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Review

Relevance of anatomical remnants for revision sinus surgery

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ABSTRACT

Objectives: Review of the scientific literature dedicated to investigating how residual structures impact surgical outcomes in chronic rhinosinusitis (CRS) patients, providing information on the frequency of anatomical remnants after endoscopic sinus surgery (ESS).
Material and methods: This review has been reported following the recommendations of the SWiM guideline. PubMed, Cochrane Library, Embase, and Web of Science were searched until April 2024. Studies selected for the systematic review were assessed about quality and risk of bias using the Oxford Centre for Evidence-Based Medicine Levels of Evidence and STROBE. The findings were analyzed descriptively and qualitatively, aligning with EPOS and ICAR guidelines.
Results: Fourteen relevant studies met the inclusion criteria for qualitative synthesis. Prospective and retrospective cross-sectional designs, focusing on revision ESS, were included. Four studies examined full-house functional ESS (FESS), three focused on frontal sinus surgery, four on conventional FESS and three did not specify the surgery type. The risk of bias was assessed, revealing significant variability in study quality and a low level of evidence. Wide variability was found in anatomical structures remaining after ESS, most notably in retained uncinate process (29.6–64%), agger nasi cell (4.5–83.33%) and frontoethmoidal cells (40.7–96.8%). Observations on concha bullosa, septal deviation and lateralization of the middle turbinate revealed distinct patterns among the included studies.
Conclusion: This systematic review underscores the persistent challenge of incomplete resection of anatomical structures in revision surgeries for CRS. The variability in the retention of key structures highlights the complexity of surgical outcomes and the need for further refinement in surgical techniques.

1. Introduction

Endoscopic sinus surgery (ESS) offers a viable option for managing chronic rhinosinusitis (CRS) in patients unresponsive to appropriate medical treatment [1]. Traditionally, surgery aimed to restore normal sinus function by reopening drainage pathways through minimally invasive access (i.e., functional ESS), achieving suitable disease control in non-severe patients [2]. However, failure rates reach 70%, particularly in polypoid phenotypes [3,4]. These high recurrence rates have shifted the focus towards personalized, mucosal-centric strategies targeting inflammation and remodeling [5]. As a result, the latest EPOS and ICAR guidelines recognize these new techniques for specific conditions, necessitating extensive resection and a mucosal treatment [6,7]. Despite advancements, disease recurrences remain a significant challenge in managing CRS patients [8,9].

Recent studies have identified various phenotypes of patients (e.g., asthmatics or NSAID-respiratory exacerbated disease patients), as well as inflammation biomarkers prone to recurrence [10,11]. Nonetheless, clinical failure is multifactorial, influenced not only by patient phenotypes but also by imprecise ESS. Incomplete cell opening and residual anatomical elements frequently necessitate reintervention, highlighting suboptimal initial surgeries [12–14]. In this line, the inflammatory load hypothesis for refractory CRS posits that the surgical benefit stems from eliminating proinflammatory factors (e.g., eosinophilic mucus, fungal and *Staphylococcus* antigens, bacterial load and osteitic bony lamellae) [15,16]. The complete removal of sinus mucosa, microbiota, intramucosal germs, and addressing significant immune dysfunction may more effectively alter CRS's natural course than piecemeal resections performed under inadequate visualization [17].

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In the realm of CRS, where conventional treatments sometimes fall short, better exploring precision surgical techniques become imperative. By examining the impact of residual structures on ESS, this study aims to elucidate the relevance of these remnants in the recurrences and the need for revision surgeries in CRS patients' management.

2. Material and methods

A systematic literature search was performed to define the frequency of incompletely resected anatomical structures in the sinonasal cavity during primary ESS. This systematic review followed the Synthesis Without Meta-analysis (SWiM) guideline of the EQUATOR network (supplementary files – Supplementary table* S1 contains the SWiM checklist fulfilled) [18]. Review protocol was registered for this study in PROSPERO (CRD-42024538477). The study was approved by the Andalusian Biomedical Research Ethics Committee.

2.1. Research question and strategy

To address this research problem, we asked which residual bone structures are most frequently identified in revision surgeries of CRS patients. The search strategy was designed using the PICOTs framework, focusing on CRS patients who were non-responders to prior ESS (P). It included any type of revision ESS as the intervention (I) and did not specify any comparison groups (C). The outcomes were the identification of residual anatomical structures via nasal endoscopy or CT scans (O), with no limitations on timing and setting (Ts). Databases searched included PubMed, The Cochrane Library, Embase via Elsevier, and Web of Science from inception until April 2024. The search strategy is described in supplementary files (Supplementary table* S2). To supplement the database search, we manually checked the reference lists of the included studies, performed a backward citation analysis, and completed a forward citation analysis.

2.2. Eligibility criteria and assessment of study quality and risk of bias

Inclusion criteria were articles written in English, featuring clinical trials, cohort studies, case-control studies, cross-sectional studies, or case series studies published in peer-reviewed journals. We did not exclude articles based on the phenotype of CRS analyzed (polyps and non-polyps), the extent of surgery performed (unilateral or bilateral), the existence of comorbidities or the use of monoclonal drug treatments, since analyzing the results of the different techniques was not the aim of this study. More conservative approaches such as polypectomy and balloon sinuplasty, as well as articles that only analyzed recurrences resulting from deficient healing after primary ESS (i.e., osteitis, middle turbinate [MT] lateralization and synechiae) were excluded. Studies selected for the systematic review were assessed about quality using the Oxford Centre for Evidence-Based Medicine Levels of Evidence [19]. The risk of bias was assessed using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for cross-sectional studies [20]. Three authors (D.M.-J., R.M.-L., S.S.-G.) independently evaluated the complete texts in accordance with the inclusion criteria and consensus solved discrepancies.

2.3. Data selection and extraction

Screening by title and abstract was conducted by three authors (S.S.-G., D.M.-J., R.M.-L.) independently. After title and abstract screening and discard, full texts were retrieved for the remaining articles. Two authors (S.S.-G., D.M.-J.) reviewed the full texts against the inclusion criteria. A standardized form (initially piloted on three included studies) was used for data extraction. Data extraction was conducted by two authors (S.S.-G., D.M.-J.). Extracted variables encompassed: the sample size of studies, the number of previous surgeries performed, the type of surgical extension studied, the use of image guidance ESS and the frequency measurements of the residual nasal anatomical structures and frequency measurements of residual structures.

2.4. Descriptive and qualitative analysis

A qualitative analysis was assessed by discussing the value and relevance of the articles included in this systematic revision. Two authors (S.S.-G., D.M.-J.) independently performed the evaluation with discrepancies being solved by consensus and reflected in the discussion section. Meta-analyses were not possible due to the outcomes' high heterogeneity between studies. In our review analysis, studies included assessed the frequency of residual anatomical structures found by endoscopic and radiological techniques in revision surgeries. Whether structure counting was done by endoscopy, CT scan or both, was reflected in the results. The frequencies were expressed as gross values and percentages. The number of surgeries was also recorded and expressed as mean and range, when it was listed in the studies.

Types of surgeries included in the studies of this review were adapted to the current descriptions of the EPOS and ICAR guidelines [6,7]: conventional functional ESS (FESS), the main objective of which is to preserve mucociliary function and ventilation of the paranasal sinuses, developing a conservative approach targeting osteomeatal complex disease [13], and full-house FESS, which offers a comprehensive clearance of macroscopic mucosal disease and restoration of sinus function [21]. Specifically, the frontal sinusotomies were adjusted according to the classification proposed by Draf, when these were specified in the analyzed articles [22].

3. Results

3.1. Articles

The systematic review's bibliographic search, conducted in April 2024, yielded 1487 potentially relevant studies. Following the removal of duplicates and application of inclusion and exclusion criteria, fourteen articles underwent qualitative synthesis for data extraction. The selection process was recorded in sufficient detail to complete a SWiM flow diagram (Fig. 1).

Table 1 outlines the included studies' quality characteristics and features, encompassing sample size, prior surgeries, type of surgery analyzed, methods for quantifying anatomical structures in revision ESS and the utilization of image guidance in ESS. All included articles were pertinent to the review's subject matter. Among them, two were cross-sectional prospective studies and the remaining twelve papers were cross-sectional retrospective studies. Notably, descriptions of surgeries prior to data collection was not uniform for all studies: four studies referred to full-house FESS without specifications about frontal sinusotomy [14,23–25]; three studies exclusively analyzed frontal sinus surgery [26–28]; four studies analyzed conventional FESS [29–32]; and the remaining three studies did not specify the type of surgery previously performed by the surgeons [12,33,34]. Additionally, only three articles documented the use of image-guided endoscopy as a tool employed in revision surgeries [12,28,30]. No article evaluated the residual bone structures after image-guided ESS. Fig. 2 and Supplementary table* S3 summarize the risk of bias assessment using the STROBE checklist. A wide variability was observed in the quality of the studies included in this review.

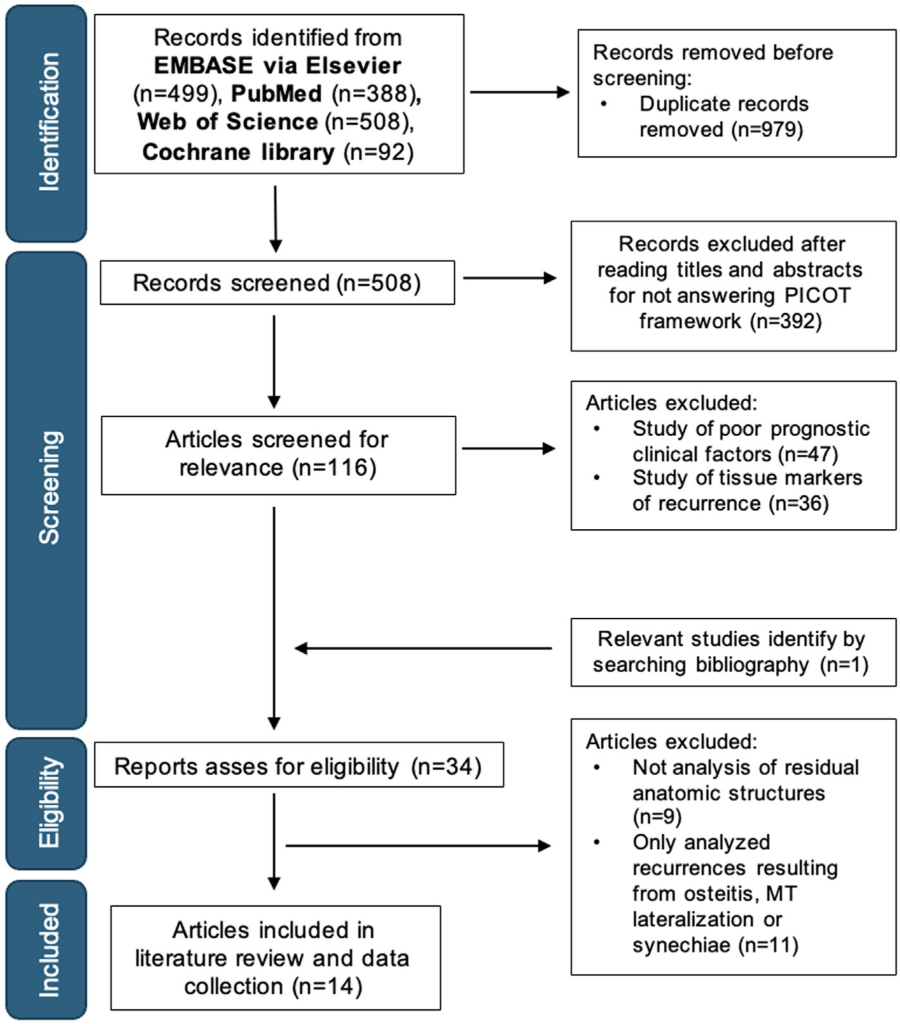

Fig. 1. Articles selection flowchart.

3.2. Clinical data

The prevalence of residual anatomical structures described in each of the included studies are shown in Table 2. Results reveal considerable variability in the retention of key structures such as the uncinate process, with percentages ranging from 29.6% to 64%, and the *agger nasi* cell, showing a wide range from 4.5% to 83.33%. Similarly, findings regarding the presence of frontoethmoidal cells span from 40.7% to 96.8%, indicating significant heterogeneity. Notably, anterior and posterior ethmoid cells exhibit frequencies ranging from 51% to 92.1% and from 20% to 96.8%, respectively, emphasizing the intricate nature of surgical outcomes. Additional observations include the prevalence of concha bullosa, septal deviation and MT lateralization, each demonstrating distinct patterns across studies.

The overall average frequency of anatomical remnants within the sinonasal cavities is shown in Fig. 3. The highest number of bony remnants is found, on average, in the anterior (31%) and posterior (28%) ethmoid cells. Lower frequencies of bony remnants causing surgical failures are detected in the maxillary, sphenoid and frontal sinuses. Notably, within the anterior ethmoid, remnants of structures initially addressed in ESS, such as the uncinate process, are revealed most frequently (43%). Lower average frequencies are noted for the ethmoidal bulla (19%), Haller cells (11%), and supraorbital and suprabullar frontal cells (8% each). Additionally, related to failures in frontal sinus approaches, remnants of frontoethmoidal cells are the most common at 41%, followed by *agger nasi* cells (35%), with the remaining 24% comprising various smaller subcategories.

4. Discussion

As reviewed in this study, the presence of residual anatomical structures may signal persistent disease necessitating further interventions. The analysis of residual cells and septa lies not only in the self-critical ability of surgeons in non-standardized surgical practice, but also sheds light on their role in the need for reinterventions. This systematic review examines the frequency of insufficiently resected anatomical structures during primary and revision ESS. Fourteen original published articles have been retrieved and the main results derived from this review are discussed below.

4.1. Scope of bone resection

Firstly, although further knowledge has been gained during the last few years regarding the inflammatory cues in CRS, patients' baseline variables representative of type-2 (T2) inflammation (e.g., asthma, NSAID-exacerbated respiratory disease, eosinophils in peripheral blood, total serum immunoglobulin E, and cycles of steroids) still have an uncertain role in the surgical management and the recurrences of the disease [3,35]. However, the significance of surgical extension in achieving favorable outcomes is increasingly apparent [8,36]. Revision surgery rates exceeding 50%

Table 1
Summary table of main characteristics of the articles included in this review.

Authorship	Year	Type and evidence of study	Sample size (sides[a])	Number of previous ESS (mean; range)	Type of surgery studied	Method to quantify residual structures	Use of image guidance in ESS
Englhard and Ledderose [29]	2023	Retrospective cross-sectional study 4[c]	253 (401[a,b])	NR	FESS	Endoscopy and CT scan	No
Baban et al. [25]	2020	Prospective cross-sectional study 3b[c]	24	1.42 (1–3)	Full-FESS	Endoscopy and CT scan	No
Nakayama et al. [14]	2018	Retrospective cross-sectional study 4[c]	129 (214[a,b])	NA	Full-FESS	CT scan	No
Cantillano et al. [33]	2017	Retrospective cross-sectional study 4[c]	27	NR	NR	Endoscopy or CT scan	No
Bewick et al. [12]	2016	Retrospective cross-sectional study 4[c]	75	2.26 (1–20)	NR	Endoscopy	Yes (27.6% of patients)
Valdes et al. [26]	2014	Retrospective cross-sectional study 4[c]	66	1.64 (1–10)	Frontal sinusotomy	Endoscopy and CT scan	No
Gore et al. [24]	2013	Retrospective cross-sectional study 4[c]	55 (110[a])	NR	Full-FESS	CT scan	No
Khalil et al. [23]	2011	Retrospective cross-sectional study 4[c]	63	NR	Full-FESS	CT scan	No
Otto and DelGaudio [27]	2010	Retrospective cross-sectional study 4[c]	149 (296[a,b])	NR (2–7)	Frontal sinusotomy	Endoscopy and CT scan	No
Ramadan [30]	2009	Retrospective cross-sectional study 4[c]	23 (children)	NR	FESS	Endoscopy and CT scan	Yes
Musy and Kountakis [31]	2004	Prospective cross-sectional study 3b[c]	70	NR	FESS	Endoscopy and CT scan	No
Chiu and Vaughan [28]	2004	Retrospective cross-sectional study 4[c]	67	1.97 (1–6)	Frontal sinusotomy	Endoscopy and CT scan	Yes
Ramadan [32]	1999	Retrospective cross-sectional study 4[c]	52	NR	FESS	Endoscopy and CT scan	No
Chu et al. [34]	1997	Retrospective cross-sectional study 4[c]	153 (265[a])	NR	NR	Endoscopy or CT scan	No

FESS: functional endoscopic sinus surgery; NA: not applicable; NR: not reported.
[a] The sample was quantified by the number of nostrils analyzed.
[b] Some sides were excluded from sample size of the study because they had not been previously addressed.
[c] Level of evidence was evaluated according to the Oxford Centre for Evidence-Based Medicine Levels.

have been reported for conventional FESS, whereas more extended surgeries (e.g., nasalization, full-house, reboot or mucoplasty) have shown to reduce these values from 8 to 23% [9,37–39]. Limited surgical approaches may compromise not only poorer sinus ventilation but also ineffective instillation of intranasal treatments, leading to early mucosal re-inflammation and CRS symptom recurrence.

The growing preference for extended surgeries underscores the imperative for enhanced surgical precision. Findings from this review reveal the challenges surgeons encounter in achieving this precision, reaching residual ethmoid cell rates exceeding 90% in certain cases (Table 2 and Fig. 3). Notably, these results are even observed in studies that analyze full-FESS, defined as a comprehensive ethmoid complex resection, with identification of the ethmoidal arteries and exposure of the anterior skull base [21]. Equally striking is the remnants of the uncinate process or the *agger nasi* cell, even in surgeries whose main goal was frontal sinusotomy, with frequencies reaching up to 64% and 83.3%, respectively, in some of the analyzed studies [26–28]. These findings raise important considerations: on the one hand, surgeries developed today may not meet the surgical standards established by the authors who initially described the different techniques; and conversely, imprecise definitions of the types of surgery in the treatment of CRS may lead to an inadequate transfer of information among otolaryngologists, in concept of research. Both aspects have already been reflected in other previous literature reviews, albeit with research objectives different from those of this study [39,40].

4.2. Considerations in mucosal treatment

Another significant challenge arising from incomplete resection of the anatomical structures of the sinonasal cavity is the proper control of mucosal inflammation. For a better understanding of the importance of this incomplete mucosal resection and its predisposition to recurrence, it is necessary to emphasize evo-devo theories and the concept of mucosa, which provide an embryological and pathophysiological explanation of CRS [5,41]. On one hand, adaptive changes in the human ethmoid labyrinth have led to the development of a non-olfactory vestigial mucosa with specific characteristics that confer a higher inflammatory tendency [42,43]. These evolutionary developmental changes underpin principles of nasalization. This surgical technique focuses on the complete

Table 2
Anatomical structures remaining after failed primary ESS in percentage.

	Englhard [29]	Baban [25]	Nakayama [14]	Cantillano [33]	Bewick [12]	Valdes [26]	Gore [24]	Khalil [23]	Otto [27]	Ramadan [30]	Musy [31]	Chiu [28]	Ramadan [32]	Chu [34]
Uncinate process	37	50		29.6	64		64	60.3			37	38.8		
Ethmoidal sinus														
Anterior cells	51	79.17		70.4			75	92.1	53		64			
Posterior cells	20	70.83		63			75	96.8			41			
Ethmoidal bulla						21.1								
Suprabullar cells	16		1.2			9.2								
Suprabullar frontal cells	4		20.3			2.7								
Supraorbital cells	1		23.7											
Haller cell	4						7.3	25.4						
Onodi cell	1	8.33					29							
Frontal sinus														
Frontal cells						24.8	45		8					
Agger nasi cell	16	83.33	4.5			73.4	64		13		49	79.1		4.9
Supra-*agger nasi* cell	16		7.7											
Supra-*agger nasi* frontal cell	6		5.6											
Frontoethmoidal cell				40.7				96.8	74			11.9	31	
Intersinus cells	1		25											
Recess stenosis (scarring)	19										50	49.3		
Recess stenosis (mucosal growth)						47.7			67	25				
Maxillary sinus														
Middle meatus (MM) antrostomy stenosis	9	37.5			15	52				27	39			
MM stenosis (scarring)				51.9	29	47.7				57				14.7
Ostium excessive opening					29									
Displacement of the ostium opening					47		68.3			15				
Sphenoid sinus														
Ostium stenosis	7	50		25.9			53							
Middle turbinate (MT)														
Concha bullosa		20.83					9.1							
MT lateralization	25	8.33		14.8			11	17.5	30		78	35.8		3
Partial/complete resection	8				35									30.2
Septal deviation		0.29		29.6			12	15.9						

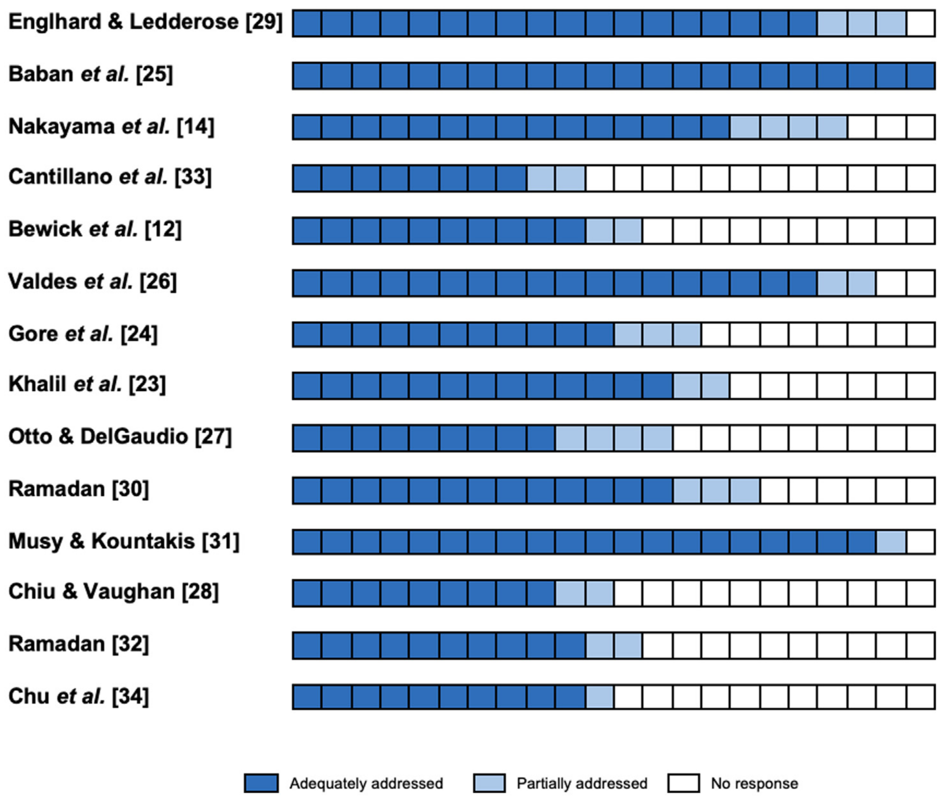

Fig. 2. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist applied to the cross-sectional studies included in this systematic review. The color graphic represents the answer to each checklist question from 1 to 22; the specific answers are shown in Supplementary table* S3.

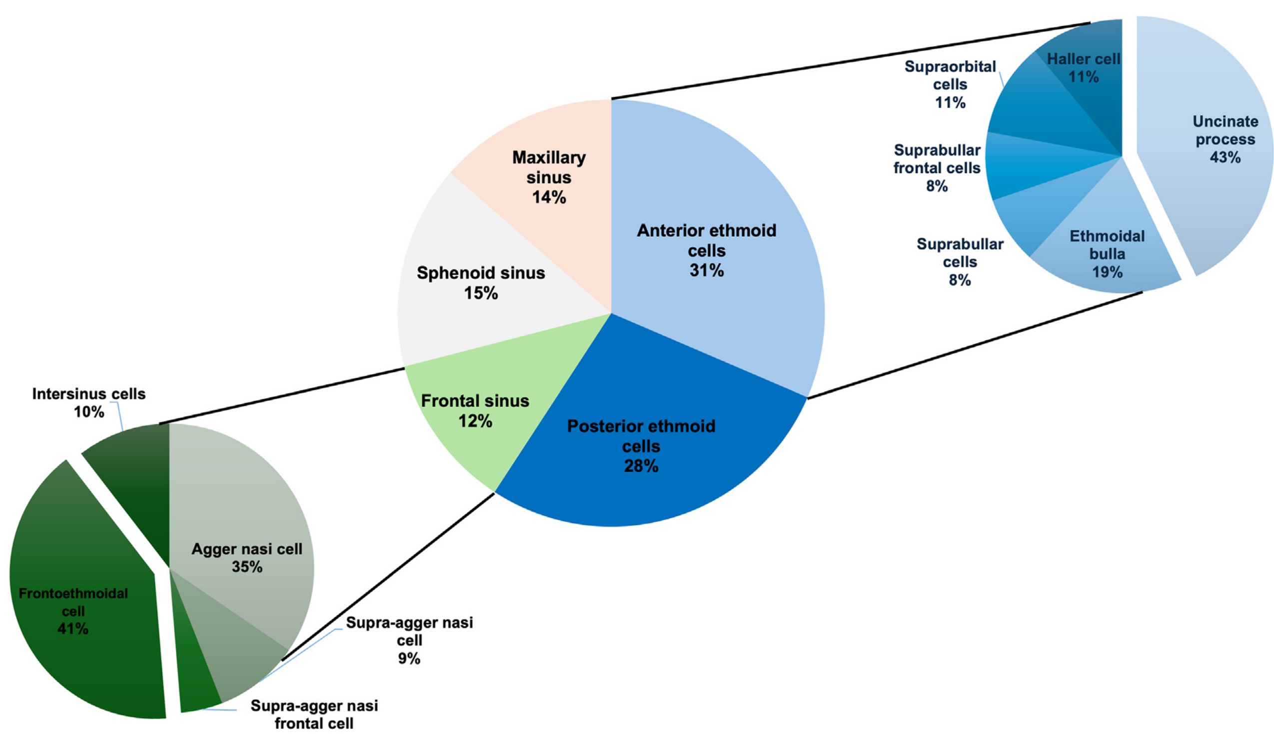

Fig. 3. Global distribution of anatomical remnants.

removal of all bony partitions within a functional sinus unit, incorporating all natural ostia into the surgical cavity. This achieves complete excision of ethmoidal mucosa while preserving mucosa on the walls of the large sinuses and around the frontal ostia [44,45].

Alternatively, since the recent concept of mucosa has been assumed, CRS has become understood as a diffuse mucosal disease rather than a simple local inflammation, due to the high probability of revision, the long-term course of the disease, and the disturbed mucosal healing under T2 inflammatory conditions [5,10]. Descriptions of molecular and cellular characteristics of mucosa in the entire sinonasal cavity have driven progress toward surgeries advocating for aggressive approaches to mucosa, not only in the ethmoid labyrinth but also throughout the other paranasal sinuses. To maximize removal of all sinus mucosa along with intramucosal germs and significant immune dysfunction, mucosal resection is intended, leaving the periosteum where possible [46]. This aims to allow healthy re-epithelialization from preserved nasal mucosa, starting from the nasal mucosa of the inferior and MTs, as well as the septum.

The presence of remaining bone fragments prevents the complete resection of both affected and unaffected mucosa, even with these more extended approaches [37,46,47]. These kinds of ESS have been based on the inflammatory theories and aim to maximally remove all sinus mucosa and enable healthy re-epithelialization from the preserved nasal mucosa to treat T2 inflammation. However, some limitations in achieving complete mucosal resection in certain areas of the sinonasal cavity have been already detected (i.e., lateral recess of the frontal and sphenoid sinuses, or the alveolar recess of the maxillary sinus) [48]. This inherent limitation of extended ESS requires surgeons to execute precise surgery, leveraging accessible anatomical structures under endoscopic vision while effectively managing mucosal pathology with meticulous technique.

4.3. Vision of image-guided ESS

A proposal to address these incomplete resections could involve the integration of image-guided ESS. This complementary technique was often used in expanded approaches and skull base surgeries, its increasing accessibility advocates for its application in more conventional ESS. Three articles in this review proposed the use of image-guided surgery as a useful tool in revision surgeries [12,28,30], but they do not analyze its added benefit, regarding non-guided surgery. Even so, it is imperative to emphasize that image-guided endoscopy offers advantages: enhanced precision, providing real-time visualization of surgical instruments within the patient's anatomy, allowing for precise navigation during surgery; improved safety, enabling surgeons to navigate complex anatomical structures more safely, thus reducing the risk of damage to critical structures; increased success rates, by ensuring accurate targeting of diseased tissue; better surgical planning and decision-making, improving the overall efficiency of the procedure; and reduced complications, with improved accuracy and visualization [49–51]. Overall, while image-guided ESS offers numerous benefits in terms of precision and safety, it also comes with associated costs and challenges that need to be considered when deciding whether to implement this technology in clinical practice. In addition, current evidence does not seem to conclude the greater utility of image-guided ESS, so although it may be a tool with potential uses, its routine use is not currently recommended [52].

In addition, other advancements in technology, such as three-dimensional imaging for preoperative planning and augmented reality for preoperative navigation, show potential in enhancing surgical precision [53,54]. These innovations aim to provide pre-surgical visualization and accurate navigation through complex anatomical structures, thereby minimizing the risk of residual anatomical structures post-surgery. Still, future studies evaluating the comparative effectiveness of these technologies in reducing revision rates and improving long-term patient outcomes are warranted.

4.4. Impact of minor surgical complications

Additionally, this review captures minor post-surgical complications resulting from inadequate healing processes, such as MT lateralization or abnormal scarring of sinus ostia (Table 2). These complications, while not having significant repercussions on the overall status following the intervention, are a potentially controllable cause of recurrence. Sinus ostia obliteration, whether favored or not by inadequate MT positioning post-ESS, results in a failure of the surgical functionality principle, hindering proper sinus ventilation and drainage and promoting the reappearance of CRS symptoms [1,55]. Thus, systematic MT resection could effectively control this issue; however, outcomes regarding disease control and nasal airflow remain uncertain, with studies both advocating for and against this approach [56,57]. Consequently, MT resection currently depends on intraoperative conditions and the surgeon's predisposition.

These modifications during postoperative care can be partially modified and controlled through the use of devices, such as silicone sheets or steroid-eluting implants, or through rigorous post-surgical follow-up in the medical office [58,59]. However, the inflammatory tendency of CRS sometimes renders these situations uncontrollable, emphasizing the importance of a precise surgical approach, ensuring proper resection of bony septa, aiming to eliminate the existence of residual anatomical structures and reduce disease recurrences.

4.5. Limitations of the review

The present systematic review is subject to limitations that warrant acknowledgment. Firstly, the review is descriptive in nature and does not incorporate a meta-analysis to quantitatively synthesize the data, due to the high heterogeneity and low quality of the studies included (Fig. 2). Additionally, the lack of consensus on the appropriate surgical procedure for treating CRS has led to comparing different types of surgeries in this review, potentially resulting in an underestimation of the outcomes. New research with stricter inclusion criteria might not resolve these issues, given the scarcity of publications referencing residual anatomical structures and the limited evidence that can be provided in surgical studies where clinical trials are not feasible. However, the introduction of new technological advancements in the field of otolaryngology could offer an intriguing avenue of research. This may involve analyzing the outcomes of pre-surgical planning using three-dimensional imaging or providing training for individualized cases through virtual surgery.

5. Conclusions

This systematic review underscores the persistent challenge of incomplete resection of anatomical structures in revision surgeries for CRS. The wide variability observed in the retention of key structures underscores the intricate nature of surgical outcomes and emphasizes the necessity for ongoing standardization in surgical techniques. The insights gained from our systematic review provide valuable guidance for the development of tailored approaches aimed at mitigating residual structures and enhancing long-term disease control. Future research should focus on refining ESS, evaluating their impact on clinical outcomes and elucidating optimal strategies for personalized management of CRS.

Disclosure of interest

The authors declare that they have no competing interest.

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Authorship contribution

Conceptualization: D.M.-J. and S.S.-G.; Data curation: D.M.-J. and S.S.-G.; Formal analysis: D.M.-J., C.G.-T. and S.S.-G.; Investigation: D.M.-J. and S.S.-G.; Methodology: D.M.-J., R.M.-L. and S.S.-G.; Project administration: D.M.-J., R.M.-L. and S.S.-G.; Resources: D.M.-J., R.M.-L., C.G.-T., J.M.-S. and S.S.-G.; Supervision: D.M.-J., R.M.-L. and S.S.-G.; Validation: D.M.-J., R.M.-L. and S.S.-G.; Visualization: D.M.-J., R.M.-L. and S.S.-G.; Roles/Writing - original draft: D.M.-J. and S.S.-G.; and Writing - review and editing: D.M.-J., R.M.-L. and S.S.-G.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.anorl.2024.09.009.

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