Table 1. Skin and lung measurements

	BLM (I)	BLM+BAR (II)	BLM+PBO (III)		Pairwise comparison		
	Mean (SD.)	Mean (SD.)	Mean (SD.)	P	I vs II	I vs III	II vs III
Dermal thickness (with H&E and MT) (µm)	430.29 (54.66)	308.00 (26.79)	452.50 (75.48)	**0.001** [a]	**<0.001**	0.721	**<0.001**
Dermal thickness (with UBM) (µm)	524.86 (116.21)	304.20 (61.45)	505.67 (88.09)	**<0.001** [a]	**<0.001**	0.919	**<0.001**
		Median (min-max)	**Median (min-max)**	**Median (min-max)**			
Ashcroft Score (0-8)	5 (2-7)	1 (0-4)	3 (2-5)	**0.001** [k]	**0.002**	0.630	0.176
	n (%)	**n (%)**	**n (%)**				
SSc-ILD in CT				0.215 [ff]			
Absent	2 (28.6)	7 (70)	2 (33.3)		ns.	ns.	ns.
Present	5 (71.4)	3 (30)	4 (66.7)		ns.	ns.	ns.

[a] OneWay ANOVA (Robuts Statistic:Brown-Forsythe); Post Hoc Test: Tukey HSD, [k] Kruskal Wallis Test (Monte Carlo); Post Hoc Test: Dunn's Test, [ff]Fisher Freeman Halton (Monte Carlo), ILD: Interstitial lung disease, UBM: Ultrasound biomicroscopy, H&E: hematoxylin and eosin staining, MT: Masson's Trichrome staining, ns.: non significant, min.: minimum, max.: maximum, SD.:Standard deviation, BLM: Bleomycine induced SSc group, BLM+BAR: Bleomycine with Baricitinib group, BLM+PBO: Bleomycine with Placebo group

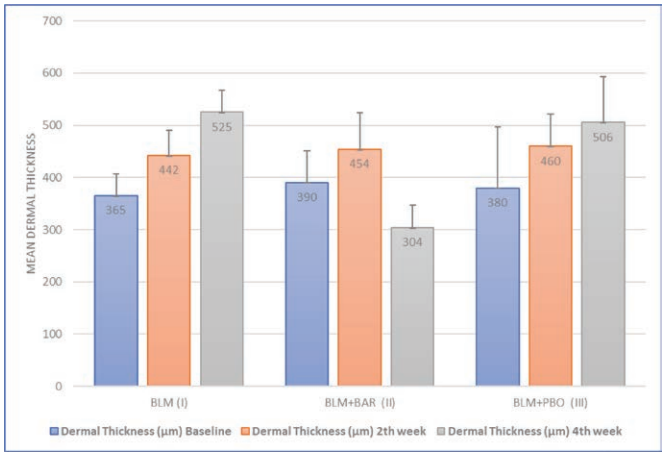

Figure 1. Dermal thickness change with UBM baseline, 2th and 4th week.

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DIFFERENT GUT MICROBIOME PROFILES AMONG PATIENTS WITH SYSTEMIC SCLEROSIS COMPARED TO RHEUMATOID ARTHRITIS

Keywords: Rheumatoid arthritis, Gastrointestinal tract, Systemic sclerosis

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Background: A growing body of evidence suggests that the gut microbiota plays a significant role in the development of autoimmune diseases. An altered microbiota composition has been associated with gastrointestinal and extraintestinal features in systemic sclerosis (SSc) patients.
Objectives: To characterize differences in the gut microbiota between SSc patients and rheumatoid arthritis (RA) patients and to look for associations between microbial profiles and SSc subtypes, disease manifestations and treatment.
Methods: SSc and RA patients seen at our center were recruited in a prospective study. The exclusion criteria included antibiotic or probiotic treatment during the month prior to recruitment, recent hospitalizations, BMI>30, diabetes mellitus or concomitant inflammatory bowel disease. Fecal samples were collected and processed and 16S rRNA gene sequences were analyzed using the QIIME2 package. Microbiome composition was determined, beta diversity and alpha diversity were calculated and ANCOM analyses was performed.
Results: During 7/2018-4/2022, 49 SSc patients (mean age [SD] 53.5[13.8] and disease duration 9.4 [8.0] years) and 21 RA patients (mean age [SD] 57.1[10.4] and disease duration 15.1[10.0] years) fulfilled the criteria and were willing to participate in the study. Significant differences in beta diversity (Unweighted q=0.019, and Weighted UniFrac q=0.005) were found between RA and SSc patients' stool microbiota, but not in alpha diversity. Composition analysis revealed higher abundance of Actinomyces and relative paucity of Coprococcus Eutactus among SSc patients compared to RA. Significant variations in beta diversity (unweighted and weighted) were associated with the subtype of SSc (diffuse - 27 vs limited - 22 patients, p [weighted] = 0.01), occurrence of interstitial lung disease (22 patients, p=0.011), renal crisis (3 patients, p=0.016), immunomodulatory treatment (33 patients, p=0.018) and biological treatment (11 patients, p=0.017). Composition analysis revealed higher relative abundance of Firmicutes in patients with GAVE [12]. Patients on biologicals (11) had higher abundance of Synergistaceae and lower of Firmicutes. The changes were consistent in recurrent fecal samples.
Conclusion: Significant differences on beta diversity were found between RA and SSc patients' gut microbiota, but not on alpha diversity. Diffuse SSc, interstitial lung disease, renal crisis and immunomodulatory treatment were associated with shifts in the microbiome of SSc patients. The impact of these changes on SSc disease progression needs further elucidation.
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