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CO.01 a CO.10

CO.01

ORAL TOLERANCE TO COL5A1 PEPTIDES ATTENUATES PULMONARY FIBROSIS THROUGH DOWNREGULATION OF PROFIBROTIC CYTOKINES IN A SYSTEMIC SCLEROSIS MODEL

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Introduction: Autoimmunity against type V collagen (Col V) has been identified in early-stage systemic sclerosis (SSc), with strong immune reactivity to COL5A1(1049) and COL5A1(1439) peptides. These peptides may contribute to the initiation of Col V–specific autoimmunity in SSc. We aimed to investigate the immunological mechanisms triggered by oral tolerance to COL5A1(1049) and COL5A1(1439) peptides and to evaluate their impact on pulmonary involvement in an experimental model of SSc.
Materials and Methods: Experimental SSc was induced in C57BL/6 mice by immunization with Col V emulsified in Freund's adjuvant (IMU-COLV, n=6). Tolerized groups received oral administration of COL5A1(1049) (n=6) or COL5A1(1439) (n=6), while controls received adjuvant alone (CT). Oral tolerance was initiated five days before immunization and reinforced twice during the subsequent week. Mice were euthanized 60 days after immunization. Lung tissue was analyzed by immunofluorescence, immunohistochemistry, and morphometry. Cytokine levels (IL-2, TGF-β1, IL-10, IL-17) were quantified in lung homogenates by ELISA, and CD4+, CD8+, and Treg subsets from mesenteric lymph nodes and spleen were characterized by flow cytometry.
Results: Lung histopathology demonstrated that COL5A1-treated mice had reduced inflammatory infiltrates ($p<0.05$) and decreased collagen deposition ($p<0.05$), particularly type I collagen ($p<0.05$). Cytokine analysis revealed significant reductions in IL-2 and TGF-β1 in both COL5A1(1049)- (TGF-β1: $p<0.0001$; IL-2: $p=0.0090$) and COL5A1(1439)-treated groups (TGF-β1: $p=0.0002$; IL-2: $p=0.0012$) compared with IMU-COLV animals, indicating modulation of the pulmonary microenvironment and suppression of profibrotic pathways. No significant differences were observed for IL-10 or IL-17. Immunophenotyping showed a reduced frequency of CD4+ T cells in mesenteric lymph nodes of COL5A1(1049)-tolerized mice ($p<0.05$), with no significant changes in LAP, PD-1, CD44^hi, or Treg expression.
Conclusion: Oral tolerance to Col V–derived peptides modulated the immune response by downregulating profibrotic cytokines, without major phenotypic changes in lymphocyte subsets. These findings highlight novel immunological mechanisms in SSc and support antigen-specific oral tolerance as a potential therapeutic strategy to control autoimmunity and pulmonary fibrosis in this disease.

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CO.02

SYSTEMIC LUPUS ERYTHEMATOSUS IS A STRONG INDEPENDENT RISK FACTOR FOR SEVERE OUTCOMES IN DENGUE HOSPITALIZATIONS: A NATIONWIDE CROSS-SECTIONAL POPULATION STUDY

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Background: Dengue is a highly prevalent infection in Brazil. Specific subpopulations, such as the elderly and immunosuppressed patients, may face severe outcomes.

Objectives: This study aimed to assess the association of Systemic Lupus Erythematosus (SLE) with adverse outcomes during dengue hospitalization.

Methods: The study included all adults (≥18 years) admissions registered at the Brazilian Hospital Information System (SIH/DATASUS) concerning dengue-related hospitalizations between October 2023-July 2024, covering the 2024 major epidemic peak from late March to mid-May, 2024. Variables included were age, sex, comorbidities, dengue hemorrhagic fever (DHF), ICU admission, length of hospital stay, and death. SLE diagnosis was assessed among the comorbidities. Unadjusted and adjusted regression models were performed to assess the associations between SLE and death, ICU admission, DHF and length of stay.

Results: A total of 104,944 patients were included. SLE was identified in 26 patients (prevalence of 24.8/100,000). SLE patients were younger (37.4 ± 11.4 vs 51.2 ± 20 years, $p<0.001$) and more predominantly female (92.3% vs. 58.4%, $p<0.001$) than general population. SLE showed higher rates of mortality (11.5% vs 2%, $p=0.016$), DHF (11.5% vs. 0.14%, $p<0.001$) and higher length of stay (5.7 ± 6.8 vs. 3.3 ± 2.9 days, $p=0.038$) in comparison to general population. The adjusted models showed SLE as independently associated with increased risk of death [odds ratio - OR: 7.56 (1.90-30.12, $p=0.004$)], longer hospital stay [mean difference with 95% confidence interval: 2.73 (1.62-3.83, $p<0.001$)], and higher risk of DHF [OR 77.2 (22.8-260.8, $p<0.001$)], despite of younger age. SLE was not associated with ICU admission ($p>0.05$).

Conclusions: This is the first national-level study demonstrating a strong and independent association between SLE and death, longer hospitalization and DHF. These findings underscore the need for prioritization of SLE patients for enhanced preventive strategies, including dengue vaccination.

References:
- Messina JP et al. The current and future global distribution and population at risk of dengue. Nat Microbiol. 2019;4(9):1508-1515.
- Shepard DS, et al. The global economic burden of dengue: a systematic analysis. Lancet Infect Dis. 2016;16(8):935-941.
- Werneck GL, et al. Comorbidities increase in-hospital mortality in dengue patients in Brazil. Mem Inst Oswaldo Cruz. 2018;113(8):e180082.
- De Abreu MM, et al. Outcomes of lupus and rheumatoid arthritis patients with

primary dengue infection: A seven-year report from Brazil. Semin Arthritis Rheum. 2018;47(5):749-755.

CO.03

Serum and Urinary Biomarkers as Predictors of Renal Response in Lupus Nephritis Patients

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Background: lupus nephritis (LN) affects up to 50% of systemic lupus erythematosus (SLE) patients and distinct immunological pathways drive inflammation, leading to variable therapeutic responses. Biomarkers have been emerging as tools for stratification and personalized management, with potential impact on diagnosis and monitoring, aiding in therapeutic decision-making. The aim of this study is to evaluate the association of serum and urinary biomarkers with achievement of Target Renal Response (TRR) at 3, 6, and 12 months and analyze semi-quantitative correlations with histological indices. **Methods**: Multicentric cohort of SLE patients ≥18 years (SLICC, 2012) and biopsy-proven active LN [classes III or IV(±V) or V] diagnosed between 2020-2024. Exclusion criteria: contraindication or refusal to kidney biopsy, insulin-dependent diabetes and pregnancy. Biopsies were blindly reviewed by a nephropathologist scoring renal score domains (glomerular, tubulointerstitial, chronicity, immunofluorescence). TRR: ±10% of baseline creatinine and proteinuria decline ≥25% at 3 months, ≥50% at 6 months, and <0.8g/24h at 12 months. CKD: eGFR<60 mL/min/1.73m² at 6 months. Baseline serum MCP-1, NGAL and KIM-1 and urinary TWEAK, NGAL, MCP-1, KIM-1, adiponectin, ceruloplasmin, and hemopexin were analyzed by ELISA. **Results:** Forty patients were included (82.5% female, mean age 32.9±8.3years). Median serum creatinine was 0.8mg/dL (0.4–2.9); 16.2% had an eGFR<60mL/min/1.73m². LN classes III or IV (± V) accounted for 80% and class V, 20%. Baseline urinary TWEAK was higher in patients who achieved TRR at 12 months [7.30 (2.83–20.8) vs. 5.85 (2.10–9.77) pg/mL; p=0.023)]. Urinary hemopexin showed a positive correlation with tubulointerstitial involvement (ρ=0.401; p=0.010) and with moderate to severe glomerulosclerosis and with interstitial fibrosis/tubular atrophy (IFTA) ≥25% [72.53 (30.9–99.5) vs. 34.73 (12.8–88.0)ng/mL; p=0.031 and 83.3 vs. 35.3ng/mL; p=0.037, respectively]. Serum NGAL showed a positive correlation with tubulointerstitial involvement (ρ=0.423; p=0.007) and was higher in the presence of interstitial inflammation [143 (99.5–267.0) vs. 99.5 (31.4–235.0)ng/mL; p=0.010). Serum KIM-1 was higher in patients with moderate/severe fibrous crescents versus absent/mild [204.41 (65.7–516) vs. 73.59 (8.99–803)pg/mL; p=0.049). **Conclusion**. TWEAK emerged as a potential predictor of TRR at 12 months, while urinary hemopexin and serum NGAL were linked to tubulointerstitial injury. Serum KIM-1 was related to fibrous crescents. These results support further investigation of biomarker-guided personalized management strategies in LN.

CO.04

MUSCLE QUALITY AND ARCHITECTURE BY ULTRASOUND BETTER REFLECT PHYSICAL PERFORMANCE THAN DXA-DERIVED MUSCLE MASS IN WOMEN WITH RHEUMATOID ARTHRITIS

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INTRODUCTION: In rheumatoid arthritis (RA), impaired physical performance reflects not only reduced muscle strength and mass, but also altered muscle quality. Although dual-energy X-ray absorptiometry (DXA) is widely used to assess muscle mass, it does not capture qualitative abnormalities such as myosteatosis. Whether muscle ultrasound (US) adds relevant information beyond conventional sarcopenia-related measures remains uncertain.
OBJECTIVES: To identify which US-derived muscle parameters are independently associated with physical performance in women with RA and to compare conventional sarcopenia-oriented models based on muscle strength plus DXA-derived muscle mass with models incorporating US-derived measures of muscle quality and architecture.
MATERIALS AND METHODS: Cross-sectional study of 128 women aged ≥40 years with RA and disease duration ≥5 years from a tertiary outpatient clinic. Physical performance was assessed by the Short Physical Performance Battery (SPPB). Muscle strength was evaluated by handgrip, body composition by DXA, including appendicular lean mass index (ALMI), and rectus femoris characteristics by US, including echogenicity, muscle thickness, cross-sectional area, muscle volume, fascicle length, and pennation angle. Associations between individual and combined US parameters and continuous SPPB were examined using adjusted multivariable linear regression. Complementary parsimonious logistic regression analyses for low physical performance (SPPB ≤8) compared conventional sarcopenia-oriented models based on handgrip strength plus ALMI with alternative handgrip-based models incorporating US-derived measures of muscle quality and architecture instead of ALMI.
RESULTS: Mean age was 56.2 ± 8.9 years, mean RA duration was 17.1 ± 8.1 years, and 47.7% of participants had low physical performance. Most had overweight/obesity (70.2%), whereas low muscle strength and low ALMI were present in 67.2% and 11.7%, respectively. In multivariable linear models adjusted for age, RA duration, disease activity, glucocorticoid exposure, handgrip strength, and adiposity, DXA-derived muscle mass was not independently associated with SPPB, whereas echogenicity, reflecting intramuscular fat infiltration, and pennation angle, reflecting muscle architecture, were independently associated with physical performance. Together, they added explanatory value (ΔR^2=0.065; p=0.0014). In complementary categorical analyses, sarcopenia-oriented frameworks replacing DXA-derived muscle mass with US-derived abnormalities discriminated low physical performance better than the conventional model based on low handgrip plus low ALMI. Low ALMI was not independently associated with low physical performance (OR 0.56, 95% CI 0.18–1.73; p=0.315). In contrast, when combined with low handgrip strength, both poor pennation angle (AUC 0.654; OR 2.55, 95% CI 1.18–5.50; p=0.017) and severe echogenicity (AUC 0.644; OR 3.21, 95% CI 1.26–8.13; p=0.014) outperformed the conventional model.
CONCLUSION: In women with RA, US-derived measures of muscle quality and

architecture were more informative than DXA-derived muscle mass for explaining physical performance. Echogenicity and pennation angle added clinically relevant information beyond conventional sarcopenia-oriented assessment, suggesting that incorporating ultrasound-based qualitative and architectural parameters may improve functional impairment assessment in this population.

CO.05

ULTRASOUND-DEFINED INFLAMMATORY BURDEN IS LINKED TO SARCOPENIA BEYOND CLINICAL DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Introduction. Ultrasound (US) is a tool for assessing inflammatory activity in rheumatoid arthritis (RA), particularly through grayscale (GS) and power Doppler (PD) detection of synovitis. Sarcopenia is a frequent comorbidity in RA, yet the relationship between US-defined inflammatory burden and sarcopenia remains poorly understood. It is also unclear whether US captures this association better than clinical composite indices.

Objective. To investigate the association between US-detected inflammatory activity and sarcopenia in RA, independently of disease activity measures.

Methods. In this cross-sectional study, women aged >40 years with RA (2010 ACR criteria) underwent standardized musculoskeletal US at a tertiary outpatient clinic. US inflammatory burden was defined a priori by severity and extent, using binary definitions (GS or PD grade ≥2 in ≥2 joint topographies) and ordinal categories reflecting increasing burden (no GS ≥2, grade ≥2 in ≥2 topographies, grade ≥2 in ≥3 topographies). Sarcopenia was defined according to EWGSOP2 as low muscle strength plus low appendicular lean mass by DXA or impaired muscle quality by rectus femoris US echogenicity, a surrogate of fatty muscle infiltration. Multivariable logistic regression examined associations with sarcopenia, and trend analyses assessed dose-response relationships across increasing US burden categories. Additional models including DAS28-CRP and US variables, separately and jointly, compared relative contributions. Sensitivity analyses adjusted for HAQ, physical activity, and pain.

Results. A total of 126 patients were included (median age 57 [49–64] years, 93% seropositive, disease duration 16 [11–22.8] years), and 57.9% had sarcopenia. In multivariable-adjusted analyses controlling for age, fat mass index, disease duration, cumulative glucocorticoid exposure, and biologic/targeted synthetic DMARD use, GS grade ≥2 in ≥2 topographies was associated with sarcopenia (OR 3.05, 95% CI 1.36–6.81; p=0.007), with a dose-response relationship across increasing GS burden (OR 1.77, 95% CI 1.10–2.84; p=0.019). Likewise, PD grade ≥2 in ≥2 topographies was associated with sarcopenia (OR 5.79, 95% CI 1.57–21.38; p=0.008), and increasing PD burden with higher odds of sarcopenia (OR 2.69, 95% CI 1.18–6.13; p=0.018). In separate models, DAS28-CRP was also associated with sarcopenia (OR 1.64, 95% CI 1.12–2.41; p=0.010); however, US-defined inflammatory burden showed stronger associations and better model fit than DAS28-CRP alone. In mutually adjusted models, both DAS28-CRP and US-defined inflammatory burden remained independently associated with sarcopenia. In domain-specific analyses, US inflammatory burden was associated with lower handgrip strength (p<0.001) and worse muscle quality (p=0.032),

but not DXA-derived lean mass (p=0.500). Findings remained consistent in sensitivity analyses.

Conclusion. In RA, US-defined inflammatory burden was independently associated with sarcopenia beyond DAS28. US variables showed stronger associations and better model fit than clinical disease activity measures, suggesting that US captures inflammatory dimensions relevant to muscle health not fully reflected by composite scores. Furthermore, the link between joint inflammation and sarcopenia appears to be driven mainly by impaired muscle strength and muscle quality rather than reduced muscle mass alone.

CO.06

MAPPING EXTRA-MUSCULOSKELETAL MANIFESTATIONS IN PATIENTS WITH SPONDYLOARTHRITIS: INSIGHTS FROM THE BRAZILIAN REGISTRY OF SPONDYLOARTHRITIS (RBE)

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Background: Extra-musculoskeletal manifestations (EMMs), such as acute anterior uveitis (AAU), psoriasis (PsO) and inflammatory bowel disease (IBD), amplify the burden of spondyloarthritis (SpA). Their epidemiology in Brazil, a country with marked racial admixture and variable HLA-B27 prevalence, is poorly characterised.
Objectives: To determine the prevalence, regional distribution, and independent predictors of EMMs in Brazilian SpA patients, and to assess their association with disease activity, functional impairment, treatment exposure, and the ASAS difficult-to-manage (D2M) classification
Methods: A multicenter, observational, cross-sectional study was conducted using data from the Brazilian Registry of Spondyloarthritis (RBE). Patients with a diagnosis of SpA, including both axial and peripheral forms, were included. Individuals were categorized into two groups based on the presence or absence of EMMs, with the latter serving as the comparator group in all analyses. Disease activity and clinical burden were assessed using validated indices, including BASDAI, ASDAS-CRP, ASDAS-ESR, BASFI, BASMI, ASQoL, and PASI, in addition to treatment-related data. Multivariate logistic regression models were constructed for each EMM as the dependent variable to identify independent predictors. Statistical analyses were performed using SPSS v20 and STATA v18, with significance set at $p < 0.05$.
Results: A total of 1,339 patients with SpA were evaluated: 946 (70.6%) had axial SpA, 304 (22.7%) psoriatic arthritis (PsA), 44 (3.3%) enteropathic arthritis, and 45 (3.4%) had other forms of peripheral SpA. At least one EMM was observed in 661 patients (49.4%), with AAU in 24.8%, PsO in 18.4%, and IBD in 4.8%. The regional distribution of EMMs across Brazil is presented in Figure 1. Co-occurrence of ≥2 EMMs was identified in 2.2% of cases. Final adjusted logistic regression models for each EMM are presented in Table 1. When the difficult-to-manage classification criteria

were applied, it was identified 13 (1.4%) patients with axial SpA and 15 (4.9%) with PsA.

Conclusion: EMM affects approximately half of Brazilian SpA patients, with low rates of overlap among them. Patients from the Southeast region exhibited a higher frequency of all EMMs compared to those from other regions, regardless ofHLA-B27 status. The increased requirement for DMARD therapy, along with greater mental health burden and treatment refractoriness in this population, suggests a higher overall disease burden and associated healthcare costs.

Figura 1: Regional Distribution of Extra-Musculoskeletal Manifestations in Spondyloarthritis. Data from the Brazilian Registry of Spondyloarthritis(RBE).

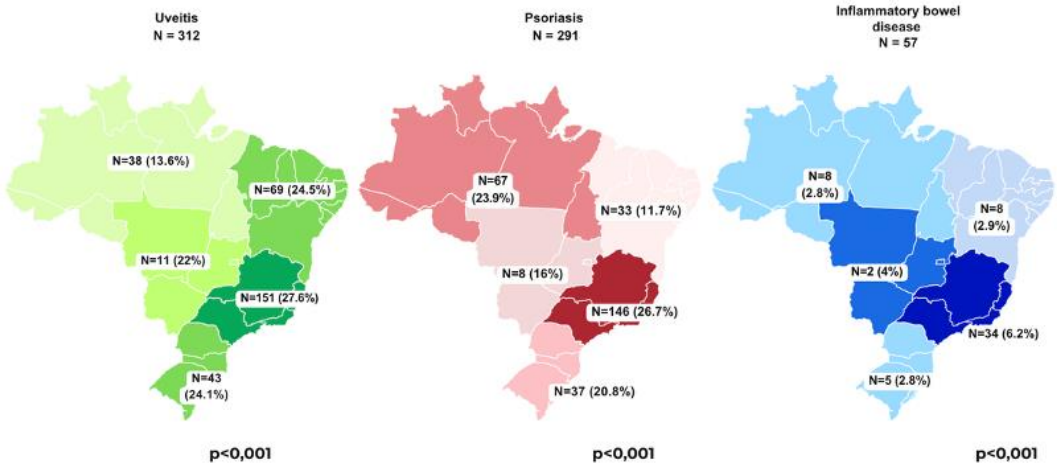

Table 1 Final regression models for each extra-musculoskeletal manifestation in patients with spondyloarthritis.

Risk Factor	AAU	Psoriasis	IBD
	OR (95% CI)	OR (95% CI)	OR (95% CI)
HLA-B27 Positive	2.30 (1.51-3.49)		
Higher BMI	1.03 (1.00-1.07)		
Anxiety	1.64 (1.03-2.60)		3.73 (1.77-7.89)
Longer Disease Duration	1.03 (1.01-1.04)	0.95 (0.92-0.97)	
Current DMARD Use	1.79 (1.28-2.51)	3.71 (2.16-6.37)	
Older Age		1.07 (1.05-1.10)	
Peripheral Involvement		4.60 (2.58-8.23)	2.14 (1.03-4.49)
Current TNF Inhibitors			2.79 (1.41-5.50)

CO.07

COLÁGENO TIPO V INTRA-ARTICULAR MODULA A APOPTOSE CONDRÓCITÁRIA E PRESERVA A CARTILAGEM EM MODELO EXPERIMENTAL DE OSTEOARTRITE

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Introdução: Modelos experimentais têm se mostrado uma importante ferramenta para entender os mecanismos envolvidos na osteoartrite (OA) e auxiliar no desenvolvimento de novas terapias. Estudos anteriores realizados pelo nosso grupo, demonstraram que injeções intra-articulares de células-tronco mesenquimais, previamente estimuladas com colágeno tipo V (Col V) *in vitro*, apresentaram efeito positivo na manutenção da integridade do tecido e inibição da apoptose dos condrócitos na cartilagem articular em modelo de OA, sugerindo o Col V, como coadjuvante no tratamento da OA.
Objetivos: Avaliar o efeito da administração intra-articular do Col V em um modelo murino de OA de evolução lenta.
Material e Métodos: Foram utilizados 40 ratos machos da linhagem Sprague Dawley, submetidos à indução de OA, por meio de meniscectomia parcial no joelho direito. Os animais foram divididos em 4 grupos: 1. OA (n=10), sem tratamento; 2. Tratamento com Col V (COLV, n=10); 3. Tratamento com ácido hialurônico (AH, n=10); e 4. Tratamento com ácido hialurônico e Col V (AH/COLV, n=10). As injeções intra-articulares foram administradas uma vez por semana, durante um mês, sendo iniciadas uma semana após a indução da OA. A caracterização histopatológica da OA foi conduzida por meio da aplicação do escore OARSI. A expressão de caspase-3 e de colágeno tipo I na cartilagem articular foi avaliada por imuno-histoquímica e imunofluorescência, respectivamente. A análise histomorfométrica foi empregada para a quantificação do número de condrócitos e aglomerados celulares (*clusters*), de proteoglicanos, da morte celular por apoptose e do colágeno tipo I.
Resultados: Os resultados mostraram efeito positivo na preservação do tecido cartilaginoso e manutenção da organização dos condrócitos no côndilo femoral dos animais do grupo COL V e AH/COL V, quando comparados ao grupo OA (p=0,0067; p=0,0326), bem como no platô tibial (p=0,0333; p=0,0011). A avaliação histomorfométrica dos *clusters* demonstrou diminuição significativa no côndilo femoral do grupo COL V, em relação ao grupo OA (p= 0,0242). Ainda, a avaliação histomorfométrica da quantidade de proteoglicanos na cartilagem articular indicou um aumento significativo após o tratamento com Col V, grupo COL V, em comparação ao grupo OA (p=0,0064; p=0,0105) e AH (p= 0,0004*)*. Adicionalmente, a análise da expressão de Col I na cartilagem articular do platô tibial do grupo COL V, evidenciou diminuição de sua expressão em relação ao grupo OA (p= 0,0025*)* e AH (p= 0,0464*)*. A avaliação quantitativa de morte celular, identificada pela imunomarcação da caspase-3, demonstrou significativa diminuição na cartilagem articular do côndilo femoral e platô tibial dos animais dos grupos COL V e AH/COLV, quando comparados aos grupos OA

e AH ($p< 0,05$; $p< 0,0001$, respectivamente).
Conclusão: O Col V, administrado por via intra-articular, apresentou efeito condroprotetor, caracterizado pela preservação da organização dos condrócitos, manutenção do conteúdo de proteoglicanos e acentuada inibição da apoptose condrocitária. Em conjunto, esses achados sugerem seu potencial como abordagem terapêutica inovadora na osteoartrite.

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CO.08

DISTINCT PULMONARY PHENOTYPES IN SJOGREN'S DISEASE: COMPARATIVE ANALYSIS OF INTERSTITIAL LUNG DISEASE AND ISOLATED PULMONARY CYSTS IN A BRAZILIAN COHORT

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Background: Sjögren's disease (SjD) is a systemic autoimmune disease associated with a broad spectrum of pulmonary manifestations. While interstitial lung disease (ILD) is a well-recognized form of lung involvement, pulmonary cysts are less clearly characterized when occurring as an isolated chest CT finding, distinct from ILD. Previous studies addressing pulmonary manifestations in SjD have been limited by heterogeneous populations and inconsistent findings, and few have specifically explored isolated pulmonary cysts as a separate imaging-defined subgroup.
Objective: To investigate the clinical and laboratory features associated with different pulmonary imaging patterns in a Brazilian cohort of patients with Sjögren's disease (SjD), particularly ILD and isolated pulmonary cysts.
Methods: This retrospective cross-sectional study included patients with SjD fulfilling the 2016 ACR/EULAR classification criteria who had undergone chest CT at a tertiary outpatient clinic in Brazil. Patients with other connective tissue diseases were excluded. All CT scans were reviewed by a single experienced radiologist blinded to clinical data. Based on chest CT findings, patients were classified as having ILD, isolated pulmonary cysts (defined as pulmonary cysts without CT features of ILD), or neither abnormality. Demographic, clinical, and laboratory features were compared across groups using Fisher's exact test, chi-square test, and Kruskal-Wallis test, followed by Bonferroni-corrected post hoc analyses and logistic regression.
Results: Among the 120 included patients, 21 (17.5%) had isolated pulmonary cysts, 45 (37.5%) had ILD, and 54 (45.0%) had neither abnormality on chest CT. In univariate analyses, isolated pulmonary cysts were associated with longer disease duration, but this association did not remain significant after multivariable adjustment. Low C4 levels (OR 0.142, 95% CI 0.029–0.704; p=0.017) and parotid enlargement (OR 0.106, 95% CI 0.011–0.996; p=0.050) were independently associated with lower odds of ILD.
Conclusion: Our findings suggest that isolated pulmonary cysts may define a distinct imaging pattern of pulmonary involvement in Sjögren's disease, separate from the more typical ILD presentation, and warranting further study. Conversely, low C4 levels and parotid enlargement — features consistent with a more systemic glandular/B-cell-driven profile — were associated with lower odds of ILD.

CO.09

ALTERAÇÕES DO PLEXO SUBBASAL DA CÓRNEA NA DOENÇA DE SJÖGREN: CORRELAÇÃO COM SUPERFÍCIE OCULAR, ATIVIDADE SISTÊMICA E DISAUTONOMIA

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INTRODUÇÃO A Doença de Sjögren (DSj) é doença autoimune cujas manifestações oculares incluem olho seco grave e dano epitelial progressivo da superfície ocular. O plexo nervoso subbasal da córnea (PSB) é o segmento mais acessível do sistema nervoso periférico para avaliação in vivo, e a microscopia confocal de córnea (MCC) permite sua quantificação automatizada pelo software ACCMetrics com parâmetros de comprimento de fibras (CNFL) e densidade de fibras (CNFD), mostrando acurácia diagnóstica para neuropatia de pequenas fibras (Giannaccare G, Graefes Arch Clin Exp Ophthalmol, 257:583, 2019). A disautonomia, avaliada pelo questionário COMPASS-31 validado (31 itens em 6 domínios autonômicos), foi documentada na DSj e pode refletir o comprometimento neurológico periférico sistêmico, embora sua relação com a denervação corneana seja pouco explorada (Sletten DM, Mayo Clin Proc, 87:1196, 2012). A córnea é uma das estruturas mais densamente inervadas do organismo e suas alterações morfológicas precedem manifestações clínicas em neuropatias sistêmicas (Villani E, Cornea, 26:26, 2007).

OBJETIVOS Avaliar parâmetros morfométricos do PSB pela MCC com ACCMetrics em pacientes com DSj e correlacioná-los com o teste de Schirmer, escala de Van Bijsterveld, atividade pelo ESSDAI e sintomas autonômicos pelo COMPASS-31.

MATERIAIS E MÉTODOS Estudo transversal com 72 pacientes com DSj segundo critérios ACR/EULAR 2016, analisando 135 olhos pela MCC (Heidelberg HRT-III/RCM) com imagens do PSB por ACCMetrics. A amostra foi estratificada pelo ponto de corte CNFL ≤14,6 mm/mm² para neuropatia de fibras pequenas, formando o **Grupo 1 com baixa densidade nervosa (n=127 olhos)** e o **Grupo 0 com inervação preservada (n=8 olhos)**. Avaliados: teste de Schirmer ≤5 mm, escala Van Bijsterveld, domínio glandular do ESSDAI, e COMPASS-31 com ponto de corte ≥30 para disautonomia. Testes de Wilcoxon e Fisher compararam os grupos ($p<0,05$).

RESULTADOS A amostra foi composta por 96% de mulheres com média etária de 56,42 ± 10,88. O Grupo 1 apresentou mediana de CNFL de 9,9 mm/mm², em comparação com 16,1 mm/mm² no Grupo 0 ($p<0,001$). A redução concomitante de CNFD ocorreu em 69% dos olhos do Grupo 1 versus 25% no Grupo 0 ($p=0,019$). Schirmer positivo: 71% no Grupo 1 versus 38% no Grupo 0 ($p=0,11$). Van Bijsterveld positivo: 65% versus 50% ($p=0,5$). O **envolvimento glandular pelo ESSDAI foi exclusivo do Grupo 1** (43% vs. 0%; $p=0,021$). O **COMPASS-31 ≥30 foi detectado em 100% do Grupo 0** versus 66% do Grupo 1 ($p=0,056$).

CONCLUSÃO Houve concordância entre a perda de CNFL e a redução da densidade nervosa, visto que no Grupo 1, 69% tiveram redução de CNFD contra 25% no Grupo 0 ($p=0,019$). A denervação corneana associou-se a maior gravidade ocular e à falência secretória, com o Teste de Schirmer mostrando 71% de ressecamento grave no grupo

mais afetado contra 38% no Grupo 0, e positividade na Escala de Van Bijsterveld de 65% versus 50%, embora sem significância estatística, possivelmente devido ao pequeno número de olhos do Grupo 0. O **envolvimento das glândulas exócrinas (domínio glandular do ESSDAI) foi observado apenas no grupo com maior atrofia nervosa** (43% vs. 0%; p=0,021). Os **sintomas de disautonomia (COMPASS-31) atingiram seu pico antes da atrofia nervosa visível** à MCC. Isso sugere que a disautonomia pode preceder a denervação morfológica, destacando a MCC com ACCMetrics como biomarcador precoce e não invasivo, além de demonstrar que o COMPASS-31 pode facilitar a avaliação do comprometimento neurológico na prática clínica.

CO.10

ORAL TOLERANCE TO α1(V) CHAIN AND COL5A1(1049)/COL5A1(1439) PEPTIDES ATTENUATES PULMONARY INFLAMMATION AND FIBROSIS IN AN EXPERIMENTAL SYSTEMIC SCLEROSIS MODEL

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Introduction: Autoantibodies against type V collagen (COLV), principally targeting the α1(V) chain and the COL5A1(1049) and COL5A1(1439) peptides, are found in early systemic sclerosis (SSc) and may contribute to disease pathogenesis.

Objectives: To test whether oral tolerance induced by α1(V) protein or its COL5A1 peptides modulates pulmonary inflammation, extracellular matrix remodeling and vascular activation in an experimental SSc model.

Material and Methods: SSc was induced in female C57BL/6 mice by COLV immunization emulsified in Freund's adjuvant (IMU-COLV). Animals (n=30) were allocated to five groups (n=6/group): α1(V) oral tolerance + IMU-COLV, COL5A1(1049) oral tolerance + IMU-COLV, COL5A1(1439) oral tolerance + IMU-COLV, IMU-COLV control (immunized + saline), and Freund's adjuvant control. Oral administrations (50 μg) were given prior to immunization. After 60 days lungs were harvested for histology, immunofluorescence, immunohistochemistry, 4-hydroxyproline assay, cytokine quantification and histomorphometry. Statistical comparisons used appropriate tests (two-tailed); $p<0.05$ was considered significant.

Results: Oral tolerance to α1(V) markedly reduced mononuclear infiltrates in peribronchovascular, perivascular and alveolar compartments versus IMU-COLV controls ($p<0.0001$). COL5A1(1049) and COL5A1(1439) tolerance also decreased inflammation ($p=0.0004$ and $p=0.0011$, respectively), with pronounced reductions in CD3+ T lymphocytes in interstitium and peribronchovascular regions ($p<0.05$). COL5A1 peptide treatments significantly downregulated IL-2 ($p=0.0095$; $p=0.0018$) and TGF-β1 ($p<0.0001$; $p=0.0002$). Total collagen deposition and 4-hydroxyproline content were markedly reduced in α1(V)- and peptide-treated groups (collagen $p<0.0001$; 4-hydroxyproline $p=0.0229$). Type I and V collagen accumulation around bronchi, vessels and septa was attenuated in treated animals ($p<0.05$). α1(V) tolerance lowered factor VIII expression ($p<0.05$), indicating reduced vascular activation, and both peptides suppressed α-SMA expression ($p=0.0054$; $p=0.0116$). Tgfβ1 mRNA was downregulated after α1(V) and COL5A1(1439) treatment ($p<0.05$).

Conclusion: Oral tolerance targeting the α1(V) chain and COL5A1(1049)/COL5A1(1439) peptides significantly modulates autoimmune, fibrogenic and vascular pathways in the IMU-COLV model of SSc. These tolerogenic interventions produced robust anti-inflammatory and antifibrotic effects, supporting

their translational potential as peptide-based therapies for SSc.

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