Glucocorticoid Receptor Isoform Expression in Peripheral Blood Mononuclear Leukocytes of Patients with Chronic Rhinosinusitis

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Abstract

BACKGROUND—In several inflammatory disorders, altered peripheral blood mononuclear leukocyte (PBML) glucocorticoid (GC) receptor isoform expression has been associated with GC resistance and disease severity. However, it is unclear if PBML GC receptor isoforms are expressed differentially and are associated with worsened disease severity in chronic rhinosinusitis (CRS).

METHODS—PBMLs were isolated from control (n = 8), CRS without nasal polyps (CRSsNP) (n = 8), atopic CRS with nasal polyps (CRSwNP) (n = 8), non-atopic CRSwNP (n = 8), and allergic fungal rhinosinusitis (AFRS) (n = 8) patients. Demographics, atopic status, asthmatic status, Sino-Nasal Outcomes Test (SNOT)-22 scores, Lund-Kennedy nasal endoscopy scores, Lund-Mackay sinus CT scores, Kennedy Osteitis scores, and GC utilization 6 months postoperatively were collected. Intracellular immunostaining was then performed for functional GC receptor α (GCR α) and non-functional GC receptor β (GCR β), followed by flow cytometry analysis of geometric mean fluorescent intensity (MFI) and the percent of cells expressing each GC receptor isoform.

RESULTS—Compared to controls, each CRS subtype had decreased PBML GCR α and GCR α :GCR β MFI expression, but no difference in GCR β expression. Decreasing PBML GCR α in AFRS was associated with increasing Lund-Mackay sinus CT scores ($r = -0.880$, $p = 0.004$). No significant associations were found between GC receptor isoform expression and other clinical measures.

CONCLUSIONS—CRS patients have reduced functional PBML GCR α expression and decreased GCR α :GCR β compared to controls. Reductions in GCR α in AFRS are associated with worsening Lund-Mackay sinus CT scores. The clinical implications of decreased functional GC receptor expression merits further investigation.

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Keywords

Chronic rhinosinusitis; steroid therapy; quality of life; flow cytometry

INTRODUCTION

Chronic rhinosinusitis (CRS) is characterized by prolonged and exaggerated sinonasal inflammation in susceptible hosts in response to a variety of environmental triggers.^{1–3} In a recent international consensus statement topical glucocorticoids (GCs) received a grade A recommendation for all forms of CRS while oral GCs received a grade A recommendation for CRSwNP.⁴ At present, there is limited understanding of the underlying pathophysiology of systemic GC resistance in CRS. Several mechanisms have been proposed, including altered GC receptor isoform expression.^{5–15} While still controversial at this point, there is a growing body of evidence that suggests that altered GC receptor isoform expression may contribute to GC resistance.^{16–20}

GC receptor functionality depends on the expression of its two known isoforms. The functional GC receptor α (GCR α) isoform mediates GC's characteristic anti-inflammatory effects. The nonfunctional GC receptor β (GCR β) isoform neither binds GCs nor participates in transactivation, though it is known to inhibit GCR α transactivation²¹ through the formation of GCR α -GCR β heterodimers.⁵ Both GCR α and GCR β are expressed in sinonasal tissue as well as systemically.^{17,22–30} Both decreased sinonasal GCR α and increased GCR β have been implicated in poor CRS treatment response,^{9,25,27,28,30–32} but it is unknown if there is differential systemic GCR α and GCR β expression in CRS. Peripheral blood mononuclear leukocytes (PBMLs) are ideal for studying systemic GC isoform expression and associated resistance due to PBMLs' role in immunoregulation and the preponderance of studies using PBMLs to examine GC resistance in other chronic inflammatory diseases.^{16–20} The objective of this study was to assess systemic GCR α and GCR β expression in PBMLs of patients with CRS without polyps (CRSsNP), atopic CRS with nasal polyps (CRSwNP), non-atopic CRSwNP, and allergic fungal rhinosinusitis (AFRS) and determine if this may influence clinical metrics.

PATIENTS AND METHODS

Patient Enrollment, Inclusion, and Exclusion Criteria

Institutional Review Board approval at the Medical University of South Carolina was obtained and all patients provided written informed consent (HR#14124). Subjects were recruited from patients who had failed appropriate maximal medical therapy⁴ for CRS and elected to undergo endoscopic sinus surgery. All CRS patients were taking intranasal GCs as part of their care. Analysis was performed on control subjects without CRS and the following four CRS subtypes: CRSsNP, atopic CRSwNP, non-atopic CRSwNP, and AFRS. Control subject peripheral blood samples were obtained from patients having surgery for cerebrospinal fluid (CSF) leaks or non-secreting pituitary tumors and were confirmed to have no sinus disease on preoperative imaging. CRS and AFRS were defined according to published guidelines³³ and the Bent and Kuhn criteria, respectively.³⁴

Exclusion criteria for all aspects of this study included the use of oral steroids, antifungal medications, or immunotherapy within 4 weeks prior to sample collection; self-reported current smoking or smoke exposure measured by analyzed hair nicotine levels;³⁵ aspirin sensitivity; ciliary dysfunction; autoimmune/inflammatory disease; cystic fibrosis; immunodeficiency; or age less than 18.

Sample Procurement and Processing

Peripheral blood was collected at the time of IV line placement, prior to the administration of anesthesia or intraoperative systemic GCs. Briefly, blood was collected in Vacutainer collection tubes containing ethylene diamine tetra-acetic acid (K2EDTA) and was centrifuged at 535 x g to separate out plasma. The remaining fraction was mixed with equal volumes of Hanks Balanced Salt Solution (HBSS) then layered over Ficoll-Hypaque and centrifuged for 15 minutes at 120 x g. PBMLs were then removed from the buffy coat, washed twice in phosphate-buffered saline (PBS) then stored in freezing media (10% dimethyl sulfoxide [(DMSO)/90% fetal bovine serum] in liquid nitrogen until later use.

Immunostaining and Flow Cytometric Analysis

Immunostaining and flow cytometric analysis were conducted as previously described.^{36–39} Briefly, each sample was washed with PBS and aliquoted at 100,000 cells per well on a 96 well plate. Viability staining was performed with a Zombie NIR™ Fixable Viability Kit (Biolegend, San Diego, CA, USA) for 30 minutes on ice. Cells were then fixed and permeabilized in a volume of 100 µL (Intracellular Fixation and Permeabilization Buffer, Foxp3/Transcription Factor Staining Buffer Set, eBioscience™, San Diego, CA, USA) for 45 minutes on ice. Nonspecific binding was blocked by incubating PBMLs in PBS with 1 mg/mL DNase buffer with 1% bovine serum albumin (BSA) then PBS with 1 mg/mL DNase buffer and Human Fc Receptor Binding Inhibitor Monoclonal Antibody (eBioscience™, San Diego, CA, USA) for 5 minutes each, respectively. Cells were then incubated with 100 µL 1x permeabilization buffer (eBioscience™, San Diego, CA, USA) containing anti-GCRα monoclonal antibody (Abcam, Cambridge, MA, USA), anti-GCRβ monoclonal antibody (Abcam, Cambridge, MA, USA) or a secondary antibody alone [F(ab')₂-goat anti-rabbit IgG secondary antibody, PE, eBioscience™, San Diego, CA] on ice for 30 minutes, washed twice with permeabilization buffer, then incubated with 100 µL permeabilization buffer containing anti-IgG-PE for 20 minutes. Cell pellets were extensively washed to remove unbound secondary antibodies, then were re-suspended in 200 µL PBS with 1 mg/mL DNase buffer. Following this, eight parameter flow cytometry was performed using a Guava 8HT flow cytometer and results were analyzed using FCS Express software (De Novo Software, Glendale, CA). Cell viability was determined by Zombie NIR™ staining and only Zombie NIR™ negative cells were included for analysis. Average cell viability was 82% with a standard deviation of 8.6%. Final statistical analysis included matched isotype control subtraction for all samples.

Sinonasal-Specific Clinical Metrics

SNOT-22 surveys measuring CRS-specific quality of life were completed on the day of sample collection.⁴⁰ Rigid sinonasal endoscopy was performed preoperatively by the attending surgeon of record and quantified according to the Lund-Kennedy nasal endoscopy

scoring system.⁴¹ Radiographic disease severity was assessed by 2 independent blinded graders using the Lund-Mackay⁴² and Kennedy Osteitis scoring systems.⁴³ Unequal scores were resolved by consensus. The number of oral GC courses during the first 6 months postoperatively were recorded.

Statistics

Statistical analysis was conducted using GraphPad Prism 7 software (La Jolla, CA). For each CRS subtype descriptive statistics were computed for age, gender, race, atopic status, asthmatic status, and all clinical metrics—SNOT-22 scores, Lund-Kennedy scores, Lund-Mackay scores, Kennedy Osteitis scores, 6-month post-operative GC utilization, and GC receptor isoform expression. Geometric mean fluorescent intensity (MFI) of GC receptor isoform expression was the primary outcome measure due to its representativeness of the absolute expression of GC isoforms among the viable cell population. The percent cells positive for each GC receptor isoform was also recorded and analyzed as a secondary outcome.

For the GC receptor isoform expression data, first normality was assessed with D'Agostino and Pearson omnibus normality testing. Following this one-way analysis of variance (ANOVA) or Kruskal-Wallis testing was performed for parametric and non-parametric continuous/ratio data, respectively. Pearson's and Spearman's correlation coefficients were then calculated for parametric and nonparametric data respectively to evaluate the relationship between GC receptor isoform expression—GCR α , GCR β , and GCR α :GCR β —compared to age and all clinical disease severity measures within each CRS subtype and among all CRS subtypes. Post-hoc Holm-Sidak's and Dunn's multiple comparison testing—for parametric and non-parametric data, respectively—were then performed with reporting of multiplicity-adjusted p-values between controls and each CRS subtype for GCR α , GCR β , and GCR α :GCR β . Unpaired t-testing and Mann-Whitney testing assessed the relationship of GC receptor isoform expression compared to gender, race, atopic status, and asthmatic status for parametric and non-parametric data, respectively. Chi-square analysis evaluated the distribution of subjects utilizing oral GCs in the 6 months postoperative period for each CRS subtype. Unpaired t-testing and Mann-Whitney U testing—for parametric and non-parametric data—compared the mean GCR α MFI between patients using oral GCs versus those not using oral GCs postoperatively. Statistical significance was defined as $p < 0.05$. All testing was two-tailed.

Power Analysis

To the authors' knowledge, no study has quantified GC receptor isoform expression in PBMLs of CRS to provide data for sample size calculation. Based on our prior flow cytometric analysis of sinonasal tissue (unpublished data) we expected to observe a difference of 25% between control and CRSwNP patients for the primary outcome of PBML GCR α MFI. This expected difference combined with an anticipated within subject standard deviation of 15% (effect size = 1.67) would require 7 subjects per group to obtain 80% power at a significance level of $\alpha = 0.05$. Thus, our sample size of 8 subjects per group was appropriate.

RESULTS

Patient Demographics and Clinical Parameters

We examined PBMLs from patients with CRSsNP, atopic CRSwNP, non-atopic CRSwNP, AFRS, and controls to quantify GC receptor isoform expression. Descriptive statistics of demographics and clinical measures are shown in Table I. We observed that 13 (41%) of the CRS patients underwent prior sinus surgery. Notably, as expected, the AFRS cohort was younger (mean 27.5 years vs 50.3 years, 95% confidence interval (CI) difference 10.75 to 34.75, $p = 0.005$) and contained a greater proportion of non-Caucasian patients (75% vs 39%, OR 7.67, 95% CI OR 1.30–45.31, $p = 0.036$). The CRSsNP cohort exhibited lower Lund-Kennedy nasal endoscopy and Lund-Mackay sinus CT scores than the other CRS subtypes, as anticipated given the association between polyposis status and higher scores with these metrics.

Compared to Control Subjects Each CRS Subtype Has Decreased GCR α and Decreased GCR α :GCR β

Next, we examined expression of PBML GCR α among each CRS subtype and, compared to controls, we found that each CRS subtype demonstrated decreased PBML GCR α MFI expression (Fig 1 and Fig. 2a). There was no difference in GCR β expression for any CRS subtype compared to controls by analysis of GCR β MFI (Fig. 2b) or of percent cells expressing GCR β (Fig 3b). Following this, evaluation of the ratio of PBML GCR α :GCR β MFI revealed that each CRS subtype demonstrated a decreased PBML GCR α :GCR β MFI ratio compared to controls (Fig. 2c). As shown in Figure 3a, analysis of percent cells expressing GCR α among total viable cells revealed that atopic CRSwNP, non-atopic CRSwNP, and AFRS were each significantly different from controls.

PBML GCR α Expression and Clinical Metrics

GCR α MFI expression inversely correlated with Lund-Mackay sinus CT scores in AFRS patients, thus indicating that AFRS patients with lower GCR α expression demonstrated greater disease burden on their CT scans ($r = -0.880$ and $p = 0.004$) (Fig. 4a). No significant associations were noted between GCR α MFI expression and Lund-Mackay sinus CT scores in other CRS subtypes (Fig. 4b, c).

No significant associations were noted between GCR α and SNOT-22, Lund-Kennedy endoscopy scores or Kennedy-Osteitis scores. [$(r = 0.01, p = 0.94)$, $(r = -0.15, p = 0.44)$, $(r = -0.16, p = 0.38)$, respectively]. GCR α MFI data comparing subjects who required oral GCs in the 6 months post-operatively versus those who did not is shown (Fig. 5). There was no statistically significant difference between GCR α MFI between subjects requiring postoperative oral GCs versus those who did not.

DISCUSSION

A number of studies have linked GC receptor isoform expression profiles with GC resistance at the local and systemic level in various inflammatory diseases, and at the local level in CRS, but this is the first study to the authors' knowledge to investigate the relationship of

systemic GC receptor isoform expression to disease severity in CRS.
5,8,17,22–25,27,28,30–32,44–47

Compared to controls, each CRS subtype demonstrated significantly decreased PBML GCR α MFI and percent cells GCR α ⁺, with the exception of percent cells GCR α ⁺ CRSsNP. These results agree with those seen in other studies of CRSwNP polyp tissue,^{9,27,31} asthmatic PBMLs, and systemic lupus erythematosus PBMLs⁴⁸ where decreased GCR α was associated with GC resistance.²³ The present study also observed that decreasing GCR α was correlated with worsening disease severity on Lund-Mackay CT scoring in AFRS patients. Next, we assessed GCR β expression due to its known dominant negative effect on GC response²¹ and the association of increased GCR β expression with GC resistance in CRSwNP polyp tissue,^{28,30} asthmatic lung tissue,^{44,49} asthmatic PBMLs,^{23,46} ulcerative colitis PBMLs,¹⁹ and mouse hybridoma cells.⁵⁰ There was no difference in GCR β expression between controls and any CRS subtype by analysis of geometric MFI or of percent GCR β ⁺ cells. PBML GCR α :GCR β scores were lower in each CRS subtype compared to controls, which is consistent with prior reports in CRSwNP polyp inflammatory cells^{9,25,30–32} and in asthmatic PBMLs.²⁴ This ratio is important to evaluate due to the known dominant negative effect of GCR β , which modifies GCR α 's functional activity.⁵¹ Our finding that PBML GCR α was decreased in CRS compared to controls—without any differential expression of GCR β —potentially suggests that GC resistance could manifest through GCR α -associated mechanisms. With fewer cells expressing GCR α , there may be fewer cells capable of responding to GCs.

The present study's use of PBMLs is significant to our understanding of CRS pathophysiology and management. Since systemic GCs are recommended for the short-term treatment of CRSwNP along with AFRS—and serve as an option for CRSsNP⁴—it is important to understand mechanisms of therapeutic response and resistance to treatments. Furthermore, we are intrigued by the potential a systemic GC receptor isoform test may offer prognostic information and optimize therapy. A test using peripheral blood samples is likely to have a more widespread clinical application than a test relying on sinonasal tissue, with the latter more difficult to obtain and likely relegated primarily to the operative setting. Given that this is the first study to assess systemic GC receptor isoform expression in CRS, the utility of a peripheral blood GC isoform test to guide clinical practice requires further investigation before any definitive recommendations can be made.

AFRS represents a distinct CRS phenotype⁵² characterized by a significant Th2 cytokine response in PBMLs exposed to fungal antigens.⁵³ Our finding that AFRS PBML GCR α expression inversely correlates with Lund-Mackay sinus CT scores suggests that patients with AFRS may be more affected than other CRS subtypes by PBML GCR α expression. This may contribute to the AFRS patients' greater clinical response to oral GCs as compared to CRSwNP patients.⁵⁴ However, to make any definitive association between these two concepts would require further studies evaluating GC receptor isoform expression among AFRS patients whose symptoms are controlled without surgical intervention, the role of GC receptor isoform expression in AFRS in response to inflammatory stimuli, and clinical response to GCs among AFRS patients whose GC receptor isoforms have been measured.

The lack of significant correlations between GC receptor isoform expression and other CRS clinical measures may be related to the multifactorial pathophysiology of CRS and its diverse subjective and objective manifestations. Differences in GC receptor isoform expression potentially contribute to some degree to disease severity, but this may be obscured by multiple other environmental, sinonasal, and systemic factors leading to the common endpoint of sinonasal mucosal inflammation. In general, it has been challenging to elucidate relationships between CRS disease severity and clinical measures such as endoscopic and radiographic findings.⁴ Future studies are needed to clarify whether alterations in GC receptor isoform expression represent an underlying factor inducing inflammation or whether these may be merely a downstream consequence of other pathologic processes.

The effects of atopy and asthma on PBML GC receptor isoform expression were evaluated due to prior reports that atopic and asthmatic status may influence GC responsiveness.^{55,56} However, in the present study no correlation between GC receptor isoform expression and atopic or asthmatic status was observed. Further studies characterizing PBML GC receptor isoform expression and inflammatory response to allergen exposure may elucidate this further.

To further understand the role of GC resistance in CRS, studies are needed to define its prevalence. In comparison, the asthma literature estimates that 15–25% of asthmatics do not respond to oral GC treatment⁵⁷ and asthmatic PBML GC resistance is associated with worse disease severity and worse response to systemic GCs.^{20,24} The lack of data on the prevalence of GC resistance in CRS is due to the lack of a standardized clinical definition. While the asthma literature defines GC resistance in asthmatics as the failure to improve morning pre-bronchodilator FEV1 values by greater than 15% of predicted value after 7 to 14 days of 20 mg of twice daily oral prednisone,⁵⁸ no clinical definition of CRS GC resistance has been proposed despite a number of studies^{8,11,25,31,59–63} commenting on the presence of GC resistance in CRS.

There are several limitations to the findings of this study and areas for further investigation. PBML samples came from CRS patients who had not used oral GCs within the four weeks prior to undergoing endoscopic sinus surgery at a tertiary care academic medical center. Thus, nonsurgical patients, patients on chronic steroids, and the general CRS population are not represented. Non-surgical CRS patients may be more likely to respond to oral and topical GCs than surgical patients and thus potentially exhibit a different GC receptor isoform profile.⁷¹ Patients on chronic oral GCs undergoing surgery may exhibit the greatest degree of GC resistance, such that they are GC-dependent in order to achieve adequate symptom control. Patients with milder disease severity than those who have undergone prior non-successful CRS treatment and are referred to a tertiary care academic medical center may have different findings. Forty-one percent of our patients had prior sinus surgery. While there are a number of reasons patients need revision surgery, this may suggest worse disease severity than the general population of patients undergoing primary sinus surgery.⁷² Furthermore, while all of the patients in this study did fail appropriate medical therapy and elected sinus surgery, we cannot necessarily define these patients as steroid resistant. Currently there is not a widely accepted definition for defining patients with CRS as steroid

responsive or steroid resistant. This would require standardized dosing of steroids with pre- and-post treatment QOL measures to determine responsiveness while controlling for numerous confounders including topical drug usage, polyp size, prior surgery, allergies, asthma and other comorbidities. Similarly, we did not collect information on preoperative oral steroid usage, as many patients were medically treated by local physicians and the dose, duration and specific steroid used vary widely and are often not included in the medical record. Even at our own institution, steroid prescriptions vary based upon patient weight, symptom severity, comorbid asthma/diabetes and physician preference. Further investigation into developing a standardized definition for GC resistance and sensitivity followed by measurement of GC receptor isoform expression in each of these groups is warranted. Additionally, a statistical limitation of our study is that although our study is powered to detect a difference in GCR α isoform expression between CRS subtypes, the relatively small sample sizes may be more susceptible to sample heterogeneity for investigating other relationships. Notably, CRS subtype groups in this study demonstrates significant differences in asthma and atopic status between cohorts, which is unable to be controlled due to the small size of the study. Furthermore, one methodologic limitation of this study is that in assessing PBMLs we have not assessed CRS sinonasal tissue directly. A number of CRS studies have examined sinonasal tissue's GC receptor isoform expression, ^{9,25,27,28,30–32} but no study to this point has evaluated systemic GC receptor isoform expression. Further studies are needed to identify the relationship between local and systemic GC receptor isoform expression in CRS. Further study is also needed to investigate the effects of intranasal GCs on systemic GC receptor isoform expression. The effect on intranasal budesonide on sinonasal GC receptor isoform expression is controversial: several studies demonstrate no effect,^{27,62} while others report decreased GCR α ⁷³ and increased GCR β .⁸ The systemic bioavailability of intranasal fluticasone is low, which may render it less likely to lead to systemic effects on GC receptor isoform expression.⁷⁴ Another area for further research is that it is not known how long after treatment with GCs it will take for GC receptor isoform expression to stabilize. In a rat model it has been demonstrated that dexamethasone-associated decreases in GC receptor mRNA and protein return to normal levels by 48–72 hours.⁷⁵ Further investigation is warranted to assess the temporal effects of GCs on GC receptor isoform expression in human PBMCs. A higher prevalence of asthma was noted for the atopic CRSwNP group and differences between groups was noted for atopic status. This may confound data analysis since the authors are not able to control for these differences due to the small sample size. Overall, it should be noted that the immunobiology of CRS and its response to GCs is complex and interactional. Multiple core inflammatory factors have been implicated in GC resistance such as NF κ B, IL-1, IL-2, IL-4, IL-6, IFN-gamma, and IL-17A.^{76–80} Further work is needed to understand the role of GC receptor isoforms from a systematic inflammatory perspective, especially the relationship between GC isoform expression and other core inflammatory markers. In future studies it may be informative to characterize the expression of GC isoforms within isolated immune cell types. Glucocorticoid resistance in T-lymphocytes, B-lymphocytes, and monocytes has been described in other diseases, but it would be intriguing to determine potential individual cellular contributions to GC resistance in CRS.^{68,81–88} While not addressed in the current study, the question of whether the downregulation of GCR α is an innate factor of CRS

patients or whether it is potentially a downstream sequelae of chronic inflammation is another area that merits further study.

CONCLUSION

PBML expression of GCR α and GCR α :GCR β is decreased in CRS patients compared to controls. Decreased GCR α is associated with worsening Lund-Mackay sinus CT scores in AFRS patients, but not other CRS subsets. Further investigation is warranted to characterize the role of PBML GC receptor isoform expression in CRS clinical outcomes.

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Figure 1.

Representative histogram of peripheral blood mononuclear leukocyte (PBML) glucocorticoid receptor alpha (GCRα) geometric mean fluorescent intensity (MFI) for controls and chronic rhinosinusitis (CRS) subtypes. Each CRS subtype demonstrated decreased GCRα expression compared to controls.

Figure 2.

(a) PBML GCR α MFI for CRS subtypes compared to controls. Holm-Sidak's multiple comparisons testing was performed between controls and each CRS subtype. Dots represent individual patient values with mean values indicated by the horizontal line. Statistically significant associations are demonstrated. (b) PBML GCR β MFI for CRS subtypes compared to controls. Dunn's multiple comparisons testing was performed between controls and each CRS subtype with no statistically significant associations noted. Dots represent individual patient values with median values indicated by the horizontal line. (c) Ratio of PBML GCR α :GCR β MFI for each CRS subtype compared to controls. Dunn's multiple

comparison testing was performed between controls and each CRS subtype with multiplicity-adjusted p-values calculated. Dots represent individual patient values with median values indicated by the horizontal line. Statistically significant associations are demonstrated.

Figure 3.

Percent peripheral blood mononuclear leukocyte (PBML) cells **(a)** $GCR\alpha^+$ and **(b)** $GCR\beta^+$ for chronic rhinosinusitis (CRS) subtypes compared to controls. Holm-Sidak's multiple comparisons testing was performed between controls and each CRS subtype with multiplicity-adjusted p-values calculated. * indicates $p < 0.05$. Mean $\pm$ standard deviations shown.

Figure 4.

Correlation between Lund-Mackay sinus CT scores and PBML GCR α MFI expression for subjects with **(a)** AFRS, **(b)** CRSsNP, and **(c)** CRSwNP

Figure 5. Comparison of mean (SD) GCRα MFI for patients requiring oral GCs with the first 6 months postoperatively for (a) CRSsNP, (b) CRSwNP, and (c) AFRS. No statistically significant relationships were observed.

Table 1

Patient Demographics and Clinical Parameters

	Control (n = 8)	CRSSNP (n = 8)	CRSsNP+Atopy (n = 8)	CRSsNP-Atopy (n = 8)	AFRS (n = 8)	P-Value
Demographics						
Age, mean (SD)	48.3 (20.9)	56.4 (10.7)	43.9 (16.7)	52.5 (15.4)	27.5 (7.4)	0.01
Male Gender, n (%)	2 (25)	2 (25)	3 (38)	4 (50)	4 (50)	0.71
Race						
Caucasian, n (%)	6 (75)	6 (75)	5 (62)	6 (75)	2 (25)	0.03
African American/Other, n (%)	2 (25)	2 (25)	3 (38)	2 (25)	6 (75)	
Prior Sinus Surgery, n (%)	0 (0)	2 (25)	3 (38)	4 (50)	4 (50)	0.17
Asthma, n (%)	2 (25)	3 (38)	6 (75)	0 (0)	4 (50)	0.03
Atopy, n (%)	2 (25)	4 (50)	8 (100)	0 (0)	8 (100)	0.01
CRS Scores						
SNOT-22, mean (SD)	-	50.6 (15.3)	56.9 (17.9)	55.9 (26.9)	56.0 (27.8)	0.94
Lund-Kennedy, mean (SD)	-	5.4 (3.1)	9.8 (3.8)	8.7 (3.0)	10.3 (2.7)	0.02
Lund-Mackay, mean (SD)	-	12.5 (3.1)	15.4 (5.3)	14.2 (7.0)	18.8 (6.7)	0.01
Kennedy-Osteitis, median (IQR)	-	0.5 (0-5)	0 (0-4)	4 (0-10)	3 (0.25-4.5)	0.30

AFRS = allergic fungal rhinosinusitis; CRSSNP = chronic rhinosinusitis without nasal polypsis; CRSsNP = chronic rhinosinusitis with nasal polypsis; KOS = Kennedy Osteitis sinus CT score; LM = Lund-Mackay sinus CT score.