Transsphenoidal approach for pituitary neuroendocrine tumor

Transsphenoidal surgery is the preferred first-line therapy for most pituitary neuroendocrine tumor (PA), and the conventional strategy of treatment is intracapsular resection(IR). The protocol of extracapsular resection(ER), which considers the pseudocapsule as the PA boundary for surgical removal, has also been introduced.

A systematic literature review was performed in the PubMed, EMBASE, Web of Science and Cochrane databases. Articles comparing IR and ER were included.

There were 7 studies containing 1768 cases in accordance with the inclusion criteria. Although the meta-analysis showed no significant difference in complete resection, a sensitivity analysis revealed that ER was more conducive to total PA resection than IR. Moreover, we found a significant difference in favor of ER regarding biochemical remission. Furthermore, there was no significant difference in the incidence rate of certain complications, such as hormone deficiency, diabetes insipidus, intraoperative cerebrospinal fluid(CSF), and postoperative Cerebrospinal fluid fistula. However, sensitivity analysis suggested that IR decreased the risk of intraoperative Cerebrospinal fluid fistula.

This meta-analysis unveiled that ER contributed to biochemical remission. To some extent, our results also showed that ER played a positive role in complete resection, but that IR reduced the incidence of intraoperative Cerebrospinal fluid fistula. However, the available evidence needs to be further authenticated using well-designed prospective, multicenter, randomized controlled clinical trials [1)]

Cerebrospinal fluid fistula after transsphenoidal surgery for pituitary neuroendocrine tumors may be prevented by skull base reconstruction with fat autograft. However, graft changes may interfere with the interpretation of postoperative images. The aim of Cossu et al. was to describe the radiological evolution of the fat autograft.

A retrospective analysis was performed, including patients undergoing transsphenoidal surgery for pituitary neuroendocrine tumors with a fat autograft for skull base reconstruction. Clinical and radiological data were collected, with an assessment of fat autograft and the extent of resection. Statistical analysis was performed using Kruskal-Wallis and Wilcoxon signed-rank test while Spearman's Rho was used to analyze the relationship between variables.

Seventy-two patients were included. Macroadenomas was diagnosed in 62 cases (86.1%) and in 21 cases an invasion of the cavernous sinus was described (29%). Gross total resection was achieved in 84.7% of cases. The volume of the fat graft significantly decreased between 3 months and 1 year after surgery ($p = 0.01$) and between 1 year and the last follow-up (mean 4.63 years, $p < 0.01$). Fat signal ratio significantly diminished between 3 months and 1 year in unenhanced and enhanced T1-weighted sequences ($p = 0.04$ and $p = 0.02$ respectively). Volume reduction was related to the decrease in the signal ratio in unenhanced T1 sequences ($p = 0.008$).

Fat resorbs with time: almost 50% of the fat volume is lost during the first year after surgery and 60% is resorbed at 4.6 years. T1-signal, before and after gadolinium injection, also decreases during the first year, probably because of the progressive fibrosis of the graft. This information will contribute to the interpretation of postoperative images [2)].

The aim of a study of Butenschoen et al. was to analyze the postoperative improvement of visual function after adenoma resection and to identify prognostic factors for the postoperative clinical recovery. They performed a retrospective analysis of all consecutive patients treated via a transsphenoidal approach for pituitary neuroendocrine tumors from April 2006 to December 2019 in a high-volume neurosurgical department. The primary outcome was postoperative visual acuity and visual field impairment; the clinical findings were followed up to 3 months after surgery and correlated with clinical and radiographic findings. In total, 440 surgeries were performed in our department for tumors of the sella region in a time period of 13 years via a transsphenoidal approach, and 191 patients included in the analysis. The mean age was 55 years, and 98% were macroadenomas. Mean preoperative visual acuity in patients with preoperative impairment (n = 133) improved significantly from 0.64/0.65 to 0.72/0.75 and 0.76/0.8 (right eye R/left eye L) postoperatively and at 3 months follow-up ($p < 0.001$). Visual acuity significantly depended on Knosp classification but not Hardy grading. The strongest predictor for visual function recovery was age. Transsphenoidal pituitary tumor resection remains a safe and effective treatment in patients with preoperative visual impairment. It significantly improves visual acuity and field defects after surgery, and recovery continues at the 3 months follow-up examination [3].

Dai et al. quantitatively synthesized the comparative efficacy and safety of the most common surgical approaches including endoscopic transsphenoidal approach, sublabial transsphenoidal microsurgery (STMS) and endonasal transsphenoidal microsurgery (ETMS) for all kinds of pituitary tumors. This systematic review and network meta-analysis were performed on randomized controlled trials (RCTs) and comparison studies from databases of Pubmed, EMBASE, and the Cochrane Library. They selected the rate of gross complete resection as the primary outcome of efficacy. And the incidence of all complications, cerebrospinal fluid (CSF) leak, diabetes insipidus, nasal septal perforation, death, and bleeding were designed as our primary outcomes of safety. Twenty-seven studies with 2618 patients were included in this network meta-analysis. On efficacy, there was no statistical difference among the three methods including ETES, STMS, and ETMS. As for safety, results indicated that the incidence of total complications of STMS (OR = 4.74; 95% CI 1.03, 40.14) is significantly superior to ETES. And the incidence of diabetes insipidus of ETMS (OR = 2.21; 95% CI 1.31, 3.81) was significantly superior to that of ETES. Besides, there was no statistical difference in the other complications including Cerebrospinal fluid fistula, nasal septal perforation, death, and bleeding. They clarified the overpraise of the efficacy of endoscopy especially the endonasal transsphenoidal approach and verified that all the approaches owned similar efficacy. Moreover, they recommended the endoscopy to be the first choice for pituitary tumors, because it demonstrated the best safety [4].

The transsphenoidal approach is the gold standard for pituitary neuroendocrine tumor resection. However, despite advances in microsurgical and endoscopic techniques, some pituitary neuroendocrine tumors can be challenging to cure.

Traditionally performed with a microscope and a sublabial incision, the implementation of the endoscopic visualization and endonasal access has rendered the transsphenoidal approach less invasive and provided improved visualization into and around the sella.

see Endoscopic transsphenoidal approach

The standard endonasal approach has been expanded to provide access to other, parasellar lesions. With the addition of the endoscope, this expansion carries significant potential for the resection of skull base lesions.

see Extended endoscopic transsphenoidal approach

Although there is limited and low quality evidence available, the use of intraoperative ultrasound appears to be a safe and effective technological adjunct to transsphenoidal surgery for pituitary neuroendocrine tumor. Advances in ultrasound technology may allow for more widespread use of such devices [5].

Suprasellar extension is regarded a drawback for complete removal of these tumors through this approach.

Is very important to evaluate the correlation between the preoperative radiologic craniocaudal extension on MRI of pituitary neuroendocrine tumors and the extent of tumor removal. A retrospective study. Tertiary care hospital. 560 patients underwent transsphenoidal removal of pituitary neuroendocrine tumors. The degree of removal of pituitary tumor in the follow-up imaging of the patients was correlated with the preoperative extension in mid-Coronal T1 W Gd. Tumors with suprasellar extension can be classified into: Type I tumors with extension confined to the sellar boundaries, resulted in complete removal in all cases (100%), type II tumors with suprasellar extension reaching the floor of the 3rd ventricle, resulted in complete removal in 70.2% of the cases, type III tumors with suprasellar extension above the 3rd ventricle, had only 13.5% of complete removal. Integration of radiologic findings into a scheme for the preoperative determination of possibility of total removal of the tumor through transsphenoidal approach, can give better correlation to the surgical outcome of pituitary tumors [6].

Costs

Geographic variations in healthcare costs have been reported for many surgical specialties.

In a study, Asemota et al. sought to describe national and regional costs associated with transsphenoidal pituitary surgery (TPS).

Data from the Truven-MarketScan 2010-2014 was analyzed. We examined overall total, hospital/facility, physician, and out-of-pocket payments in patients undergoing TPS including technique-specific costs. Mean payments were obtained after risk-adjustment for the patient- and system-level confounders and estimated differences across regions.

The estimated overall annual burden was $43 million/year in our cohort. The average overall total payment associated with TPS was $35,602.30, hospital/facility payment was $26,980.45, physician payment was $4,685.95, and out-of-pocket payment was $2,330.78. Overall total and hospital/facility costs were highest in the West and lowest in the South (both $P<0.001$), while physician reimbursements were highest in the North-east and lowest in the South ($P<0.001$). There were no differences in out-of-pocket expenses across regions. On a national level, there were significantly higher overall total and hospital/facility payments associated with endoscopic compared to microscopic procedures (both $P<0.001$); there were no significant differences in physician payments nor out-of-pocket expenses between techniques. There were also significant within-region cost differences in the overall total, hospital/facility, and physician payments in both techniques as well as in out-of-pocket expenses associated with microsurgery. There were no significant regional

differences in out-of-pocket expenses associated with endoscopic surgery.

These results demonstrate significant geographical cost disparities associated with TPS. Understanding the factors behind disparate costs is important for developing cost containment strategies [7].

Complications

Transsphenoidal approach complications.

Post-operative surveillance

A comprehensive review of the literature quantified the pituitary neuroendocrine tumor recurrence rates for commonly observed pituitary neuroendocrine tumors after transsphenoidal surgical resection with curative intent. Findings suggest that surveillance within 1 year may be of low yield. Further, clinical trials and cohort studies investigating the cost-effectiveness of surveillance schedules and their impact on the quality of life of patients under surveillance will provide further insight to optimize follow-up [8]

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