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Sublabial Transseptal Approach to Pituitary Adenomas with Special Emphasis on Rhinological Complications

Rinolojik Komplikasyonlara Özel Vurguyla Hipofiz Adenomlarına Sublabial Transsfenoidal Yaklaşım

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ABSTRACT

OBJECTIVE: The aim of this presentation is to show that the sublabial transseptal transsphenoidal approach to pituitary adenomas is the least invasive anatomic route with the lowest postoperative complication rates.

PATIENTS and METHOD: This study was based on a retrospective analysis of 276 patients with a diagnosis of pituitary adenoma who were surgically treated via the sublabial transsphenoidal route.

RESULTS: The overall complication rate of the presented series was 14.8%. The recurrence rate was 14.1%; there were no deaths or intranasal complications in this series. Postoperative rhinological complications, such as septal perforation, synechiae, and mucosal tear which impaired nasal function, occur rarely with this approach compared to other approaches.

CONCLUSION: Besides the technical advantages of this approach, performance of the initial phase of the operation by an otorhinolaryngologic surgeon is the basis of the low intranasal complication rate in our series.

KEY WORDS: Complication, Pituitary adenoma, Sublabial approach, Rhinological compticatıons

ÖZ

AMAÇ: Bu çalışmanın amacı sublabial transsfenoidal yolun hipofiz adenomlarına yaklaşımda en az komplikasyon gelişen, en az invaziv anatomik yol olduğunu göstermektir.

YÖNTEM ve GEREÇ: Bu çalışma, hipofiz adenomu tanısı ile sublabial transsfenoidal yolla ameliyat edilen 276 hastanın geriye dönük değerlendirmesini içermektedir.

BULGULAR: Bu serinin genel komplikasyon oranı %14.8, nüks oranı %14,1'dir. Bu seride hasta kaybı veya intranazal komplikasyon yoktur.

SONUÇ: Bu yaklaşımın teknik avantajları yanında açılış fazının bir kulak burun boğaz hastalıkları uzmanınca yapılması da düşük rinolojik komplikasyon oranında rol oynamıştır.

ANAHTAR SÖZCÜKLER: Hipofiz adenomu, Komplikasyon, Sublabial yaklaşım, Rinolojik Komplikasyonlar

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INTRODUCTION

Adenomas arising from the anterior pituitary lobe comprise about 10-12% of all intracranial mass lesions (18). Although they are benign in nature, they may compress the optic apparatus, hypothalamic and cerebrospinal fluid (CSF) flow pathway, and invade the cavernous sinus. Pituitary adenomas (PA) may lead to hormonal dysfunction syndromes (18). Thus, adequate treatment of these neoplasms is of importance. Surgical removal should be performed in cases where medical treatment is insufficient or not indicated. The preferred way for achieving this goal is the transsphenoidal route because of its low postoperative complication rate and direct access to the sella without retraction of brain tissue (10). There are several transsphenoidal routes defined in detail in the literature (1,4,6,8,9,10,12,14,17,18,19,21,22,24,26). Attempts to reduce the postoperative complication rate associated with this procedure are continuing. The aim of this analysis is to designate the sublabial transseptal transsphenoidal (STT) route as one of the least invasive approaches for the removal of PA, and to emphasize that this procedure is among the routes with the lowest complication rates, especially with regard to rhinological complications.

MATERIAL and METHODS

This study was based on a retrospective analysis of 276 patients with a diagnosis of PA who were surgically treated via the STT route at the Second Neurosurgery Clinic of the Yildirim Bayezit Training and Research Hospital in Ankara, Turkey between 1994 and 2006. This project was reviewed and the protocol was approved by the Institutional Review Board of the Dışkapı Yildirim Bayezit Training and Research Hospital. Patients who were lost to follow-up and under the restrictions of our Institutional Review Board (i.e., pregnant women, minors, mentally disabled persons, and persons incarcerated, on parole, on probation, or awaiting trial) were excluded.

Rhinological complication rates and several parameters of some big series in the literature were compared to our results. Advanced statistical methods were not used as they were not necessary in this manner.

The mean age of the patients was 39.8 years (range, 19 to 67 years) and the mean follow-up time was 34.6 months. The overall female:male ratio was approximately 1.6. This ratio was 8.9 for prolactinomas, 0.2 for non-secreting adenomas, and 1.3 for growth hormone (GH) adenomas. We used a classification system based on the type of hormone secreted. Besides this classification, the patients were divided into groups according to the size, invasiveness, and extension of the adenomas. One hundred eight patients (39.1%) had prolactinomas, 67 patients (24.3%) had non-secreting adenomas, 63 patients (22.8%) had growth hormone adenomas, 37 patients (13.4%) had pluri-hormonal adenomas secreting both prolactin (PRL) and GH, and 1 patient (0.4%) had an adrenocorticotropic hormone (ACTH) adenoma. We performed 315 operations on 276 patients. Twenty-nine patients were operated on twice, 7 of these 29 patients were operated on three times, and 3 of them were operated on four times. Twenty-eight of the recurrent cases were GH adenomas (44.4%), 9 were prolactinomas (8.3%), and 2 (5.4%) were pluri-hormonal adenomas. Two hundred four of the patients had macroadenomas (73.9%). Since the first line treatment option for prolactinomas was medical and only the patients with drug-resistant adenomas and adenomas with a mass effect were operated on, the rate of macroadenomas in the prolactinoma group was 89.8%. In the non-secreting adenoma group, symptomatology depended on the mass effect of the adenoma only, so all non-secreting adenomas operated on were macroadenomas. Fourteen (5%) of the adenomas exhibited a locally invasive character according to the modified Hardy system (26).

Hourglass adenomas expanding into the suprasellar cistern, and adenomas expanding to the parasellar area, were removed via transcranial, transsphenoidal, combined, or two-stage operations; those patients were excluded from the study. Asymptomatic non-secretory adenomas were followed up until they became symptomatic from their mass effect. Patients with prolactinomas were first treated medically if the hormone levels were less than 200 or higher than 450 ng/mL or there were no compression symptoms, like visual field defects.

The preoperative evaluation consisted of a complete history, physical and neurological examinations, and radiological assessment. T1-weighted (T1W), T2-weighted (T2W), and post-contrast sequences of magnetic resonance imaging (MRI) and coronal reformatted computed tomography (CT) for evaluation of bony structures and nasal contents were performed on all patients. The position of the sphenoid sinus septum and the

other minor septa and mucosal foldings which could be recognized during the operation, in particular, were recorded. The relationship of the sellar floor and the sphenoid sinus septum and the posterior attachment of the sphenoid septum were considered for planning the opening site in the sellar floor. The Neuroophtalmology Department evaluated all patients for their visual acuity, visual fields, and fundus findings. Otorhinolaryngologic examination and diagnostic nasal endoscopy (DNE) were performed on all patients. The diagnosis of PA was confirmed histopathologically in all cases. Postoperative follow-up MRIs were performed immediately after the operation, in the fourth month, and in the first year after the operation.

Tumor control was defined as normalization of a basal hormonal level, clinical remission of visual, endocrinologic, and gonadal dysfunction and lack of progression of the adenoma on imaging studies.

Criteria of cure

Patients were considered cured of disease if the following criteria were met:

1. PRL-secreting adenomas: Normalization of basal PRL levels (<20μg/mL), without dopaminergic therapy for at least 3 months.
2. GH-secreting adenomas: Oral glucose tolerance test-suppressed GH level < 1μg/mL and age-related insulin-like growth factor-1 (IGF-1) level within normal limits.
3. ACTH-secreting adenomas: Presence of hypocortisolism requiring glucocorticoid substitution therapy or, in the case of normal serum and urinary cortisol levels, suppression of serum cortisol level after an overnight low-dose dexamethasone test.
4. Thyroid stimulating hormone (TSH)-secreting adenomas: Normalization of TSH, free triiodothyronine (T3), and free thyroxine (T4) levels in hyperthyroid patients; normal suppression of TSH levels after the administration of 25 μg T3 orally every 6 hours for 10 days in patients who had previously received thyroablative therapies.
5. Non-functioning adenomas: Absence of residual tumor on the first postoperative MRI, performed 3 months after surgery (17).

Operative Techniques

In the operating room, the head of the patient was slightly flexed and rotated to the surgeon. The legs were positioned lower than the head to minimize surgical bleeding. This head position provided an approximately 300 angle with the sella and hard palate making the surgeon's view parallel to the operating route. The C arm fluoroscope was prepared preoperatively, but not placed around the patient's head unless it was necessary.

Hypotensive anesthesia was preferred for lowering intraoperative bleeding. The gingivobuccal sulcus and septum were infiltrated with lidocaine HCl with 1/200000 epinephrine to ease dissection and reduce bleeding.

A horizontal sublabial incision was performed 1 cm above the gingivobuccal sulcus, extending between the alae nasalis. The incision was continued through the periosteum of the premaxilla, which was elevated superiorly to the pyriform aperture, the anterior nasal spine, and the anterior edge of the nasal septum. The anterior edge of the septal cartilage perichondrium was incised after recognizing the anterior edge of the nasal septum by blunt dissection. A left superior tunnel was opened after the subperichondrial space was found. From the anterior maxillary spine, the left inferior tunnel was also opened and both tunnels were communicated by sharp dissection. The quadrangular cartilage was separated from the floor of maxilla and posterior bony septum. The right superior tunnel of bony septum was formed after that right inferior tunnel was formed for replacing the cartilage septum more laterally. The bony septum was excised until the anterior wall of sphenoid septum was reached. Part of the bony septum was reserved for repairing the sellar floor during the closure. A suitable size Hardy retractor was placed between the mucosal flaps and the remnant of the bony septum and fixed in the midline. The blades of the Hardy retractor were equidistant to the midline. This stage of the operation was performed with a headlamp and the operating microscope was then used. The mucoperiosteum was elevated on both sides step-by-step from the anterior wall of the sphenoid sinus and the blades of the Hardy retractor were opened maximally. Both sphenoid sinus ostia were sought and found as a useful anatomic landmark for opening the anterior wall of the sphenoid sinus. The bone between the two ostia was removed on entering the sinus. After revealing the sphenoid sinus anatomy, the anterior opening was widened. The sphenoid sinus septum was removed, but a small piece was left for the correlation and orientation of radiologic anatomy.

The mucosa of the sellar floor was peeled off and the sellar floor was elevated by chisel and widened by Kerrison rongeur. The dura was incised; the tumor was removed with various types of angled pituitary forceps and curettes in a piecemeal fashion. After hemostasis, the sellar floor defect was repaired with a septal bone graft. Several grooves were made on the bony graft to fix it on the sellar floor. The cartilaginous septum was pulled back to the midline and mucoperiostal flaps replaced. The nasal cavity was packed with tampons to fix the mucoperiostal flaps. The package material was removed on the third postoperative day.

RESULTS

The extent of removal for each group of adenomas was different. Gross total and subtotal removal rates for PRL-secreting macroadenomas were 79.4 and 20.6%, respectively. These rates were 71.6 and 28.4% for non-secreting macroadenomas, 57.9 and 42.1% for GH-secreting macroadenomas, and 66.7 and 33.3% for pluri-hormonal macroadenomas, respectively. Complete recovery of ophthalmologic signs was observed in 59.6% of the patients who had a visual field defect due to the mass effect of the macroadenoma. Partial improvement in the visual field defect was observed in 28.4% of patients and 12.0% of patients showed no improvement in ophthalmologic signs during the postoperative follow-up period. Overall endocrine cure rate was 25.9% for all prolactinomas. For PRL-secreting microadenomas, the endocrine cure rate was 63.6%. In the macroadenoma group, an endocrine cure was achieved in only 21.6% of the patients. The endocrine cure rate for GH adenomas was 22.2% and was approximately the same in both the macro- and micro-adenoma groups. The overall tumor control rate was 74.8%. In articles reporting the surgical results of prolactinomas, some authors use stable residual mass during long-term follow-up without mass effect as the goal of treatment (9,10,17,18,24,26). From this point of view, the tumor control of prolactinomas was 78.0% in our study, which is similar to that reported in the literature (5,10,16,18).

Transient or permanent fluid-electrolyte imbalance and diabetes insipidus (DI) was the most common postoperative complication (8.3% of the patients) in the presented series. Rhinorrhea occurred in 4.3% of the patients as the second most common complication. The other complications are listed in (Table I). Nine of the postoperative rhinorrhea patients were treated surgically. Late onset postoperative rhinorrhea occurred in two patients.

With a 14.8% overall complication rate, a 14.1% recurrence rate that required surgery, and no mortality, the results of this series are similar to or slightly better than most of the major series in the literature (4,5,6,7,18,22).

DISCUSSION

Since Schloffer first used the TSA for removal of pituitary adenomas in 1907, it has become the method of choice for removal of intrasellar tumors, even those which extend to the parasellar region. The decision to choose an approach to the sella for removing an adenoma should be guided by the technical facility, the surgeon's experience, and the morbidity rate of the chosen surgical route. Each route that is used for removal of an adenoma has some operative advantages. The most important consideration during the decision period must be the complication rate, which is dependent on the chosen approach. Other components such as the working distance, the need for additional specialized equipment, and the surgeon's comfort can be compensated for.

The transcolumellar transseptal (TCTS) route provides a more direct midline access to the sella. The TCTS route requires a columellar incision and retention sutures, which frequently results in an external scar. Furthermore, a medial crural reduction may sometimes be needed (1). The septal perforation rate related to this route has been reported as approximately 2.4% (24). The external rhinoplastic approach (ER) also has scarring problems, and results in nasal tip edema (8,19).

All of the above mentioned advantages and disadvantages of those routes are about intraoperative difficulties or facilities. Safety, efficacy, postoperative results, and complications related to the surgery must be a more important concept of modern pituitary surgery. The major advantage of the STT approach over the other routes is its low complication rate, especially in the intranasal cavities. Diastasis or fracture of the hard plate is a complication that results from wide opening of the speculum and can lead to malocclusion. This complication was reported in some TS surgery series (12,15), but we have not experienced this complication because one does not have to use extra

Table I: Complication rates

Complications	Number of patients n=276	Percentage of patients n=276	Percentage of operations n=315
Fluid –electrolyte imbalance and DI* (permanent or temporary)	23	8.3	7.3
Rhinorrhea	12	4.3	3.8
Neurodeficits due to vascular accidents	5	1.8	1.6
CN 3, 4, 6 palsies	3	1.0	0.9
Iatrogenic panhypopituitarism	2	0.7	0.6
Postoperative thrombotic disorders	1	0.4	0.3
Additional visual deficit (scotomas or acuity disorders)		0	0
Nasal passage obstruction		0	0
Septal perforation		0	0
Mortality		0	0
Total	41**	14.8**	13.0**

*DI: Diabetes insipidus, **Total number is smaller than the sum of the above numbers and percentages because some patients had more than one complication.

force to open the speculum during the STT approach. This route provides a wider opening than the other routes in any case. Septal perforation is a complication of TS approaches, with a 1.0% incidence in some series of TS surgery (20); septal perforations are not life-threatening, but extremely function-limiting and disturbing for a lifetime. Repair of these perforations is one of the most technically challenging for the rhinologic surgeon (21). Nasal complications are seen frequently in the endonasal (EN) approaches without an endoscope. The septal perforation rate related to this approach has been reported as 19% (14). Besides dissections being made deeply in the nasal cavity, inserting the speculum into the mucosal incision may be the cause of mucosal tears and septal perforations. Although endoscopic approaches are different disciplines and beyond the scope of this manuscript, they will improve and develop parallel to technological advancements (27). Lesions of the pituitary gland are increasingly being resected via the endoscopic, endonasal, transsphenoidal approach (11,27). Endoscopic transsphenoidal surgery is a valuable microinvasive technique with its effectiveness and safety (27). The pituitary gland, inside the adenoma and lateral wall of the cavernous sinus can be visible by this approach (3,23). Besides the pure endoscopic approach, combination with a microscope is being used in some pituitary centers (13). This technique also leads to shorter total anesthesia time and less blood loss (2). Transnasal approaches (TN) can preserve nasal form and offer excellent operative sterility, but they need an alatomy incision which results in scar tissue. The septal perforation rate related to the TN approach has been reported to be approximately 8 % (9).

The septal perforation rate related to the STT approach is reported to be 0%, as in our series (24) (Table II). The STT route facilitates septal dissections; as the starting point of the septal dissection is always anterior to the septal structures, the risk of septal perforation during dissection remains minimal. Moreover, the STT provides septal alignment with improvement in nasal function (25).

CONCLUSION

The STT route is one of the most direct and safest surgical routes to pituitary tumors. It is of course impossible to conclude that this approach is the least invasive one with the lowest complication rate by a retrospective analysis. Postoperative rhinologic complications, such as septal perforation, synechiae, and mucosal tears which impair nasal function are very rare with this approach compared to other approaches. Septal alignment provided by this approach seems to improve nasal function, such as nasal obstructive symptoms. The incidence of

Table II: Septal perforation rates in the literature

Author, year	TS route	Septal perforation rate (%)
Koltai PJ, 1994 (10)	EN,ER	19*
Reese BR, 1992 (17)	ER	15.4
Dew AL, 1999 (7)	TN	8
Arden RL, 1999 (1)	TCTS	7.7
Kennedy DW, 1984 (9)	EN	7
Spencer WR, 2000 (19)	TCTS	2.4
Spencer WR, 2000 (19)	STT	0
Urquhart AC, 1996 (20)	STT	0
Dew AL, 1999 (7)	STT	0
Present series	STT	0

*Only 7% were symptomatic. EN: Endonasal, ER: External rhinoplasty, TN: Transnasal, TCTS: Transcolumellar transseptal, STT: Sublabial transseptal transsfenoidal.

procedure-related complications, especially intranasal complications, appears to be insignificant compared with the benefits derived from this approach. Besides the technical advantages of this approach, performing the initial phase of the operation with an otorhinolaryngologic surgeon may be the basis of the low intranasal complication rate in our series.

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