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Computed Tomography Scans as an Objective Measure of Disease Severity in Chronic Rhinosinusitis

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Abstract

Objectives—A truly objective method of measuring disease severity in chronic rhinosinusitis (CRS) has only recently existed. We evaluated computed tomography (CT) scans of CRS patients using this novel objective 3D computerized system and compared results with a novel 2D computerized analysis of a single coronal slice through the osteomeatal complex (OMC) and subjective methods including Lund-Mackay and Zinreich's modified Lund-Mackay.

Study Design—Prospective multicenter study.

Setting—Two academic tertiary referral centers.

Subjects and Methods—Forty-six adults with a diagnosis of CRS underwent CT examination and received an intramuscular triamcinolone injection, dosage weight dependent, followed by CT scan 4 to 5 weeks later. Recruitment lasted 21 months. Scans were evaluated with all 4 scoring methods over 5 months.

Results—The Lin's concordance class correlation (CCC) of the OMC method revealed the best correlation to the 3D volumetric computerized values (0.915), followed by the Zinreich (0.904) and Lund-Mackay methods (0.824). Posttreatment results demonstrated that both the OMC

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Author Contributions

Micah M. Likness, lead author, study design, data collection and analysis, critical revision and approval; **John F. Pallanch**, manuscript writing, study design, experimentation, teaching, methodology, data collection and analysis, critical editing and approval; **David A. Sherris**, teaching and design, study conception, revision, and approval; **Hirohito Kita**, experimental design and methodology, teaching, study conception, manuscript editing and approval; **Terry L. Mashtare Jr**, data analysis and interpretation, manuscript drafting and approval; **Jens U. Ponikau**, study conception and design, data analysis, manuscript editing and approval.

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(0.824) and Zinreich's (0.778) methods had strong agreement with the 3D volumetric methods and were very sensitive to change, whereas the Lund-Mackay (0.545) had only moderate agreement.

Conclusion—Computerized CT analysis provides the most comprehensive, objective, and reproducible method of measuring disease severity and is very sensitive to change induced by treatment intervention. A 2D coronal image through the OMC provides a valid, user-friendly method of assessing CRS and is representative of CRS severity in all sinuses. Zinreich's subjective method correlated well overall, but the Lund-Mackay method lagged behind in disease representation and sensitivity to change.

Keywords

chronic rhinosinusitis; computed tomography; staging system; volumetric scoring; disease severity; objective

No current validated objective endpoint of successful treatment of chronic rhinosinusitis (CRS) exists. The Food and Drug Administration's guidance statement of clinical development programs for sinusitis outlines the necessity for existence of validated objective measures for CRS.^{1,2} Imaging techniques are one method of objectively measuring disease status and change in the paranasal sinuses. Summary Statement 27 from "A Practice Parameter Update" by the Joint Council of Allergy, Asthma, and Immunology (2005) stated that computed tomography (CT) is the optimal technique for evaluating the ethmoid sinuses and for preoperative evaluation of the nose and paranasal sinuses, including assessment of the osteomeatal complex (OMC) areas.³ The 2007 American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) "Clinical Practice Guidelines" for adult sinusitis emphasized the requirement of using radiographic imaging to quantify inflammation.¹

The necessity of quality staging systems for evaluation of severity and treatment response in sinusitis are not new concepts. Caldwell outlined this as early as 1893.^{4,5} A century later, Kennedy⁶ proposed that surgical outcomes could be affected by assessment of disease extent by staging systems. The following year, the Lund-Mackay staging system was described as a simple tool to guide treatment intervention.⁷ Multiple scoring systems now exist for assessing disease status,^{5,7–15} and their ability to standardize disease severity has globally fostered objective analysis of treatment interventions and outcomes. Oluwole et al¹⁴ determined the Lund-Mackay to be the best system for clinical practice based on interscorer agreement and ease of use after analyzing 4 systems: Jorgensen, May and Levine, Lund and Mackay, and Newman. Zinreich¹⁵ summarized 4 staging systems, the Kennedy Staging System, the Harvard Staging system, the Levine and May Staging system, and the Lund-Mackay staging system, in 2004 and noted that the Lund-Mackay system was the most widely accepted, objective, and reproducible of those systems but that it has the drawback of the inability to "subgrade" the volume of inflammatory disease. He thus proposed modifications to further stratify grade levels.^{8,15}

Despite the existence of multiple scoring systems, a truly objective method of measuring disease severity of CRS with CT scans was only recently described.¹⁶ Theoretically, 3-dimensional (3D) CT scanning scoring systems should provide the most complete objective measurement of the status and volumetric contents of the sinuses available through imaging.

Because of its comprehensive nature, 3D scoring techniques lack both simplicity and ease of use.

We evaluated disease severity of CRS patients using 4 CT scoring methods: Lund-Mackay, Zinreich modification of Lund-Mackay, a novel 3D digital format system to yield a numerical score of disease status using a complete volumetric percentage of disease measurement of all sinuses, and a novel 2D digital format system using volumetric measurement of a single coronal slice image through the OMC. Study objectives were to identify if correlation exists among results of scoring systems on measurements of disease severity and response to treatment intervention and which system is the most complete, valid, and user-friendly method available. The primary hypothesis was that a 3D CT scanning scoring system provides the most comprehensive and objective method of measuring disease severity and successful response to treatment in patients with CRS. The secondary hypothesis was that a 2D single-slice coronal image through the OMC provides a valid, objective, user-friendly method of assessing CRS that is representative of the inflammation in all sinuses.

Materials and Methods

Institutional Review Board Approval

This study received exemption from the University at Buffalo Health Sciences Institutional Review Board.

Study Design

This study was a multicenter review of data collected from a prospective nonrandomized trial of CRS patients.

Subjects

Forty-six male and female adult patients were included who met the AAO-HNS definition for CRS, demonstrated at least 5 mm of mucosal thickening in some of the sinuses, had no air-fluid levels on CT, and had no contraindication to treatment with Kenalog (triamcinolone) intramuscularly or follow-up CT scanning. Patient recruitment lasted 21 months, and CT analysis occurred later over a 5-month time frame. Thirty-seven patients had visible nasal polyps, 45 had frontal sinus disease, and 43 patients had sphenoid disease.

Experimental Procedures

Patients underwent pretreatment CT examination of the sinuses and then received a single dose of triamcinolone (Kenalog) injection, 60 mg (body weight <70 kg) or 80 mg (body weight ≥ 70 kg), to the gluteus maximus, followed by a posttreatment CT scan 4 to 5 weeks later. Analysis of CT data was performed with Analyze 6.0 to 11.0 (Mayo Biomedical Imaging Resource) software, using the 4 unique CT staging systems reviewed below in Tables 1 and 2 and Figures 1 and 2.

The Lund-Mackay staging system (Table 1) assigns a value of 0, 1, or 2 to each of the following sinuses: maxillary, anterior ethmoid, posterior ethmoid, frontal, and sphenoid.

Score assignments are 0 if the sinus is totally patent, 1 if the sinus is partially opacified, and 2 if the sinus is completely opacified. The OMC is scored either 0 if not occluded or 2 if occluded. The maximum score for each side is thus 12, with a total score determined out of 24.

Zinreich modified the Lund-Mackay staging system (Table 2) by increasing the scale to range from 0 to 5. Each sinus is assigned a score based on the percentage of opacification from mucosal thickening as follows: 0 = 0%, 1 = 1% to 25%, 2 = 26% to 50%, 3 = 51% to 75%, 4 = 76% to 99%, and 5 = 100% or completely occluded. The OMC is given a score of 0 to 2, depending on whether it is completely patent, partially obstructed, or completely obstructed. Similar to the Lund-Mackay system, each side is graded and their sum is the total score out of maximum of 54.

The 3D volumetric scoring system method (Figure 1) uses the set of heuristics previously developed by Pallanch et al¹⁶ to consistently repeat segmentation, the definition of the 3D space occupied by the sinuses, by analyzing the total outline and volumetric contents of the sinuses. Segmentation defined the voxels of CT data, cubes of 0.4 mm per edge, which comprised each sinus. Optimal range of Hounsfield units, a radiodensity measure of tissue on CT scans, were previously determined to be -1024 to -500 for air volume and -500 to +250 for tissue or disease volume.¹⁶ All slices that define an individual sinus are segmented by outlining the borders starting at the lowest level of the sinus and progressing upward to the most superior slice. Segmentation was manual as no automated system was available during the study, but tools to speed the process exist. Parts of this process can use automation to increase efficiency. Once the entire sinus has been segmented, the total volume, air volume, and volume of disease can be calculated. Each individual sinus total volume percentage of disease was then calculated by the following equation: $\text{percentage disease volume} = 100 \times (\text{volume disease}) / (\text{volume disease} + \text{volume air})$. The 2D coronal OMC method uses the same principles and software but segments only a single coronal slice through the OMC. The user requires a knowledgeable instructor and several hours of instruction. The only time-consuming 3D segmentation is the first one done for a given patient, which takes 1 to 2 hours once proficient, and after that, the defined sinus volumes can be used for any further studies on the same patient. The 2D coronal OMC method uses the same principles and takes only 10 minutes per patient once proficient.

The 2D coronal OMC scoring system (Figure 2) uses a volumetric segmentation of a single coronal CT image standardized by review of the coronal cut through the OMC, showing the maxillary sinus ostium and supported by distinctive bony landmarks unique for that plane. The selected slice chosen had the maximal height of the ethmoid and width of the maxillary sinuses while visualizing the OMC. Calculation of the percentage disease volume for this slice occurred by the same method as the 3D equation after a single segmentation to include all sinonasal contents visible. Bony boundaries were the skull base and cribriform plate superiorly, the medial and inferior orbital walls, the lateral and inferior maxillary sinus walls, and the bony maxilla of the nostril sill to the midline maxillary crest.

Statistical Methods

Statistical analysis of data was performed by the SUNY UB Biostatistics Department. Spearman rank correlations examined the associations between methods for determining disease percentage. Lin's concordance class correlation and corresponding bootstrap 95% confidence intervals were computed to compare the measure of agreement among the 4 methods for determining disease proportion. Each analysis was performed for pretreatment, posttreatment, and differences between pretreatment and posttreatment groups.

Results

The Lin's concordance class correlation (CCC) of pretreatment comparison (Figure 3) of staging systems revealed all methods to have strong correlation. Note that CCC values from 0 to 0.4 are considered poor agreement, 0.4 to 0.7 are considered moderate agreement, 0.7 to 0.9 are considered high agreement, and >0.9 have very high agreement. The 2D coronal OMC method revealed the best correlation with the 3D volumetric system values (0.915), followed by the Zinreich (0.904) and Lund-Mackay methods (0.824). The Zinreich and Lund-Mackay systems had the third highest correlation (0.864). In general, confidence intervals increased with decreasing CCC.

Comparison of posttreatment correlation (Figure 4) revealed the Zinreich modification to have the best correlation to the 3D volumetric Scoring system (0.837) ahead of the 2D OMC method (0.767). This may have been secondary to the 2D OMC method's being less inclusive. The remaining comparisons showed only moderate correlation and increased confidence intervals between values.

Comparison of the difference between pre- and posttreatment results (Figure 5) demonstrated that both the 2D coronal OMC (0.824) and Zinreich (0.778) systems had strong agreement with the 3D volumetric scoring system and were very sensitive to change, whereas the Lund-Mackay method (0.545) had only moderate agreement. The 2D OMC and Zinreich methods also have strong correlation with each other (0.788). The mean, range, and standard deviation for each method's results on both pretreatment and posttreatment analysis can be found in Table 3.

Discussion

We evaluated disease severity and response to treatment intervention of CRS patients' CT scans with the most popular and user-friendly method currently used (Lund-Mackay) and a variation of this method created to better subgrade diseases and thus increase sensitivity (Zinreich) against 2 novel objective computerized methods (3D volumetric and 2D coronal OMC) to determine how well results of these systems correlated in determining severity of disease and response to treatment. There is little doubt that the 3D volumetric scoring method, which is able to yield a numerical score of total disease percentage by complete volumetric measurement of all sinuses, is the most accurate and objective scoring tool yet created. By setting the 3D volumetric scoring system as the standard against which to compare the other systems, we can determine how well results of these other methods depict disease status and sensitivity to change.

All methods tested were found to be replicable and with satisfactory intersystem agreement when compared with the 3D method on pretreatment scoring. However, there was a pronounced difference in the strength of agreement between systems, which became more apparent on subsequent data sets. The 2D coronal OMC method had the best correlation on pretreatment and the difference between pre- and posttreatment analysis. The Zinreich system had the second best agreement on analysis pretreatment and difference data sets and had the best agreement on posttreatment examination. When comparing each system to the others, the 3D volumetric, 2D coronal OMC, and Zinreich systems had the strongest correlations with each other on all 3 analyses. When looking only at the Lund-Mackay and Zinreich methods, the best agreement was seen on pretreatment scoring, but this decreased on subsequent analysis of posttreatment and difference values. The lack of correlation between the Lund-Mackay results with the actual percentage volume of disease calculated by the 3D volumetric scoring system is consistent with previous findings.¹⁶

Correlation differences between staging systems tested reflect their sophistication and inclusiveness. The Lund-Mackay staging system was intentionally simplified by design to minimize subjective variation in interpreting the CT scans and to allow quick, competent use by those without formal radiology training.^{12,17} Although for years it has been the most widely accepted, objective, and reproducible scoring system, it does have, among others, the limitation of the inability to subgrade the volume of inflammatory disease.¹⁵ This affects its sensitivity to change, which is important for outcome measurement. Zinreich attempted to enhance the sensitivity of Lund-Mackay by increasing the scale from 0–2 to 0–5.^{7,8,15} This improved sensitivity to change but does decrease the facility of application of this system as predicted by the original creators of the Lund-Mackay system¹² and allows variation of interpretation of disease severity, especially when determining whether a sinus is 74% or 76% occluded, which yields differing score values. While describing the Lund-Mackay system, Lund and Kennedy¹² stated that “simplicity is the key to usefulness.” While we do not argue that the Lund-Mackay staging system was the most simple and easy to master of the methods tested, our findings indicate decreased correlation with more comprehensive methods. Although prior literature has stated the Lund-Mackay and Zinreich scoring systems to be more objective than others, ultimately both remain subjective and dependent on evaluator skill level and prone to bias. Zinreich¹⁵ noted that the ideal staging system for CRS objectively quantifies the disease volume, is easy to use and reproducible, and considers patency of specific anatomic bottlenecks.

Both objective computerized methods tested are replicable and address the OMC. The only task that allows subjectivity is the outlining of sinus boundaries during segmentation, a skill quickly obtained by tracing over the bony landmarks. Deviation outside of these landmarks could falsely increase the percentage of disease score by incorporating orbital, brain, or infraorbital nerve tissue, which has similar density to mucosa on CT. Once the initial outlining is complete, multiple editing tools allow exact delineation of sinus boundaries for each segmentation. After each slice of the sinus is segmented (or in the case of the 2D coronal OMC method, the single slice chosen is segmented), the total volume, volume of air, and volume of disease are calculated. By recognizing different Hounsfield units, the 3D and 2D computerized methods are able to discern the percentage disease volume through the equation mentioned previously in Figure 1, percentage disease volume = $100 \times (\text{volume}$

disease)/(volume disease + volume air). For the 3D method, a percentage disease volume is calculated for each sinus, from which the mean is the total volume of disease for that patient. The 2D method derives a single volume calculation incorporating bilateral maxillary and ethmoid sinuses and OMC. Thus, beyond segmenting correctly, the actual scoring of disease is outside the influence of the evaluator.

Of the 46 CRS patients in this study, 37 had visible nasal polyps, 45 patients had frontal sinus disease (2 others had absent frontal sinus unilaterally but disease in the present side), and 43 patients had sphenoid disease (1 other patient had unilateral absent sphenoid but complete opacification of the other side). By nature, the 2D coronal OMC scoring system does not evaluate the sphenoid or frontal sinus, and we are not stating that it does directly assess either the presence or the severity of disease in these sinuses. One of the very interesting findings of this study is that in a population of 46 patients with CRS, including a majority with sphenoid and frontal disease, a method examining a single coronal slice through the OMC correlated well with 3 methods that do assess disease in these sinuses and correlated the best with the most comprehensive scoring system analyzed. Thus, our results found it to be a reliable diagnostic tool for CRS disease severity and response to treatment, outside of the presence of isolated frontal or sphenoid pathology.

Software availability is an obvious and realistic limitation of the computerized methods. Three-dimensional analysis of sinonasal CT data is a relatively new science, having recently gained attention as a tool to improve preoperative planning and intraoperative success in facial plastic surgery¹⁸ and by mapping of frontal sinus and nasofrontal ducts.^{17,19–21} As 3D CT analysis is in its relative infancy, interested parties are hampered by a paucity of different software and limited access to existing programs. To our knowledge, use of such programs to facilitate scoring systems for CRS had not been described until the recent 3D volumetric scoring paper.¹⁶ An additional constraint is the time required both to learn and to perform the technique of volumetric calculation. This is inevitable with a system as comprehensive as 3D volumetric segmentation of every CT slice. The challenge of ease of use in the 3D system is what fostered the idea that a single coronal slice through the OMC may be representative of the entire disease status of the sinuses and dramatically cut down on the learning curve to comprehend and perform each analysis.

Other limitations not unique to computerized analysis but present in all CT scoring systems are cost, patient risk from radiation exposure, and that the CT image represents a static picture of the variable and changing topography of the sinuses. The nasal cycle and hypertrophic turbinates were of particular concern with the 2D coronal OMC system, where thickened septal mucosa or hypertrophied turbinates could falsely increase a disease percentage score. This was not found to significantly affect the correlation of this method with the other systems tested. One alleged problem is the poor correlation of CT with symptoms and quality-of-life (QOL) information.^{12,15} The report regarding 3D computed CT scoring showed there was a correlation between change in disease on CTs with change in CRS symptoms, polyp size by endoscopy, and disease-specific QOL parameters and that the correlation is significantly better for 3D volumetric staging over the Lund-MacKay staging system.¹⁶ Future investigations should examine if by calculating the quantity of disease volume by the 2D coronal OMC system there is also a better correlation with patient

symptoms. In the future, if an automated system can be developed with decreased time constraints and improved software availability and ease of use, then 3D volumetric computerized analysis of CT scans will become the gold standard of measurement of disease extent and response to treatment in CRS. Until then, the easier and more practical objective method is the 2D coronal OMC method, and the best subjective method is the Zinreich-modified Lund-Mackay method.

Conclusion

Computerized CT analysis provides an objective and reproducible method of measuring disease extent in CRS and is very sensitive to change induced by treatment intervention. The 3D volumetric CT scoring system provides the most comprehensive and objective method of measuring disease extent and successful response to treatment in patients with CRS but may have decreased use secondary to its complex nature and limitations from lack of technique knowledge and software access. The 2D coronal OMC system provides a valid, less complex method of assessing CRS and correlates well with CRS severity in all sinuses. The subjective Zinreich method correlated well with the objective 2D and 3D methods overall. Despite its popularity and ease of use, the Lund-Mackay staging system lagged behind the other methods tested in disease representation and sensitivity to change.

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Figure 1.

Three-dimensional (3D) volumetric scoring system. The 3D space and volumetric contents of a sinus are defined by segmentation. The percentage disease volume is calculated by the following: $\text{percentage disease volume} = 100 \times (\text{volume disease}) / (\text{volume disease} + \text{volume air})$.

Figure 2.

Two-dimensional (2D) coronal osteomeatal complex (OMC) scoring system. The 2D coronal OMC scoring system uses a volumetric segmentation of coronal computed tomography image standardized by review of the coronal cut through the OMC.

Figure 3.

Pretreatment comparison of computed tomography staging systems.

Figure 4.
Posttreatment comparison of computed tomography staging systems.

Figure 5.

Difference between pretreatment and posttreatment comparison of computed tomography staging systems.

Table 1

Lund-Mackay staging system.

Lund-Mackay Staging System	
Scores Each Sinus 0–2, OMC 0 or 2	
0 = Normal, 1 = Partial Opacification, 2 = Total Opacification	
Right	Left
Maxillary	
Anterior ethmoid	
Posterior ethmoid	
Sphenoid	
Frontal	
Osteomeatal complex	
Total (maximum = 24)	

Table 2

Zinreich staging system.

Zinreich Staging System (Modification of Lund-Mackay)	
Scores Each Sinus 0–5, OMC 0–2	
0 = 0%, 1 = 1%–25%, 2 = 26%–50%, 3 = 51%–75%, 4 = 76%–99%, 5 = 100%	
Right	Left
Maxillary	
Anterior ethmoid	
Posterior ethmoid	
Sphenoid	
Frontal	
Osteomeatal complex	
Total (maximum = 54)	

Table 3

Statistical comparison of computed tomography analysis methods.

Staging/Scoring System	Treatment Time Frame					
	Mean		Range		Standard Deviation	
	Pre	Post	Pre	Post	Pre	Post
Lund-Mackay	14.33	10.63	2–23	0–16	4.68	3.57
Zinreich	31.91	19.96	7–53	4–40	13.35	9.54
3D Volumetric, %	69.1	50.4	28–97	23–87	21.4	15.9
2D Coronal osteomeatal complex, %	65.3	42.4	12–100	11–92	26.4	20.7