



Guanti bianchi technique for resection of selected pituitary adenomas

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ABSTRACT

Introduction: Since the introduction of the endoscopic endonasal approach (EEA) to skull base, the nasal phase has been a true challenge as it represents the moment of definition of the corridor, thus defining the instruments maneuverability at tumor removal phase. The longstanding cooperation between ENT and neurosurgeons have provided the possibility of creating adequate corridor with maximal respect toward nasal structures and mucosa. This sparked the idea of entering the sella as thieves, so we named "Guanti Bianchi" technique a lesser invasive variation of the approach for the removal of selected pituitary adenoma.

Research Question: The purpose of this study is to present the preliminary results of "Guanti Bianchi" technique. **Material and Methods:** Data from 17 patients undergoing "Guanti Bianchi" technique (out of 235 standard EEA) at our center, were retrospectively analysed. ASK Nasal-12, a quality-of-life instrument developed specifically to assess patient perception of nasal morbidity, was administered pre- and postoperatively.

Results: 10 (59%) patients were men and 7 (41%) women. The mean age was 67.7 (range 35-88). The average duration of the surgical procedure was 71.17 minutes (range 45-100). GTR was achieved in all patients, no postoperative complications were observed. Baseline ASK Nasal-12 was near normal in all patients, 3/17 (17,6%) experienced transitory very mild symptoms without any worsening at 3 and 6 months.

Discussion and Conclusions: This minimally invasive technique does not require turbinectomy or carving of the nasoseptal flap, it alters the nasal mucosa as little as necessary, and it is quick and easy to perform.

1. Introduction

Pituitary adenomas are in the vast majority of cases benign neoplasms, defined by a prevalence ranging from 1/865 up to 1/2688 people; more recently, the rate of diagnosis increased along with the refinement on neuroradiological techniques, so that nowadays microadenomas reach up an incidence of ca. 10% at magnetic resonance imaging (Villalonga et al., 2019; Solari et al., 2019a).

A discrete number of pituitary adenomas require to be treated surgically in accordance with strict indications, well refined along the years: pituitary surgery has been evolving rapidly, offering improvement of outcomes along with reduction of morbidity and mortality rates, with the transphenoidal either microscopic or endoscopic the standard approach to the pituitary area (Doglietto et al., 2005; Kanter et al., 2005; Cappabianca and de Divitiis, 2004; Leonhard et al., 2003; Perneczky et al., 1999). The transphenoidal approach is currently adopted in more than

95% of all surgeries for the treatment of pituitary adenomas and, more recently, the EEA is commonly used in many centers throughout the world (Cappabianca et al., 2010).

The possibility of accessing the skull base from a ventral corridor, namely the nasal route, has represented a true challenge as it required a concrete paradigm shift to understand the instruments maneuverability, especially at tumor removal phase. The close cooperation with ENT surgeons (Jho et al., 1996; Jankowski et al., 1992; Sethi and Pillay, 1995) have favored the definition of adequate surgical corridors to the skull base with maximal respect toward nasal structures and mucosa.

The "pure" endoscopic endonasal approach, has been adopted by our group in Naples (Cappabianca et al., 1998, 2004, de Divitiis et al., 2003), since the 1997 firstly to remove the sellar area lesions and nowadays it represents a viable route for different median and paramedian skull base lesions.

Standard approach to manage mostly infradiaphragmatic lesions was

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initially run via a monostril approach, without the removal of any nasal structure (Cappabianca et al., 1998); thereafter, the use of a dynamic technique, requiring two nostrils with bilateral middle turbinate lateral luxation and removal of posterior aspect of the nasal septum took over (Cappabianca et al., 2008; Cavallo et al., 2012).

Along with the introduction of the so-called extended approaches, the Pittsburgh group defined the paradigm of nasal structures removal - including monolateral and/or bilateral middle turbinectomy, monolateral and/or bilateral anterior and posterior ethmoidectomy, combined with a larger posterior septectomy - to achieve superior exposure and adequate surgical freedom (Kassam et al., 2005a). Upon the expanding of the indications, there have been many controversies regarding the adequate enlargement of the nasal corridor, i.e., the extent of removal of nasal structures to ensure a comfortable surgical corridor. It should be kept in mind that in these approaches, a wider dissection of nasal mucosa is required per harvesting of the pedicled nasoseptal flap, being considered this latter the most resilient technique to provide watertight reconstruction of the osteodural defect (Hadad et al., 2006; Rivera-Serrano et al., 2011; Cavallo et al., 2019). Therefore, the risks of nasal complications (Friedman et al., 2000; Houser, 2006; Marchioni et al., 2008; Nyquist et al., 2010) cannot be underestimated and can cause similar discomfort as compared to the threatened neurosurgical ones.

Following the analysis of surgical freedom and exposure of the endonasal endoscopic corridor we noticed that extensive removal of paranasal structures is not worth in every case (de Notaris et al., 2014). Thanks to the evolution of the techniques and development of a solid surgical experience, we though reduced the invasiveness in regard to the paranasal structures; nowadays, adequate corridor is created according to the intradural pathology in order to achieve to maximum possible/allowed tumor resection along with the maximum possible sparing of the nasal structures.

Hence, in case of infradiaphragmatic intra-suprasellar lesions, we are adopting a minimally invasive one and a half nostril technique, in order to keep as much as possible intact the nasal mucosa. Accordingly, one of the Argentinian fellows (JFV) working at our Division got the idea of entering the sella as thieves, and thereafter named this technique “Guanti Bianchi” (i.e. white gloves thief technique) [Fig. 1], in allusion to the theft of the Mona Lisa from the Louvre Museum by the Italo-Argentinian duo of Vincenzo Peruggia and the Marquis Eduardo Valfermo (Hugh, 1984).

Whether ideally one can consider the nostril as the magnificent Louvre Museum with different arts.

- the nasal structures -, the pituitary tumor represents the Mona Lisa: the neurosurgeon should move gently and respectfully along the way – the nasal corridor – to reach the masterpiece – the pituitary adenoma -.

The purpose of this study is to present the preliminary results of the application of the “Guanti Bianchi” technique in the resection of selected pituitary adenomas.

2. Material and methods

2.1. Patients' series

We retrospectively reviewed the data of 17 patients (10 men and 7 women) with a mean age of.

67.7 years (range 35–88 years) who underwent the “Guanti Bianchi” technique for resection of pituitary adenomas between January 2019 and January 2022, at the Neurosurgery Division of the Università degli Studi di Napoli “Federico II”, Naples, Italy.

The series consists of 1 of GH-secreting microadenoma and 16 macroadenomas; in these latter group 12 were non-functioning lesions, 3 cases presented apoplexy (1 was a Prolactinoma), and finally 1 case of GH secreting tumor.

All patients underwent postoperative MRI at 3 months with detailed imaging, including fat suppression sequences.

Demographics, preoperative evaluation (e.g., endocrine, visual status and presenting signs), tumor characteristics, surgical outcomes, and complications were retrieved from our dedicated database and analyzed retrospectively.

Patients were followed up for a mean of 23 months (median 25 months, range 7–37 months). Follow-up comprised MRI of the sellar region, endocrinology evaluation, as well as clinical and ophthalmic examinations. Furthermore, the ASK Nasal-12, a QOL instrument developed specifically to assess patient perception of nasal morbidity was administered to patients preoperatively, and 7 days, 3 and 6 months after surgery (Little et al., 2012, 2013; Sarris et al., 2021, van der Meulen et al., 2022). It consists of 12 items assessing the presence and severity of nasal symptoms on a six-point Likert scale (0 = No problem, 5 = Severe problem) (van der Meulen et al., 2022); accordingly, we considered ASK-12 score of 2 or higher as complaint of nasal complications.

This study was conducted in accordance with the ethical standards stated in the 1964 Declaration of Helsinki. According to its retrospective nature IRB waived the need for written consent.



Fig. 1. The white glove thieves of the Mona Lisa. 1) The Italian weekly of that time, *La Domenica del Corriere*, shows on its cover an illustration of the theft. 2) Portrait of Vincenzo Peruggia, the perpetrator of the theft. 3) Famous photograph of the Louvre Museum showing the empty space and four bare hooks on the wall after the theft of the painting.

2.2. Surgical technique

All the patients underwent standard endoscopic endonasal approach to the sellar area using a rigid 0-degree endoscope, 18 cm in length and 4 mm in diameter (Karl Storz Endoscopy, Tuttlingen, Germany), as the sole visualizing tool (Cappabianca et al., 2008, de Divitiis et al., 2002).

As previously depicted, the surgery goes through three main phases plus the reconstruction, which is tailored upon the intraoperative findings; we hereafter report the significant variations in regard to the nasal and sphenoidal parts.

The procedure consists in four different steps: the nasal, the sphenoid, the sellar and the reconstructive phase.

2.2.1. Nasal phase

When the endoscope (18 cm in length, 4 mm in diameter) is introduced, it is possible to identify the main anatomic landmarks, such as the inferior turbinate laterally, the nasal septum medially and the roof of the choanal inferiorly. Cottonoid pledgets soaked with diluted adrenaline (2:100 000) or with xylometazoline hydrochloride are positioned between the middle turbinate and the nasal septum; then, the middle turbinate is gently pushed laterally in order to get access to the surgical corridor along to the sphenoidal-ethmoidal recess. Posterior nasoseptal

mucosa is minimally coagulated where the posterior nasal septum attaches to the rostrum sphenoidalis. Coagulation is performed halfway in between the choana's roof and sphenoid sinus (10/12 mm above the choana roof), having the body of the middle turbinate as lateral limit of the surgical field (Figs. 2.1-2.3). Coagulation is stopped as soon as the bone of the rostrum sphenoidalis is exposed. The nasal septum mucosa is slightly detached from the sphenoid rostrum and drilling is started (Figs. 2.4-2.6) to detach the posterior portion of the nasoseptal septum by a soft contralateral pressure. The sphenoid rostrum is fully exposed, and the sphenoidal phase is started (Figs. 2.6-2.7).

2.2.2. Sphenoidal phase

The anterior bony wall of the sphenoid sinus is widely opened, whilst only a little window over the mucosa covering it at the left nostril is obtained (Figs. 3.1-3.2). This corridor represents the access through 1 + ½ nostril, so called the “Guanti Bianchi” technique. From this point on, the surgeon performs a bimanual dissection while a coworker holds the endoscope dynamically, (Castelnuovo et al., 2006). (Fig. 3.3) The endoscope is held by the assistant in the patient's right nostril; this is stretched upward (at 12 o'clock) by and a suction tube is held by the first surgeon, in the most inferior position in the same nostril (at 6 o'clock) with the main instrument sliding in the left nostril (Solari et al., 2019b).

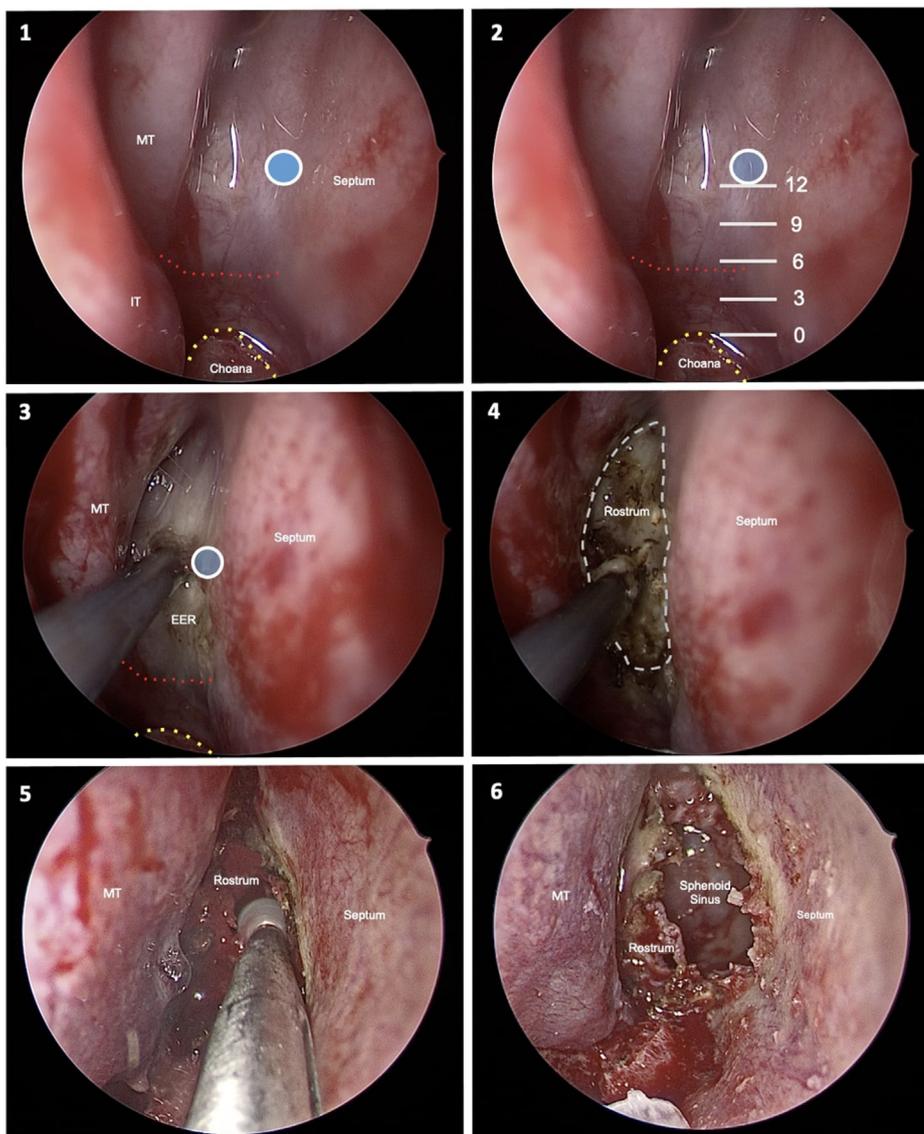


Fig. 2. Nasal phase. Section of the sphenoid mucosa step by step. 1) The starting point in the EER is objective. Here it is shown where to place the exact point to coagulate, in a latero-medial direction, just at the junction of the septum with the sphenoid rostrum. 2) Shows the height (mm) of the point with respect to the choana. 3) Beginning of the coagulation of the mucosa of the sphenoid face from the mentioned point. 4) Coagulation stops when the rostrum is exposed. 5) Start of drilling with a diamond bur, with slight contralateral dislocation of the nasoseptal septum separating it from the sphenoid rostrum. 6) Exposure of the sphenoid sinus from the right nostril. MT: middle turbinate; IT: inferior turbinate. The celestial and white point is the exact place where the sphenoidal mucosa should begin to coagulate. The red dotted line and red arrow correspond to the nasoseptal artery (a branch of the sphenopalatine artery). The yellow dotted line corresponds to the upper border of the choana.

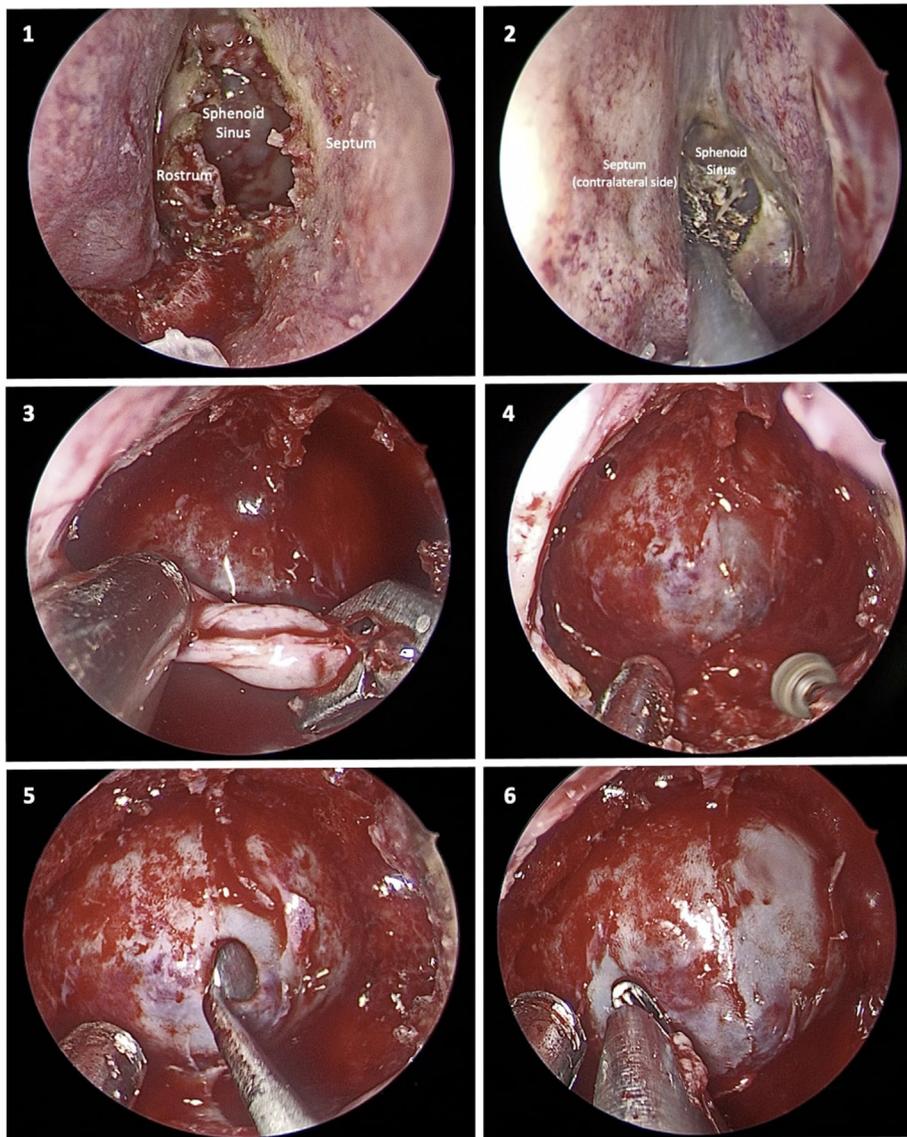


Fig. 3. Sphenoidal phase. 1–2) Bilateral sphenoid opening. 3) Bimanual dissection of the sphenoid mucosa. 4) Drilling of sphenoid septa and sella. 5–6) Opening of the posterior sphenoid wall of sella, with dissector and Kerrison punches.

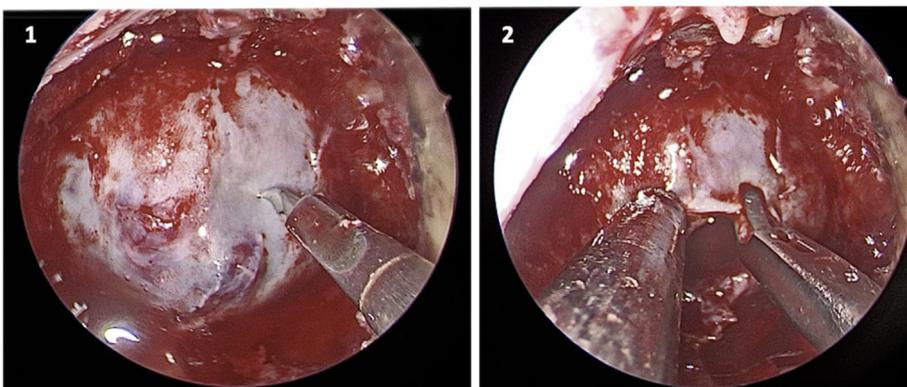


Fig. 4. Sellar phase. 1) Dura mater incision with micro-knife, 2) Posterior opening with cutting forceps.

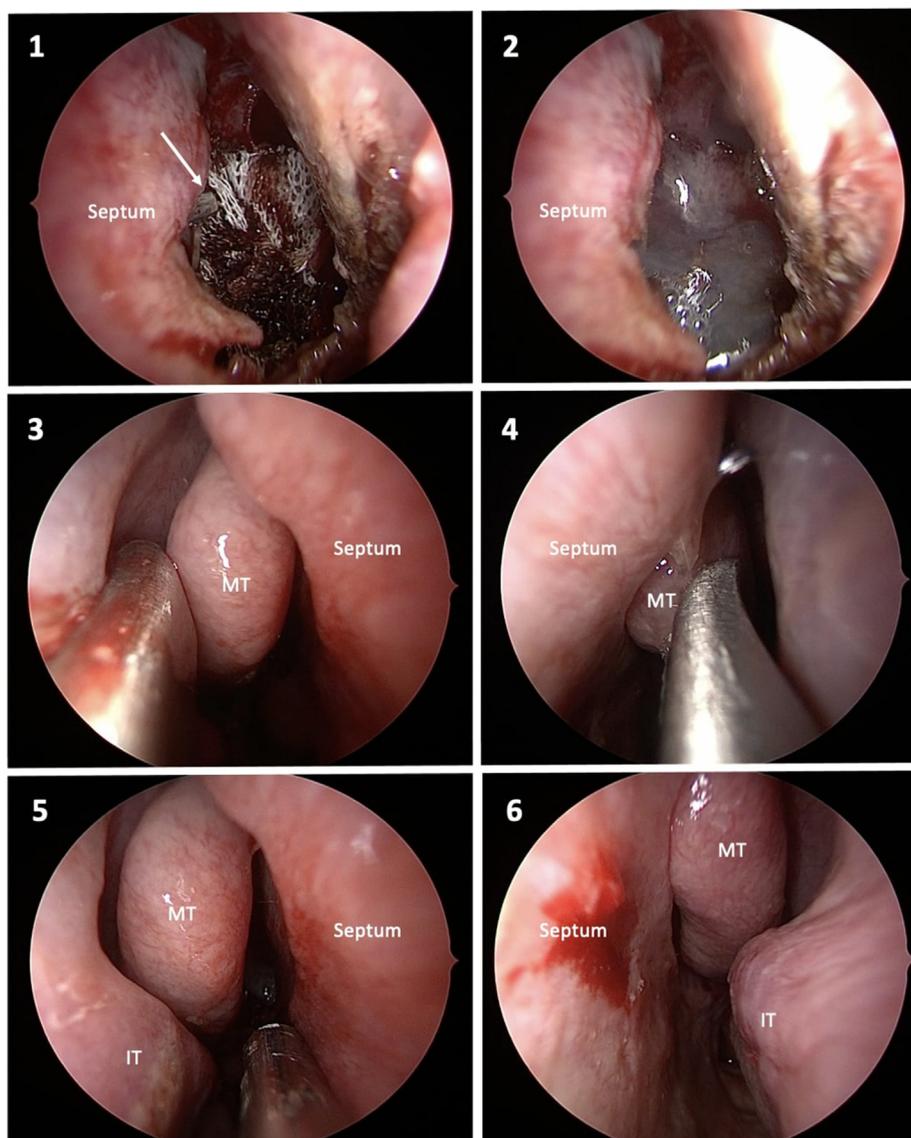


Fig. 5. Reconstruction. 1–2) Sellar reconstruction with hemostatic agents (oxidized cellulose and subsequent fibrin glue). The white arrow indicates a forceps holding oxidized cellulose from the contralateral nostril to the optic. 3–4) Medialization of the right and left middle turbinates, respectively. 5–6) Final view of both nostrils. MT: Middle Turbinate; IT: Inferior Turbinate.

Finally, the sellar floor is opened and the dural plane is exposed until to see the “four blues” (Prevedello et al., 2013). (Figs. 4.4–4.6)

2.2.3. Sellar phase

The dural opening is made in the center with a micro-knife (Fig. 4.1). Then it is extended “to measure” according to the location of the tumor with a cutting forceps (Fig. 4.2). We proceed to a resection “en bloc”, “extracapsular” (Prevedello et al., 2013) or “piecemeal” as appropriate (Cavallo et al., 2007; Oldfield and Vortmeyer, 2006). Hemostasis is achieved and, thereafter, the absence of CSF leak is secured.

2.2.4. Reconstruction

After lesion removal, closure of the sellar floor is required: usually, packing with heterologous materials (i.e oxidized cellulose polymer - fibrin glue) was performed. In the cases of a weak sellar barrier or CSF minimal weeping, we seal with autologous fat and fibrin glue (Cappabianca et al., 2002).

At the end of the procedure, hemostasis is obtained, and the middle

turbinate is gently moved medially to its original position (Fig. 5). Packing of the nasal cavity is not necessary.

3. Results

Patients’ overall preoperative features are summarized in Table 1: 82.35% of the patients (14/17) presented non-functioning adenomas, 11.76% of patients (2/17) presented GH secreting lesions and 1 prolactinoma (5.88%); 17.64% presented with apoplexy (2 non-functioning and 1 prolactinoma).

In the preoperative period, 6 patients presented visual defects- 4 complaining of minor visual acuity loss and two presenting bitemporal hemianopia -, 2 cases of galactorrhea and 1 case of acromegaly. On the other hand, 7 patients presented some hormonal alterations; visual disturbance improved in 66.6% of patients (4/6), and there were no cases of transient or permanent worsening of visual functions.

Gross total removal was recorded in all patients, with a mean follow-up of 23 months.

Table 1
Preoperative features, and extent of removal in the series of patients that underwent surgery by means of “Guanti Bianchi” technique.

N°	Sex	Age (years)	Size & Location	Pathology	Clinical Presentation	Extent of Removal
1	M	58	Intrasellar Microadenoma	GH secreting	Incidental	GTR
2	F	66	Intra-Infasellar Macroadenoma	Non-Functioning	Incidental	GTR
3	F	35	Intra-Infasellar Macroadenoma	Non-Functioning	Galactorrhea	GTR
4	F	63	Intra-suprasellar Macroadenoma	Non-Functioning	Incidental	GTR
5	M	47	Intra-parasellar Macroadenoma	GH Adenoma	Acromegaly	GTR
6	F	72	Intra-parasellar Macroadenoma	Non-Functioning	Incidental	GTR
7	M	70	Intra-suprasellar Macroadenoma	Non-Functioning	Apoplexy	GTR
8	M	88	Intra-suprasellar Macroadenoma	Non-Functioning	Visual acuity loss	GTR
9	M	82	Intra-suprasellar Macroadenoma	Non-Functioning	Visual acuity loss	GTR
10	F	61	Intra-suprasellar Macroadenoma	Non-Functioning	Visual field defect	GTR
11	F	40	Intra-suprasellar Macroadenoma	Non-Functioning	Galactorrhea	GTR
12	M	78	Intra-suprasellar Macroadenoma	Non-Functioning	Visual field defect	GTR
13	F	75	Intra-suprasellar Macroadenoma	Non-Functioning	Incidental	GTR
14	M	72	Intra-suprasellar Macroadenoma	Non-Functioning	Visual acuity loss	GTR
15	M	63	Intra-suprasellar Macroadenoma	Non-Functioning	Visual acuity loss	GTR
16	M	35	Intra-suprasellar Macroadenoma	Prolactinoma	Apoplexy	GTR
17	M	61	Intra-suprasellar Macroadenoma	Non-Functioning	Apoplexy	GTR

F: Female; M: Male; GH: Growth Hormone;; GTR: Gross Total Removal.

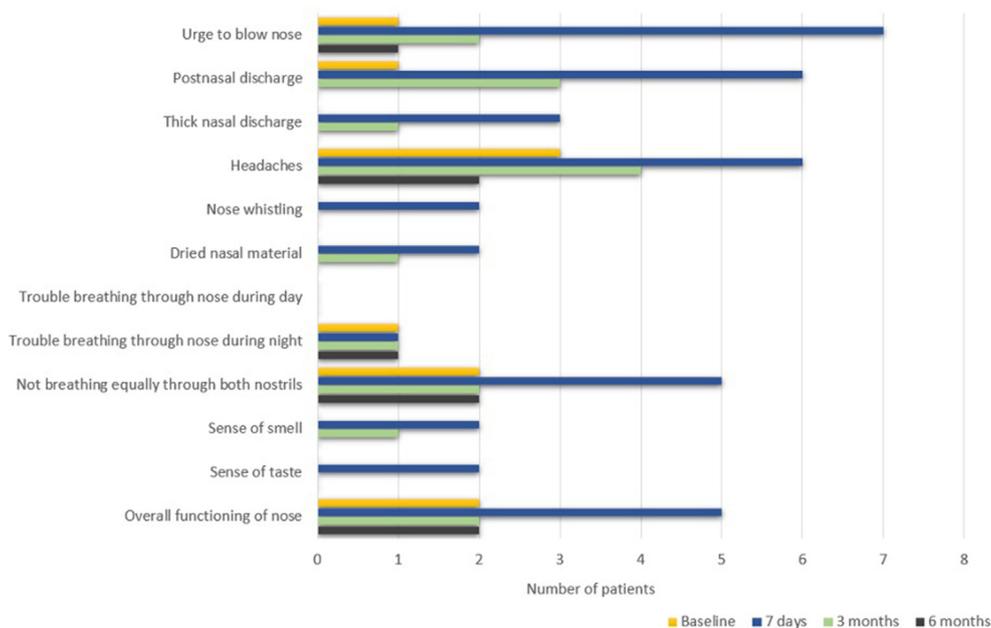


Fig. 6. ASK Nasal-12 results. Horizontal bar chart showing ASK Nasal-12 questionnaire results at baseline, 7 days, 3 and 6 months after surgery.

The mean duration of the procedure was 71.17 min, with a range between 45 and 100 min. No infections, hematomas, or CSF leaks were observed, nor early or late complications. Only in one case, minimal CSF leak was evidenced during the intraoperative time. In this case, abdominal fat was used during the reconstruction phase. No case presented CSF leak in the postoperative period. According to Ask survey score, preoperative status was considered normal in all patients (100% total score <2). 17,6% of patients (3/17) presented with nasal symptoms at 7 days after surgery: all of them reached a total score >2, although maximum score of 1 (=very minor problem) was revealed at each item apart.

No worsening of preoperative score at 3 and 6 months was detected (Fig. 6).

4. Discussion

The nasoseptal flap has revolutionized endoscopic cranial base reconstruction; Being based on the posterior septal artery, a branch of the sphenopalatine artery, it is a robust flap with a great arch of rotation (Pinheiro-Neto et al., 2019). However, this technique can be associated

with a series of complications. These complications can occur beyond the immediate postoperative period and are associated with donor site morbidities such as septal perforation, prolonged crusting, and cartilage necrosis (Soudry et al., 2015). This seldom can be underestimated in the attempt of achieving the most resilient skull base reconstruction. We believe extensive manipulation of mucosa and harvesting of nasal pedicled flap e can be avoided in several surgeries that do not require extended approaches. The “Guanti Bianchi” technique in its philosophical conception respects the ancestral precepts of pituitary microscopic surgery and is part of the vanguard in endoscopy.

Our technique shares some principles with the “rescue” flap praised by Prevedello and Carrau (Rivera-Serrano et al., 2011), and the “one and half” approach (Wen et al., 2016):1) it tries to reduce the nasal morbidity, 2) it aims to provide a good surgical exposure and 3) and an adequate corridor to grant performing maneuvers according to 3–4 hands technique. It differs from these, in that practically does not manipulate the nasal mucosa, it enters and leaves without leaving any trace in the nose.

Further, although on a limited series of patients we had the opportunity to retrieve their satisfaction in terms of postoperative nasal

discomfort. Indeed, “Guanti Bianchi” technique has shown a minimal impact on nasal morbidity as validated at the ASK-12 questionnaire, with near normal sinonasal status in all patients 3 months after surgery, confirmed at 6 months follow up.

It should be said that this lesser invasive variation of the endoscopic endonasal approach does not require any additional surgical instrument nor technological advanced tool; thus far it can be considered a viable option also in those neurosurgical centers that do not feature a higher standard intraoperative technology.

“Guanti Bianchi” technique is useful to resect selected pituitary adenomas. This technique excludes the use of flaps in the reconstructive phase, so that it is crucial to carefully indicate its adoption. We suggest to not adopt it in patients with increased risk of CSF leak and/or in case indication for extended EEA stands preoperatively. We nowadays recommend an extended EEA with the harvesting of nasoseptal flap preferably in patients with dumb-bell shape, supra or parasellar extension (e.g., invasion of III ventricle and encasement of carotid artery), fibrous or rubbery consistency or recurrent tumors (Kassam et al., 2005a, 2005b; Cappabianca et al., 2000; Cappelletti et al., 2019).

4.1. Selection of the surgical technique

The neurosurgeon must be very careful in the selection of patients to operate, their tactics and surgical technique. Therefore, both teams (Naples-Tucuman) are working on a classification that allows us to predict the intraoperative risk of CSF leakage and help to define which surgical technique we should use (Villalonga et al., 2022).

5. Conclusions

The “Guanti Bianchi” technique can be considered a viable, an effective technique in the treatment of intrasuprasellar infradiaphragmatic tumors, mostly pituitary adenomas.

It is a minimally invasive approach that alters as least as required the anatomy of the nasal mucosa, thus reducing the overall risks of nasal complications. On the other hand, the surgeon receives advantages in terms of reduction of nasal phase surgical time.

Author contributions

Conceptualization, J.F.V. and D.S.; methodology, D.S., G.L.F., and M.B.; validation P.C., L.M.C. and A.C. writing—original draft preparation, G.L.F., M.B., and D.S.; writing—review and editing, D.S., J.F.V. and L.M.C.; supervision, P.C. and L.M.C. All authors have read and agreed to the published version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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