# Analysis of risk factors for cerebrospinal fluid leakage in endoscopic endonasal surgery for neuroendocrine pituitary tumors.

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## Introduction

Neuroendocrine pituitary tumors (PitNET) account for approximately 15% of primary intracranial neoplasms. The endoscopic endonasal approach (EEA) is currently the most common surgical technique used to treat this pathology. One of the main complications of this procedure is the CSF leakage.

## Materials and Methods

A retrospective analysis was conducted on patients operated by the same surgeon between **2019 and 2023** with a diagnosis of PitNET using EEA. The final sample size was of **121 patients**. Clinical, radiological, surgical, and oncological variables associated with intraoperative CSF leakage (FiOP) and postoperative CSF leakage (FpOP) were analyzed.
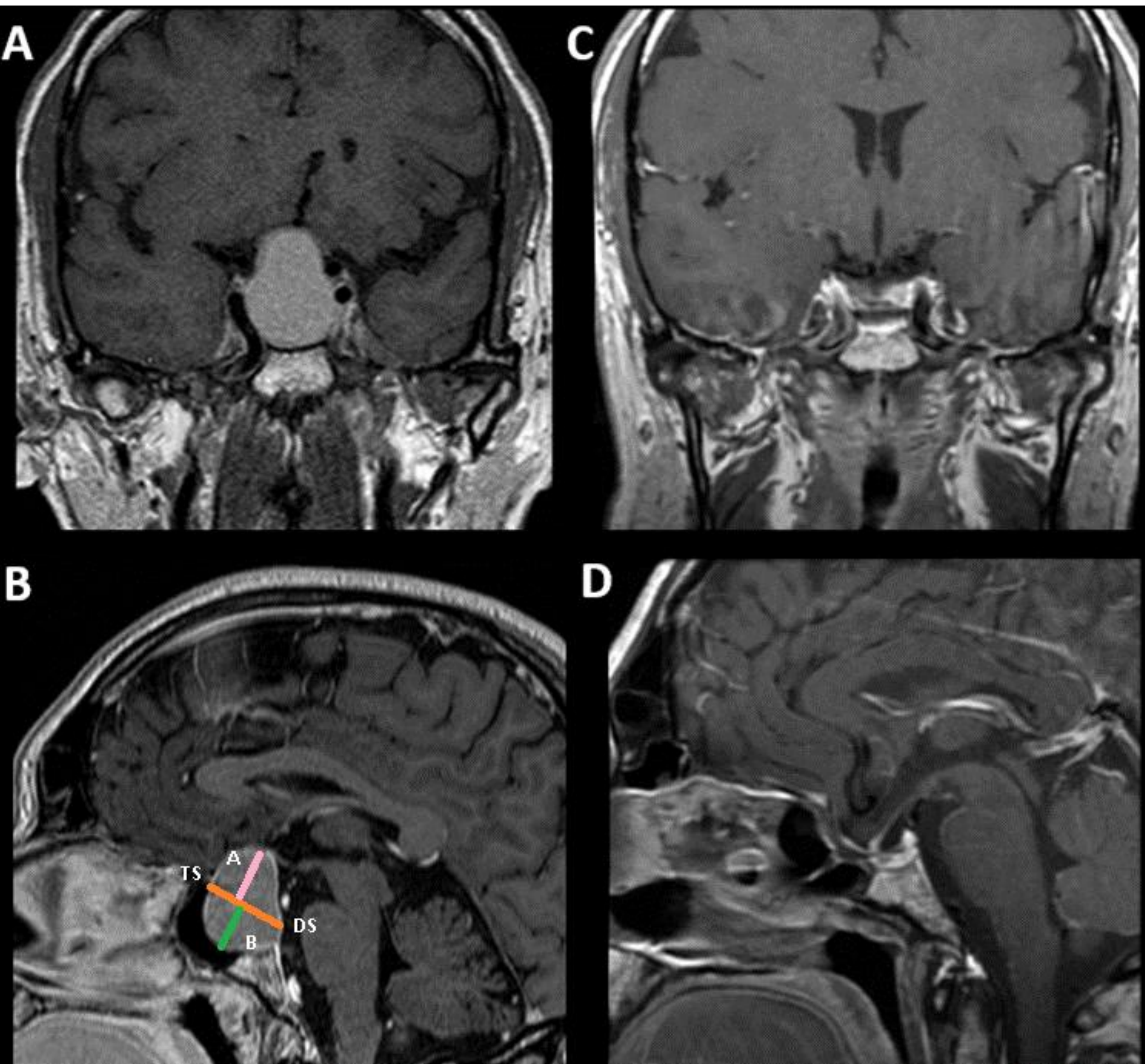


Figure 1. T1 weighted with gadolinium MRI of a PitNet case.
A. Preoperative coronal image. B. Preoperative sagittal image depicting: the "tuberculum sellae - dorsum sellae" (TS-DS) plane and variables of tumor extension overlying the TS-DS plane and the tumor extension underlying the TS-DS plane. By measuring these variables, we obtain the "sellar coefficient" (CS= A / B). C&D show postoperative coronal and sagittal images.

## Results

The incidence of **FiOP** was **41.3%.** Univariate analysis identified several significant risk factors for this complication. In multivariate analysis, four factors showed independent association: pituitary apoplexy, suprasellar tumor extension above tuberculum sellae - dorsum sellae (TS-DS) plane, subtotal tumor resection, weak sellar barrier, and sellar coefficient. Regarding **FpOP**, its incidence was **3.3%**. The grade of FiOP was the main determinant factor. Additionally, FpOP was associated with an increased risk of complications such as **meningitis and vasospasm**.

## Discussion

The anatomical features of tumor growth were crucial in determining the risk of FiOP.

The sellar coefficient, which represents the ratio of tumor extension above to below the tuberculum sellae-dorsum sellae (TS-DS) plane, proved to be a crucial predictor. ROC curve analysis determined an optimal cutoff value of 0.75, with values above this threshold significantly increasing the likelihood of moderate to severe FiOP (Esposito Kelly grades 2 and 3). Logistic regression further validated this result, as can be seen in Table 1. This finding, as well as the association of the superior extension over the TS-DS line, imply that cephalic tumor growth, limited by the sellar diaphragm, could lead to diaphragmatic compromise, thereby raising the risk of FiOP.

The sellar barrier concept reinforces these findings, with its weakness acting as a prognostic factor for the risk of FiOP (p 0,002). These observations highlight the significance of assessing sellar anatomy during preoperative planning to predict the risk of intraoperative complications.

The pathophysiology behind the relationship between pituitary apoplexy and the risk of FiOP may be related to the fact that post-ischemic edema or rapid tumor growth caused by intralesional hemorrhage, both of which impair the structural integrity of the sellar region. The most vulnerable areas, including the sellar roof and lateral edges, are especially prone to disruption, reducing the strength of the sellar diaphragm and making it more susceptible to intraoperative injury.

Finally, the relationship between subtotal resection and risk of FiOP may be in relation to the fact that invasive tumors usually require more aggressive maneuvers and more prone to be sub totally resected.

| Variable | OR | CI | p value |
|---|---|---|---|
| Subtotal resection | 1.5 | 0.15; 1.2 | 0,05 |
| Apoplexy | 1.73 | 0.56; 5 | 0,05 |
| Weak sellar barrier | 2.1 | 1.7; 3.9 | 0,002 |
| Superior extension TS-DS line | 4.5 | 0.48; 7.2 | 0,04 |
| "Sellar coefficient" | 1.67 | 1.4; 1.8 | 0,02 |

Table 1. Factors associated with intraoperative CSF leak (multivariate logistic regression R2 0.76)

## Conclusions

CSF leaks in EEA for PitNET have an impact on **surgical time**, **hospital stay**, and increase the risk of **complications**. This emphasizes the importance of comprehensive preoperative evaluation and precise surgical planning. By integrating a deeper understanding of risk factors and employing tools such as the sellar coefficient, we aim to improve surgical planning, minimize complications, and ultimately enhance patient care.

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