10.5±11.7 (2–56) days, respectively, and 45.7% of the patients did not need intensive care. Demographic data, anesthetic agent consumption and hemodynamic data of the patients are presented in Table 1.

The MAP value of the patients before the induction was 76.28±5.13 mmHg, the MAP value after the induction was 64.36±3.23 mmHg, and the MAP value during sevoflurane anesthesia was 68.26±4.30 mmHg. The relationship between MAP values before and after induction, during induction and sevoflurane anesthesia, is presented in Figure 1.

<table>
<thead>
<tr>
<th>Table 1. Other system and organ injuries</th>
<th>Mean±SD (n=46)</th>
<th>Min–Max (n=46)</th>
</tr>
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<tbody>
<tr>
<td>Age (year)</td>
<td>56.6±15.1</td>
<td>18–70</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.06±8.95</td>
<td>55–90</td>
</tr>
<tr>
<td>Propofol (mg)</td>
<td>106.5±13.42</td>
<td>82.5–135</td>
</tr>
<tr>
<td>Sevoflurane (ml)</td>
<td>13.70±2.82</td>
<td>8.70–19.57</td>
</tr>
<tr>
<td>EtCO₂</td>
<td>37.65±1.84</td>
<td>35–40</td>
</tr>
<tr>
<td>Temperature (ºC)</td>
<td>36.43±0.27</td>
<td>36–36.9</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>97.39±1.02</td>
<td>96–99</td>
</tr>
<tr>
<td>Heart Rate (/dk)</td>
<td>67.52±6.14</td>
<td>55–80</td>
</tr>
<tr>
<td>GCS</td>
<td>13.2±3.4</td>
<td>4–15</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>8.7±4.0</td>
<td>4–25</td>
</tr>
<tr>
<td>ICU Time (day)</td>
<td>5.4±12.1</td>
<td>0–56</td>
</tr>
<tr>
<td>Hospital Time (day)</td>
<td>10.5±11.7</td>
<td>2–56</td>
</tr>
</tbody>
</table>

EtCO₂: End–tidal CO₂; SpO₂: Peripheral oxygen saturation; GCS: Glasgow coma scale; ICU Time: Intensive care unit time; SD: Standard deviation; Min: Minimum; Max: Maximum.

Figure 1. Comparison of MAP values before and after induction and during sevoflurane anesthesia of patients. */**/***: p<0.001, MAP I: mean arterial pressure before induction, MAP II: mean arterial pressure after induction, MAP III: mean arterial pressure during sevoflurane anesthesia.
The aneurysm localization of the patients is presented in Table 2.

There was a statistically significant difference between the preoperative and peroperative values of cerebral artery diameters measured from three different locations in patients with anterior cerebral artery aneurysm (p<0.001). A statistically significant difference was observed between the preoperative and peroperative measurements of LPCA diameters of patients with posterior cerebral artery aneurysm (p=0.005) (Table 3).

In Pearson correlation analysis, there was a strong relationship between the percentage of MAP change and the percentage of ICA diameter change (p<0.001, p=-0.785) and a moderate relationship with the percentage of MCA diameter change (p=0.033, p=-0.338) (P: Pearson’s Rho Correlation Coefficient) (Fig. 2).

No complications developed in any patient during the procedure. Mortality developed in six patients (13.04%).

To determine the independent risk factors that affect the development of mortality, logistic regression analysis, including age, sex, GCS, duration of operation, aneurysm diameter,
MAP change percentage and change percentages of cerebral artery diameters, was performed. Low GCS scores (OR: 1.658, p=0.037, 95% CI: 1.030–2.668) were determined as independent risk factors affecting mortality development.

DISCUSSION

Most neurointerventional procedures are performed under general anesthesia as it provides greater patient safety and better image quality due to patient immobilization.[9]

We also preferred general anesthesia in our patients to standardize conditions that may have cerebral vasodilator effects. Anesthesia induction was achieved with propofol and remifentanil, and sevoflurane was added as a volatile agent to remifentanil during maintenance. Anesthesia depth was monitored with BIS (40 <BIS <60), and <1 MAC sevoflurane was applied to the patients.

In normal intracranial pressure (normal neurological examination) ruptured or unruptured aneurysm, a maximum of 140 mmHg should be targeted so that the patient has normal systolic blood pressure. MAP should be targeted to be ≥60 mmHg.[12] It has been shown that 1 MAC sevoflurane, which is often used, does not have systemic hemodynamic effects.[13]

In a study in which propofol fentanyl was used for the induction and sevoflurane for maintenance, MAP decreased in the induction phase, while aortic and pulse pressure increased. In the later phases, there was no significant change in hemodynamic parameters, and it was emphasized that sevoflurane had no systemic effect. Peripheral vasodilation in this induction phase has been linked to propofol use.[10]

Similar to the aforementioned study, in our patient group, there was a significant decrease in MAP after induction compared to baseline values. This significant decrease was also observed during sevoflurane anesthesia. Although this decrease was more pronounced in the induction phase, none of the patients had MAP values below 60 mmHg, and no inotropic agent was used. <1 MAC sevoflurane anesthesia was significant in patients undergoing FDD procedure according to the baseline value, and the systemic effect of sevoflurane was significant.

In the traditional concept of cerebral autoregulation, the steady-state CBF remains relatively stable despite large changes in arterial blood pressure.[14] CBF reacts quickly to temporary changes in arterial blood pressure.[15] The cerebral vascular bed buffers these changes in CBF caused by temporary changes in arterial blood pressure. Changes in perfusion pressure produce marked changes in cerebrovascular resistance, thus preserving CBF relatively.[10]

Inhalation anesthetics are cerebral vasodilators. While reducing cerebral metabolic rate (CMR), they can blunt cerebral autoregulation by separating CBF and metabolism, thereby increasing CBF and intracranial pressure.[14,17] In <1 MAC values, the net effect is a modest decrease in CBF, and generally, CO2 responsiveness is maintained. However, CBF increases more noticeably at >1 MAC concentrations.[14,19] Inhalation anesthetic agents have been shown to provide a dose-dependent increase in CBF. The magnitude of this increase is dependent on the balance between the agent’s intrinsic vasodilatory action and the vasodilatation secondary to flow–metabolism coupling.[9] Previous studies have indicated that sevoflurane between 0.5–1.0 MAC has a minimal direct vasodilator effect on brain arterioles.[20,21]

In our study, peroperative cerebral artery diameters were significantly higher than preoperative diameters. The reason why this significance was low in posterior cerebral artery diameters was attributed to the low number of cases in the measurement of posterior cerebral artery diameters. The change percentages of cerebral artery diameters measured from ICA and MCA were correlated with the change percentages in MAP. However, it was observed that cerebral artery diameter change percentages and MAP change percentages had no role in the development of mortality.

In most of the studies performed so far, CBFv was evaluated using MCA in this evaluation. It was emphasized that CBFv, as measured from MCA, is not a direct CBF measurement. However, it has also been shown that changes in CBFv are reliably correlated with changes in CBF in the presence of fixed vessel diameter.[22–26]

One advantage of our study is that the cerebral artery diameters of our patients were directly visualized by DSA and the cerebral artery diameters under baseline and anesthesia were compared. In our study, ICA and ACA diameters were evaluated besides MCA, where CBF was commonly evaluated in the literature. The increase in the cerebral artery diameters compared to baseline showed significance in all three regions. Our study has some limitations. One of the limitations was that different MAC values of sevoflurane were not compared. However, in the literature, although it was stated that sevoflurane was a minimal vasodilator between 0.5–1 MAC values, it was observed in our study that the vasodilatory effect of <1 MAC sevoflurane in cerebral arteries was significant, and it is likely this significance would be observed in >1 MAC sevoflurane.

The second limitation of this study was that only cerebral artery diameters were evaluated, and simultaneous CBF was not evaluated. However, it was stated that CBFv measured by Doppler is not a direct measure of CBF; but CBFv correlates to CBF only in the presence of fixed cerebral artery diameter. In conclusion, in patients undergoing FDD procedure under sevoflurane anesthesia, <1 MAC sevoflurane has a hemodynamic effect and creates significant vasodilation in the cerebral artery diameters. There is a significant correlation between cerebral artery diameter changes (ICA-MCA) and
MAP changes, but these variables have no effect on mortality. Prospective randomized studies are needed to support all these data in the future.

**Ethics Committee Approval:** Approved by the local ethics committee.

**Peer-review:** Internally peer-reviewed.


**Conflict of Interest:** None declared.

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Intrakraniyal anevrizmanın endovasküler tedavisinde sevofluran anestezisinin hemodinamik ve serebral arter çaplarına etkisi: Pilot çalışma

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AMAÇ: Serebral otoregülasyon, arteriyel kan basıncındaki büyük değişikliklere rağmen kararlı durum serebral kan akımının sabit kalmasını sağlar. İnhalasyon anestezikleri serebral vazodilatörlerdir. <1 MAC değerlerinde, net etki serebral kan akımında ılımlı bir azalma ve karbondioksit yanıt verilmesinin korunmasıdır. Bu çalışmanın amacı, genel anestezi altında akış saptırıcı cihaz yerleştirme uygulanan hastalarda kararlı durum sevofluran anestezisinin hemodinamik ve serebral arter çap ölçümlerine etkisini araştırmaktır.


BULGULAR: Hastaların yaş ortalaması 56.6±15.1’ idi. Hastaların indüksiyon öncesi OAB; 76.28±5.13 mmHg, indüksiyon sonrası OAB; 64.36±3.23 mmHg ve sevoflurane anestezisi sırasında OAB; 68.26±4.30 mmHg idi ve istatistiksel olarak anlamlı bir farka sahip idi. Anterior yerleşimli anevrizmanın ameliyat öncesi ve ameliyat tarihi arasında istatistiksel olarak anlamlı bir farka sahipti (p<0.001, p=-0.785) ve posterior yerleşimli anevrizmanın ameliyat öncesi ve ameliyat tarihi arasında istatistiksel olarak anlamlı bir farka sahip idi (p=0.033, p=-0.338) ve bu arada bir ilişki mevcuttu.

TARTIŞMA: Akış saptırıcı cihaz yerleşimi uygulanan hastalarda, <1 MAC sevofluranın hemodinamik etkisi vardır ve serebral arter çaplarında anlamlı olarak vazodilatasyon yapmaktadır.

Anahtar sözcükler: Akış saptırıcı cihaz; genel anestezi; serebral arter çap; sevofluran.