ANATOMICAL VARIATIONS OF THE NOSE AND PARANASAL SINUSES FOUND ON CT SCAN IMAGES OF ADULT CHRONIC RHINOSINUSITIS PATIENTS

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ABSTRACT

Background: Anatomical variations of the nose and paranasal sinuses are one of the contributing factors in developing Chronic Rhinosinusitis (CRS) predisposing factor and complications during surgery complicating factors. CT Scan has an important role in diagnosing. One of the tools used to identify and detecting thesediagnose anatomical variations. in patients is CT scans.

Objectives : To study theexamine prevalence of anatomical variations of the nose and paranasal sinuses found on CT Scanscans images of adult chronic rhinosinusitis patients. with CRS.

Methods: The research conduct through aA retrospective descriptive studyresearch was conducted using CT scans images of 43 nose and paranasal sinuses CT Scans of the adult CRS patients who went tovisited the Allergy Rhinology Polyclinic at Dr. Hasan Sadikin hospital,Hospital in Bandung; on 1 between January-31 1 and December 31, 2019. Anatomical variations assessment of the nosewere assessed and paranasal sinuses divided into:categorized as CRS predisposing and surgery-complicating factors. CRS factors include septal deviation, Agger nasi, frontal bullae, concha hypertrophy, bullae ethmoid, pneumatized septum, concha bullosa, accessory ostium, bullous uncinate process; paradoxical, secondary, and sinus concha. While surgery complicating factors are depth of olfactory fossa, fronto ethmoid cells, inter frontal sinus septal cells, Haller cells, supraorbital cells, Onodi cells, intra maxillary sinus septum, and uncinate process attachment. Other include infraorbital nerve, anterior ethmoid artery, optic nerve, internal carotid artery, vidian canal dehiscence, atelectasis uncinate processus, intra sphenoid sinus septum, frontal, maxilla, and sphenoid sinus pneumatization.

Results: The result showed that the most common CRS predisposing factors were septal deviation (90.8%), concha hypertrophy (72.2%), and Agger Nasi Cells (65.1%);%). Regarding surgery -complicating factors are, the most prevalent ones were Keros II (72.2%), sellar sphenoid sinus (69,.8%), and Kuhn I (58,.1%).

Conclusion: SeptalIn conclusion, septal deviations, concha hypertrophy, and Agger Nasi cells asCells are the most common anatomical variations associated with CRS predisposing factors;predisposition. Additionally, Keros II, sellar sphenoid sinus sellar, and Kuhn I were identified as the most frequent complicating factors for surgery. These findings emphasize the importance of considering these anatomical variations in managing CRS.

***Keywords**:* Anatomical Variations, Prevalence, Nose, Paranasal Sinuses, CT Scans, Adult, CRS, Predisposition, Surgery Complications, Management.

INTRODUCTION

According to the 2020 European Position Paper on Rhinosinusitis and Nasal Polyposis, Chronic Rhinosinusitis is defined as the presence of a minimum of two major symptoms and additional minor symptoms persisting for a duration of at least 12 weeks. Major symptoms encompass nasal blockage, obstruction, or congestion, as well as nasal discharge (either anterior or posterior nasal drip). On the other hand, minor symptoms include facial pain or pressure and a reduction or loss of the sense of smell. To accurately diagnose CRS, it is necessary to consider not only the symptoms but also specific observations made during nasal endoscopy and CT Scans) imaging of the paranasal sinuses. Nasal endoscopy allows for the identification of various indicators, such as the presence of nasal polyps, mucopurulent discharge, and edema or mucosal obstruction, primarily located in the middle meatus. On the other hand, CT scans imaging provides valuable information regarding mucosal changes occurring within the Ostiomeatal Complex (OMC) and the sinuses. By utilizing the EPOS 2020 criteria, medical professionals can comprehensively assess patients with suspected CRS by considering the presence and persistence of major and minor symptoms, as well as utilizing nasal endoscopy and CT scans imaging to identify specific findings related to nasal polyps, mucopurulent discharge, edema/mucosal obstruction, and mucosal changes within the OMC and sinuses. This comprehensive approach aids in making an accurate and thorough diagnosis of CRS.[1]

Prevalence of Chronic Rhinosinusitis (CRS) in the United States, as reported in the 2012 National Health Survey, indicated that 1 in 8 adult suffers from CRS, highlighting the significant burden of the condition among the population. A research conducted in Europe in 2011, involving 57,128 CRS patients, found prevalence rate of 10.9% among individuals aged 15-75 years. In Indonesia, the predominance of CRS was reported to be 12.6% in 2004, estimating 30 million CRS patients in the country. Furthermore, at the Polyclinic of Allergy Rhinology Otorhinolaryngology-Head and Neck Surgery (ORL-HNS) in Hasan Sadikin Hospital (RSHS), a total of 206 CRS patients (11%) visited during 2012-2013. Among these patients, the age group with the highest representation was 20-29 years, accounting for approximately 33.09% of the cases. [2–5]

Chronic Rhinosinusitis (CRS) is a widely prevalent health issue that not only imposes significant financial burdens due to high medical costs but also demands long-term care. This chronicity of CRS disease necessitates ongoing management and treatment, further contributing to the overall expenses associated

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with this condition. In addition to the financial implications, CRS has been found to have a profound impact on various aspects of individuals' lives, including emotional well-being and overall quality of life (QoL).

The burden that CRS places on an individual's QoL is comparable to that of other chronic diseases such as COPD, asthma, and diabetes. Similar to these conditions, CRS affects individuals' daily functioning, social interactions, and emotional states. The persistent and bothersome symptoms of CRS, such as nasal congestion, facial pain, and a diminished sense of smell, can greatly impede one's ability to engage in regular activities and fulfill responsibilities. Moreover, the emotional toll of living with CRS should not be overlooked. The constant discomfort, frustration, and limitations imposed by the condition can lead to emotional dysfunction, including symptoms of depression and anxiety. The impact on mental health is particularly significant when individuals experience recurrent or refractory CRS that does not respond well to treatment.

Consequently, the detrimental effects of CRS on both physical and mental well-being underline the importance of comprehensive management approaches that not only focus on symptom relief but also address the broader impact on patients' lives. By recognizing and addressing the multifaceted nature of CRS, healthcare professionals can strive to improve not only the physical symptoms but also the emotional and psychological well-being of individuals living with this chronic condition, ultimately enhancing their overall QoL.[2]

CT scans is essential in diagnosing and describing the extent of CRS disease and detecting anatomical variations of the nose and paranasal sinuses. Anatomical variations such as concha bullosa, septal deviation, uncinate process pneumatization, and Haller cells have the potential to obstruct the OMC. This obstruction can contribute to the development of CRS and increase the risk of CRS recurrence. In cases where surgical intervention is required, complications can arise due to specific anatomical variations observed on CT Scans. For instance, dehiscence of the infraorbital nerve canal, optic nerve canal, and internal carotid artery canal in the sphenoid sinus, as well as the presence of Onodi cells, can pose challenges during surgery. These complications can potentially cause severe bleeding, vision impairment, or neurological sequelae. CT scans imaging of paranasal sinuses is crucial in preoperative planning, enabling surgeons to evaluate anatomical variations and choose appropriate surgical techniques.[1,6–8]

In 2017, Wardani found a frequent coexistence of septal deviation, concha bullosa, and lateral deflection of the uncinate process with ipsilateral maxillary rhinosinusitis. Research conducted at Cipto Mangunkusumo between 2005 and 2009 revealed a correlation between obstruction of the OMC and the presence of maxillary, anterior ethmoid, and frontal rhinosinusitis.[9] Kranti Gouripur in 2017 found commonly anatomical variations found on CT scans imaging of CRS patients were Agger Nasi Cells, anterior ethmoid cells, septal deviation.[10] Similarly, Mendiratta in 2016 discovered Agger Nasi Cells, bullous concha, and paradoxical middle concha as frequently observed anatomical variations.[11]

MATERIALS AND METHODS

This research focused on conducting CT scans of paranasal sinuses in adult aged 18 years and above. This selection was based on the fact that most CRS patients seeking treatment at the Allergy Rhinology Polyclinic, ORL-HNS, RSHS Bandung were adult, accounting for 33.09% of the cases. Additionally, it is known that anatomical structure of the nose and paranasal sinuses reaches its optimal shape and size after the age of 18 years.[7,12,13]

A retrospective descriptive research study was conducted to analyze 43 computed tomography (CT) scans of paranasal sinuses obtained from adult patients diagnosed with Chronic Rhinosinusitis (CRS) at RSUP Dr. Hasan Sadikin Bandung, Indonesia. The study period spanned from January 1 to December 31, 2019. The inclusion criteria for the study comprised adult CRS patients (aged 18 years and above) with either unilateral or bilateral CRS, and the CT scans needed to have axial, coronal, sagittal, and 1-2 mm sections obtained using the bone window technique. However, patients with a history of nasal or paranasal sinus surgery, any nasal mass, and facial anomalies were excluded from the analysis.

By conducting a retrospective analysis of these CT scans, the researchers aimed to gain a better understanding of the radiological characteristics and findings associated with CRS in adult patients. The selection of CT scans meeting specific criteria ensured that the study focused on a homogeneous group of patients with CRS, thereby minimizing potential confounding factors.

The research team utilized a descriptive research design to provide a detailed account of the radiological features observed in the CT scans. This approach allowed for the systematic evaluation of the paranasal sinuses, including the identification of anatomical variations, mucosal changes, and any other abnormalities associated with CRS.

The data collected from this study can contribute to the existing knowledge base regarding the radiological manifestations of CRS in adult patients. By excluding CT scans from patients with a history of surgery, nasal masses, and facial anomalies, the researchers aimed to isolate and analyze the specific characteristics of CRS-related changes in the paranasal sinuses. This information may prove valuable in improving the diagnosis and management of CRS, as well as providing insights into potential treatment strategies for affected individuals.

The minimum sample size of 43 was determined using a formula specific to nominal data research. During the specified period, 113 adult CRS patients were identified, but CT scans data were available for only 58 of them. Fifteen patients were excluded due to not meeting the inclusion criteria. The recorded data included anatomical variations as well as characteristics such as age, gender, occupation, history of atopy, and comorbidities.

The observations of paranasal sinuses CT scans were conducted using a DICOM viewer program. The results encompassed identifying anatomical variations on the right side, left side, and both sides of sinuses. To calculate the total percentage of each anatomical variations, the percentages of variations found on the right side, left side, and both sides were summed together.

The septal deviation is categorized into seven types according to the Mladina classification, namely types 1, 2, 3, 4, 5, 6, and 7. However, when calculating the total percentage of septal deviation, Mladina type 7 is excluded. This is because Mladina type 7 represents a combination of types 1 to 6.

Anatomical variations assessment of the nose and paranasal sinuses was divided into two groups, CRS predisposing and surgery complicating factors. CRS predisposing factors included septal deviation, Agger Nasi Cells, frontal bullae, concha hypertrophy, bulla ethmoid, pneumatized septum, concha bullosa, accessory ostium, bullous uncinate process, paradoxical concha, secondary concha, and sinus concha. On the other hand, surgery complicating factors included the depth of olfactory fossa according to Keros classification, fronto ethmoid cells according to Kuhn classification, interfrontal sinus septal cells, Haller cells, supraorbital cells, Onodi cells, intra maxillary sinus septum, attachment of the uncinate process, infraorbital nerve dehiscence, anterior ethmoid artery dehiscence (AEAD), optic nerve dehiscence, internal carotid artery dehiscence, vidian canal dehiscence, atelectasis uncinate processus, intra sphenoid sinus septum, and frontal, maxilla, and sphenoid sinus pneumatization. The results of observations on paranasal sinuses CT Scans of adult

CRS patients were collected and described descriptively in the statistical measure of number as well as percentage for categorical data. The collected data was then organized and presented in a table format. Statistical description methods were applied to process the collected data, and the findings were utilized to prepare and write the scientific paper.

RESULT

General Characteristics of Subjects

Table 1. General Characteristics of Subjects

Characteristics	Total n=43	
	n	%
Age (years)*		
18-25 Late adolescence	11	25,6
26-35 Early adulthood	7	16,2
36-45 Late adulthood	6	14,0
46-55 Early old age	9	20,9
56-65 Late old age	6	14,0
>65 Elderly	4	9,3
Gender		
Man	24	55,8
Woman	19	44,2
Ocupation		
Civil Servant	5	11,6
Entrepreneur	4	9,3
Private sector employee	9	20,9
Housewife	9	20,9
Student	10	23,3
Doctor	2	4,7
Laborer	1	2,3
Unemployment	3	7,0
History of Atopy		
Present	30	69,8
Absent	13	30,2
Comorbid		
Allergic Rhinitis	21	48,7
Dental caries	10	23,3
Asthma	3	7,0
Absent	9	21

NOTE: *Age category according to the Health Ministry of Indonesia in 2009

Table 1 shows the general characteristics of the research subjects, with the majority late adolescence, male, students, had a history of atopy and comorbid allergic rhinitis.

Anatomical Variations Of The Nose And Paranasal Sinuses

Anatomical Variations as CRS Predisposing Factors

Table 2. Anatomical Variations as CRS Predisposing Factors

NO	Anatomical Variation	(n=43)	Percentage %	Total Percentage %
1.	Nasal Septum			
	Normal	8		18,6

SD Mladina 1	4	9,3	90,8
Mladina 2	3	7	
Mladina 3	12	27,9	
Mladina 4	10	23,3	
Mladina 5	9	21	
Mladina 6	1	2,3	
PS	9		20,9

	Anatomical Variation	**Right (n=43)**		**Left (n=43)**		**Both**		**Percentage**	**Total Percentage**
		n	%	n	%	n	%	%	(n=43) %
2.	Nasal Concha								
	Normal								(7) 16,3
	CB Media	7	16,3	2	4,7	5	11,6	32,6	
	Inferior	2	4,7	0	0	4	9,3	14	
	Superior	0	0	0	0	0	0	0	
	CH Media	3	7,0	1	2,3	26	60,5	69,8	
	Inferior	3	7,0	2	4,7	26	60,5	72,2	
	Superior	0	0	0	0	0	0	0	
	PC Media	0	0	1	2,3	1	2,3	4,6	
	Inferior	0	0	0	0	1	2,3	2,3	
	Superior	1	2,3	0	0	1	2,3	4,6	
	SIC Media	0	0	0	0	1	2,3	2,3	
	Inferior	0	0	0	0	1	2,3	2,3	
	Superior	0	0	0	0	0	0	0	
	SEC Media	1	2.3	0	0	1	2,3	1,5	
	Inferior	1	2,3	0	0	2	4,7	2,3	
	Superior	0	0	0	0	0	0	0	
3	AO	0	0	3	7	0	0		7
	Without OA								93

4.	BUP	0	0	1	2,3	2	4,7	7
	Without BUP							93
5.	AN	3	7	1	2,3	24	55,8	65,1
	Without AN							34,9
6.	BE	2	4,7	0	0	8	18,6	23,3
	Without BE							76,7

NOTE: SD: Septal deviation, PS: , pneumatized septum, CB: concha bullosa, CH: concha hypertrophy, PC: paradoxical concha, SIC: sinus concha, SEC: secondary concha, AO: accessory ostium, BUP: bullous uncinate process, AN: Agger Nasi Cells, BE: bulla ethmoid.

Table 2 shows prevalence of the nose and paranasal sinuses anatomical variations as a predisposing factor for CRS. As the third most predisposing factor for CRS, anatomical variations are septal deviations, concha hypertrophy, and Agger Nasi Cells.

Anatomical Variations as Surgery Complicating Factor

Table 3. Anatomical variations as Surgery Complicating Factor

NO	Anatomical Variation	Right (n=43)		Left (n=43)		Both (n=43)		Percentage Total
		n	%	n	%	n	%	(n=43) %
1.	Maxillary Sinus							
	Normal							(16) 37,2
	HiMS	1	2,3	1	2,3	4	9,3	14
	MSA	1	2,3	0	0	0	0	2,3
	MSH	0	0	0	0	0	0	0
	IMSS	4	9,3	0	0	2	4,7	14
	IOND	6	14	5	11,6	6	14	39,6
2.	PU							
	AUP	0	0	0	0	0	0	100
	Without AUP							
	UPA							
	UPA Type I	4	9,3	2	4,7	7	16,3	30,3
	UPA Type II	2	4,7	3	7	5	11,6	23,3
	UPA Type III	2	4,7	3	7	13	30,2	41,9
	Others UPA	3	7	3	7	7	16,3	30,3
3.	Frontal Sinus							
	Normal							(8) 18,6
	FSA	1	2,3	0	0	1	2,3	4,6
	FSH	5	11,6	1	2,3	1	2,3	16,2
	IFSSC	0	0	0	0	0	0	0
	FC							
	Kuhn Type 1	8	18,6	8	18,6	9	20,9	58,1

	Kuhn Type 2	3	7	4	9,3	4	9,3	25,6
	Kuhn Type 3	4	9,3	3	7	5	11,6	27,9
	Kuhn Type 4	4	9,3	5	11,6	0	0	21
	Keros							
	Keros Type I	3	7	3	7	8	18,6	32,6
	Keros Type II	3	7	2	4,7	26	60,5	72,2
	Keros Type III	1	2,3	2	4,7	2	4,7	11,7
4.	Ethmoid Sinus							
	Normal							(16) 23
	AEAD	1	2,3	6	14	3	7	23,3
	SOC	3	7	5	11,6	7	16,3	34,9
	HC	4	9,3	1	2,3	3	7	18,6
	OC	5	11,6	1	2,3	9	20,9	34,9
5.	Sphenoid Sinus							
	Normal							(16) 37,2
	ISSS	6	14	5	11,6	9	20,9	46,5
	OND	1	2,3	2	4,7	6	14	21
	ICAD	3	7	5	11,6	0	0	18,6
	VCD	2	4,7	5	11,6	8	18,6	34,9
	SSP							
	SSA	1	2,3	1	2,3	0	0	4,6
	SSC	1	2,3	1	2,3	2	4,7	9,3
	SSPS	2	4,7	0	0	9	20,9	25,6
	SSS	0	0	2	4,7	28	65,1	69,8

NOTE: SMHi: Sinus Maksila Hiperpneumatisasi, HiMS: Hyperpneumatized Maxillary Sinus, SMA: Sinus Maksila Agenesis, MSA: Maxillary Sinus Agenesis, SMHo: Sinus Maksila Hipoplasia, MSH: Maxillary Sinus Hypoplasia, SISM: Septum Intra Sinus Maksila, IMSS: intra Maxillary Sinus Septum, KNIOD: Nervus Infra Orbita Dehisen, IOND: Infra Orbital Nerve Dehiscence, AUP: Atelectasis Uncinate Processus, Uncinate Process Attachment: UPA, FSA: Frontal Sinus Agenesis, FSH: Frontal Sinus Hypoplasia, IFSSC: Inter Frontal Sinus Septal Cells, FC: Frontal Cell, AEAD: Anterior Etmoid Artery Dehisence, SOC: Supra Orbital Cells, HC: Haller Cells, OC: Onodi Cells, ISSS: Intra Sphenoid Sinus Septum, OND: Optic Nerve Dehisence, ICAD: Internal Carotid Artery Dehiscence, VCD: Vidian Canal Dehisence, SSP: Sphenoid Sinus Pneumatization, SSA: Sinus Sfenoid Agenesis, SSC: Sphenoid Sinus Concha, SSPS: Sphenoid Sinus Pre Sellar, SSS: Sphenoid Sinus Sellar

Table 3 shows prevalence of the nose and paranasal sinuses anatomical variations as surgery-complicating factors. Anatomical variations of the nose and paranasal sinuses that serve as the third most common surgery-complicating factors are Keros type II, sphenoid sinus sellar, and Kuhn type I.

DISCUSSION

Research Characteristics

According to the present research, most CRS patients were adult, comprising 3.2% of the total population, and 16.2% and 14% were early and late adult. These findings are consistent with the research by Multazar in 2008 that 20.61% of CRS patients fell into the early adulthood category. Thomas (2020) stated that CRS patients aged 40-64 years (late adult and seniors) were 48.5%.[12] In contrast, research at Udayana Hospital in 2018 found that generally, CRS patients aged 46-60 years (early elderly and seniors) were 37,7%[13] and at Haji Adam Malik Hospital Medan in 2013, 21.7% aged 46 -60 years (early elderly and seniors). [14]

Based on this research and previous ones, it was found that CRS patients were generally adult and the elderly. Although there are little variations in the age distribution, it is likely attributed to differences in the research population, sample size, and the specific age categories used for classification.

Prevalence of CRS increases with age, averaging 2.7%, 6.6% and 4.7% in 20-29, 50-59 and above 60 age groups (EPOS, 2012). The incidence of CRS is commonly observed in adult productive age group, likely due to their increased outdoor activities and potential exposure to allergens or pollutants.[12–15]

Generally, approximately 55% of CRS patients were male, consistent with previous research conducted in 2010 in North America, where there were twice as many male CRS patients as females. The Korea National Health and Nutritional

Examination Survey in 2011 also reported a higher prevalence of CRS in males than females. Several factors contribute to the higher prevalence of CRS in men, including a higher likelihood of smoking (2.25 times more likely) and exposure to dust and chemicals (2.48 times more likely) compared to women. These factors can irritate the nasal mucosa and paranasal sinuses, leading to inflammation.[15,16]

Different things were found in Canada, with 5.7% female CRS patients and 3.4% male patients. However, data from The Longitudinal Health Insurance Database of Taiwan in 2014 showed a slightly higher prevalence of CRS in females (51%) than males (49%). Predisposition of women to CRS is thought to be related to the smaller size of the sinus ostium, which makes it more susceptible to obstruction. According to Fokkens et al., hormonal effects on the nasal mucosa and blood vessels, such as estrogen, progesterone, and placental growth hormone, can increase the inflammatory response and contribute to the occurrence of CRS. Women are also more likely to report CRS symptoms and seek medical care, which can result in biased data and an apparent increased prevalence of CRS.[13,16]

The Global Allergy and Asthma European Network multi-center research conducted in 2011 showed no significant gender difference in CRS patients across Europe. The pathophysiology of the gender-related prevalence of CRS is not yet clearly known, and this is still a matter of debate.[16]

The majority of CRS patients in this research were identified as students, comprising 48.7% of the total participants. This finding is similar to the research by Salsabila in 2018 at Dr. Sardjito Hospital, which also reported a high proportion of CRS patients among students (33.06%).[17] However, a contrasting pattern emerged from the research conducted at Udayana Hospital in 2018, where most CRS patients were found to be private-sector employees, accounting for 43.40%.[13] Research conducted by Lubis in 2014 highlighted that civil servants constituted 24.2% of CRS patients, while according to Sitinjak (2015) entrepreneurs accounted for 28.2% of the cases.[14]

Variations in occupation observed in this research and previous ones are attributed to differences in the population and sample sizes. The higher incidence of CRS among certain occupations can be attributed to frequent exposure to pollutants or irritants, which can lead to inflammation of the nasal and paranasal sinuses mucosa and impairment of the nasal mucociliary system.[13,14,16]

In this research, it was observed that students constituted the largest occupational group among the participants, particularly in the age range of 18-25 years, accounting for 23.3% of the sample. They are particularly susceptible to exposure to pollutants and irritants within the school environment and during their commute to and from school due to exposure to dust, lime, and vehicle fumes.[13,17]

Based on the findings, a significant proportion of CRS patients, specifically 69.8%, had a history of atopy. This aligns with the research conducted by Benjamin in 2019, where prevalence of atopy among CRS patients was reported as 60%.[18] Jin-Young Min in 2015 found the atopy prevalence in CRS patients was 30-80%.[19]

Atopy refers to the tendency of an individual to develop allergic reactions and produce immunoglobulin E (IgE) antibodies in response to common environmental exposures. The findings from this research and previous ones indicate that a history of atopy is commonly observed in patients with CRS. Ho (2018) stated that CRS patients with atopy tend to have more severe symptoms but do not cause a decrease in QoL of patients.[23] Additionally, prevalence of atopy was higher in CRS patients with nasal polyps (76%) than those without nasal polyps (52%). CRS patients with atopy also had a higher recurrence rate than those without atopy. Based on this, it is essential to diagnose the presence of atopy in CRS patients for proper and optimal CRS management.[20,21,22,23]

Allergic rhinitis is considered one of the manifestations of atopy. Robinson (2006) stated that approximately one-third of individuals with atopy will develop allergic rhinitis.[22] In line with this, the current research identified a significant comorbidity of allergic rhinitis in CRS patients, with prevalence of 48.7%. Furthermore, in 2018, Philpott reported a high prevalence of inhalant allergies (84.63%) among CRS patients.[24] Green (2014) stated that 73% of CRS patients exhibited positive allergen extracts in the skin prick test, indicating sensitization to allergens.[24] In 2017, Hamizan found that CRS patients with nasal mucosa and paranasal sinuses endoscopic features were polypoid oedema mucosa associated with inhalant allergy.[24]

Allergic rhinitis occurs when the body's immune system becomes sensitized to foreign proteins, known as allergens, that are able to breach the protective mucosal barrier. These allergens initiate a cascade of immune responses, starting with their interaction with dendritic cells and CD4-positive lymphocytes. This interaction activates antigen-specific Th2 lymphocytes and plasma cells, which then produce IgE antibodies.

The IgE antibodies, once bound to the surface of mast cells, trigger the process of degranulation, leading to the release of various inflammatory mediators. These mediators include histamine, leukotrienes, and cytokines, which contribute to the characteristic symptoms of allergic rhinitis such as nasal congestion, sneezing, and itching.

Beyond the IgE-mediated response, allergens possess another characteristic feature called protease activity. These proteases have the ability to directly interact with epithelial cells lining the respiratory tract. This interaction prompts the release of type 2 activating cytokines and chemokines, which are important signaling molecules in immune responses.

These type 2 activating cytokines and chemokines, including interleukins such as IL-4, IL-5, and IL-13, play a crucial role in the development and progression of CRS. They contribute to the recruitment and activation of immune cells, the remodeling of nasal tissues, and the perpetuation of inflammation.

The combined effects of the IgE-mediated response and the protease activity of allergens create a complex and multifaceted immune response in individuals with allergic rhinitis. This response involves the activation of various immune cells, the release of inflammatory mediators, and the recruitment of cytokines and chemokines that collectively contribute to the pathogenesis of CRS.

Understanding these underlying mechanisms is important for developing targeted therapeutic strategies aimed at managing allergic rhinitis and its complications, such as CRS. By targeting specific components of the immune response, it may be possible to alleviate symptoms, prevent disease progression, and improve the overall quality of life for individuals affected by these conditions. Further research is necessary to elucidate the precise interplay between allergens, immune cells, and inflammatory mediators in order to develop more effective treatment options..[20,24]

According to preliminary research, allergic inflammation is believed to contribute to the mucosal inflammation observed in CRS. Allergic inflammation can lead to mucosa swelling, impaired mucociliary clearance, and the release of pro-inflammatory mediators. In patients with CRSwNP (CRS with Nasal Polyps), the mucosal inflammation mediated by Th2 cell cytokines resembles the inflammation seen in allergic conditions, particularly in individuals with a predominant eosinophilic infiltrate in the tissue. There is an association between allergy and specific phenotypes such as CCAD (Central

Compartment Allergic Disease) and AFRS (Allergic Fungal Rhinosinusitis), as highlighted in the EPOS 2020 guidelines.[20,21,24]

Anatomical Variations of The Nose And Paranasal Sinus

Anatomical variations of the nose and paranasal sinuses was the most predisposing factor, had 90.8% septal deviation, while the most complicating factor for surgery was Keros type II at 72.2 %.

Anatomical Variations as CRS Predisposing Factors
Septal Deviation

Septal deviation is the predominant anatomical variations of the nose and paranasal sinuses in CRS patients, accounting for 90.8% of cases. Research by Hamid (2019) [25] and Shivakumar (2018)[26] found 75% (from 100 subjects) and 71% septal deviation. Additional research by Maru et al. (2011) [27] and Fadda et al. also identified septal deviation as one of the most common anatomical variations of the nose and paranasal sinuses, with prevalence rates of 55% and 60%, respectively.[26]

Individuals with a perfectly straight nasal septum are rare due to deviation on the ear, nose and throat dysfunction with or without symptoms. These deviations can have a significant impact on the ventilation flow and drainage of the maxillary sinuses, leading to the thickening of the maxillary sinus mucosa and an increased risk of developing CRS.[25,26,28]

In this research, the most prevalent type of septal deviation observed was Mladina type 3, accounting for 27.9% of cases. This finding is in accordance with research conducted by Zulaikhah in 2020, which reported prevalence of 54.4% for Mladina type 3 septal deviation.[29] Mladina type 3 septal deviation is characterized by a deviation resembling the letter "C" when viewed from above. It is commonly found in CRS patients due to its proximity to the head of the middle concha, potentially obstructing the communication (COM) pathway. The contralateral side of the septal deviation, despite having a wider area, does not provide a physiological stimulus for the airway mucosa. As a result, it can transform cylindrical epithelial cells into stratified squamous epithelial cells in the COM. Patients with Mladina type 3 septal deviation were found to have a 6.3-fold higher probability of developing ethmoidal rhinosinusitis and a 7.5-fold higher probability of developing maxillary rhinosinusitis compared to patients without septal deviation. Conversely, the research by Toluhala identified Mladina type 5 septal deviation in 38.6% of 70 CRS patients. Variations in the types of septal deviations observed in this research and previous research may be attributed to differences in the research population and sample size.[29,30,31]

Concha Hypertrophy

The most common anatomical variations observed in CRS patients was concha hypertrophy, accounting for 72.2% of cases. This finding is consistent with the research conducted by Sayan in 2019, which reported prevalence of 34% for inferior concha hypertrophy.[32] Grewal (2019) stated that 58.7% of the 92 CRS patients had inferior concha hypertrophy.[33]

Nasal obstruction, a common symptom in CRS patients, can be attributed to various factors, including septal deviation and different degrees of inferior concha hypertrophy. Inferior concha hypertrophy is a physiological compensation mechanism to protect the nasal mucosa from dry air and excessive crusting caused by increased airflow. When the nasal septum shifts, the inferior concha becomes enlarged to fill the empty space in the nasal cavity. However, inflammatory factors can exacerbate this condition, leading to chronic nasal congestion and an increased predisposition to CRS.[34]

Concha hypertrophy can manifest as either bilateral or unilateral enlargement. Bilateral concha hypertrophy is commonly associated with both allergic and nonallergic conditions. Nonallergic factors such as exposure to air pollutants like dust and tobacco smoke can contribute to developing concha hypertrophy. In these cases, hypertrophy is primarily observed in the mucosal lining of the concha. On the other hand, unilateral concha hypertrophy is often linked to septal deviation, particularly in cases involving Mladina type 3 septal deviation. In these instances, the hypertrophy is mainly attributed to the thickening of the bony component of the concha.[35]

The choice of technique for concha reduction depends on the dominant tissue affected by hypertrophy. In cases of concha hypertrophy associated with allergic rhinitis, where only the medial mucosa is hypertrophied, conservative methods such as limited mucosal resection using diathermy or other techniques may be sufficient. It is crucial to avoid total or partial removal of concha tissue in these cases to prevent complications such as the empty nose syndrome or atrophic rhinitis. However, the submucosal diathermy technique is impractical for addressing concha hypertrophy, as it primarily affects concha thickening. Turbinoplasty, a surgical procedure aimed at reducing the size of the concha, is recommended in such cases.[35,36]

Inferior concha hypertrophy is a common occurrence, with the majority of hypertrophied concha being the inferior concha. Chronic nasal obstruction resulting from inferior concha hypertrophy affects over 20% of the population. This research also found that most concha hypertrophy cases involved the inferior concha, accounting for 72.2% of the cases. The inferior concha, being larger and situated in the most anterior position, is more exposed to antigens, pollutants, and other irritants.[35,36]

Agger Nasi Cell

Anatomical variations involving Agger Nasi Cells are commonly observed in CRS patients. Research by Dul Afif at Dr. Sardjito Hospital in 2015 reported prevalence of 88% Agger Nasi Cells among 144 CRS patients.[37] Ahmed in 2013 found 90% of Agger Nasi Cells from 140 patients who underwent FESS.[38] In contrast, the research by Julyanti (2013) at Dr. Wahidin Sudirohusodo Hospital reported a much lower prevalence of 5.9% Agger Nasi Cells among 119 CRS patients.[32]

Based on this research and numerous previous research, it has been consistently observed that Agger Nasi Cells are a common anatomical variation. Agger Nasi Cells are the most frequently encountered among the cells in the frontal recess area.[38] When these cells are large, they can cause constriction of the frontal recess, leading to an increased susceptibility to frontal rhinosinusitis, either posteriorly or laterally.[17] Additionally, Agger Nasi Cells are situated adjacent to the nasolacrimal duct, creating a potential pathway for infection to spread from the frontal sinus to the nasolacrimal duct. On the other hand, small-sized Agger Nasi Cells may contribute to the thickening of the frontal beak, resulting in a narrowing of the frontal sinus ostium.[13,39,40]

Ethmoid Bulla

Approximately 23,3% of ethmoid bullae were found in this research, similar to the one conducted by Julyanti in 2013, which found 26.9% of it from 119 CT scans of CRS patients.[32] Furthermore, Poorey (2014) and Gouripur (2017) found 28.35% and 30% of 67[41] and 50 CT scans.[42] The presence of ethmoid bulla is a common occurrence in CRS patients. During functional endoscopic sinus surgery (FESS), it is crucial to remove the ethmoid bulla to ensure proper drainage of the frontal recess and prevent the recurrence of CRS.[32,41,42,43]

Anatomical Variations as Surgery Complicating Factor
Depth of the Olfactory Fossa

This research found that a significant proportion of patients with CRS exhibited Keros type II olfactory fossa depth. This observation is consistent with previous research by Fabian in 2019, where Keros type II was identified in approximately 82.3% of the 249 CT scans of CRS patients. Similarly, a research conducted by Basti in 2018 reported that the majority of CRS patients had Keros type I, accounting for around 62% of 500 CT Scans of CRS patients.[44,45]

It can be concluded that Keros type II is the most common olfactory fossa depth among CRS patients, followed by Keros type I, while Keros type III is the least prevalent.[44,45]

This research also highlighted the vulnerability of Keros type III to trauma during FESS due to the lower position of the lateral lamellae of the cribriform plate compared to other Keros types. The research revealed that the depth of the Keros type III olfactory fossa was greater on the left side (9.4%) than on the right side (7%). In contrast, a research by Murthy in 2015 found a higher prevalence of Keros type III on the right side (13%) compared to the left side (5%). The lower location of the lateral lamella in Keros type III increases the risk of intracranial penetration and trauma to anterior ethmoid artery (AEA). Patients with Keros type III have an elongated ethmoid roof, and AEA is situated below the skull base, making it more susceptible to injury during FESS. [44,45,46,47]

These variations in findings between different research may be attributed to differences in ethmoid roof configurations among various ethnic and racial populations.

Sphenoid Sinus Pneumatization

This research revealed that the majority of patients with CRS had sellar-type sphenoid sinus pneumatization, accounting for approximately 69.8% of cases. This finding is in accordance with the research conducted by Shivaprakash in 2018, which reported complete-type sphenoid sinus pneumatization in 76.6% of 500 CT scans of the Indian population, with incomplete-type pneumatization observed in 22.2% of cases. Similarly, sellar-type pneumatization was found in 98.8% of Caucasian and East Asian populations. Another research by Catalina research in 2015, focusing on patients undergoing dental procedures, identified sellar-type pneumatization in 55.1% of 25 CT scans.[48,49]

Based on this research and previous research, sellar-type sphenoid sinus pneumatization was consistently the most prevalent among CRS patients. The degree of sphenoid sinus pneumatization affects factors such as bone dehiscence, the presence of critical neurovascular structures protruding into the sinus, and the choice of surgical approach for transsphenoid procedures. Sellar-type pneumatization offers wider pneumatization, facilitating easier access for transsphenoid surgical procedures. This pneumatization often involves the protrusion of critical neurovascular structures, such as the internal carotid artery and optic nerve, into the sinus. Consequently, there is an increased risk of iatrogenic trauma, including cerebrospinal fluid (CSF) leakage and injury to neurovascular structures.[48,49] Conversely, concha-type pneumatization is unsuitable for transsphenoid surgical procedures due to the need for extensive removal of thick and dense bone, resulting in longer operating times.[48,49]

Fronto Ethmoid Cells

This research found that most patients with CRS had fronto-ethmoid cells of type 1 Kuhn (K1), accounting for approximately 58.1% of cases. This corresponds to the findings of Ozum in 2012, which reported K1 cells in 49.1% of 167 CT scans of CRS patients.[38]

Accessing fronto-ethmoid cells during FESS is challenging due to their small diameter, location within the frontal bone, proximity to orbital structures, the skull base, and the frontal recess. These factors make it difficult to identify fronto-ethmoid cells using endoscopic techniques.[50]

Based on this research and previous research, most fronto-ethmoid cells observed were of K1 and type 2 Kuhn (K2). This finding has implications for the surgical approach. K1, K2, and type 3 Kuhn (K3) cells can typically be removed endoscopically from below through the frontal recess. However, removing type 4 Kuhn (K4) cells is more complex due to their extensive pneumatization into the frontal sinus. This situation necessitates endoscopic management from below through the frontal recess in combination with an approach through the anterior frontal sinus table.[51]

Intra Sphenoid Sinus Septum

According to this research, prevalence of multiple intra-sphenoid sinus septa (ISSS) in CRS patients was found to be 46.5%. Similar findings were observed in other research. A research by Battal in 2014 found an incidence of 34.1% in 314 CT Scans;[52] Kapur in 2012 reported 54.1% in 200 CT Scans;[53] Kashyap in 2017 found 27.5% in 80 CT Scans,[52] and Gautam in 2019 observed an incidence of 17.29% in 52 CT Scans.[52]

Understanding anatomical characteristics of sphenoid sinus septation is crucial for performing successful FESS and trans-sphenoid skull base endoscopic surgery. ISSS can manifest as a single septum, multiple septa, or even an absence of septa. This research specifically focused on prevalence of multiple ISSS, which poses a higher risk of attachment to vital neurovascular structures such as the internal carotid artery, optic nerve, and vidian nerve. Considering that nearly half of CRS patients exhibited multiple ISSS, preoperative evaluation of sphenoid sinus septation through CT scans is essential to prevent potential injury to these neurovascular structures. The research also examined the number of ISSS present and their proximity to critical neurovascular structures. ISSS that is located posterolaterally in the sphenoid sinus, superolaterally to the optic nerve, or inferiorly to the vidian nerve suggests adhesion to the internal carotid artery.[52,53,54]

ISSS has a significant association with prominent neurovascular structures surrounding the sphenoid sinus. [52,53,54] This research revealed the rates of dehiscence or protrusion of these critical neurovascular structures into the sphenoid sinus namely, Vidian Canal Dehiscence (34.9%), Optic Nerve Dehiscence (21%), and Internal Carotid Artery Dehiscence (18.6%).

Uncinate Process Attachment

This research found that among CRS patients, the attachment sites of the uncinate process were as follows, 37.2% to the median concha, 30.3% to the lamina papyracea, 25.6% to the skull base, and 16.3% to other locations. In addition, some uncinate processes were attached to the ethmoid bulla or the Agger Nasi Cells.

Research conducted by Arun in 2017 reported attachment rates of 67.5% to the lamina papyracea, 18.5% to the skull base, 9.5% to the median concha, and 4.5% located freely in the middle meatus, based on 100 paranasal sinus CT scans.[55]

It is crucial to assess the attachment site of the uncinate process prior to FESS using paranasal sinus CT scans to guide the surgeon in locating the frontal recess and preventing damage to surrounding critical structures. Unsinectomy, the removal of the uncinate process, is an important step during FESS. Complications associated with unsinectomy depend on the attachment site of the uncinate process.[13,56]

The majority of uncinate process attachments were observed on the median concha, which causes the frontal recess to be situated further posteriorly than the Agger Nasi Cells. Therefore, removing the Agger Nasi Cells is necessary to access the frontal recess.[15,16] Complications specifically related to unsinectomy in FESS with this configuration are not widely reported, but it could potentially lead to trauma to the median concha.[13,56]

According to preliminary research, the most common attachment site of the uncinate process is the lamina papyracea, and this site can lead to complications such as orbital penetration, orbital fat prolapses, bleeding, tear duct injury, and epiphora. Attachment to the skull base can lead to CSF leakage. The different results between this research and previous research may be attributed to variations in the research population and sample size.[55]

Infra Orbital Nerve Dehiscence

In this research, it was discovered that 39.6% of CRS patients had infraorbital nerve. Similar findings were reported by Gulay in 2017, which found 36,2% from 200 CT scans of CRS patients;[57] Ference in 2015 found 39,5%;[18] Yenigun in 2016 found 51,2%. while Lifeng in 2000, found 70% from 20 cadavers.[57]

Infraorbital nerve dehiscence is quite common in CRS patients. Therefore, it is crucial to evaluate infraorbital nerve dehiscence through paranasal sinus CT scans prior to procedures to prevent iatrogenic injury to the nerve. Iatrogenic infraorbital nerve injury has been reported during interventions like FESS, Caldwell-Luc surgery, and orbital reconstructive surgery. This is because such injuries can lead to hypoesthesia or anesthesia of the infraorbital nerve. Temporary hypoesthesia incidence due to iatrogenic injury has been reported as 0.5%. Infraorbital nerve dehiscence is associated with iatrogenic injury and poses a risk of infection or tumor spread from the maxillary sinus to the orbit.[18,57]

Onodi Cell

In this research, prevalence of Onodi cells was found to be 34.9%. Huang (2020) reported a higher prevalence of 52.3% among 216 patients who underwent FESS.[57] Conversely, Basis in 2016 found a lower prevalence of 25.3% in 400 paranasal sinuses CT scans.[50] A research by Shivakumar in 2018 identified Onodi cells in only 8.6% of 138 CRS patients, while Adeel in 2013 found prevalence of 10% among 77 CRS patients.[51]

In rare cases, onodi cells are situated adjacent to the internal carotid artery and can be found medial or around the optic nerve. Onodi cells pose a risk of injury to the optic nerve and internal carotid artery during procedures such as posterior ethmoidectomy, transsphenoidal surgery, and other skull base surgery.[17] Optic nerve injury can lead to immediate or delayed vision loss, while internal carotid artery injury can result in bleeding. Due to their low prevalence, internal carotid artery injuries are not extensively documented in the literature.[26,50,51,52]

Performing surgical maneuvers behind the Onodi cells, such as opening the sphenoid sinus, carries a risk of damaging the optic nerve and internal carotid artery. It is essential to locate the ostium before entering the sphenoid sinus and to remain inferior and medial to the posterior ethmoid cells to ensure safety. When Onodi cells are identified, the endoscopic anatomy should be correlated with CT scans findings, and access to the sphenoid sinus should be obtained through the medial floor of the Onodi cells. It is not recommended to follow the lamina papyracea with the posterior ethmoid cells to access the sphenoid sinus.[50,51,52]

The clinical implications of Onodi cells are associated with the risk of optic nerve and internal carotid artery injury, and their identification during endoscopy is often mistaken for the sphenoid sinus. This can occur when there is incomplete sphenoid sinus removal and sphenoid rhinosinusitis recurrence.[50,51,52]

Prevalence variations observed are attributed to differences in the research populations and sample sizes.

AEAD

In this research, it was found that 23.3% of the participants had AEAD. Similar findings were reported by a research carried out by Guarnizo in 2020, which found AEAD in 13.2% of 1008 CT scans, Moon found AEAD in 11%, and Floreani found AEAD in 16%. In contrast, a research by Ferrari in 2017 found AEAD in as much as 46.4% of 14 cadavers, and a research conducted by Abdullah in 2019 reported AEAD incidence ranging between 40% and 67% in other countries.[53,54,55]

AEA is at risk of injury during FESS procedures due to its proximity to the lamina papyracea and its protrusion into the orbital cavity. AEAD is categorized into three segments namely, intra-orbital, ethmoid, and intracranial segments.[53,54,55]

AEAD can be identified through coronal and sagittal sections of CT scans. The sagittal section provides the best visualization of the protrusion degree of the right AEA into the ethmoid sinus and AEA segment groove. According to Lannoy-Penisson et al., AEA canal is classified based on its relationship with the skull base, with three levels, namely, level I on the roof of the ethmoid, level II under the ethmoid roof and protruding, and level III connecting AEA canal to the ethmoid sinus roof with a distance of approximately 5 mm.[53,54,55]

The location of AEA is relatively safer when it is situated in the ethmoid fovea or lateral lamella. However, when there is supraorbital pneumatization or anterior ethmoid cells in the superior anterior ethmoid depression, AEA becomes more prominent in the ethmoid sinus and more susceptible to injury. AEA injury can lead to accelerated retroorbital hematoma due to retraction of the injured blood vessel into the orbit. Cauterization of AEA is necessary to prevent further complications.[53,54,55]

Variations in prevalence of AEAD is attributed to differences in ethmoid roof configurations among different ethnic and racial populations. Additionally, variations in research methods, such as anatomical dissection techniques with microscope or endoscope magnification, can contribute to different sensitivity and results.[53,54,55]

CONCLUSION

In conclusion, the predominant anatomical variations observed in this research pertaining to the nose and paranasal sinuses was septal deviation, accounting for 90.8% of cases. Among the various anatomical variations researched, three factors, namely septal deviations, concha hypertrophy, and Agger Nasi Cells, were found to be the most common predisposing factors for CRS. Furthermore, three specific anatomical variations, namely Keros type II, sphenoid sinus sellar, and Kuhn type I, were identified as the most complicating factors for surgery. These anatomical variations warrant attention in management of CRS. Further research is needed to explore the potential association between the nose and paranasal sinuses anatomical variations, CRS occurrence, and surgical complications.

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