Validation of modular endoscopic medial maxillectomies for inverted papilloma of the maxillary sinus*

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Abstract

Background: Treatment of inverted papilloma of the maxillary sinus (IPMS) has a lower success rate compared to other IPs. As such, its correct management generally needs trans-nasal endoscopic medial maxillectomy (EMMs) for adequate resection. The aim of this manuscript is to describe outcomes and major prognostic factors of a cohort of patients with IPMS who were treated with EMM.

Methodology: In this multicentric study, patients affected with IPMS and treated with EMMs were included. The site of origin of the IPMS were studied as well as the type of EMM performed. The histological features (IP vs dysplasia), type of mucosal resection (total vs. pedicle oriented), and post-operative complications were analyzed.

Results: 310 patients were included (212 primary and 98 recurrent cases). After a mean follow-up of 45.4 months, 15 patients experienced recurrence (4.8%) due to the application of EMMs tailored to the surgical insertion point. Dysplasia was significantly associated with a higher risk of recurrence. The rates of early and late complications were 11.6% and 11.9%, respectively.

Conclusions: IPMS resection via tailored EMM is associated with excellent disease control, thus excluding the systematic use of extended EMMs, which can however be justified in case of dysplastic IPMS given its significant impact on recurrence.

Key words: sinusitis, maxillary sinus, paranasal sinuses, paranasal sinus diseases, paranasal sinus neoplasms

Introduction

Inverted papilloma of the maxillary sinus (IPMS) is a benign pathology that accounts for 34-49% of all IPs and is characterized by local aggressiveness and potential malignant transformation, reported in 6.6% of cases [(1)]. Although different surgical approaches have been proposed over past decades, the management of IPs is nowadays primarily through a trans-nasal endoscopic approach and has a recurrence rate ranging from 5% to 30% [(2,3)]. However, when specifically considering IPMS, a reduction in terms of disease control (recurrence rate 16-30%) has been reported [(4)], due to heterogenous wall geometry and presence of areas that renders the complete IPMS removal challenging (e.g. alveolar recess and zygomatic recess) [(3,4)]. Unfortunately, little is currently known about the actual pathologic involvement of these blind spots and the consequent optimal approach, leaving the management of IPMS to the expertise of the center at which the patient is treated.

As such, the correct management of this pathology generally seems to require more extensive procedures, namely trans-nasal endoscopic medial maxillectomies (EMMs) [(5)], which are performed to gain sufficient exposure of the maxillary sinus and allow adequate resection of the IP. However, as the extension of

the endoscopic approach increases, so does post-operative morbidity [6,7]. In the last years, two different classifications of EMMs have been introduced with the aim to standardize the nomenclature of this surgical approach and facilitate their comparison. One was anatomy-based and validated in a preclinical setting according to the exposure and the working volume guaranteed by each EMMs [8]; the other was clinically oriented and validated on a large mono-institutional retrospective series [9] (Table 1). Both incorporated the concept of modularity, thus suggesting the possibility to intra-operatively tailor the extension of EMMs. However, the benefit of applying these endoscopic surgical procedures in the management of IPMS still needs clinical validation.

The aim of this manuscript is to describe the outcomes of a large, international, multi-institutional cohort of patients with IPMS who were treated with EMMs and analyze the prognostic factors that influence the final success rate.

Materials and methods

Study design

This is a multicentric retrospective observational study performed at four tertiary care referral centers (Hospital Lariboisière, Paris, France; ASST Spedali Civili di Brescia-University of Brescia, Italy; University of Insubria, Ospedale di Circolo e Fondazione Macchi, Varese, Italy; University of Padua, Italy). Inclusion criteria were: a) IPMS (either primary or recurrent) operated on via a trans-nasal endoscopic approach; b) availability of follow-up data (minimum 6 months); c) older than 18 years. Exclusion criteria were: a) combined or external approaches; b) presence of invasive carcinoma. Informed consent was obtained from each patient for treatment and use of de-identified clinical data for study purposes; the study, which was conducted according to the ethical standards of the Declaration of Helsinki revised in 2011, was approved by Hopital Lariboisiere review board (CNIL No. 2225234), and the respective Boards of Ethics at Insubria (approval number 0033025/2015), Padua, and Brescia (NP 3616).

Patient management and study variables

In all cases, the diagnostic work-up included a pre-operative radiological study (computed tomography [CT] and/or contrast-enhanced magnetic resonance imaging [MRI]), associated with biopsy under local anesthesia when feasible. The information regarding the site of origin of the IPMS was retrieved by both pre-operative imaging and intra-operative findings and classified as located in the anterior, lateral, posterior, medial, superior, or inferior walls of the MS or multiple localizations. In addition, the involvement of the retro-lacrimal, zygomatic, and alveolar recess was evaluated (Figure 1).

The EMMs performed on each patient were intra-operatively modulated according to the insertion point and the areas involved within the maxillary sinus; the approach was retrospectively classified by independent clinicians in each center following the classifications of Schreiber et al. [8] and Turri-Zanoni et al. [9]. The extension of the mucosal resection, defined as complete (total removal of MS muco-periosteum with extended drilling) or pedicle oriented (which focused the mucosal resection and bony drilling only at the level of the IP attachment), was studied. In all cases, the bony origin of the tumor was identified and drilled out.

Follow-up visits were based on in-office endoscopic evaluation every 6 months for the first 2 years and then yearly for 5 years. In cases in which the maxillary sinus was not completely assessable, MRI was indicated with the same schedule of the clinical visits. The frequency of follow-up evaluations was arbitrarily increased (every 3 months for the first year, every 6 months for the next 2 years and then yearly for 3 years) in case of an expected higher risk of recurrence (i.e., recurrent tumors, multifocal disease, dysplasia).

In line with World Health Organization (WHO) criteria, histological reports were classified as either IP with no precancerous changes or IP with dysplasia/carcinoma in situ so that no further

Table 1. Description of the different medial maxillectomies applied, related to the classification of Turri-Zanoni et al. and Schreiber et al. MM= medial maxillectomy.

Type of maxillectomy Turri-Zanoni et al. [8]	Type of maxillectomy Schreiber et al. [7]	Description	N (%)
Type 1	Type A	Wide antrostomy, borders of resection: inferior turbinate insertion, orbital floor, palatine bone and nasolacrimal duct	8 (2.6)
Type 2	Type B	Type 1/A with the additional removal of the inferior turbinate and medial maxillary wall posterior to the lacrimal pathway	35 (11.3)
Type 3A	Type C	Type 2/B with the additional resection of the maxillary sinus medial wall anterior to the lacrimal pathway, up to the pyriform aperture (transection of the lacrimal pathway)	167 (53.9)
Type 3B-4	Type D	Type 3A/C plus the removal of the anterior wall of the maxillary sinus to the infraorbital foramen, eventually enlarged as far as the zygomatic bone	61 (19.7)
Type 3A mod	Type D mod	Known as the pre-lacrimal medial maxillectomy, that allows the access to the maxillary sinus passing through the so called pre-lacrimal recess, a corridor between the pyriform aperture and the nasolacrimal duct, preserving the inferior turbinate	39 (12.6)

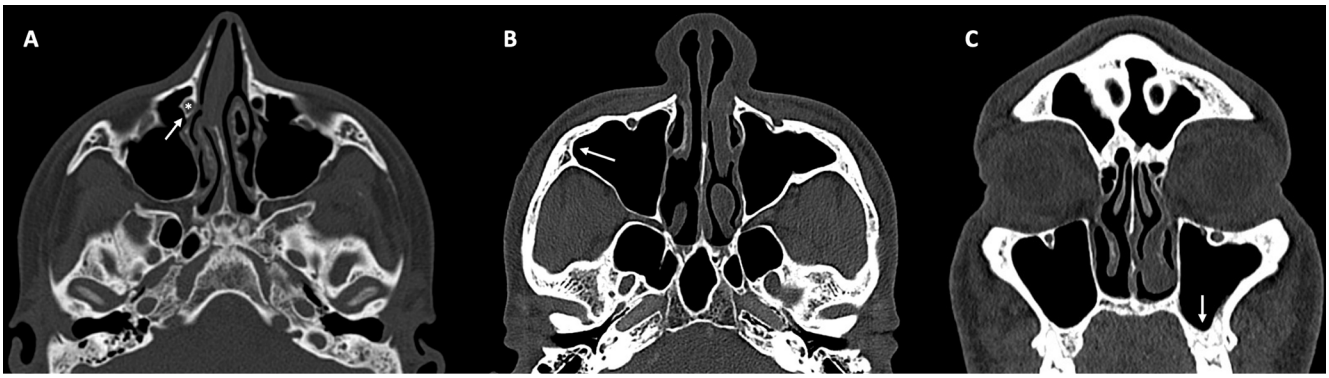

Figure 1. CT scans showing the specific localization of retro-lacrimal, alveolar, and zygomatic recesses. Retro-lacrimal recess (A, white arrow): located between the posterior wall of the lacrimal pathway (*), antero-medial aspect of the natural ostium of the maxillary sinus, and uncinate process; Zygomatic recess (B, white arrow): lateral pneumatization of the maxillary sinus towards the zygomatic bone and located between the superior, anterior, and lateral walls of the MS; Alveolar recess (C, white arrow): inferior pneumatization of the maxillary sinus towards the alveolar process of the maxilla bone, and located between the inferior, anterior, and medial walls of the MS.

sub-analysis on the grade of histology was performed.
Post-operative complications were divided into early (less than 10 days) and late, evaluated at 1, 2, and 6 months. Specifically, post-operative epistaxis was considered a complication when requiring intervention, infection if requiring antibiotics (decided post-operatively on clinical signs and symptoms), and epiphora when the Munk scale was ≥2 [10].
Data on age, sex, laterality of the lesion, symptoms referred, Krouse staging [11], follow-up updated in August 2022, and recurrence were also collected.

Study objectives

Primary endpoint was the assessment of the recurrence rate and the cumulative recurrence free survival. Secondary endpoints were: a) definition of prognosticators of higher risk of recurrence; b) association between EMMs, insertion point, and outcome; c) analysis of complications and correlation with the extent of surgery.

Statistical analysis

Statistical analysis was performed with SPSS version 26 (IBM Corp. in Armonk, NY, USA). Data are reported as mean ± standard deviation or percentage, as appropriate. Chi-square test or Fisher's exact test were used to evaluate the association of recurrences and complications with qualitative clinical factors. The cumulative time-dependent risk of recurrence was analyzed with Kaplan-Meier analysis and the log-rank test was used to evaluate the association of the variables with recurrence (primary vs secondary surgery, Krouse staging, site of insertion, involvement of recesses, histology, total vs. pedicle oriented mucosal resection, type of endoscopic medial maxillectomy). The Cox proportional hazard method was used to build a multivariate model with factors that were significantly associated with the log-rank test. The level of statistical significance was set at $p< 0.05$.

Results

In total, 310 patients were included in the study. The clinical characteristics of the series are summarized in Table 2. Of note, 68.4% were primary IPMS, whereas 31.6% were recurrences. Among presenting symptoms, in the majority of cases nasal obstruction (59.9%) or epistaxis (12.5%) were referred; in 18.5% of cases, the diagnosis was incidental. The pre-operative work-up was more commonly based on a CT scan associated with a contrast-enhanced MRI (77.3%); a pre-operative biopsy was made in all primary cases and in clinical suspicion of recurrent lesions. The IPMS was confined to the maxillary sinus in 159 cases (51.3%), whereas, even if it was primary pedicled at the level of the MS, it presented an extension to the anterior ethmoid, posterior ethmoid, and frontal sinus in, respectively, 48 (15.4%), 87 (28.1%), and 16 (5.2%) cases.
After a mean follow-up of 45.4 months, 15 patients experienced a recurrence (recurrence rate 4.8%, in all cases inside the maxillary sinus). Mean time to recurrence was 44 months (median 22 months, range 4-180). Considering the cumulative time-dependent risk of recurrence, 3, 5 and 10-year recurrence-free survival was 96%, 94%, and 80%, respectively. Nine of 15 recurrences were detected after more than 5 years of follow-up.

Prognostic factors

The EMMs used were classified following the classifications of Schreiber et al. [8] and Turri-Zanoni et al. [9] (Table 1). Considering the different setting of validation of these two classifications and the subject of this study, for the sake of simplicity we only use the latter hereafter.
EMM type 3A was the most frequent (53.9%). As expected, the

Table 2. Main clinical characteristics. SD=standard deviation; *= percentages expressed on available data.

	N=310
Age, mean (SD)	56.7 (14.1)
Gender, N (%)	
Male	207 (66.8)
Female	103 (33.2)
Laterality of the lesion, N (%)	
Right	153 (49.4)
Left	157 (50.6)
Primary vs. revision surgery, N (%)	
Primary	212 (68.4)
Revision	98 (31.6)
Pre-operative symptoms, N (%) *	
Nasal obstruction	139 (59.9)
Epistaxis	29 (12.5)
Rhinorrhea	14 (6.1)
Epiphora	4 (1.7)
Maxillary pain	3 (1.3)
Incidental	43 (18.5)
Pathologic recurrence, N (%)	15 (4.8)
Early complications, N (%)	36 (11.6)
Late complications, N (%)	37 (11.9)
Follow-up (months), mean (range)	45.4 (6-250)

EMM used varied according to the site of insertion. An EMM 1-2 was primarily used in IPs located at the posterior aspect of the medial wall or medial aspect of the posterior wall; when dealing with an IP pedicled on the anterior and/or lateral wall, an EMM 3A or 3B was usually required ($p < 0.05$). Of note, no correlation between the EMM applied and recurrence-free survival was demonstrated ($p = 0.9$). Similarly, the involvement of the retro-lacrimal, alveolar, and zygomatic recesses was associated with a more extended approach (i.e. type 3A EMM or larger, $p < 0.01$), but did not impact the final result (log rank $p = 0.89$, 0.46, and 0.47, respectively).

Considering other potential factors influencing the final rate of recurrence (Table 3), neither primary vs. secondary surgery ($p= 0.42$) nor the Krouse staging ($p = 0.95$) was significant. Conversely, dysplasia/Ca in situ (log rank $p= 0.02$, Figure 2) and extension of mucosal resection (log rank $p = 0.04$) showed a significant influence on recurrence at univariate survival analysis. Nevertheless, when a multivariable Cox proportional hazard model was applied with histology and type of mucosal resection (total vs pedicle oriented), only dysplasia maintained significant impact on the recurrence free-survival.

Table 3. Analysis of variables with a potential influence on the final success rate. P-values were obtained using log-rank test (Kaplan-Meier analysis).

Pathologic recurrence N (%)	No	Yes	p-value
Primary vs revision surgery	0.42		
Primary surgery	200 (64.5)	12 (3.9)	0.42
Revision surgery	95 (30.6)	3 (1)	
Krouse staging	0.95		
Stage 2	63 (20.3)	6 (1.9)	0.95
Stage 3	224 (72.3)	8 (2.6)	
Stage 4	8 (2.6)	1 (0.3)	
Site of insertion	0.28		
Anterior wall	43 (13.9)	3 (1)	
Lateral wall	25 (8.1)	2 (0.6)	
Posterior wall	46 (14.8)	2 (0.6)	0.28
Medial wall	64 (20.6)	2 (0.6)	
Inferior wall	17 (5.5)	0	
Superior wall	32 (10.3)	2 (0.6)	
Diffuse	68 (21.9)	4 (1.3)	
Alveolar recess involvement (N= 27, 8.7%)	27	0	0.46
Zygomatic recess involvement (N= 25, 8.1%)	25	0	0.47
Retro-lacrimal recess involvement (N= 75, 24.3%)	70	5	0.89
Histology	0.02		
Inverted papilloma	272 (87.7)	10 (3.2)	0.02
Carcinoma in situ	23 (7.4)	5 (1.6)	
Type of surgery	0.04		
Total mucosa resection	114 (43.3)	3 (1.2)	0.04
Pedicle-oriented mucosal resection	140 (53.2)	6 (2.3)	

Complications

Early and late complications, related to the different medial maxillectomies applied, are shown in Table 4. Early complications occurred in 36 patients (11.6%): 5 epistaxis, 20 infections, 4 transient epiphora, 1 orbital hematoma, 2 cerebrospinal fluid leak (due to the extension into the frontal sinus), 2 orbital fat exposure, and 2 oro-antral fistula. At univariate analysis of potential factors causing these events (type of mucosal resection [when data available], type of EMM, lacrimal pathway, alveolar and zygomatic recess involvement, and surgical insertion point), only the type of mucosal resection showed significance ($p = 0.01$), emphasizing the negative influence of complete mucosal resection on early morbidity.

Among late complications, 37 cases were reported (11.9%): 17 epiphora, 5 anterior-superior alveolar nerve hypoesthesia

Table 4. Early and late complications related to the different medial maxillectomies. ASAN= anterior-superior alveolar nerve.

Type of maxillectomy Turri-Zanoni et al. [8]	Early complications (n= 36)	Late complications (n= 37)
Type 1	n= 2 - 1 infection - 1 epistaxis	n= 0
Type 2	n= 6 - 3 infections - 2 epistaxis - 1 orbital fat exposure	n= 2 - 2 nasal synechia
Type 3A	n= 16 - 10 infections - 3 transient epiphora - 1 orbital hematoma - 1 orbital fat exposure - 1 cerebrospinal fluid leak	Tn= 28 - 15 epiphora - 7 fronto-ethmoidal mucocele - 4 ASAN hypoesthesia - 2 frontal sinus blockages
Type 3B-4	n= 10 - 6 infections - 1 epistaxis - 1 transient epiphora - 1 cerebrospinal fluid leak - 1 oro-antral fistula	n= 3 - 2 epiphora - 1 ASAN hypoesthesia
Type 3A mod	n= 2 - 1 epistaxis - 1 oro-antral fistula	n= 4 - 2 frontal sinus blockages - 1 nasal synechia -1 ethmoidal mucocele

(ASAN), 3 nasal synechiae, and 2 frontal sinus blockages: the more aggressive the surgical approach (≥ type 3A EMM), the higher the likelihood to experience a late complication (p = 0.03, Cramer's V value 0.185). Specifically, among patients that experienced epiphora, all were treated with a type 3A or 3B EMM. Similarly, patients experiencing ASAN paresthesia had partial/complete drilling of the pyriform aperture.

Discussion

The main finding of the present study is that, in contrast with previous reports, IPMS showed a lower recurrence rate (4.8%), which is comparable to other sino-nasal localizations. Moreover, we demonstrated that the involvement of maxillary recesses is not a risk factor for recurrence, in contrast with the precancerous changes that showed significant impact on the recurrence rate. These findings support the concept that whenever the endoscopic resection follows oncological principles [adequate exposure, subperiosteal dissection of the involved mucosa, drilling of the bony insertion point(s)], the outcomes are excellent regardless of the site of origin. To the best of our knowledge, this study is the first that specifically correlates management of IPMS to the adequacy of EMMs.

Over the past decades, different surgical approaches have been described in the management of IPMS, both external and endoscopic endonasal, with the latter being generally preferred due to reduced post-operative morbidity [4]. Some authors have argued that the antero-lateral/inferior portion of the MS is difficult to dominate so that an endoscopic approach should be assisted with a Caldwell-Luc one, even if it leads to pain and facial/dental numbness in up to 75% of cases [12]. However, its real benefit in terms of success rate is not unanimous and a recent meta-analysis demonstrated that EMMs are associated with a higher success rate compared to an endoscopic endonasal-assisted Caldwell-Luc approach, underlying that proper resection of IPMS can be achieved via a trans-nasal endoscopic route [13]. Overall, the success rate of EMMs in the management of IPMS is highly variable. Bertazzoni et al. reported a 95% success rate in a cohort of patients treated with a 3B EMM, commonly known as Sturmann-Canfield's procedure [14]. Kamel achieved a 75% success rate after a mean follow-up of 8.8 years, in contrast to our result of 95.2% of success at 45 months [15]. Ferrari et al. reported cumulative recurrence rates at 5- and 10-years of 89.3% in case of maxillary involvement [3], in contrast with our cumulative data of, respectively, 94% and 80.3%. Notwithstanding, it should be noted that in that study cumulative recurrence referred to IP with maxillary sinus involvement rather that a primary IPMS, making the data difficult to compare. In fact, as already pointed out, the involvement of maxillary recesses and presence of different wall shapes make the management of primary IPMS challenging, for which the application of a modular intra-operative expansion of the EMMs driven by intra-operative findings, seems to be crucial to ensure such a high success rate.

In this series, the insertion area of the IPMS drove the decision of the EMM extension, and such a modular approach results in a reliable outcome that was not influenced by the tumor origin (p = 0.28). Nevertheless, for the same insertion area, some technical difficulties emerged from our experience, favoring a more extended approach. In particular, when addressing a pedicle located on the anterior and lateral walls, the clinician should be aware that the anterior wall can present different shapes that, in some cases, would render management challenging and man-

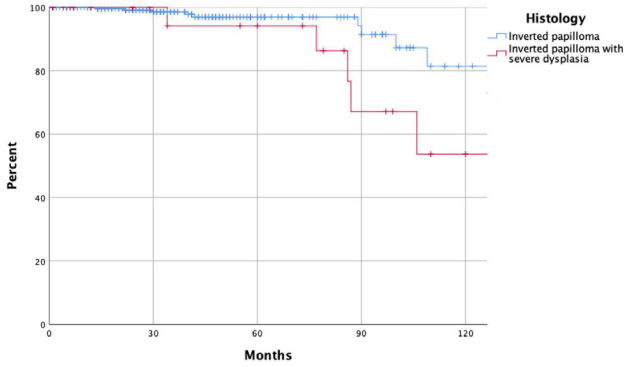

Figure 2. Kaplan-Meier survival curve showing the local control rate based on histological findings.

date a 3B EMM to achieve sufficient exposure. The posterior and superior walls are generally more easily approachable, especially when the pathology is confined to the medial aspect of these walls. On the contrary, considering IPMS pedicled on the medial wall, if the retro-lacrimal recess is involved, its management is more challenging. However, the involvement of this region, located between the posterior wall of the lacrimal pathway, the antero-medial aspect of the natural ostium of the maxillary sinus, and the uncinate process, did not directly influence the recurrence rate ($p = 0.89$), but usually required resection of the lacrimal pathway (type 3A EMM or larger). The inferior wall of the maxillary sinus is affected by the potential presence of recesses caused by dental roots that could render total removal of the IP more difficult. Similarly, the presence of pneumatized alveolar and zygomatic recesses renders the management of IPMS more demanding: from our data it emerged that involvement of these recesses did not directly influence the recurrence rate ($p = 0.46$ and 0.47, respectively) as long as they were properly addressed with, at least, a 3A EMM.

When considering factors associated with recurrence, primary vs. recurrent IPMS is one of the most widely recognized; in fact, it has been demonstrated that in secondary cases multifocal attachment is more common, which has a negative impact on recurrence [16]. Even if this evidence is different from what we observed in our cohort ($p = 0.42$), it should be considered that in redo surgery the IP attachment site is generally indistinguishable from surrounding scarring tissue, leading to residual disease that according to Lund et al. is the primary risk factor in IP recurrence [17]. As such, this benign pathology was originally approached with a centripetal compartmental resection which consisted of complete removal of muco-periosteum of the maxillary sinus with extended drilling; however, the non-negligible local sequelae and similar outcomes compared to the pedicle-oriented approach which focused the mucosal resection and bony drilling only at the level of the IP attachment [18] led surgeons to shift to this more conservative approach [3,18,19]. Nevertheless, to date, our data are the first that specifically address the question of the real benefit of complete mucosal resection in IPMS: indeed, at univariate survival analysis it was found that complete mucosal resection of IPMS was associated with better outcomes ($p = 0.04$), although the significance was lost at multivariable analysis. However, our patients experienced a higher rate of early complications in case of complete mucosal resection, confirming previous reports [18]. Considering the importance of post-surgical morbidity, oncological safety, and the difficulties in achieving clear margins of 5-10 mm in IPMS, usually advisable for some authors [4,20], a solution to this scenario can be the application of a pedicle-oriented resection assisted with intra-operative frozen sections. The actual benefit of this surgical practice is still open to debate since some studies did not find an association with decreased rate of recurrence [4], while others cited its high reliability [21,22].

In view of the above-mentioned evidence and the results from the current series, this multicentric study group proposes two possible alternatives: 1) apply an upfront pedicle-oriented resection in favor of a less morbidity, and reserve complete mucosal resection only in the few patients with recurrence; 2) pre-operatively identify patients with higher risk of recurrence/residual disease (i.e. inverted papilloma with dysplasia), and selectively treat these patients with more aggressive surgery. In fact, the presence of precancerous changes was the only independent risk factor for recurrence ($p = 0.02$). This finding has been already demonstrated [3,23] and related to a more local aggressiveness of the pathology.

Another factor studied in the literature is the correlation between HPV infection in sinonasal IPs and increased recurrent rate. This was not investigated in the current study, but could be of interest in a future prospective work [24].

Considering the complications associated with EMMs in the management of IPMS, the available studies generally present heterogenous descriptions and little is known about their association with different types of EMMs [14]. It seems reasonable that the greater the extension of the EMM, the greater the likelihood to have complications: in our cohort, a relation was not present with early complication, but rather with late ones. Specifically, if general surgical complications (i.e. infection and bleeding) are excluded, 17 patients (6.4%) reported epiphora that required surgical treatment, 5 ASAN hypoesthesia (1.8%), and 3 nasal synechia: among patients that experienced epiphora, all were treated with a type 3A or 3B EMM. Likewise, patients that referred ASAN paresthesia had undergone partial/complete drilling of the pyriform aperture. Overall, the complication rate is low but non-negligible, which should prompt the surgeon to conduct adequate preoperative counselling with the patient. ASAN numbness is one of the most frequent adverse events in case of extended EMMs (3A and 3B) and is reported in 15.7%-52.4% of cases [25]. It is thought to be caused by injury of V2 branches during bone drilling and soft tissue resection around the ASAN. It is plausible that the ASAN is generally injured during enlargement of the pyriform aperture, although the complex network that connects the anterior, middle, and posterior alveolar nerves compensate ASAN injury in about 20% of cases [26,27].

Another common adverse event in case of EMMs is epiphora, and specifically in EMMs that require transection of the lacrimal pathway (3A and 3B/4) with an incidence of 0-16% [13,28]. Overall, the data in the literature are heterogenous regarding the best management of lacrimal stenosis after EMMs and its management is infrequently reported [29]. Our data are in line with the literature, reporting 6.4% of cases with long-term epiphora, defined as at least 6 months of clinical follow-up with daily external massage of the lacrimal sac that did not resolve and required surgical dacryocystorhinostomy.

Of note, all centers involved shared the same strategy of treatment for IPs throughout the study period, thus ensuring uniformity in terms of treatment outcomes; in addition, the recurrence rate was assessed not only as cumulative risk but also as a time-dependent event (i.e. recurrence-free survival), which is a more reliable parameter of treatment failure. However, the increasing surgical experience acquired in the centers involved could be considered a potential confounder of the analysis; in addition, it should be noted that not only its retrospective nature can be considered as another limitation of this study, but the low number of recurrences may have also hidden potential risk factors for IPMS failure.

Conclusion

The encouraging outcomes observed in this case series validates the strategy that a surgical approach for IPMS should be tailored to the disease, thus avoiding the systematic use of extended EMMs. Likewise, if properly addressed, the involvement of maxillary recesses does not represent a risk factor in the overall success rate; in contrast, the evidence of dysplastic IPMS should justify a more aggressive surgical approach given its significant influence on recurrence.

Authorship contribution

AV, DM, MTZ, AS, MF, VR., AK, MV, SA, FC, VP, PG, ID and TS made substantial contributions to conception, design and acquisition of data, drafted the article, revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; BV, CP, PN, PC and PH made substantial contributions to conception of the data, revised it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of interest

None

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