Eur Arch Otorhinolaryngol
DOI 10.1007/s00405-011-1744-2

REVIEW ARTICLE

Traditional endonasal and microscopic sinus surgery complications versus endoscopic sinus surgery complications: a meta-analysis

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Received: 1 May 2011 / Accepted: 1 August 2011

Abstract The aim of this study was to compare the incidence of complications of endoscopic sinus surgery (ESS) to the incidence of complications of traditional and microscopic sinus surgery. A meta-analysis was carried out on 28 series of patients (a total of 13,405) who had undergone ESS, 8 series of patients (3,887 in total) who had undergone traditional endonasal sinus surgery and 7 series of patients (1,630 in total) who had undergone microscopic sinus surgery. The authors used the Bayesian inference package WinBUGS operating from within the statistical computer program R (version 2.7.1). Major complications had a higher incidence after traditional sinus surgery than ESS but this fact did not cause a significant statistical difference, whereas microscopic surgery had significantly more complications than ESS ($p < 0.05$). Carrying out our meta-analytic study, comparing major and minor complications of endonasal surgical approaches, was very difficult due to several methodological biases of data extraction and evaluation from studies concerning a broad timespan. Regarding major complications, we only found a significant statistical difference ($p < 0.05$) between the endoscopic (1%) and the microscopic methods (2.0%), but, if we had analyzed the data considering the natural learning curve of the latest ESS surgical approach, and if we had not considered the results produced in the first 10 years (1988–1998) concerning ESS in our meta-analysis, we would have found a statistically significant difference ($p < 0.05$) between the endoscopic (0.4%) and the traditional (1.1%) approach as well.

Keywords Sinusitis · Surgical procedures · Operative · Surgical complications · Meta-analysis

Introduction

The specific risks of endonasal sinus surgery (ESS) have long been recognized. In the first study that quantified complications related to ESS, Stankiewicz [1], reported, in a group of 90 patients, a 8% major and 21% minor complication rate, the most common being synechiae. In a follow-up study, Stankiewicz [2] reported on the complication rate of a subsequent group of 90 patients, and noted a 2.2% rate which compared favorably with previous reports of complications as reported by Freedman and Kern in 1979 using conventional intranasal methods [3]. This significant drop in the complication rate was attributed to the greater operational experience, concurrent cadaveric dissection, and the initial use of limited ethmoidectomy, with gradual progress on to more extensive procedures.

Several studies have subsequently shown a further decline in the incidence of complications of ESS [4–27].

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Published online: 09 October 2011

A previous meta-analysis of case series that included 4,693 patients found an 1.1% overall major complication rate with no significant difference between conventionally and endoscopically treated patients (0.9 vs. 1.3% respectively) [18].

In our study, the incidence of complications in endoscopic sinus surgery (ESS) was determined in 28 series [1, 2, 4–27] of patients (13,405 total) and this was compared to the incidence with traditional and microscopic sinus surgery as described in published reports by others [3, 28–40]. Considering that minor complications, particularly sinechiae, presented many methodological biases (different definitions, pick-up methods, follow-up and damage evaluation), we do not think a comparison of this kind of complications is possible.

Materials and methods

All the published studies encompassing the period from 1979 to 2007 that reported on complications of traditional, microscopic and endoscopic endonasal sinus surgery were identified using a Medline/OldMedline, Embase, and Cochrane Central databases search [41–43] and cross-referencing.

Our primary objective was to estimate the risk of major and minor complications of sinus surgery with traditional, microscopic and endonasal endoscopic methods, as well as evaluating the methodological quality of the relevant studies.

We performed a meta-analysis of all reports with no language restrictions and consisting of at least 50 patients that satisfied the participation criteria of the meta-analysis established prior to the bibliographic research.

The clinical participation criteria comprised only patients with:

Age > 18 years.

Surgery for inflammatory disease limited to paranasal sinuses.

Surgery for chronic rhinosinusitis with or without nasal polyposis.

Surgery for benign lesion of paranasal sinuses.

Follow-up evaluations performed for 6 months or longer for patients with complications.

The clinical exclusion criteria included patients with severe underlying diseases and patients who had undergone surgery for malignant lesions of paranasal sinuses.

Complications of sinus surgery were classified as major or minor according to the degree of morbidity and treatment needed to prevent permanent serious sequelae (Table 1).

Major complications of sinus surgery included cerebrospinal fluid (CSF) leak, retrobulbar hematoma, hemorrhage requiring transfusion, and symptomatic lacrimal duct obstruction requiring surgical correction.

Minor complications of surgery on the paranasal sinus included periorbital edema or ecchymosis, epistaxis, and formation of symptomatic adhesion between the middle turbinate and the lateral nasal wall.

Table 1 Classification of sinus surgery complications (May, 1994) [17]

Minor complications	Major complications
Temporary, requiring no treatment	Corrected with treatment
Subcutaneous periorbital amphysema	Orbital hematoma
Periorbital ecchymosis	Loss of vision
Dental or lip pain or numbness	Diplopia
Temporary, corrected with treatment	Epiphora (requiring dacryocystorhinostomy)
Symptomatic sinechiae	Hemorrhage requiring transfusion
Epistaxis requiring packing	Cerebrospinal fluid leak (CSF)
Sinus infection	Meningitis
Permanent and not correctable	Brain abscess
Dental or lip pain or numbness	Focal brain hemorrhage
Loss of smell	Permanent despite treatment
	Death
	Blindness
	Diplopia
	Central nervous system deficit

Identification of studies

The main sources for this systematic review were the Medline/OldMedline, Embase, and Cochrane Central databases [41–43], beginning with the first quotation of sinus surgery until July 2007.

The literature search strategy started with MEDLINE, EMBASE, and COCHRANE databases [41–43] where we combined the following medical subject headings (or their equivalent in other databases): “sinusitis” and “surgical procedures, operative”.

Abstracts were screened for potentially relevant articles which were then obtained as full texts. In a second step, the references of these articles were cross-checked for further potentially relevant articles. No language restrictions were applied. Abstract publications were not included.

The search strategy achieved a high sensitivity (which means that missing a relevant study was unlikely). On the other hand, it provided low specificity (that is, many trials not meeting the inclusion criteria proved irrelevant during later selection steps).

We selected those trials that examined types of sinus surgery suitable for this review from the entire pool of studies.

Data extraction

Using the established key-words, and cross-referencing, 78 publications were extracted from the database, 40 of which had a design meeting the selection criteria.

In the study, we included our series of patients (1,032 patients underwent ESS at the Department of Otorhinolaryngology of Bologna University and 242 patients underwent ESS at the Department of Otorhinolaryngology of the Polytechnic University of Marche. All the patients met the rating criteria for inclusion).

The meta-analysis was carried out on 28 series of patients (13,405 total) who had undergone ESS [1, 2, 4–27], 8 series of patients (3,887 total) who had undergone traditional endonasal sinus surgery [3, 28–34] and 6 series of patients (1,630 total) who had undergone microscopic sinus surgery [35–40].

Statistical methods

Homogeneity analysis

A preliminary homogeneity analysis was performed to test whether the assumption that all of the proportions of complications are estimating the same population mean, is a reasonable assumption.

The test of hypothesis was performed using the Q statistic homogeneity. For each surgery method, its value, reported in Table 2, showed that homogeneity must be rejected, the distribution of proportions (ratios) is heterogeneous.

Q resulted significant and we assumed that the excess variability across effect sizes derived from random differences across studies.

Taking into account the heterogeneity of complications, a hierarchical normal random- effect model was assumed for their distribution.

Furthermore, each study specific mean, is assumed to be drawn from a normal distributed superpopulation of complication ratio with mean μ and variance τ^2 (hyperparameters of the model).

The assumption of normality seems reasonable given the sample size observed.

The meta-analysis was performed using the Bayesian inference package WinBUGS, operating from within the statistical computer program R (version 2.7.1) [44–47].

Table 2 Values of the Q statistic homogeneity rates

Method	Qw	*df*	*p* value
Traditional	32.24	6	<0.001
Microscopic	32.71	5	<0.001
Endoscopic	29.91	15	<0.001

As WinBUGS requires proper prior distributions for the hyperparameters, we expressed non-informative prior distribution for mean μ and variance τ^2 by proper distribution with large uncertainties:

μ was given a normal distribution with mean 0 and standard deviation 1,000 and τ^2 had a uniform distribution from 0 to 1,000. These are certainly non informative priors, given that the data all fall well below unity.

Results

Our results are summarized in Tables 3, 4, 5, 6, 7 and 8. Tables 3, 4 and 5 showed the incidence of major and minor complications in each study. In Table 6, the overall incidence of ESS complications is compared to the overall

Table 3 Incidence of endoscopic sinus surgery complications in each study

References	No. patients	Major complications (%)	Minor complications (%)
Stankiewicz [1]	90	8	21
Friedrich [4]	65	1.5	3.1
Kennedy [5]	50	1	0
Stankiewicz [2]	90	1.1	1.1
Schaefer [6]	100	0	14
Toffel [7]	170	0.6	3.5
Wigand [8]	220	1.3	4
Rice [9]	100	0	10
Stammberger [10]	500	0.2	6
Levine [11]	250	0.7	8.3
Massegur [12]	150	2	21
Kennedy [13]	120	0	0.8
Vleming [14]	667	1	6.3
Lopez-Cortijo [15]	189	1	12.1
Lund [16]	650	0.3	–
Dessi [17]	1,192	1.3	–
May [18]	2,108	0.85	6.9
Ramadan [19]	337	1.5	15.1
Castillo [20]	553	2.2	13.4
Friedman [21]	500	0.6	19.6
Rudert [22]	1,172	1.1	–
Lopez-Cortijo [23]	100	0	8
Jakobsen [24]	237	0.4	20
Sprekelsen [25]	266	1.1	20
Hopkins [26]	2,145	0.4	6.6
Pasquini 2007	1,032	0.2	2
Re 2007	242	0.8	4.4
Guerrero [27]	110	0	21
Total	13,405	1	6.6

Table 4 Incidence of traditional sinus surgery complications in each study

References	No patients	Major complications (%)	Minor complications (%)
Freedman [3]	565	1.9	0.9
Eichel [28]	123	3.2	–
Tylor [29]	284	1.4	2.8
Stevens [30]	87	6.9	9.2
Sogg [31]	146	0	1.5
Friedman [32]	582	1.2	4.4
Sogg [33]	1,500	0.4	18.8
Lawson [34]	600	1.1	0.8
Total	3,887	1.1	8.9

Table 5 Incidence of microscopic sinus surgery complications in each study

Author no.	No patients	Major complications (%)	Minor complications (%)
Bagatella—Mazzoni, 1986 [35]	155	3.9	8.4
Amedee, 1990 [36]	325	0	0
Ilberg, 1990 [37]	221	1.4	1.8
Teatini, 1991 [38]	100	0	16.5
Weber—Draf, 1992 [39]	590	5.4	6.8
Yanez, 1993 [40]	239	1.4	2
Total	1,630	2.0	5.9

Table 6 Overall incidence of endoscopic sinus surgery complications compared to the overall incidence of complications in the traditional endonasal and microscopic sinus surgery approach

	Endoscopic surgery (%)	Traditional surgery (%)	Microscopic surgery (%)
Major complications	1	1.1	2.0
Minor complications	6.6	8.8	5.9

incidence of complications with traditional endonasal and microscopic sinus surgery while in Tables 7 and 8 each group of major and minor complications are compared among the different approaches.

Major complications

The Bayesian estimates of the population mean incidences of major complications, a 95% credible intervals for the estimates and between-study standard deviation using random-effect model were reported in Table 9.

Even though the estimated mean incidence of major complications after traditional surgery was higher than the incidence of major complications after endoscopic surgery, there was only a significant difference ($p < 0.05$) between the endoscopic (1%) and microscopic methods (2.0%).

Minor complications

The Bayesian estimates of the population mean incidences of minor complications, a 95% credible intervals for the estimates and between-study standard deviation using random-effect model were reported in Table 10.

The estimated mean incidence of minor complications after endoscopic (6.6%), traditional surgery (8.8%) and microscopic surgery (5.9%) was comparable between the three methods, so there was no evidence to believe that the mean incidences of minor complications are different among the methods.

In other words, the differences of the incidence of minor complications between the three methods were not statistically significant.

Discussion

There are several general aspects that impact on the risk of performing sinus surgery. The first is patient selection. Multiple studies have quoted an increased risk of complications associated with ESS performed on patients with polyposis, prior to surgical intervention and in those who have had a long-standing disease [6, 10, 11, 13, 18].

A recent multivariate analysis on a prospective multicenter study of 3,128 patients [26], confirmed that the risk of complications depended on patient's characteristics rather than on the surgical technique used; particularly, the same study showed that the complication rate was linked to the extent of polyposis, the opacity level of the sinuses on computerized tomography, and the presence of co-morbidity, but not surgical characteristics such as the extent of surgery or grade of surgeon. In this study, major complications were observed in 11 patients (0.4%): there were 7 reported orbital complications (0.3%), 2 intracranial complications (0.05%) and 2 major hemorrhage cases (0.05%).

The minor complication rate reported in this study was 6.6%; most frequently reported minor complications were excessive perioperative hemorrhage bleeding (5%) as well as postoperative hemorrhage requiring treatment (0.8%); however, the incidence of minor complications, in this study were underestimated due to a methodological bias: the study did not collect findings from clinical examinations carried out in the post-operative period and, as a consequence, adhesions were not included in the reported complication rate.

Table 7 Comparison of each group of major and minor complications among the different approaches

Complications	Traditional surgery (3,887 pt) [3, 28–34]	Endoscopic surgery (11,467 pt) [1, 2, 4–20, 22, 24, 26, 27]	Microscopic surgery (1,630 pt) [35–40]
Major complications (%)			
Intracranial	0.4	0.3	1.8
Orbital	0.2	0.3	0
Haemorrhage	0.5	0.2	0.1
Lacrimal	0.0	0.1	0.1
Total	1.1	1.0	2.0
	Traditional surgery (3,764 pt) [3, 29–34]	Endoscopic surgery (9,625 pt) [1, 2, 4–15, 18–20, 22, 24, 26, 27]	(Microscopic surgery 1,630 pt) [35–40]
Minor complications (%)			
Orbit	7.6	1.5	4.3
Epistax	0.5	2.4	0.1
Synechiae	0.1	2.6	1.4
Other	0.7	1.1	0.1

In the single previous meta-analysis of case series [18], the overall incidence of major complications in the two groups (traditional and endoscopic) was not statistically significantly different ($p < 0.05$). There was, however, a statistically significant difference ($p > 0.05$) in the incidence of major orbital complications. The incidence of major orbital complications was significantly higher ($p > 0.05$) for the traditional (0.5%) approach versus ESS (0.1%).

In the same study, the overall incidence of minor complications was significantly higher ($p > 0.05$) for endoscopic sinus surgery (6.1%) versus traditional (2.8%) and the difference was determined by orbital and synechiae complications, higher in the endoscopic approach.

A comparison of the observed complication rate between Hopkins's prospective study [26] and May's meta-analysis case series [18], however, is hampered by differences in definitions. For example, the meta-analysis of case series carried out by May included epistaxis that required packing as a minor complication, but did not include perioperative bleeding and postoperative hemorrhage requiring treatment as included in Hopkins's study.

The meta-analysis in our article has some limitations. All, but three [9, 24, 26], of the patient series included in the analysis used a retrospective design.

The patient population being treated with ESS, microscopic and traditional sinus surgery may be heterogeneous, as each series varies with regard to patient selection criteria, severity of sinusitis (no staging system has uniformly been used), and presence of underlying systemic disease.

There is no homogenous definition of the extent/intensity of the surgery—e.g. the definition of "pansinus—surgery" differs in the various surgical centers and schools.

Table 8 Comparison of major complications between endoscopic surgery and traditional and microscopic surgery

Major complications	Endoscopic/ traditional	Endoscopic/ microscopic
Intracranial	$p > 0.05$	$p < 0.05$
Orbital	$p > 0.05$	$p > 0.05$
Haemorrhage	$p < 0.05$	$p > 0.05$
Lacrimal	$p > 0.05$	$p > 0.05$
Total	$p > 0.05$	$p < 0.05$

The type of surgery performed varies from patient to patient and from series to series, as most patient are treated with middle meatal antrostomy and anterior ethmoidectomy, while other patients may have more extensive sinus surgery.

In some series, we have a mixture of methods and some of the papers about microscopic surgery used a combined micro-endoscopic method.

There are no homogenous inclusion criteria as regards some complications; some authors, for example, define excessive bleeding as bleeding of 400 ml or more, or bleeding that made it difficult to proceed with the operation [19]. We believe that 400 ml of bleeding could be a low threshold as, for example in extensive polyposis with aspirin sensitivity or in a hypertensive patient with bacterial sinusitis complicating their paranasal sinus pathology. Considering haemorrhage as a complication would require more homogenous inclusion criteria; it would be necessary to determine whether it was something that was just a bother during surgery, if it called for reintervention, if it required coagulation of the anterior ethmoidal artery or the sphenopalatine artery and whether or not a blood transfusion was necessary.

Table 9 Comparison of the estimated population ratio of major complications and between-study standard deviation using a random-effect model

Pr. major compl.	Mean	SD	2.50%	25%	50%	75%	97.50%
Endoscopic method							
μ	0.0057	0.0007	0.0044	0.0052	0.0057	0.0062	0.0070
τ	0.0022	0.0003	0.0017	0.0020	0.0022	0.0024	0.0027
Microscopic method							
μ	0.01959	0.00321	0.01351	0.01736	0.01945	0.02174	0.02638
τ	0.0076	0.00114	0.00552	0.00679	0.00753	0.00832	0.00999
Traditional method							
μ	0.00884	0.00134	0.0062	0.00795	0.00888	0.00972	0.01146
τ	0.00281	0.00045	0.00199	0.00249	0.00277	0.0031	0.00372

One major factor distinguishing the different groups is the method of follow-up. Following traditional surgery, for example, injury to the skull base, specially small CSF leaks, may go unnoticed for a long time following the surgery without the benefit of high resolution CT imaging and nasal endoscopy. This probably results in an underestimation of complications in the traditional surgery group.

As outlined by some authors [48], one major determinant of complications besides the method is the surgeon, and in many papers there is no reference to the expertise of the surgeons—e.g. in academic centers having younger surgeons (residents) complications are much more likely to occur in comparison with special centers with few well-trained and skilled surgeons.

Furthermore, case series from single centers are unlikely to be submitted for publication if they demonstrate a complication rate which is higher than expected.

To overcome these potential biases, a large prospective multicenter study should be carried out with specific and homogeneous patients selection criteria, uniformed staging system of sinusitis, uniformed type of surgery performed and more homogenous inclusion criteria as regards some complications and particularly regarding minor complications.

However, the results of our meta-analysis showed that even though the estimated mean incidence of major complications after traditional surgery was higher than the incidence of complication after endoscopic surgery, there is only a significant difference ($p < 0.05$) between endoscopic (1%) and microscopic (2.0%) method.

Considering the specific group of major complications we can observe that, as regards intracranial complications, there was a statistically significant difference ($p < 0.05$) between endoscopic (0.3%) and microscopic (1.8%) surgery but not between traditional (0.4) and endoscopic (0.3) surgery; there was moreover, considering the haemorrhagic complications, a statistically significant difference ($p < 0.05$) between endoscopic (0.2%) and traditional (0.5%) surgery (Tables 7, 8).

Regarding minor complications, the differences of the incidence between endoscopic and traditional surgery were not statistically significant.

However, considering that minor complications, particularly sinechiae, showed several methodological biases (different definitions, pick-up methods, follow-up and damage evaluation), we do not think a comparison of this kind of complications is possible.

The most common ESS minor complications was synechiae (particularly between the middle turbinate and the lateral nasal wall), which occurred in 3% of patients. This prevalence was significantly higher compared to synechiae found in the traditional and microscopic approach. Adhesions of the middle turbinate do not occur as frequently after traditional sinus surgery because the middle turbinate is often removed. This minor complication occurs relatively frequently after ESS, however, because the attempts are usually made during ESS to preserve the middle turbinate. When the middle turbinate is preserved, the possibility of opposing raw surfaces due to surgical manipulation is real. Synechiae occur anteriorly in the nose either between the inferior turbinate and the septum or the anterior middle turbinate and lateral wall. The middle turbinate has a tendency to drift laterally after surgery and may become contiguous with the lateral wall, thus increasing the possibility of synechiae. Synechia is occasionally asymptomatic (when it is posterior, i.e. it does not obstruct the infundibulum) and was taken into account in many series regardless of the symptoms giving rise to it. For these reasons this result could be due to an important methodological bias, that is the possibility to find synechiae in an endoscopic control after ESS, which is usually not performed after the traditional and microscopic approach.

Finally, we should point out another aspect of ESS; the first studies that quantified complications concerning ESS have been reported since 1988. Every new surgical approach has a natural learning curve, considered as an improvement of surgeon skills, development of surgical techniques and video endoscopic technology and as an introduction of more and more dedicated instruments. Therefore, if we had not considered the incidence of ESS major and minor complications produced in the early 10 years in our meta-analytic study, taking into account all

Table 10 Comparison of the estimated population ratio of minor complications and between-study standard deviation using a random-effect model

Prop. minor compl.	Mean	SD	2.50%	25%	50%	75%	97.50%
Endoscopic method							
μ	0.08198	0.00246	7.70E−02	8.04E−02	0.082	0.08359	0.08688
τ	0.01721	0.00132	1.47E−02	1.63E−02	0.01723	0.0181	0.01974
Microscopic method							
μ	0.04025	0.0044	0.03184	0.03727	0.04023	0.0432	0.04894
τ	0.01093	0.00152	0.00806	0.00989	0.01087	0.01194	0.01402
Traditional method							
μ	0.07951	0.00423	0.07137	0.07658	0.07958	0.08242	0.08776
τ	0.0198	0.00171	0.0167	0.01861	0.01971	0.02092	0.02321

Table 11 Overall incidence of endoscopic sinus surgery complications, considering the 1998–2007 period, compared to the overall incidence of complications with traditional endonasal and the microscopic sinus surgery approach

	Endoscopic surgery (1998–2007) (%)	Traditional surgery (%)	Microscopic surgery (%)
Major complications	0.4	1.1	2.0
Minor complications	7.4	8.8	5.9

Table 12 Comparison of each group of major complications between the different approaches considering the 1998–2007 period for endoscopic sinus surgery

Complications	Traditional surgery (3,887 pt) [3, 28–34]	Endoscopic surgery (5,038 pt) [22–24, 26, 27]	Microscopic surgery (1,630 pt) [35–40]
Major complication (%)			
Intracranial	0.4	0.1	1.8
Orbital	0.2	0.1	0
Haemorrhage	0.5	0.1	0.1
Lacrimal	0.0	0.1	0.1

Table 13 Comparison of major complications between endoscopic surgery (1998–2007) and traditional and microscopic surgery

Major complications	Endoscopic/ traditional	Endoscopic/ microscopic
Intracranial	$p < 0.05$	$p < 0.05$
Orbital	$p > 0.05$	$p > 0.05$
Haemorrhage	$p < 0.05$	$p > 0.05$
Lacrimal	$p > 0.05$	$p > 0.05$
Total	$p < 0.05$	$p < 0.05$

the ESS studies from 1997, we would have observed that the estimated mean incidence of major complications after endoscopic sinus surgery (0.4%) should have been lower than microscopic (2.0%) and traditional (1.1%) surgery and the difference should have been statistically significant ($p < 0.05$) (Tables 11, 12, 13).

Conclusions

Carrying out a meta-analytic study, comparing major and minor complications of endonasal surgical approaches, was very difficult due to many methodological biases of data extraction and evaluation from studies concerning a broad timespan. Our significantly valuable statistics method is based on less valid data. Considering that traditional and microscopic surgical approaches are procedures that will be used less and less often, it will not be possible to wait for or carry out more correct studies from a methodological point of view in the future. We believe that a completely different evaluation should be made between major and minor complications. Minor complications presented many methodological biases in the different studies: different definitions, pick-up methods, follow-up and damage evaluation. In conclusion, even considering our reported results, we think that an evaluation and comparison of this kind of complications is not possible. The evaluations of major complications are completely different. In this case a more uniform description and evaluation of complications has allowed a more statistically significant analysis of the collected data. We can therefore state that the incidence of major complications after traditional sinus surgery was higher than the incidence of complications after endoscopic sinus surgery, although, there is only a statistically significant difference ($p < 0.05$) between the endoscopic (1%) and the microscopic (2.0%) method. This result becomes even more significative if we analyze the data considering the natural learning curve of the latest ESS surgical approach [49]. The learning curve is considered as a

development of surgical techniques, video endoscopic techniques and as an introduction to dedicated instruments. As a matter of fact, if we had not considered the results produced in the first 10 years (1988–1998) concerning ESS in our meta-analysis, the statistical differences among the different surgical approaches would have increased and become statistically significant. All the endonasal surgical approaches have the potential to determine minor complications and especially major complications. Nevertheless, even considering the exponential increase of the number of procedures carried out in the world, endoscopic surgery has not proved to be a more dangerous technique than others. Probably the reasons are to be found in the fact that since its introduction, thanks to the Graz school, a precise didactic setting has been achieved with multiple year courses that are numerous even now, and also considering the ongoing development of dedicated technology and instruments.

Conflict of interest None.

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