Hemodynamic response, coughing and the incidence of cerebrospinal fluid leakage on awakening with an endotracheal tube or laryngeal mask airway in place after transsphenoidal pituitary surgery: a randomized clinical trial

Paola Hurtado  
Hospital Clinic of Barcelona

Javier Tercero  
Hospital Clinic of Barcelona

Marta García-Orellana  
Hospital Clinic of Barcelona

Joaquim Enseñat  
Hospital Clinic of Barcelona

Luis Reyes  
Hospital Clinic of Barcelona

Gemma Cabedo  
Hospital Clinic of Barcelona

Jose Rios  
Hospital Clinic of Barcelona

Enrique Carrero  
Hospital Clinic of Barcelona

Nicolas Riva  
Hospital Clinic of Barcelona

Jaume Fontanals  
Hospital Clinic of Barcelona

Isabel Gracia  
Hospital Clinic of Barcelona

Isabel Belda  
Hospital Clinic of Barcelona

Anna Lopez  
Hospital Clinic of Barcelona

Neus Fabregas  
Hospital Clinic of Barcelona
Research Article

**Keywords:** Laryngeal mask airway, neuroanesthesia, awakening, cerebral hemodynamic response, systemic hemodynamic response, cerebrospinal fluid leakage

**DOI:** https://doi.org/10.21203/rs.3.rs-208707/v1

**License:** This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Background:

We aimed to compare systemic and cerebral hemodynamic variables and cough incidence during emergence from general anesthesia after pituitary surgery in patients after extubation of an endotracheal tube (ETT) or after replacing the ETT with a laryngeal mask airway (LMA).

Methods:

Patients undergoing pituitary surgery were randomized (open-label parallel trial) to awaken with the ETT in place or after it had been replaced with a LMA before extubation. We recorded mean arterial pressure (MAP), heart rate, middle cerebral artery (MCA) flow velocity, regional cerebral oxygen saturation (SrO2), cardiac index, norepinephrine plasma concentrations, need for vasoactive drugs, coughing during emergence, and incidence of postoperative cerebrospinal fluid (CSF) leakage.

Results:

Forty-five patients were included. MAP was lower during emergence than at baseline in both groups. More patients required antihypertensive drugs in the ETT group (34.8% vs 14.3%; P = 0.17). MCA flow velocity was higher in the ETT group (e.g., mean [95% confidence interval] at 15 min, 103.2 [96.3–110.1] vs 89.6 [82.6–96.5] cm s⁻¹; P = 0.003). SrO₂, cardiac index, and norepinephrine plasma levels were similar. Coughing was more frequent in the ETT group (15% vs 81%; P < 0.001). CSF leakage occurred in 3 patients (13%) in the ETT group only.

Conclusions:

Placing a LMA before removing an ETT during emergence from anesthesia after pituitary surgery favors a safer cerebral hemodynamic profile and reduced coughing. This strategy may also lower the risk for CSF leakage.

Trial registration number:

NCT02988804 (clinicaltrials.org) (09/12/2016).

Background

The transnasal transsphenoidal endoscopic approach to the sella turca for pituitary surgery and the expanded endonasal approach to the skull base have both improved over the last decade. [1–2] The goal
of anesthetic management in pituitary surgery is to guarantee adequate depth of anesthesia, control arterial blood pressure to enhance endoscopic visibility in the surgical field, and ensure a smooth awakening to prevent bleeding associated with Valsalva maneuvers or hypertension. Recovery from general anesthesia usually involves sympathetic activation and catecholamine release, which increase blood pressure and heart rate and, thus, elevate cerebral blood flow and oxygen consumption. There is some evidence that rough emergence and poor hemodynamic control during endotracheal extubation may also favor such brain complications as edema or haemorrhage.[3] Measures to prevent agitation, hypertension, shivering, and coughing are therefore very well justified in neurosurgical patients. [4–5]

LMA removal has been reported to have a better safety profile than tracheal extubation, with a lower incidence of coughing, retching, and laryngospasm.[6] In this context, replacing an ETT with a LMA at the end of a procedure has been recommended to allow for smooth emergence in at-risk extubations,[7] in patients with highly irritable airway or in surgical procedures, such as after neurosurgery, where cardiovascular stimuli during extubation is not advisable. However, few studies have been done to test the effect of this recommendation. Our group showed that neurosurgical patients emerged from anesthesia with a more favorable hemodynamic profile, a lower incidence of coughing and less cerebral hyperemia when a LMA was placed just after removal of the endotracheal tube (ETT) but before emergence after undergoing a supratentorial cranectomy.[8]

The transnasal transsphenoidal endoscopic approach has been reported to have less associated morbidity than open surgery, [9–10] but postoperative cerebrospinal fluid (CSF) leakage remains a major limitation of this technique.[11] The incidence of CSF leakage was 8% in a patient series in our hospital. [2] Studies have linked this complication to postoperative coughing and lower airway disease.[12]

The aim of this randomized controlled trial was to study the effect on emergence of placing a LMA before removal of the ETT in the minimally invasive endoscopic endonasal transsphenoidal pituitary surgery. To that end, we compared systemic and cerebral hemodynamic variables and cough incidence during emergence from general anesthesia under two conditions: after ETT extubation, according to standard procedure or after replacement of the ETT with a LMA just before extubation. A secondary objective was to assess the effect of this approach in the incidence of CSF leakage in these patients.

**Patients And Methods**

This single-site randomized open-label parallel trial was approved by the research ethics committee of Hospital Clínic de Barcelona (file number HCB/2016/0781) and registered at clinicaltrials.org (NCT02988804) on December 9, 2016. A data analysis and statistical plan was written and posted on ClinicalTrials.gov and in the institutional review board (research ethics committee of Hospital Clínic de Barcelona) files before data were accessed. The study was performed according to the Declaration of Helsinki Criteria, and this manuscript adheres to the CONSORT guidelines. Patients provided written informed consent and were randomly allocated to one of two study groups.
Adult patients undergoing elective endoscopic endonasal transsphenoidal pituitary surgery were recruited from February 2017 until September 2019. We applied the following exclusion criteria before randomization: anticipated difficult airway (severe acromegaly, limited mouth opening) or unexpected Cormack–Lehane grade IV detected during laryngoscopy, risk of bronchial aspiration (e.g., gastroesophageal reflux disease or lower cranial nerve palsy), uncontrolled arterial hypertension during preoperative assessment, and contraindication for early emergence based on anesthetic criteria. Surgical complications (e.g., severe bleeding, surgical approach modification) after randomization but before extubation were also exclusion criteria.

Patient characteristics (age, body mass index, sex) and relevant aspects of past medical history were recorded. We also did a cough test during the preanesthetic evaluation.[13]

1.2.1 Anesthetic procedure

In the operating room, patients were premedicated with intravenous midazolam (1–2 mg). Standard monitoring consisted of electrocardiography, pulse oximetry, continuous arterial pressures (S/5; Datex Ohmeda, Helsinki, Finland), depth of anesthesia (bispectral index) (BIS Brain Monitoring System; Covidien, Mansfield, MA, USA), neuromuscular blockade (response to train-of-four stimulation), temperature and urine output, cerebral regional oxygen saturation (SrO₂) (INVOS 5100C Cerebral/Somatic Oximeter; Minneapolis, MN, USA), and cardiac index (LiDCOplus™; LiDCO, London, UK). A transcranial Doppler ultrasound monitor (Intraview; Rimed, Singen, Germany) was fixed at the temporal window to monitor middle cerebral artery (MCA) flow velocity during induction and emergence.

General anesthesia was provided with an intravenous site-effect target-controlled infusions of 4 µg mL⁻¹ propofol, 2 g mL⁻¹ remifentanil (Orchestra Infusion Workstation, Primea Base; Fresenius Vial, Bad Homburg v.d.H., Germany), and an intravenous perfusion of rocuronium. Propofol and remifentanil infusions were set to maintain the BIS index between 40 and 60. Rocuronium doses were given to maintain a response between T0 and T1 in train-of-four stimulation. After intravenous injection of 1.5 mg kg⁻¹ of lidocaine, we performed direct laryngoscopy and orotracheal intubation with a reinforced ETT (Lo-Contour Oral/Nasal cuffed tracheal tube; Mallinckrodt, Covidien, Tullamore, Ireland) in all patients. Tube sizes were assessed by the anesthetist according to a patient's sex and weight. We recorded the Cormack–Lehane grade, the number of intubation attempts, and the need for additional equipment (tube introducer, videolaryngoscope). The ventilator (Primus; Dräger Medical Hispania, Madrid, Spain) parameters were set to maintain normocapnia and a partial pressure of oxygen in arterial blood of 150–200 mm Hg. A pharyngeal tamponade was inserted to prevent the passage of blood to the stomach during surgery. One puff of xylometazoline 0.05% nasal spray was applied every 5 min for 1 hour before surgery in the ward.

During the surgical procedure, arterial blood pressure was kept low, at about 20% below a patient’s baseline but always with a MAP above 50 mm Hg; the SrO₂ was kept above 50 and no lower than 20%
below baseline. Antihypertensive agents (urapidil or clevidipine) were administered when needed, and the doses were recorded.

1.2.2 Randomization

At the end of surgery, with general anesthesia and muscle relaxation still in effect, we administered paracetamol (1 g) and ondansetron (4 mg) through the intravenous line and removed the pharyngeal tamponade.

The first author (P.H.) opened a sequentially numbered, sealed envelope with patient allocation to either the standard procedure (tracheal extubation, ETT group) or replacement of the tracheal tube with a Proseal LMA mask (Laryngeal Mask Co. Ltd., Le Rocher, Victoria, Mahe Seychelles) (LMA group) before emergence from anesthesia. We used a software-generated randomization list in a 1:1 ratio and unstratified blocks of four patients. The anesthetist was not blind to group assignment.

1.2.3 Study procedures

In the ETT group intravenous infusions of propofol, remifentanil and rocuronium were stopped and sugammadex (200 mg) was given to reverse the neuromuscular blockade. When the patient was breathing spontaneously and could follow simple commands, the tube was removed.

In the LMA group, after withdrawing the pharyngeal tamponade and aspirating pharyngeal secretions and with the patient still under general anesthesia, we inserted a size 4 or 5 LMA, according to the manufacturer’s recommendations, using a guided Bailey technique.[14–15] Specifically, the anesthetist first inserted a suction catheter 8–10 cm beyond the distal end of the drainage tube of the LMA to be used, and then inserted the mask behind the ETT, allowing the suction catheter to enter the esophagus and guiding the tip of the LMA into the correct position. After the cuff of the LMA was inflated to a pressure of 60 cm H$_2$O according to a cuff manometer (VBM Medizintechnik GmbH. Sulz, Germany), the ETT cuff was deflated and the tube removed. Ventilation continued with the same parameters through the LMA. Intravenous infusions of propofol, remifentanil and rocuronium were then stopped and sugammadex (200 mg) was given. Gentle manual ventilator assistance was provided until the patient resumed spontaneous breathing and responded to simple commands. The LMA was then removed. Ondansetron to prevent nausea was continued in the postoperative period.

Hemodynamic variables (blood pressure, cardiac index, heart rate, SrO$_2$, MCA flow velocity) were recorded at 8 moments: baseline: before anesthetic induction; end of surgery: before extubation (ETT group) or before ETT replacement (LMA group); and throughout emergence at 1, 5, 10, 15, 30, and 60 min after extubation or LMA removal. The last blood pressure and heart rate measurements were taken in the postoperative recovery room. Respiratory variables (including end-tidal carbon dioxide concentration) and arterial blood gases were recorded during mechanical ventilation.

We measured norepinephrine plasma concentrations with a radioimmunoassay kit (Noradrenalin RIA, IBL, Hamburg, Germany) before induction and 30 min after extubation. The normal norepinephrine
concentration range in our laboratory is $136–364 \text{ pg mL}^{-1}$.

Any coughing episode during emergence was recorded. Postoperative events were recorded as follows: epistaxis and CSF leakage, defined as clinically important rhinorrhea diagnosed by the neurosurgeon and requiring repair of the fissure in the nasal cavity. The patients were expected to be discharged on the fourth postoperative day, and all were followed for one month after surgery.

1.2.4 Statistical analysis

The primary endpoint was postoperative MAP. We calculated that we would need 21 patients in each group to detect between-group differences of 10 mm Hg in MAP, assuming a standard deviation (SD) of 11 mm Hg, with a type-1 error of 5% and power of 80%.

Mean (SD) results and 95% confidence intervals (CI) were calculated for each group. The global estimated group effects and 95% CI adjusted to baseline were calculated for each variable. Longitudinal models were constructed, using the generalized estimating equation method to account for within-subject correlations over time by means of an unstructured correlation matrix. These models were used to analyze the effect of the intervention on MAP and the secondary endpoints ($\text{SrO}_2$ and cough incidence) during emergence. The main independent factors were time from baseline (end of surgery) and study group (standard extubation vs extubation after prior placement of a LMA). To evaluate the statistical significance of differences at each data recording time, the model, including the time interaction by group, was run again for each dependent variable. Bonferroni correction of P values was used to adjust for multiplicity in time-by-time analyses.

Homogeneity of groups at baseline was tested. A post-hoc analysis was performed to compare the hypertensive patients to all the patients enrolled. All analyses were done with SPSS version 25 (IBM, Armonk, NY, USA), assuming the superiority of the intervention and a 2-tailed type I error of 5%.

Results

Forty-five patients were randomized. No differences in patient characteristics were found between groups at baseline (Table 1). One patient was lost from the ETT group because extubation was delayed due to life-threatening intraoperative bleeding (carotid artery puncture) (Fig. 1).
Table 1
Patient characteristics

|                        | ETT group | LMA group |
|------------------------|-----------|-----------|
| Age (yr)               | 51.7 (14.9) | 52.3 (11.4) |
| Sex (female/male)      | 12/11     | 13/9      |
| BMI (kg m\(^{-2}\))    | 27.8 (3.6) | 29.3 (5.5) |
| Cough test (positive)  | None      | None      |
| Sleep apnea            | 2 (9%)    | 2 (9%)    |
| Acromegaly             | 3 (13.6%) | 3 (13.6%) |
| Well-controlled hypertension | 11 (50%)  | 11 (50%) |

*Values are expressed as mean (SD) or number of patients (percentage).

ETT indicates endotracheal tube; LMA, laryngeal mask airway; BMI, body mass index.

The Cormack-Lehane grade was II or lower in all cases, and all the ETTs were easily inserted. The LMA was successfully inserted on first attempt in all LMA-group patients. No respiratory complications were observed during device replacement and emergence from anesthesia in the LMA group. Nor did partial pressure of oxygen in arterial blood or increases in end-tidal carbon dioxide concentration in expired air decrease during device replacement in the LMA group. No complications related to ETT replacement with a LMA were detected.

Hemodynamic variable changes are listed in Table 2 and plotted in Figs. 2 and 3. Thirteen patients (29.5%) required intraoperative antihypertensive drugs to keep blood pressure low and within the range established for each patient. One patient needed ephedrine for an intraoperative hypotensive episode. Compared to baseline, blood pressure was significantly lower at all measured times during emergence from anesthesia in both groups. The greatest difference occurred at the end of surgery (P < 0.001) (Fig. 2).
Table 2
Hemodynamic data of patients in both groups

|                     | Baseline | Before extubation | 1 min | 5 min | 10 min | 15 min | 30 min | 60 min |
|---------------------|----------|-------------------|-------|-------|--------|--------|--------|--------|
| **Systolic blood pressure (mm Hg)** |          |                   |       |       |        |        |        |        |
| ETT                 | 135.8 (28) | 100.8 (24)*       | 123 (21)# | 123.9 (20) | 127.4 (20) | 126.4 (16) | 124.7 (21)# | 126.3 (19) |
| LMA                 | 138.6 (25) | 91.9 (11)*        | 112.8 (23)* | 120.1 (22)* | 122.1 (23)* | 120.4 (20)* | 118.1 (18)* | 118.7 (16)* |
| **Diastolic blood pressure (mm Hg)** |          |                   |       |       |        |        |        |        |
| ETT                 | 81.1 (16)  | 62.7 (17)*        | 72.3 (12)# | 71.4 (14)# | 70.3 (13)* | 72.1 (13)* | 73.6 (11)* | 72.0 (11)* |
| LMA                 | 81.6 (14)  | 57.1 (9)*         | 67.1 (12)* | 72.1 (11)# | 72 (12)* | 71.1 (14)# | 69.4 (11)* | 69.9 (8)* |
| **Heart rate (beats per min)** |          |                   |       |       |        |        |        |        |
| ETT                 | 63.6 (11)  | 62.3 (15)         | 63.3 (17) | 64 (16) | 64 (14) | 65.1 (13) | 64 (11) | 60.8 (11) |
| LMA                 | 69.8 (12)  | 69.5 (12)         | 74.3 (13) | 75.9 (12)# | 76.4 (11)# | 73.4 (11) | 72.7 (11) | 73 (11) |
| **Cardiac index (L min⁻¹)** |          |                   |       |       |        |        |        |        |
| ETT                 | 2.9 (1)    | 2.1 (1)*          | 2.4 (1)# | 2.4 (1)# | 2.5 (1) | 2.6 (1) | 2.7 (1) | –      |
| LMA                 | 3.1 (1)    | 2.48 (1)#         | 2.58 (1)# | 2.7 (1) | 2.97 (1) | 2.8 (1) | 2.7 (1) | –      |

Values are expressed as mean (SD).

ETT indicates endotracheal tube; LMA, laryngeal mask airway; MCA, middle cerebral artery; SrO₂, regional cerebral oxygen saturation.

P value: comparisons between groups; Comparisons of group means for intraindividual differences with respect to baseline: *P < 0.001; #P < 0.05.
### Emergence from anesthesia

|                  | P value | SrO\(_2\), (%) |
|------------------|---------|-----------------|
|                  |         | ETT             | LMA             |
| SrO\(_2\), (%)   |         |                 |                 |
|                  |         | 67.7 (8)        | 65.5 (8)        |
|                  | 0.543   | 66.8 (7)        | 65.8 (10)       |
|                  | 0.184   | 69.1 (8)        | 68.9 (10)       |
|                  | 0.723   | 69.3 (8)        | 70.9 (9) #      |
|                  | 0.477   | 70.0 (7)        | 70.1 (8)        |
|                  | 0.240   | 70.9 (7)        | 70.4 (8)        |
|                  | 0.580   | 70.5 (7)        | 70.4 (9)        |
|                  | 0.990   |                 |                 |
| P value          |         | 0.366           | 0.687           |
|                  |         | 0.946           | 0.982           |
|                  |         | 0.541           | 0.845           |
|                  |         | 0.953           |                 |

| Mean MCA flow velocity (cm s\(^{-1}\)) |
|---------------------------------------|
| ETT                                   |
| 57.0 (15)                             |
| 50.2 (17)                             |
| 59.4 (17)                             |
| 63.3 (20)                             |
| 65.8 (24)                             |
| 66.5 (18)                             |
| 62.0 (18)                             |
| LMA                                   |
| 55.8 (13)                             |
| 42.2 (12)*                            |
| 57.7 (19)                             |
| 56.6 (17)                             |
| 58 (18)                               |
| 55.7 (13)                             |
| 55.2 (13)                             |
| P value                               |
| 0.783                                 |
| 0.063                                 |
| 0.759                                 |
| 0.216                                 |
| 0.204                                 |
| 0.020                                 |
| 0.146                                 |

Values are expressed as mean (SD).

ETT indicates endotracheal tube; LMA, laryngeal mask airway; MCA, middle cerebral artery; SrO\(_2\), regional cerebral oxygen saturation.

P value: comparisons between groups; Comparisons of group means for intraindividual differences with respect to baseline: *P < 0.001; #P < 0.05.

Although there were no significant between-group differences in blood pressure, more ETT group patients required antihypertensive drugs during emergence (34.8% vs 14.3%, P = 0.116) (Fig. 2). Heart rate and the cardiac index did not significantly change from baseline and were similar in the two groups.

The peak MCA flow velocity measurements were significantly higher during ETT extubation compared to LMA removal at 5, 10, 15 and 30 min (Fig. 3) (P = 0.003). Mean MCA flow velocity was also significantly higher at 15 min, P = 0.020), but SrO\(_2\) was similar in the 2 groups (Table 2).

Mean (SD) norepinephrine plasma levels were higher than at baseline at the end of emergence within each group, rising from 86.1 (65.9) to 103.7 (103.7) pg mL\(^{-1}\) in the ETT group and from 95.1 (59.2) to 175.5 (331.7) pg mL\(^{-1}\) in the LMA group. The difference between the groups was not significant (P = 0.329).
The analysis of hemodynamic variables in the subgroup of patients with a history of hypertension in each group showed that these patients did not differ from the full cohort of patients enrolled.

Significantly more patients had coughing episodes in the ETT group than in the LMA group: 18 (81%) vs 5 (15%) patients, respectively (P < 0.001). Postoperative epistaxis was recorded in 4 patients (18.2%) in the ETT group and 3 (15%) in LMA group. Postoperative CSF leakage occurred in 3 patients (13%) in the ETT group; all underwent surgical repair and required an extended hospital stay of at least one week (range, 8–16 days). No patients in the LMA group had this complication. However, the differences were not significant.

**Discussion**

Arterial blood pressure during emergence from anesthesia was stable in both groups but lower than baseline values, regardless of whether the ETT was replaced with a LMA or not before the patient awoke. Blood pressure tended to be nonsignificantly higher in the ETT group patients, even though they received more antihypertensive treatment during emergence. However, the rise was not clinically relevant.

These findings contrast with the different hemodynamic profile of our previous study performed in patients after supratentorial craniotomy with a similar protocol. [8] In our former clinical trial on supratentorial craniotomy patients, baseline mean arterial pressure was lower than in this present study (about 20 mmHg lower). We speculate that the preoperative administration of a quite high dose of xylometazoline could provoke a similar mild hypertensive effect in all included patients. Moreover, the present studied population had a 50% of well controlled chronic hypertensive patients in both groups, compared with an 18% in our previous study. On the other side, strict intraoperative control of arterial blood pressure, maintaining values within the lowest safe threshold, to optimize the surgical field through the endoscopic procedure is a unarguable clinical objective in this type of surgery. For all these reasons, the intraoperative tight control of blood pressure control in this study could minimize the differences observed during the emergence. Finally, our systematic treatment of any hypertensive peak during emergence and prompt extubation after resumption of spontaneous breathing may explain the absence of a difference in MAP between the two groups. Another possible explanation for the similarly relative low emergence MAP values in both groups in the present study compared to our previous one is that pain immediately after transsphenoidal pituitary surgery may be less than after craniotomy, making blood pressure easier to control.[16]

Although we did not find between-group differences in MAP during emergence, we did see a higher mean MCA flow velocity in the ETT group. Since the anesthetic management and ventilation parameters were identical in both groups and no patient was hypercapnic at any moment during the study, the difference in MCA flow velocity was probably caused by slight differences in MAP, even though the group means did not differ significantly.

Norepinephrine measured levels were low and similar in both groups. Our patients were anesthetized with target-controlled intravenous propofol-remifentanil, so our observation of this stress hormone is
consistent with a recent study that found that adrenocorticotropic hormone levels were significantly lower immediately after this type of anesthesia than after balanced anaesthesia.[17] However, since a better stress hormone response has been reported with LMA use in laparoscopic gastric banding[18] and elective orthopedic surgery or general surgical procedures,[19] we did expect to see even lower values in the LMA group. We attribute the lack of difference in our study to the strict control of blood pressure and gentle extubation that is so necessary in neurosurgery.

Another main finding of our study was that patients in the LMA group had significantly fewer coughing episodes during emergence compared to the ETT group. This finding is in line with our previous study [8] and other studies that showed fewer episodes of postoperative cough, hypoxemia, and nausea or vomiting associated with the LMA removal than with extubation. [18–19] Smooth emergence, without coughing, is particularly important in skull base surgery, justifying LMA placement before removing the ETT.

The higher rate of coughing in the ETT group could be related to the 3 episodes of CSF leakage in this group. Hanba and colleagues [12] suggested that lower airway disease, commonly associated with frequent coughing, might be a risk factor for postoperative CSF rhinorrhea. Their patients undergoing pituitary surgery who had this condition had almost a two-fold higher incidence of rhinorrhea compared to a cohort of disease-free patients. Their findings are consistent with those of a retrospective analysis of 2918 patients, 84 (2.9%) of whom were readmitted or reoperated for CSF leakage within 30 days of skull base surgery.[20] Chronic obstructive pulmonary disease was significantly associated with CSF leakage in those patients. In our study, the 3 patients with rhinorrhea required reintervention (flap closure of the fistula), prolonging the hospital stay. None of the 3 patients had chronic obstructive disease, but two of them were active smokers. Our study was not designed to find differences in CSF leakage, however. The small sample size to demonstrate an association between coughing and this complication is a limitation of the study. Nevertheless, all our patients were operated by the same team of surgeons, and the procedures were similar in both groups.

Replacing an ETT with a LMA at the end of the procedure has been recommended to allow a smooth extubation in “at-risk” patients, such as smokers, asthmatics and other patients with irritable airways or those in whom the surgical repair may be compromised by cardiovascular stimulation.[7] Emergence is the most intense moment for systemic and cerebral hemodynamic changes, even when extubation is performed meticulously.[4] Using the Bailey manoeuvre[14] in selected patients still under adequate depth of anesthesia is a fast, effective and safe way to avoid apnea and a possible increase in PaCO₂, which could disturb systemic and cerebral hemodynamics. However, it is not recommended in patients with anticipated or known difficult airway or at high risk of bronchial aspiration.[7] We used the Proseal LMA because it seals the airway better than first generation devices, allows evacuation of gastroesophageal contents, and guided insertion is possible. This LMA has been successfully used in other neurosurgical settings as lumbar spine microsurgery,[21] ventriculoperitoneal shunt [22] and awake craniotomy.[23]

**Conclusion**
In conclusion, placing a LMA before removing an ETT and ventilating through the mask during emergence from anesthesia after pituitary surgery favors a safer cerebral hemodynamic profile and reduced coughing. The possibility that this strategy may also lower the risk for CSF leakage warrants further investigation.

**List Of Abbreviations**

ETT  
Endotracheal tube  
LMA  
Laryngeal mask airway  
MAP  
Mean arterial pressure  
SrO2  
Regional cerebral oxygen saturation  
CSF  
Cerebrospinal fluid leakage

**Declarations**

**Ethics approval and consent to participate**

This single-site randomized open-label parallel trial was approved by the research ethics committee of Hospital Clínic de Barcelona (file number HCB/2016/0781). Patients provided written informed consent.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The datasets used and analysed during this study are available from the corresponding author on reasonable request.

**Competing interests**

Dr López has received material and funding for academic or scientific purposes from Teleflex, Ambu A/S and Bioser, and as a consultant for Ambu A/S.

Dr Valero has received consulting fees from Medtronic.

The other authors declare that they have no conflict of interest.

**Funding statement**
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Support was provided solely from departmental sources.

**Author contributions**

PH: Conceptualization, Methodology, Formal analysis, Investigation, data curation, writing; JT: investigation, writing; MGO: investigation, writing; JE: investigation, writing; LR: investigation, writing; GC: Investigation, writing; JR: Conceptualization, Methodology, Formal analysis; EC: Investigation, writing; NR: Investigation, writing; JF: Investigation, writing; IG: Investigation, writing; IB: Investigation, writing; AL: Investigation, writing; NF: Investigation, writing; RV: Conceptualization, Methodology, Formal analysis, Investigation, data curation, formal analysis, writing.

**Acknowledgments**

The authors thank neurosurgery nurses Ana Quintana, Gloria Pastor for their assistance with the biochemistry analyses; and Dr Manuel Morales and their laboratory support staff for their measurements of norepinephrine plasma concentrations (Biochemistry and molecular genetics laboratory, Hospital Clinic de Barcelona, Spain). Mary Ellen Kerans advised on English usage in some versions of the manuscript.

**References**

1. Lund VJ, Stammberger H, Nicolai P, Castelnuovo P, Beal T, Beham A et al. European position paper on endoscopic management of tumours of the nose, paranasal sinuses and skull base. Rhinol Suppl. 2010 Jun 1;22:1–143.

2. Ensenat J, de Notaris M, Sanchez M, Fernandez C, Ferrer E, Bernal-Sprekelsen M et al. Endoscopic endonasal surgery for skull base tumours: technique and preliminary results in a consecutive case series report. Rhinology. 2013 Mar;51(1):37–6. doi: 10.4193/Rhino12.090.

3. Schubert A. Cerebral hyperemia, systemic hypertension, and perioperative intracranial morbidity: is there a smoking gun. *Anesth Analg* 2002; <background-color:#FFCC66;bu>94</background-color:#FFCC66;bu>:485–487. doi: 10.1097/00000539-200210000-00002.

4. Bruder, N. J. Awakening management after neurosurgery for intracranial tumours. *Curr Opin Anaesthesiol* 2002; 15(5), 477–82. doi: 10.1097/00001503-200210000-00001.

5. Fábregas, N., & Bruder, N. Recovery and neurological evaluation. *Best Pract Res Clin Anaesthesiol* 2007; 21(4), 431–47. doi: 10.1016/j.bpa.2007.06.006.

6. Amorocho MC, Fat I. Anesthetic Techniques in Endoscopic Sinus and Skull Base Surgery.*Otolaryngol Clin North Am.* 2016 Jun;49(3):531–47. doi: 10.1016/j.otc.2016.03.004.

7. Difficult Airway Society Extubation Guidelines Group, Popat M, Mitchell V, Dravid R, Patel A, Swampillai C et al. Difficult Airway Society Guidelines for the management of tracheal extubation. *Anaesthesia.* 2012 Mar;67(3):318–40. doi: 10.1111/j.1365-2044.2012.07075.x.
8. Perelló-Cerdà L, Fàbregas N, López AM, Rios J, Tercero J, Carrero E et al. ProSeal Laryngeal Mask Airway Attenuates Systemic and Cerebral Hemodynamic Response During Awakening of Neurosurgical Patients: A Randomized Clinical Trial. J Neurosurg Anesthesiol. 2015 Jul;27(3):194–202. doi: 10.1097/ANA.0000000000000108.

9. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH. Endoscopic skull base surgery: a comprehensive comparison with open transcranial approaches. Br J Neurosurg 2012; 26(5):637–48. doi:10.3109/02688697.2012.654837.

10. Rioja E, Bernal-Sprekelsen M, Enriquez K, Enseñat J, Valero R, de Notaris M et al. Long-term outcomes of endoscopic endonasal approach for skull base surgery: a prospective study. Eur Arch Otorhinolaryngol. 2016 Jul;273(7):1809–17. doi:10.1007/s00405-015-3853-9.

11. Ruggeri AG, Cappelletti M, Giovannetti F, Priore P, Pichieri A, Delfini R. Proposal of Standardization of Closure Techniques After Endoscopic Pituitary and Skull Base Surgery Based on Postoperative Cerebrospinal Fluid Leak Risk Classification. J Craniofac Surg. 2019 Jun;30(4):1027–32. doi:10.1097/SCS.0000000000005540.

12. Hanba C, Svider PF, Jacob JT, Guthikonda M, Liu JK, Eloy JA et al. Lower airway disease and pituitary surgery: Is there an association with postoperative cerebrospinal fluid leak? Laryngoscope. 2017 Jul;127(7):1543–50. doi: 10.1002/lary.26216.

13. Morice AH, Fontana GA, Belvisi MG, Birring SS, Chung KF, Dicpinigaitis PV et al. ERS guidelines on the assessment of cough. Eur Respir J. 2007 Jun;29(6):1256–76. doi:10.1183/09031936.00101006.

14. Nair I, Bailey PM. Review of uses of the laryngeal mask in ENT anaesthesia. Anaesthesia. 1995;50:898–900. doi: 10.1111/j.1365-2044.1995.tb05860.x.

15. García-Aguado R, Viñoles J, Brimacombe J, Vivó M, Lópe-Estudillo R, Ayala G. Suction catheter guided insertion of the ProSeal laryngeal mask airway is superior to the digital technique. Can J Anaesth. 2006; 53:398–3. doi: 10.1007/BF03022507.

16. Chowdhury T, Garg R, Sheshadri V, Venkatraghavan L, Bergese SD, Cappellani RB et al. Perioperative Factors Contributing the Post-Craniotomy Pain: A Synthesis of Concepts. Front Med (Lausanne). 2017 Mar;4:23. doi: 10.3389/fmed.2017.00023.

17. Yhim HB, Oh HM, Yoon HK, Kim YH, Park HP. A Retrospective Observational Study of the Neuroendocrine Stress Response in Patients Undergoing Endoscopic Transsphenoidal Surgery for Removal of Pituitary Adenomas: Total Intravenous Versus Balanced Anesthesia. J Neurosurg Anesthesiol. 2019 Aug 23. doi:10.1097/ANA.0000000000000638. [Epub ahead of print]

18. Carron M, Veronese S, Gomiero W, Folotto M, Nitti D, Ori C et al. Hemodynamic and hormonal stress responses to endotracheal tube and ProSeal Laryngeal Mask Airway™ for laparoscopic gastric banding. Anesthesiology. 2012 Aug;117(2):309–20. doi: 10.1097/ALN.0b013ef31825b6a80.

19. Dahaba AA, Prax N, Gaube W, Gries M, Rehak PH, Metzler H. Haemodynamic and catecholamine stress responses to the Laryngeal Tube-Suction Airway and the Proseal Laryngeal Mask Airway. Anaesthesia 2006; 61:330–4. doi: 10.1111/j.1365-2044.2006.04548.x.
20. Perry A, Kerezoudis P, Graffeo CS, Carlstrom LP, Peris-Celda M, Meyer FB et al. Little Insights from Big Data: Cerebrospinal Fluid Leak After Skull Base Surgery and the Limitations of Database Research. World Neurosurg. 2019 Jul;127:e561-e569. doi: 10.1016/j.wneu.2019.03.207.

21. Hurtado P, Fàbregas N, Forero C, Tercero J, Carrero E, de Riva N et al. Laryngeal Mask Ventilation During Lumbar Spine Neurosurgery in Knee-Chest Position is Feasible. J Neurosurg Anesthesiol. 2017 Jul;29(3):317–321. doi: 10.1097/ANA.0000000000000277.

22. Hurtado P, Valero R, Tercero J, Carrero E, de Riva N, López AM et al. Experience with the proseal laryngeal mask in ventriculoperitoneal shunting. Rev Esp Anestesiol Reanim. 2011 Jun-Jul;58(6):362–4. doi: 10.1016/s0034-9356(11)70085-8.

23. Tongier WK, Joshi GP, Landers DF, Mickey B. Use of the laryngeal mask airway during awake craniotomy for tumor resection. J Clin Anesth. 2000 Dec;12(8):592–4. doi: 10.1016/s0952-8180(00)00211-7.