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**REVIEW ARTICLE** 

# Safety of restarting continuous positive airway pressure (CPAP) therapy following endoscopic endonasal skull base surgery

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### Abstract

**Objectives:** Patients with obstructive sleep apnea (OSA) are at increased risk of perioperative and postoperative morbidity. The use of continuous positive airway pressure (CPAP) in the perioperative period may be of potential benefit. However, among patients who have undergone endonasal skull base surgery, many surgeons avoid prompt re-initiation of CPAP therapy due to the theoretical increased risk of epistaxis, excessive dryness, pneumocephalus, repair migration, intracranial introduction of bacteria, and cerebrospinal fluid (CSF) leak. The objective of this article is to review the most up-to-date literature regarding when it is safe to resume CPAP usage in the patient undergoing endonasal skull base surgery.

**Data Sources and Methods:** This review combines the most recent literature as queried through PubMed regarding the safety of CPAP resumption following endonasal skull base surgery.

**Results:** Recent surveys of skull base surgeons demonstrate little consensus regarding the post-operative management of OSA. Recent cadaveric studies suggest that approximately 85% of delivered CPAP pressures are transmitted to the sphenoid sinus. Further, at frequently prescribed CPAP pressure settings, common sellar reconstruction techniques maintain their integrity while preventing very little transmission of pressure into the sella. In small retrospective case series, patients with OSA who received CPAP immediately following transsphenoidal pituitary surgery had similar rates of surgical complications as OSA patients who did not receive CPAP in the immediate post-operative period. Concerns of reinitiating CPAP too early, such as the development of pneumocephalus, rarely develop.

**Conclusions:** There remains a paucity of objective data regarding when it is safe to resume CPAP following endonasal skull base surgery. Recent cadaveric studies and small retrospective case series suggest that it may be safe to resume CPAP earlier than is often practiced following endonasal skull base surgery.

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#### KEYWORDS

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Continuous positive airway pressure, Endoscopic skull base surgery, Obstructive sleep apnea, Transsphenoidal surgery

# Key points

- There is no consensus regarding the time course of when it is safe to resume CPAP therapy following endonasal skull base surgery.
- Following endonasal skull base surgery there are potentially unique risks of initiation of CPAP including epistaxis, excessive nasal crusting/drying, graft migration, pneumocephalus, CSF leak, and intracranial introduction of bacteria.
- Cadaveric modeling suggests that only a fraction of the delivered CPAP pressure is actually transmitted into the sella, and even the simplest sellar repair techniques can withstand low to moderate pressures.
- Small case series' do not demonstrate increased rate of post-operative complications in patients with OSA who received CPAP immediately after surgery.
- The decision to start CPAP postoperatively must be tailored to each patient based on the severity of his/her OSA, intraoperative findings, and the type of skull base repair employed.

## INTRODUCTION

Obstructive sleep apnea (OSA) is a common condition characterized by episodes of partial and complete airway obstructions during sleep leading to ventilatory disturbance. It has an estimated prevalence between 4% and 50%, with a mean prevalence of 22%, in the general population.<sup>1</sup> However, patients with certain skull base pathologies are at increased risk of developing OSA. Functioning pituitary adenomas, including adrenocorticotropic hormone-, growth hormone-, and prolactin-secreting tumors, are independently implicated in the development of OSA both because of resulting anatomic changes to the upper airway and direct hormonal influences.<sup>2–4</sup>

It is well established that patients with diagnosed and unrecognized OSA are at increased risk of experiencing perioperative complications following major surgery.<sup>5,6</sup> Specifically, comorbid OSA in patients undergoing endonasal skull base surgery are at increased risk of post-operative hypoxemia and pulmonary and airway complications.<sup>7,8</sup> However, while the American Society of Anesthesiology guidelines recommend early postoperative initiation of continuous positive airway pressure (CPAP) ventilation in OSA patients, there are no specific recommendations regarding timeline for re-initiation. Furthermore, these guidelines do not risk stratify post-operative patients based on surgery performed.<sup>9</sup>

For patients undergoing endonasal skull base surgery, risks of early re-initiation of CPAP have been reported and theorized. Some of these proposed risks are minor, such as epistaxis, excessive dryness, and crusting. However, others, such as skull base repair migration and introduction of bacteria intracranially may lead to significant morbidity including pneumocephalus and/or cerebrospinal fluid (CSF) leak and intracranial infection.<sup>8,10-13</sup> Due to a historic paucity of objective data, there is no consensus regarding the time course of when it is safe to resume CPAP therapy following endonasal skull base surgery. Recently, studies have been published objectively evaluating the effects of CPAP on sinonasal pressures and how effective commonly used reconstruction techniques are at withstanding these pressures. These studies, as reviewed below, will ultimately aid in an effort to develop an evidence-based recommendation regarding the re-initiation of CPAP following endonasal skull base surgery.

# PERIOPERATIVE RISK OF OSA

For patients undergoing endonasal skull base surgery with comorbid OSA, the optimal time to re-initiate CPAP therapy is uncertain. While there are theoretical risks of resuming CPAP too soon as addressed above, there are also significant safety concerns associated with withholding this therapy. There may be potential benefit to the early re-initiation of CPAP therapy in post-operative patients, as patients with untreated OSA may be at risk of pulmonary complications post-operatively.<sup>8</sup> Additionally, early post-operative CPAP usage decreases the number of apneas and hypopneas and hospital length of stay.<sup>14</sup> The benefit of resuming positive pressure ventilation as soon as possible after surgery may outweigh the theoretical risks. However, there are currently no evidence-based recommendations regarding the optimal timing of CPAP re-initiation after endonasal skull base surgery.

## CURRENT SURGICAL PRACTICE

Due to the lack of objective data regarding the extent of CPAP pressures transmitted to the skull base and how well various skull base repair techniques withstand these transmitted pressures, there has been no consensus as to when it is safe to restart CPAP. A survey of the American Academy of Otolaryngology members in 2013 revealed that surgeons ranged from not stopping at all to withholding CPAP for 8 weeks or longer after sinonasal surgery.<sup>10</sup> Another survey, specifically of endoscopic skull base surgeons, found that CPAP is commonly withheld anywhere from 10 days to 6 weeks after endoscopic transsphenoidal pituitary surgery, again, emphasizing the variable practices.<sup>15,16</sup> There is great variability amongst skull base surgeons with respect to how long they typically recommend withholding CPAP following endonasal skull base surgery due to a lack of objective data to help guide practice. Not only is there a lack of consensus regarding when it is safe to resume CPAP, but there is often a lack of a plan at the time of surgery. In a cohort of 69 patients with documented OSA at the time of endonasal transsphenoidal pituitary surgery, White-Dzuro et al. report only 36% of these patients had a documented post-operative plan that addressed management of their OSA.<sup>12</sup> Further, in a 2020 survey of the members of the North American Skull Base Society, while a majority of respondents felt that a patient's OSA status had an effect on perioperative decision-making, only 18% of respondents reported use of a preoperative OSA screening protocol.<sup>17</sup> This highlights the lack of attention that has historically been given to the peri-operative management of OSA in the endonasal skull base patient population.

# CLINICAL AND CADAVERIC MODEL DATA

In an effort to make more well informed, data-guided decisions regarding when it is safe to resume CPAP following endonasal skull base surgery, Rimmer et al.<sup>18</sup> created a cadaveric model to measure the pressure delivered to the nasal cavity, sphenoid, and sella. In this study, three fresh cadaver heads were studied - all with pituitary gland, diaphragm sella, and cranial base dura intact and with the trachea and major cervical vessels oversewn to avoid pressure loss. CPAP equipped with size appropriate full-face masks were then applied to each cadaver head with pressures ranging from 5 to 20 cm H<sub>2</sub>O in fixed pressure mode. Intranasal pressures using microsensors were then recorded. Pressures were first recorded in the midnasal cavity before any endoscopic sinus surgery. Then, wide sphenoidotomies with a limited posterior septectomy was performed to simulate an endonasal transsphenoidal approach. Microsensors were placed along the floor of the sphenoid and pressures were recorded. Then, the sellar bone and dura were opened, microsensors were placed within the sella and sphenoid, and pressures were once again recorded. The results of this cadaveric model demonstrated excellent reliability and suggest that, on average, 81% of delivered CPAP pressures are transmitted to the midnasal cavity, 88% to 90% of delivered CPAP pressures are transmitted to the sphenoid sinus, and

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80% to 84% of delivered CPAP pressures are transmitted to the sella.18

This same group then used this validated cadaveric model to assess the effectiveness of various skull base repair techniques at withstanding positive pressure ventilation.<sup>19</sup> Three cadaver heads were again prepared as described above. In this study, a cruciate opening in the sellar dura was made, a complete hypophysectomy performed, and a 3 mm sellar diaphragm defect was surgically created. Pressure microsensors were placed in the sphenoid endonasally and in the sella transcranially, with position confirmed endonasally. Three commonly employed skull base repair techniques were analyzed on each of the three cadaver heads: (1) an onlay of two lavered sheets of oxidized cellulose (Surgicel<sup>TM</sup>, Ethicon, Inc. Somerville, NJ), (2) a synthetic dural substitute (Durepair<sup>TM</sup>, Medtronic, Minneapolis, MN) inlay with dural sealant glue (DuraSeal® Cranial Sealant System, Integra Lifesciences Corporation, Plainsboro, NJ) onlay, and (3) a synthetic dural substitute inlay with nasoseptal flap and dural sealant glue onlay. The cadaver calvaria were filled with water, and CPAP applied at various pressure settings ranging from 5 to 20 cm H<sub>2</sub>O. The integrity of the repair was considered 'breached' when air bubbles were visualized originating from the sellar region when viewed from the cranial cavity. The corresponding CPAP setting was defined as the breach point. Not surprisingly, the least robust repair technique - the oxidized cellulose onlay - breached in all three specimens between 11 and 14 cm H<sub>2</sub>O of delivered CPAP pressure; the synthetic dural substitute inlay repair only breached in one specimen at a delivered CPAP pressure of  $20 \text{ cm H}_2O$ ; and the most robust repair technique - the synthetic dural substitute inlay with the nasoseptal flap onlay - maintained integrity up to a delivered pressure of 20 cm of H<sub>2</sub>O in all specimens without evidence of breach. Also, of critical note, while between 79% and 95% of delivered CPAP pressure was transmitted to the sphenoid in all specimens at all levels of CPAP pressures, significantly less pressure was transmitted into the sella with the repairs in place. Between 22% and 56% of delivered CPAP pressures were transmitted into the sella with the first repair technique, but only between 0% and 20% were transmitted into the sella with the second repair technique, and only 0% to 13% was transmitted into the sella with the third repair technique.<sup>19</sup> This further supports the effectiveness of the repair techniques.

These novel cadaveric studies suggest that even with a simple oxidized cellulose onlay reconstruction, only a fraction of the delivered CPAP pressure is actually transmitted into the sella. Further yet, while this simplest reconstruction did not withstand positive pressure as effectively as the second and third repair techniques, breach did not occur until 11 cm H<sub>2</sub>O. When common auto-CPAP settings have been investigated, the usual median CPAP settings are only between 5.2-7.2 cm H<sub>2</sub>O.<sup>20</sup> These settings are notably lower than the breach point seen even with the least robust repair technique as demonstrated in the above referenced study.<sup>19</sup> Therefore, although this most simple onlay repair technique is less effective than the other two tested techniques at withstanding the effects of positive pressure ventilation, it may be just as effective as

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the more robust repair techniques in OSA patients who only require a low-pressure profile.

Given the cadaveric nature of these studies, the effect of human factors such as lung compliance could not be evaluated. In consideration of this, the group evaluated the pressures transmitted to the midnasal cavity in live subjects utilizing the same methodology and same pressure microsensors as presented above.<sup>21</sup> The results were consistent with those of the cadaver model study - approximately 85% of delivered CPAP pressure was transmitted to the midnasal cavity. While this supports the results of the cadaver model as it applies to actual patients, this human study was performed utilizing healthy subjects only and could not account for the effect of post-operative factors such as crusting, blood clot, nasal packing and mucosal edema. As such, the same group is actively engaged in a prospective study of post-operative patients in order to evaluate the aforementioned effects on the sinonasal transmission of CPAP pressure and the safety of early reinitiation of CPAP. In addition to these models studying the effects of CPAP on sinonasal pressures, small retrospective case series have been published endorsing the safety of early re-initiation of CPAP. In a retrospective review, Rieley et al. report 8 patients who underwent endoscopic transsphenoidal pituitary surgery with sellar reconstruction utilizing a synthetic and fat repair and received CPAP ventilation immediately post-operatively in the post-anesthesia care unit. They report similar rates of post-operative complications in patients with OSA who received CPAP immediately after surgery with those who did not (12% rate of post-operative CSF leak vs 5%, respectively, no reported statistically significant difference) and no cases of post-operative pneumocephalus.<sup>13</sup>

White-Dzuro et al.<sup>12</sup> report an additional 2 patients treated with early re-initiation of CPAP following transsphenoidal surgery and no cases of pneumocephalus. Thus, despite the sporadic reports of pneumocephalus following transsphenoidal surgery, the risk of post-operative CPAP related pneumocephalus may be less than initially assumed.<sup>15,22</sup>

# DISCUSSION

Ultimately, the decision to start CPAP postoperatively must be tailored to each patient based on the severity of his/her OSA, intraoperative findings, and the type of skull base repair employed. Based on the findings of the above studies it is likely safest to re-initiate CPAP on patients who have undergone more robust reconstructions, such as those including synthetic dural substitute inlay grafts with or without the addition of a nasoseptal flap onlay. Additionally, resuming CPAP at the lowest possible pressure setting is likely safest.

# CONCLUSIONS

There is a paucity of literature regarding when it is safe to resume CPAP ventilation following endonasal skull base surgery. Due to the lack of objective data, there is great variability in practice amongst practitioners. Recent studies employing cadaveric models and retrospective case series suggest that it may be safe to re-initiate CPAP therapy in the immediate post-operative period following endonasal skull base surgery. Critically understanding these pressures will help to develop practice guidelines based on objective data as to when, at what pressure, and on whom, CPAP may be safely restarted following endoscopic skull base surgery.

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#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available upon request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

#### ETHICS STATEMENT

This literature review was considered exempt from IRB review.

## DECLARATION OF COMPETING OF INTEREST

None.

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