EXPERIENCE IN THE SURGICAL TREATMENT OF PITUITARY ADENOMAS AT THE GUILLERMO ALMENARA HOSPITAL IN 2019-2020

Experiencia en el tratamiento quirúrgico de adenomas de hipófisis en el Hospital Guillermo Almenara en 2019 – 2020

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ABSTRACT

Introduction: Pituitary adenomas constitute 25% of the primary benign neoplasms of the brain and can be functional or non-functional, or depending on their size they can be microadenomas, macroadenomas and giant adenomas. They are mainly treated by surgery using either transcranial or transsphenoidal approach.
Objective: To know the experience in the surgical treatment of pituitary adenomas in the Guillermo Almenara National Hospital from January 2019 to May 2020.
Methods: Descriptive, retrospective, cross-sectional epidemiological study. 84 cases of patients operated on for pituitary adenoma were found. The data was collected from the medical history and images in the hospital's PACS system. Chi square was applied as a statistical test.
Results: Of the total of patients, 50% were operated by transcranial surgery and 50% by transsphenoidal surgery. Hypertension, Cushing's disease, and acromegaly were statistically significant in favor of transsphenoidal resection. 69.05% were macroadenomas in transsphenoidal resection (TSR) and 61.90% in transcranial resection (TCR). In the TSR there were 4.76% of intraoperative complications, and in the TCR it was 19.05%. The total resection grade was greater than 50% in both groups.
Conclusions: Pituitary adenomas are a frequent pathology and can be treated by transcranial or transsphenoidal approach, with good resection rates. Prospective studies are required to determine the causal relationship between the variables.

Keywords: *Pituitary Neoplasms, Acromegaly, Craniotomy, Endoscopy (Source: MeSH NLM)*

RESUMEN

Introducción: Los adenomas de hipófisis constituyen el 25% de las neoplasias benignas primarias del cerebro y pueden ser funcionantes o no funcionantes, o según su tamaño pueden ser microadenomas, macroadenomas y adenomas gigantes. Se tratan principalmente por cirugía ya sea por vía transcraneal o transesfenoidal.
Objetivo: Conocer la experiencia en el tratamiento quirúrgico de los adenomas de hipófisis en el Hospital Nacional Guillermo Almenara de enero de 2019 a mayo de 2020.
Métodos: Estudio descriptivo, retrospectivo, transversal de tipo epidemiológico. Se encontraron 84 casos de pacientes operados de adenoma de hipófisis. Los datos fueron recolectados de la historia clínica y de las imágenes en el sistema PACS del hospital. Se aplicó chi cuadrado como test estadístico.
Resultados: Del total de pacientes, 50% fueron operados por vía transcraneal y 50% por vía transesfenoidal. La hipertensión, enfermedad de Cushing y acromegalia tuvieron significancia estadística a favor de la resección transesfenoidal. 69.05% fueron macroadenomas en la resección transesfenoidal (RTE) y 61.90% en la resección transcraneal (RTC). En la RTE hubo 4.76% de complicaciones intraoperatorias, y en RTC fue del 19.05%. Grado de resección total fue mayor del 50% en ambos grupos.
Conclusiones: Los adenomas de hipófisis son una patología frecuente y pueden ser tratados por vía transcraneal o por vía transesfenoidal, con buenas tasas de resección. Se requieren estudios prospectivos para determinar la relación causal entre las variables.

Palabras Clave*: Neoplasias Hipofisiarias, Acromegalia, Craneotomía, Endoscopía. (Fuente: DeCS Bireme)*

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Pituitary adenomas are approximately 15% of all primary brain tumors and 25% of primary benign neoplasms of the brain, varying in incidence by population, from 3 to 94 cases / 100,000 habitants. On the other hand, in children it represents only 2% of all primary brain tumors. It can occur in all ages but has a higher incidence between the fourth and seventh decade of life. Functional tumors tend to be more common in young adults, while non-functioning tumors are more common in older age. Regarding sex, studies show that they are more frequent in women, especially in premenopausal women. [2]

Tumors of the stellar region include a wide range of benign and malignant neoplasms. These include pituitary adenomas, inflammatory lesions, craniopharyngiomas, and metastases [3]. Clinically and endocrinologically they are classified as functional (or hyperfunctional) or nonfunctional. Functional people can secrete prolactin (PRL) that give an amenorrhea-galactorrhea phenotype, growth hormone (GH) whose phenotype is acromegaly or gigantism, adrenocorticotropic hormone (ACTH) with phenotype of Cushing's disease or Nelson syndrome, hormone stimulating the thyroid (TSH) with secondary hyperthyroidism phenotype, follicle stimulating hormone (FSH) and luteinizing hormone (LH) whose phenotype is hypogonadism. Non-functioning adenomas include null cell adenomas, oncocytomas, and various silent adenomas. [2]

Pituitary adenoma surgery is indicated when there is a mass effect, especially that associated with loss of the visual field, excess hormonal secretion not controlled by medical treatment, or in cases of pituitary apoplexy. Due to its systemic effects, both preoperative and postoperative hormonal supplementation is necessary. [2]

Transsphenoidal surgery of a tumor in the selar region can affect the patentness and function of the nasal airways, smell, and sinonasal quality. For this, there are necessary anatomical parameters that must be known to avoid injuring the olfactory nerve and its nervous fillets. Hondronikos et al showed in their study that these types of complications have a low incidence [6].

The COVID-19 pandemic has changed the care protocols for pituitary adenomas, since these patients have risk factors such as hypopituitarism, diabetes mellitus, high blood pressure, obesity, and cardiovascular disease, making them susceptible to increased morbidity due to COVID-19. Furthermore, transsphenoidal procedures are known to increase the risk of contagion in medical personnel, since they are exposed to patient aerosols for a longer time. [5]

METHODS

The sample universe of this study is known, and it is every person of any age who was treated at the Guillermo Almenara Irigoyen National Hospital (HNGAI) between January 2019 and May 2020. The size of the universe is finite but unknown. The study population is any patient of any age who had a radiological clinical diagnosis of pituitary adenoma at the HNGAI between January 2019 and May 2020 and who underwent surgical treatment, either by the transsphenoidal or transcranial route. Patients with pituitary adenoma who have had only medical treatment are excluded.

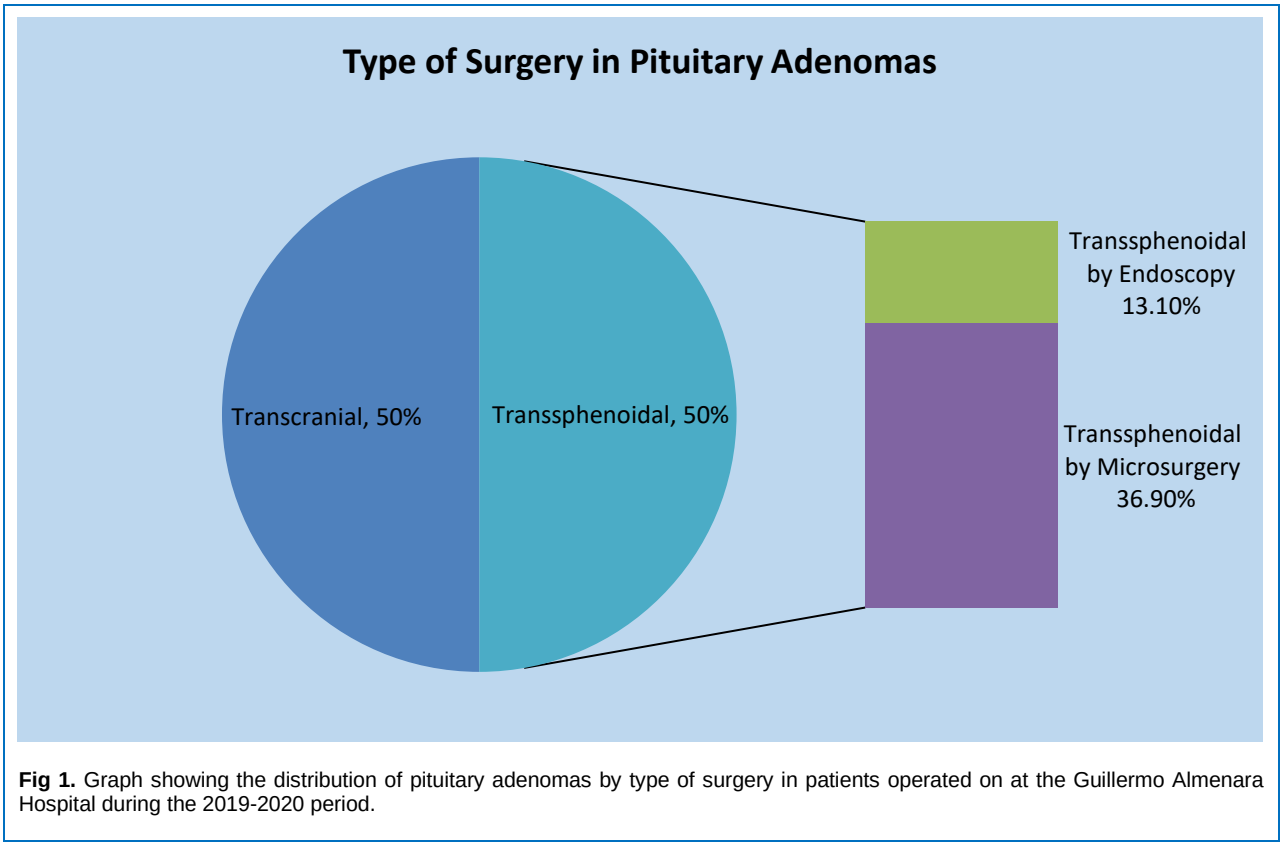

Fig 1. Graph showing the distribution of pituitary adenomas by type of surgery in patients operated on at the Guillermo Almenara Hospital during the 2019-2020 period.

To obtain the sample, an accidental non-probabilistic sampling was used, because all the patients with a diagnosis of pituitary adenoma in the mentioned study period were considered. Being the sampling unit the clinical history of hospitalization of the HNGAI Vascular Neurosurgery and Tumors Service between January 2019 and May 2020.

The present study is observational because the variables were not deliberately manipulated, and retrospectively because the events had already happened. Likewise, it is of a descriptive cross-sectional type since the characteristics of the study subjects were analyzed using data collection in a single moment. Finally, it is epidemiological in nature because it sought to find measurable rates on the variables to be studied.

Data collection was performed using the statistics of the Vascular and Tumor Service of the Guillermo Almenara National Hospital as a source, where patients were searched according to the diagnosis of "pituitary adenoma", "pituitary macroadenoma", "giant adenoma of pituitary "," microadenoma of pituitary ", or by its ICD10" D35.2 ", obtaining a total of 84 cases in the period studied. They then proceeded to conduct a thorough review of medical records in the hospital file, in addition to reviewing the hospital imaging system (PACS) to take measurements of the size of the tumor. Finally, Microsoft Excel was used for data processing.

In data collection and processing, the proportions of all the variables considered were found, to then apply the statistical chi-square test and assess the statistical significance, if the p is less than 0.05.

Regarding age, patients were grouped into those under 40 years old, between 40 and 49 years old, 50 and 59 years old, 60 and 69 years old, 70 and 79 years old, and 80 years old and older. To assess Wilson and Knosp's modified Hardy's classifications, in addition to the averages of the caudal skull, anteroposterior and transverse dimensions, the images in the hospital's PACS system were reviewed by 2 different researchers to reduce bias.

On the other hand, any tumor with a maximum diameter of less than 10mm was considered a microadenoma, as a tumor with a maximum diameter of 10mm or more, but less than 40mm; and finally, a tumor with a maximum diameter of 40mm or more was considered a giant adenoma.

For the definition of improvement of visual fields, it was coded from 1 to 7, depending on whether their greatest visual defect corresponded to none, unilateral quadrantanopsy, bilateral quadrantanopsy, unilateral hemianopia, bilateral hemianopia, unilateral amaurosis or bilateral amaurosis, respectively. Then, a difference was made between the preoperative and postoperative visual defects, if this was 1 it was considered as a slight improvement and if it was greater than 1 it was considered as an obvious improvement. For this, a follow-up time of 1 month was also taken, which was reviewed directly from the medical evaluations recorded in the medical record both in hospitalization and in the outpatient clinic.

Finally, the degree of resection was considered as total if in the tomographic control with contrast the degree of resection was 100% (no residual tumor was evident), subtotal if the degree of resection was 90 to 99%, partial if the degree of resection was from 50 to 89% of resection, and biopsy if the resection was less than 50%.

RESULTS

It was determined that of the 84 patients who underwent surgical treatment for pituitary adenoma, 50% underwent transcranial resection (TCR) and 50% under transsphenoidal resection (TSR). In turn, of those who underwent transsphenoidal resection, 11 patients (13.1%) underwent endonasal endoscopic resection, while 31 patients (36.9%) had transeptal microsurgical resection, as seen in Figure 1.

Regarding the epidemiological profile, it was identified that in the group of patients undergoing transsphenoidal resection there was a predominance of women with 57.14%, while in the transcranial resection group the prevalence was towards men with 54.76%, as can be seen in Table N ° 1. When applying the chi square test with respect to age, a p of 0.20 was obtained. In the same table, in both groups the age predominance was in adults, 78.57% occupying the children under 60 years in the TSR group and 66.67% in the TCR group. Likewise, it is observed that the patients with TCR,

Table 1: Distribution by gender and age group in patients operated on pituitary adenomas at Guillermo Almenara Hospital in the period 2019-2020

Characteristic		*TSR*		*TCR*	
		Number	**%**	**Number**	**%**
Sex	Male	18	42.86	23	54.76
	Female	24	57.14	19	45.24
TOTAL		**42**	**100**	**42**	**100**
Age	Less than 40 years old	9	21.43	9	21.43
	40 to 49 years old	9	21.43	7	16.67
	50 to 59 years old	15	35.71	12	28.57
	60 to 69 years old	5	11.91	10	23.81
	70 to 79 years old	3	7.14	4	9.52
	80 to more	1	2.38	0	0
TOTAL		**42**	**100**	**42**	**100**

Table 2: Medical history in patients operated on pituitary adenomas at Guillermo Almenara Hospital in 2019-2020

Characteristic	*TSR*		*TCR*	
	Number	*%*	*Number*	*%*
Hypertension	10	23.81	4	9.52
Diabetes Mellitus	7	16.67	4	9.52
Panhipopituitarismo	8	19.05	8	19.05
Hypothyroidism	9	21.43	11	26.19
Acromegaly	13	30.23	3	7.14
Cushing's disease	6	14.29	1	2.38

the patients between 60 and 69 years old, occupied a good percentage with 23.81%, that is to say almost a quarter of patients. The chi square test was applied at age obtaining a p of 0.15.

Regarding the medical history of these patients, it is observed in Table 2 that in the group of patients undergoing TSR there was a high percentage of acromegaly with 30.23%, arterial hypertension with 23.81%, hypothyroidism with 21.43% and panhypopituitarism with 19.05%. While in the TCR group, those who occupied a high percentage were hypothyroidism with 26.19% and panhypopituitarism with 19.05%. When analyzing each background individually with the chi-square test, it was found that arterial hypertension with a p of 0.05, acromegaly with a p of 0.003 and Cushing's disease with p of 0.03 were statistically significant.

It was also shown that patients undergoing surgery for a pituitary adenoma, about a quarter or a fifth had had previous surgery for the same lesion and were reoperated for recurrence or residual tumor. As can be seen in *Table 3*, the patients who underwent TSR had a prior TSR of 19.05% and a previous TCR of 4.76%. On the other hand, in those subjected to TCR, the antecedent was a previous TSR of 7.14% and a previous TCR of 11.91%. The chi square test was applied to these variables, finding a p of 0.07 for the antecedent of TSR and a p of 0.17 for the antecedent of TCR.

Regarding the imaging characteristics, it was observed that 69.5% of the patients undergoing TSR were macroadenomas, 26.19% microadenomas and 4.76% were giant adenomas; while in the TCR group 61.9% were macroadenomas, 38.1% were giant adenomas and none were microadenomas, as observed in *Table 4*. The chi-square test was applied to the variable classification by size, finding significance statistic with p of 0.0000. When applying to each type of adenoma by size, statistical significance was found for microadenomas with a p of 0.0005 in favor of TSR and for giant adenomas with a p of 0.0005 in favor of TCR.

Regarding the functionality of the adenomas, as observed in *Table 4*, in the group of TSR, 57.14% were non-functioning, 28.57% were producers of growth hormone (GH) and 14.29% were producers of adrenocorticotropic hormone. (ACTH). In the TCR group, 88.10% were non-functioning, 7.14% were GH producers, 2.38% were ACTH producers and 2.38% were prolactin (PRL) producers. When applying the chi square test, statistical significance is evident with the GH-producing adenoma with a p of 0.01 and the ACTH-producing adenomas with a p of 0.04, in favor of TSR.

Regarding the classification of Hardy modified by Wilson, as observed in *Table 4*, when the extension was evaluated, in the TSR group the majority of patients were grade O (30.95%) or grade B (26.19%), while in the TCR group the majority was grade D (47.62%) or grade C (28.57%), and when applying the chi square test, statistical significance is found in grade O (p of 0.0002), grade A (p of 0.05) and grade B (p of 0.007) in favor of TSR, while grade D (p of 0.0001) and grade E (p of 0.04) in favor of TCR. Regarding the degree of invasion, in the TSR group the majority were grade I (28.57%) or grade IV (28.57%), while the TCR group the majority was grade IV (66.67%) or grade III (26.19%).), and when applying the chi-square test, statistical significance was found for grade I (p of 0.001) and grade II (p of 0.02) in favor of TSR, while grade IV with p of 0.006 to favor of the TCR.

When lateral extension was evaluated according to the Knosp classification *(table 4),* it was found that in the TSR group the majority were grade 0 (38.1%) or grade 2 (23.81%), while the TCR group the majority They were grade 4 (42.86%) or grade 3 (26.19%), and when applying the chi square test, statistical significance was shown in grade 0 (p of 0.0005) for the TSR and grade 4 (p of 0.0006) for the TCR. The last mentioned in said table are the averages of the maximum diameters of the tumor in the 3 planes, finding

Table 3: Surgical history in patients operated on pituitary adenomas at Guillermo Almenara Hospital in the period 2019-2020

Characteristic		*TSR*		*TCR*	
		Number	*%*	*Number*	*%*
History of pituitary adenoma surgery	TSR	8	19.05	3	7.14
	TCR	2	4.76	5	11.91

Table 4: Characteristics of images in patients operated on pituitary adenomas at Guillermo Almenara Hospital in the period 2019-2020

Characteristic		*TSR*		*TCR*	
		Number	*%*	*Number*	*%*
Type of Pituitary Adenoma by Size	Microadenoma	11	26.19	0	0
	Macroadenoma	29	69.05	26	61.90
	Giant Adenoma	2	4.76	16	38.10
TOTAL		**42**	**100**	**42**	**100**
Type of Pituitary Adenoma according to Function	Not Functioning	24	57.14	37	88.10
	GH producer	12	28.57	3	7.14
	ACTH producer	6	14.29	1	2.38
	PRL producer	0	0	1	2.38
TOTAL		**42**	**100**	**42**	**100**
Hardy's classification modified by Wilson, Invasion Grade	I	12	28.57	1	2.38
	II	9	21.43	2	4.76
	III	9	21.43	11	26.19
	IV	12	28.57	28	66.67
	V	0	0	0	0
TOTAL		**42**	**100**	**42**	**100**
Hardy's classification modified by Wilson, Extension Grade	0	13	30.95	0	0
	A	7	16.67	2	4.76
	B	11	26.19	2	4.76
	C	8	19.05	12	28.57
	D	2	4.76	20	47.62
	And	1	2.38	6	14.29
TOTAL		**42**	**100**	**42**	**100**
Knosp classification	0	16	38.10	2	4.76
	1	7	16.67	2	4.76
	2	10	23.81	9	21.43
	3	6	14.28	11	26.19
	4	3	7.14	18	42.86
TOTAL		**42**	**100**	**42**	**100**
Average Size	Cranio-caudal	2.09cm		3.56cm	
	Antero-posterior	1.57cm		2.71cm	
	Transverse	1.96cm		3.30cm	

that in the TSR group, the average of the caudal skull diameter was 2.09cm, the anterior was 1.57cm and the transverse it was 1.96cm; while in the TCR group, the mean of the caudal skull diameter was 3.56cm, from the anterior posterior one it was 2.71cm and from the transverse one it was 3.30cm.

Regarding the result of the surgery, it was observed that most of the patients improved in their visual fields, being 54.76% in the TSR group and 59.53% in the TCR group, while there was no variation in the visual defect in 45.24% of the TSR group and in 35.71% of the TCR group. Only in the TCR group was there visual impairment by 4.76%.

All this can be seen in *Table 5*, as well as most patients improved within the first 2 weeks, being 69.56% in the TSR and 80% in the TCR. When applying the chi square test for the effects on the visual fields, a p of 0.06 was obtained and for the time in which the visual function was recovered it was a p of 0.09. When the rate of intraoperative complications was assessed with the chi square test, statistical significance was found with a p of 0.03, concluding that the TCR were more complicated.

Regarding the degree of tumor resection (*Table 6*), it was evident that in the TSR group 71.44% had total resection, 7.14% had subtotal resection, 11.9% was partial and a biopsy was performed in 9.52%; while in the TCR group 50% had total resection, 11.90% had subtotal resection, 19.05% was partial and 19.05% underwent a biopsy. The chi square test was also applied and a p of 0.10 was found.

DISCUSSION

Zhu et al evidenced, in their study on pituitary adenomas of the suprasellar region, that the average age of presentation was 36.73 years, the majority being women with 61.5%, while our study showed no significant difference with respect to sex in all the treated cases, but when divided by

Table 5: Result of surgery in patients operated on pituitary adenomas at Guillermo Almenara Hospital in the period 2019-2020

Characteristic		*TSR*		*TCR*	
		Number	*%*	*Number*	*%*
Effect on visual fields	Obvious Improvement	13	30.95	8	19.05
	Mild Improvement	10	23.81	17	40.48
	No Variation	19	45.24	15	35.71
	Worsening	0	0	2	4.76
TOTAL		**42**	**100**	**42**	**100**
Time when visual function was recovered	In a day	6	26.09	2	8.00
	In two weeks	16	69.56	20	80.00
	In a month	1	4.35	3	12.00
TOTAL		**23**	**100**	**25**	**100**
Intraoperative Complications		2	4.76	8	19.05

TSR or TCR group, it turns out that in the TSR group the predominance is female, while in the TCR group the predominance is male [4]. In contrast, Das et al found that the predominance was in males, with 59% [8].

The imaging classification is based on microadenomas if their maximum diameter is less than 10mm, macroadenomas if their maximum diameter is greater than or equal to 10mm, and giant adenoma if their maximum diameter is greater than or equal to 40mm. In addition, to assess pituitary adenomas, Hardy's classification modified by Wilson is used, which assesses invasion from grade I to V, with I being microadenomas, II macroadenomas that cause broadening of the Sella, III is a focal destruction of the Sella turcica, IV is a diffuse destruction of the Sella turcica and V is a spread by CSF or hematogenous. It also evaluates the extension from 0 to E, being 0 an intraselar tumor, A is a tumor that reaches the suprasellar cistern, B that which reaches the anterior recess of the III ventricle, C is the one that elevates the floor of the III ventricle, D is that that has intradural intracranial growth and E is the one that has a tumor that invades laterally towards the cavernous sinus [2].

The use of MRI has increased the diagnosis of pituitary microadenomas. These are a heterogeneous group of tumors with different biological behavior, endocrine secretion, and clinical presentation. Treatment is mainly based on endocrine secretion. Active endocrine tumors will require medication such as prolactinoma, or surgical management as in the case of acromegaly or Cushing's disease. For inactive tumors, called microincidentalomas, follow-up is the appropriate option [1].

The Knosp classification is also used to assess its lateral extension and the involvement of the supracavernous and intracavernous carotid, where 3 imaginary lines are made, one that passes through its internal border, one that passes through the middle and one that passes through the external border. Grade 0 if the tumor is inside the inner line, grade 1 between the inner and midline, grade 2 between the median and outer line, grade 3 that passes the outer line, and grade 4 if it involves the carotid [2].

Likewise, Zhu et al reported in their study a predominance of non-functioning adenomas with 36.5%, and in a second place they had ACTH secretors with 34.6%. In our study, we also found non-functionaries first, both in the TSR group and in the TCR group, but unlike Zhu, we found GH producers second. Zhu et al also mentioned in their study that they mainly had macroadenomas with 68.9%, similar to our findings since both the TSR and TCR groups found a predominance of macroadenomas, with more than 60% in each case [4].

In our study it was also evidenced that arterial hypertension, acromegaly and Cushing's disease showed statistical significance in favor of TSR, this association is probably due to the fact that Cushing's disease and acromegaly are mainly expressed as microadenomas, since the Hormonal hyperproduction results in early symptoms, and these two

Table 6: Degree of Resection in patients operated on pituitary adenomas at Guillermo Almenara Hospital in the period 2019-2020

Degree of Resection		*TSR*		*TCR*	
		Number	*%*	*Number*	*%*
Total	100%	30	71.44	21	50.00
Subtotal	90-99%	3	7.14	5	11.90
Partial	50-89%	5	11.90	8	19.05
Biopsy	Less than 50%	4	9.52	8	19.05
TOTAL		**42**	**100**	**42**	**100**

diseases can lead to high blood pressure.

Goshtasbi et al 7 found in their study that patients undergoing endoscopic treatment for pituitary adenoma had a smaller tumor, with p <0.01, similar to our findings, since we found a significant difference with a p of 0.0005 in favor of TSR. for microadenomas. It is also evident that tumors undergoing TSR have a lower degree in imaging classifications, which also showed statistical significance.

Our study also showed that the rate of intraoperative complications was higher in the TCR (p of 0.03), probably explained by the fact that giant adenomas compromised the optic nerves and sometimes involved important vascular structures that could be injured during surgery. Likewise, Billings et al in their study found that giant pituitary tumors have a higher risk of cranial nerve paresis (p of 0.019) and a higher risk of vascular complications (p of 0.0001) [9]. Regarding the degree of resection, Goshtasbi et al 7 found that the resection rate had no statistical significance with a p of 0.34, similar to our findings where we also found no statistical significance with a p of 0.10.

The COVID-19 pandemic has changed the canons established in the treatment of patients with pituitary adenoma, due to the fact that it has been shown that patients undergoing transsphenoidal treatment generate greater exposure to medical personnel [5]. That is why the present study had to be suspended in May 2020 due to the aforementioned pandemic, the last surgery being performed in March 2020.

It is worth mentioning that a statistically significant association was found in several of the variables studied, without implying a causal relationship; therefore, it can only be said that a variable is more frequent in some type of surgery. In the future, prospective studies with multivariate analysis are required to determine this causal relationship. Thus, a larger sample is also necessary to be able to compare subgroups such as endoscopic and microsurgical transsphenoidal resection, which will give us more insight into the preoperative and postoperative profile in each case.

CONCLUSIONS

Pituitary adenomas are a frequent pathology and can be treated transcranial or transsphenoidal, achieving good resection rates, although with a higher rate of intraoperative complications in the transcranial route. Through the transsphenoidal route, smaller and smaller grade lesions are treated in the different classifications, the most frequent being adenomas that cause Cushing's disease and acromegaly; while by the transcranial route, larger and higher degree injuries are treated in the classifications. Prospective, randomized and controlled studies are required to determine the causal relationship of these variables.

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