Turk Neurosurg, 2024

Original Investigation

Received: 20.08.2023
Accepted: 21.09.2024

DOI: 10.5137/1019-5149.JTN.45315-23.2

Published Online: 15.10.2024

Impact of Tumor Resection Volume on Visual Outcomes and the Need for Secondary Surgery Following Transsphenoidal Surgery in Suprasellar Extended Non-Functionial Pituitary Adenomas

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ABSTRACT

AIM: To investigate the surgical outcomes in patients with nonfunctional pituitary adenomas (NFPAs) exhibiting visual field defects (VFDs) in order to ascertain the impact of the volume of adenoma excised during surgery on recurrence rates and improvements in VFDs.

MATERIAL and METHODS: From a cohort of 150 individuals diagnosed with NFPAs and exhibiting suprasellar extensions accompanied by VFDs, we selected 114 patients who fulfilled the inclusion criteria for further analysis after a comprehensive retrospective review. All selected patients underwent pituitary magnetic resonance imaging (MRI) examinations, and volumetric measurements were conducted on T1 contrast sequences using the Syngo.via software. Measurements were derived from MRI scans taken 24 h preoperatively, 24 h postoperatively, at 3 months, and at the end of the first year postsurgery. Volumetric values were compared between patients who underwent subsequent surgeries due to recurrence and those who did not. Similarly, the variables were evaluated in patients experiencing an improvement in VFD, those whose VFD remained stable, and those experiencing a deterioration in VFD.

RESULTS: The recurrence rate was 19.3%. Among patients who underwent a second surgery due to recurrence, the presurgical adenoma volume, the adenoma volume removed based on the 24-h postoperative MRI, and the volumes recorded in the 3-month and 1-year postoperative imaging were significantly greater than those in patients who did not require a second surgery. Remarkable improvements were identified in 84.2% of patients with VFD complaints and 62.5% of those with visual acuity complaints.

CONCLUSION: Adenoma volume measurements exerted a significant impact on recovery from VFDs and the need for a second surgery. Although the choice of surgical methodology does not definitively affect outcomes, an in-depth evaluation of variations in adenoma volume can provide valuable prognostic insights.

KEYWORDS: Retrospective Studies, Pituitary Adenomas, Visual Field Defects, Prognosis, Recurrence

ABBREVIATIONS: ETS: Endonasal transsphenoidal surgery, **MRI:** Magnetic resonance imaging, **VA:** Visual acuity, **VFD:** Visual field defects

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INTRODUCTION

Nonfunctional pituitary adenomas (NFPAs) are commonly diagnosed as "macroadenomas" and frequently present with "visual symptoms" that lead individuals to become symptomatic (2,20,23). The visual symptoms of NFPAs are primarily reported as visual field defects (VFDs) and a decline in visual acuity (VA) (14,21,24). Surgical treatments for NFPAs aim to reduce and/or completely alleviate these visual symptoms (2,20,23,27). To some extent, the concepts of "cure" and "recurrence" in NFPAs are closely related to visual symptoms. Residual tumor volume in NFPAs is considered a "cure" as long as the tumors do not become symptomatic (6,12,20,27).

As in the case of sellar and parasellar pathologies, endonasal transsphenoidal surgery (ETS) is a primary treatment option for NFPAs (6,22,23). The success rate of treatment for various parasellar and sellar pathologies is approximately 90% (2,20,23). ETS can be performed both endoscopically and microscopically. Both methods are aimed to excise the adenoma with the maximum safe volume, reducing optic nerve compression and consequently improving optical findings.

The objective of this study was to comparatively analyze the results of contrast-enhanced pituitary magnetic resonance imaging (MRI) taken in the early postoperative period (within the first 24 h), at 3 months postoperation, and at 1 year in patients with NFPA diagnosed with visual symptoms and treated with ETS in our clinic. Another aim was to explore the effect of the obtained volumetric variables on visual symptoms and the need for secondary surgery. Furthermore, we determined the predictive volumetric values required for improving visual symptoms in patients with NFPAs.

MATERIAL and METHODS

This study was approved by the Selçuk University Medical Faculty Hospital Ethics Committee, number 2022-189.

Patient Selection

Between 2011 and December 2022, we retrospectively evaluated 150 patients diagnosed with pituitary macroadenomas compressing the optic chiasm, all of whom exhibited visual field constriction and had been treated with ETS. These patients were categorized into two groups, viz., endoscopic and microscopic, based on the ETS application method. For this study, we included 114 patients who consistently attended their followup appointments and underwent comprehensive radiological examinations.

Inclusion Criteria

- Patients with pituitary macroadenomas causing compression of the optic chiasm and resulting in VFDs.
- Patients without hormonal imbalance, with pathology results classified as nonfunctional.
- Patients whose surgical treatments and followups were conducted at our clinic.
- Patients who attended regular followup examinations.
- Patients with complete pituitary MRI data at the time of diagnosis and followup available in our hospital's Enlil PACS software system.
- Patients who fully cooperated with visual field examinations.

Exclusion Criteria

- Patients who underwent their initial surgery at a different center.
- Patients who did not undergo a pituitary MRI examination within the first 24 h postsurgery.
- Patients lacking pituitary MRI data at 3 months and 1 year postsurgery.
- Patients with inconsistencies in visual field evaluations during followup appointments.
- Patients whose pathology results did not classify their adenomas as nonfunctional.
- Patients with symptoms of hormonal imbalance in addition to decreased VA and/or VFDs.
- Patients classified as stage 3 or 4 in the preoperative Knosp assessment.

Imaging and Volume Measurements

Preoperative, postoperative day 1, 3-month, and 1-year pituitary MRI scans of the 114 patients were analyzed. Tumor volumes were measured using the Enlil PACS software and Syngo.via imaging software (Figure 1). Tumor volumes before and after surgery (day 1, 3 months, and 1 year) were compared, and based on the MRI results from 24 h postsurgery, the volume of the excised tumor was determined. Tumor volumes were analyzed according to the surgical method (microscopic or endoscopic). The tumor volumes of patients with significantly reduced or completely resolved optic chiasm compression postsurgery were compared with those of patients whose symptoms persisted. Moreover, volumetric measurements of patients requiring a second surgery were compared with those of patients who did not require a second surgery. The predictive excisional volumetric value required for the improvement of symptoms was determined.

Statistical Analysis

For descriptive statistics, mean ± standard deviation was used to express continuous data with a normal distribution. Continuous variables without a normal distribution were expressed using median with minimum–maximum values. Categorical variables were expressed using number and percentage. The Kolmogorov–Smirnov test was used to evaluate the normal distribution of numerical variables. For variables without a normal distribution, the Mann–Whitney U test was used to compare two independent groups. Differences between categorical variables were compared using Pearson's chi-square tests. Statistical analyses were conducted using SPSS version 22.0, with the significance level (p value) set at 0.05.

Table I: Demographic and Clinical Characteristics of the Patients

Variables	n (%) / Mean ± SD	Min-Max
Age (years)	50.14 ± 15.18	[14-56]
Gender		
Female	55 (48.2%)	
Male	59 (51.8%)	
Surgery Type		
Microscopic	75 (65.8%)	
Endoscopic	39 (34.2%)	
Tumor Dimensions		
Measurement 1 (mm)	21.05 ± 9.61	[1-50]
Measurement 2 (mm)	18.27 ± 9.26	[0.7-44]
Preoperative Volume (cm³)	7.69 ± 2.98	[4.24-12.91]
Evacuated Volume (cm³)	4.14 ± 1.72	[2.50-8.24]
Postoperative Volume (cm³)		
3rd Month	2.82 ± 1.07	[1.52-5.24]
1st Year	2.22 ± 0.91	[1.28-4.44]
Follow-up Time (months)	54.21 ± 28.93	[9-128]
Number of Patients Who Underwent Recurrent Surgery	22 (19.3%)	

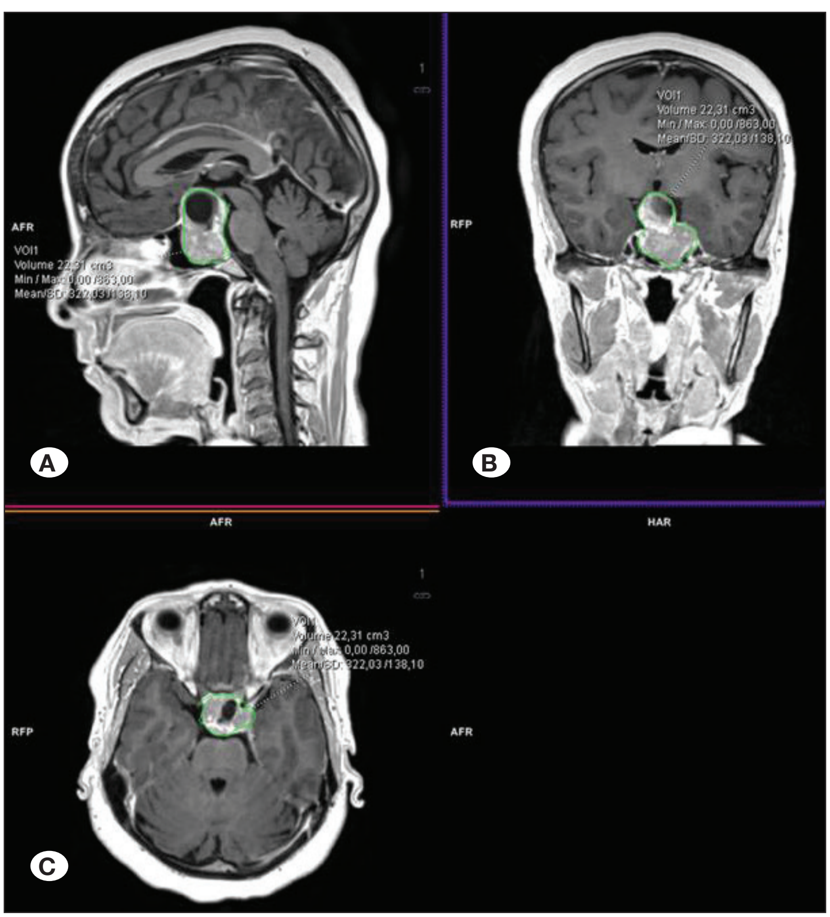

Figure 1: Volume measurements using Synog.via program on images taken from pituitary MRI T1 contrast-enhanced sequences in the Enlil PACS program (**A:** sagittal, **B:** coronal, **C:** axial).

RESULTS

Demographic Characteristics of the Study Population

We evaluated 150 patients who underwent surgery for NFPAs between December 2011 and 2022, of whom 114 patients who met the inclusion criteria were included in this study. We excluded 36 patients for various reasons, viz., noncompliance with visual field examination (n=5), surgery performed at another center (n=8), nonattendance at followup examinations (n=8), symptoms due to high anterior pituitary hormone levels (n=6), no VFDs detected in the preoperative ophthalmologic examination (n=2), cognitive impairments (n=3), KNOPS stage 3 or 4 (n=20), and disease-related death (n=2). Patients could be excluded for multiple reasons.

Among patients included in this study, 48.2% were women, with a mean age of 50.14 ± 15.18 (range: 14–76) years. The mean followup duration was 54.21 ± 28.93 (range: 9–128) months.

Table I shows the demographic characteristics of the 114 patients and the effects of different variables.

Clinical Findings

All study patients had VFDs, and 48 (42.1%) patients also had VA defects. Complete vision loss (anopia) was observed in both eyes of one patient (0.87%) and in one eye of two patients (1.75%). Anterior pituitary hormone levels were within normal ranges, and macroadenomas were identified by pituitary MRI. In the visual field tests, 56.1% (n=64) of patients had bitemporal hemianopia, 34.2% (n=39) had temporal VFD, 7% (n=9) had nasal hemianopia, and 2.6% (n=3) had anopia.

Size and Volume Changes in Pituitary Macroadenomas

The average size of the pituitary macroadenomas was 21.05 ± 9.61 × 18.27 ± 9.26 mm^2. The average preoperative volume was 7.69 cm^3 (IQR=4.24–12.91), whereas the average volume evacuated postsurgery was 4.14 cm^3 (IQR=2.50–8.24). The average postoperative volume at 3 months was 2.82 cm^3 (IQR = 1.52–5.24), and the average postoperative volume at 1 year was 2.22 cm^3 (IQR=1.28–4.44) (Table I).

Evaluation of Patients With and Without the Need for Recurrent Surgery

A total of 22 (19.3%) patients required recurrent surgery. Four patients (3.6%) underwent surgery three times, and one patient (0.9%) underwent surgery four times. Recurrence was classified as early in 6 of 22 patients (27.3%) who were diagnosed within the first year of followup. No significant difference was observed between the volumetric measurements of patients with early recurrence and those of patients with later recurrence.

Among patients who underwent recurrent surgery due to recurrence, no statistically significant difference was observed between the preference for microscopic or endoscopic surgical approach (Pearson's chi-square, p=0.499).

The followup duration for patients who required a second surgery due to recurrence was significantly longer than that for patients who did not require an additional surgery (Mann–Whitney U, p=0.004) (Table II).

The presurgical adenoma volume, the adenoma volume evacuated during the initial surgery based on the 24-h postoperative MRI, and the adenoma volumes at 3 months and 1 year postsurgery were significantly higher in patients who required a second surgery due to recurrence than in patients who did not require an additional surgery (Mann–Whitney U: p<0.001, p=0.025, p<0.001, and p<0.001, respectively) (Table II).

Evaluation of Endoscopic and Microscopic Approaches

Patients who underwent the microscopic approach had a higher resected volume (3.98 [2.41–8.27] cm^3) than patients who underwent the endoscopic approach (4.29 [2.54–7.6] cm^3). However, the difference in recurrence rates between the two approaches was not statistically significant (Mann–Whitney U, p=0.990).

Postoperative Visual Results

All patients with preoperative VFDs (n=114, 100%) and VA complaints (n=48, 42.1%) were evaluated after surgery. In the postoperative 24-hour evaluation, 71.9% (n=82/114) of patients showed improvement in VFDs, and 58.3% (n=28/48) showed improvement in VA.

Table II: Comparison of Patients Who Underwent and Did Not Undergo Recurrent Surgery

Variable	Recurrent Surgery Absent (n=92)	Recurrent Surgery Present (n=22)	p-value
Microscopic Surgery†	14 (63.6%)	8 (36.4%)	p=0.499**
Follow-up Time (months)‡	46 [26-64.5]	77.5 [19.0-90.0]	**p=0.004***
Preoperative Volume (cm^3)‡	6.58 [4.02-10.59]	11.57 [9.36-25.07]	**p<0.001***
Evacuated Volume (cm^3)‡	3.61 [2.21-6.96]	7.15 [2.75-14.96]	**p=0.025***
Postoperative Volume (cm^3)‡			
3rd Month	2.26 [1.39-3.98]	6.57 [2.91-12.66]	**p<0.001***
1st Year	1.76 [1.13-3.22]	6.27 [3.03-14.04]	**p<0.001***

*†: n (%), ‡: median [min-max], *: Mann-Whitney U test, **: Pearson Chi-Square test.*

Table III: Analysis of Volumetric Evaluations of Patients Whose VFD Worsened (5.2%, n=6) and/or Remained Stable (10.5%, n=12) at One Year Post-Operative Evaluation Compared to Patients with Improvement in VFD (n=94, 84.2%)

Variable	Patients with Improvement in VFD (84.2%, n=94)	Patients with Worsened and/or Stable VFD (15.8%, n=18)	p-value
Preoperative Volume (cm^3)	7.69 (4.24-12.91)	12.50 (8.00-18.50)	**<0.001***
Resection Volume (cm^3)	4.14 (2.50-8.24)	4.50 (2.80-8.80)	0.650
Residual Volume (cm^3)			
3rd Month	2.82 (1.52-5.24)	3.00 (1.80-5.80)	0.320
1st Year	2.22 (1.28-4.44)	2.40 (1.50-4.90)	0.480

***:** *Mann-Whitney U test.*

In the 24-hour postoperative examination, we observed deterioration in both VFDs and VA in two patients (1.7%), requiring urgent surgical intervention. One patient underwent multilayer duraplasty and fat grafting due to a cerebrospinal fluid (CSF) leak during the initial surgery. Improvement in visual symptoms was observed after removing the fat grafts during the second surgery. The other patient had a history of anticoagulant use. An early postoperative MRI revealed a hematoma in the sellar region, prompting an emergency surgery. Improvement in the exacerbated visual symptoms after the initial surgery was observed after the evacuation of the hematoma. Both cases were considered complications, and their urgent secondary surgeries were not considered recurrences.

At the 3-month followup, the improvement rate in VFDs was 80.7% (n=92/114), whereas the improvement rate in VA was 62.5% (n=30/48). At the 1-year follow-up, 10.5% (n=12) of the patients showed stable VFDs without changes. At the 1-year checkpoint, the overall improvement rate was 84.2% in VFDs and 62.5% in VA. Remarkably, deterioration in both VFDs and VA was evident in six patients (5.2%), with control MRI scans confirming recurrences.

Distribution analysis of the 12 patients with no improvement in VFDs by preoperative VFD groups was as follows: anopia 16.6% (n=2), bitemporal hemianopia 50% (n=6), nasal hemianopia 8.3% (n=1), and temporal VFDs 25% (n=3). Although there were no significant differences in VFD improvement across these groups, patients with anopia had the lowest improvement rates. At the 1-year followup, patients with no improvement in VFDs had statistically significantly higher preoperative volumes (Mann–Whitney U, p<0.001) (Table III). In the early postoperative period, there was no improvement in VFDs in patients with tumor excision rates <42%.

DISCUSSION

All patients were subjected to a “wait and see” followup system. During followups, patients who experienced deterioration in visual symptoms that had initially improved after surgery, or those whose visual symptoms that did not improve in the early stages persisted beyond the first year, were evaluated for recurrence. When followup pituitary MRI scans indicated an increase in adenoma volume consistent with their visual symptoms, those cases were classified as “recurrence,” and the patients underwent an additional surgery.

In the literature, the recurrence rates for pituitary adenomas, including NFPAs, range from 20.5% to 67.9% during an average followup period of 60–180 months (4,5,8,12). In our study, the recurrence rate, which resulted in a second surgery, was 19.3% (n=22), consistent with the literature (4,5,18). Our average followup duration was 54.21 ± 28.93 (range: 9–128) months. The literature indicates a statistically significant increase in recurrence rates for NFPAs with an increase in the followup duration (5,17,18). Our statistical analysis corroborates this trend, demonstrating a significant correlation between the recurrence rate and followup duration (Mann–Whitney U, p=0.004).

Studies have indicated that younger age in patients with NFPAs is associated with a higher risk of recurrence. The risk of recurrence decreases by 3% for each additional year of the patient’s age (12,25,27,28). In our study, the mean age of patients was 50.14 ± 15.18 (range: 18–76) years. However, we found no significant correlation between age and recurrence in our statistical analysis. This lack of correlation may be attributed to the relatively low number of younger participants in our study, which could have limited the ability to detect an age-related effect on the risk of recurrence.

In patients who underwent a second surgery due to recurrence, the preoperative adenoma volumes, the adenoma volume evacuated based on imaging results within the first 24 h postoperation, and the adenoma volumes observed in MRI scans at 3 months and 1 year were significantly higher than those in patients who did not require a second surgery (Mann–Whitney U, p<0.001, p=0.025, p<0.001, p<0.001, respectively) (Table II). These results suggest that larger adenoma volumes are associated with a higher risk of recurrence and indicate the need for additional surgical intervention.

Although the literature reports studies on tumor volume calculations (3,10,13), most of these studies have focused on the limitations of traditional methods in evaluating gross total and subtotal tumor resection, especially in cases with irregularly shaped tumors and/or significant cavernous sinus invasion, such as those observed in Cushing’s disease and acromegaly. These studies suggest that volumetric measurements provide valuable insights in such contexts. However, our study specifically evaluated the effects of volumetric variables on recurrence and VFD improvement in patients with NFPAs exhibiting suprasellar spread. To our knowledge, no similar volumetric studies focusing on this specific patient population and context have been reported in the literature.

NFPAs are typically diagnosed based on visual symptoms, which can include VFDs and reduced VA. The literature reports VFD rates of 14%–84% and VA reduction rates of 28%–100% (1,9,17,19). In our study, which included only patients with VFDs, this rate was 100%. However, there was a reduction in VA in 42.1% (n=48) of the patients. These findings are consistent with rates reported in the literature.

The goal of surgical treatment for NFPAs is to improve visual symptoms. A meta-analysis reported visual symptom improvement rates of 80.8% for VFDs and 67.5% for VA reduction, with postoperative deterioration rates of 2.3% for VFDs and 4.5% for VA (9,19). Our study revealed an 84.2% improvement rate for VFDs, a 62.5% improvement rate for VA, and a 5.2% deterioration rate for VFD. These data, measured 1 year after surgery, are consistent with the average values reported in the literature. The deterioration rate for VFDs observed 24 h post-surgery was 1.75% (n=2). Nevertheless, this was considered a complication rather than a deterioration related to the primary surgery, because these patients experienced improvements in visual symptoms after emergency interventions.

The 1-year follow up revealed a VFD deterioration rate of 5.2%, which included six patients who underwent early recurrence surgery. There were no statistically significant differences in any variable between patients with early recurrence and those with later recurrences.

We evaluated the variables of the 12 patients with stable VFDs and the 6 patients with VFD deterioration at the 1-year followup and found that the preoperative adenoma volume was significantly higher in the latter group than in the former group (Mann–Whitney U, p<0.001) (Table III). This finding is consistent with reports showing a correlation between the onset time of visual symptoms and the delay in postoperative improvement, suggesting that the observed data are related to prolonged optic nerve compression (7,16,25,26,28).

An objective of our study was to evaluate the required adenoma volume evacuation for VFD improvement; however, no significant predictive value was achieved. Nonetheless, an analysis of the ratio of adenoma volumes evacuated during surgery to their preoperative volumes, using the first 24-h postoperative MRI, revealed that in patients with stable VFDs, <42% of the tumor volume had been removed. This finding has not been documented in the existing literature. Values reported in meta-analyses are specific to endoscopic ETS (EETS) (9,19,21). Our study statistically evaluated the combined results of both microscopic and endoscopic ETS methods, as well as their separate outcomes. Among patients who underwent repeat surgeries due to recurrence, the choice of the surgical method– whether microscopic or endoscopic– did not show a statistically significant difference (Pearson's chi-square, p=0.499). Similarly, there was no statistically significant difference between the endoscopic and microscopic ETS in terms of VA and VFD improvements. The choice of endoscopic or microscopic surgical approach exerted no statistical effect on the outcomes. These results suggest that postoperative visual outcomes in patients are related more to other factors (such as tumor size and excision rate) than to the choice of the surgical technique.

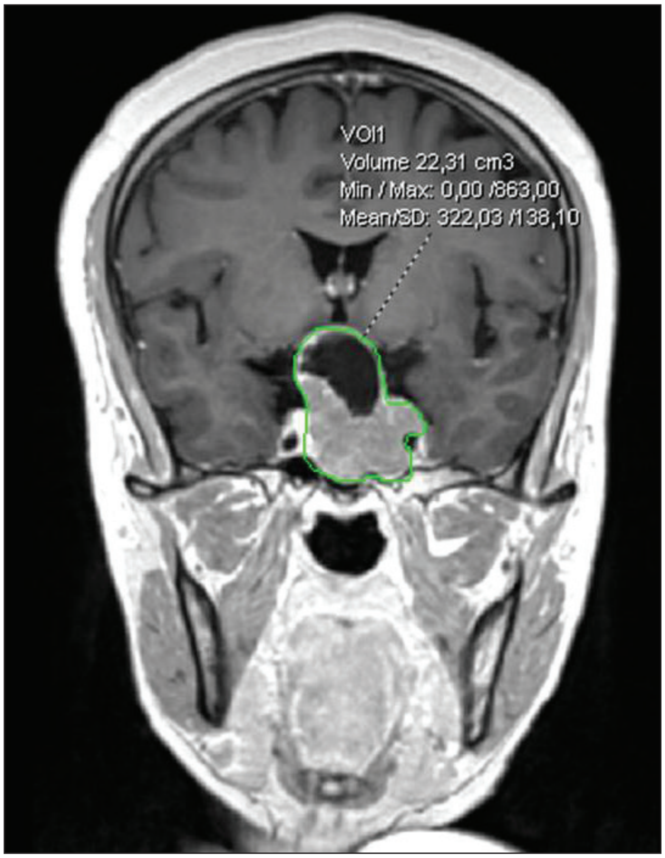

Figure 2: T1W-contrast enhanced coronal magnetic resonance imaging of a patient who was excluded from the study. The tumor was classifed as Knosp stage 3 when evaluated with the Syngo. via program.

Studies examining the distribution of patients affected by VFDs reported that approximately one-third of the patients presented with a typical bitemporal hemianopia (14,21,24). In our study, this proportion was 56.1% (n=64). As our aim was to analyze patients with VFDs based on volumetric measurements before and after surgery, we excluded patients with NFPAs in Knosp stages 3 and 4, which do not play a role in the development of VFDs but have a significant residual volume postsurgery (Figure 2). We considered only macroadenomas exhibiting suprasellar extensions. Other studies that investigated the visual outcomes of patients with NFPAs did not incorporate volumetric evaluations (11,15,21,24,28).

CONCLUSION

This study provides valuable insights into the volumetric evaluations associated with NFPAs and their correlation with VFDs and VA. Although recurrence rates were consistent with the existing literature, our findings emphasized a significant relationship between adenoma volume and the risk of recurrence. Furthermore, a remarkable correlation was identified between the preoperative adenoma volume and stable VFDs. The surgical approach, either endoscopic or microscopic, exerted no statistically significant effect on the outcomes, suggesting that other factors, such as tumor size and excision rate, play a more pivotal role. The emphasis on volumetric evaluations in our study highlights the importance of incorporating these measures into clinical practice, especially when considering the prognosis and management of patients with NFPAs.

ACKNOWLEDGEMENTS

The authors would like to thank Enago (www.enago.com) for the English language review."

Declarations

Funding: There is no funding to report.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

AUTHORSHIP CONTRIBUTION

Study conception and design: DKG, EK

Data collection: DKG, MAB, AB

Analysis and interpretation of results: DKG, EK, MŞ, BG, HK

Draft manuscript preparation: DKG, EK

Critical revision of the article: DKG, EK

All authors (DKG, BG, MŞ, EK, HK, MAB, AB) reviewed the results and approved the final version of the manuscript.

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