COMUNICAÇÕES ORAIS

Comunicações Orais

002 - PORTUGUESE RECOMMENDATIONS FOR THE MANAGEMENT OF RAYNAUD'S PHENOMENON AND DIGITAL ULCERS IN SYSTEMIC SCLEROSIS AND OTHER CONNECTIVE TISSUE DISEASES

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Objective: To develop evidence-based recommendations for the non-pharmacological and pharmacological management of Raynaud's phenomenon (RP) and digital ulcers (DUs) in patients with systemic sclerosis and other immune-mediated connective tissue diseases (CTDs).
Methods: A task force comprising 21 rheumatologists, two surgeons (vascular and plastic), two nurses, and one patient representative was established. Following a systematic literature review performed to inform the recommendations, statements were formulated and discussed during two meetings (one online and one in-person). Levels of evidence, grades of recommendation (GoR), and level of agreement (LoA) were determined.
Results: Five overarching principles and 13 recommendations were developed. GoR ranged from A to D. The mean ± standard difference (SD) LoA with the overarching principles and recommendations ranged from 7.8±2.1 to 9.8±0.4. Briefly, the management of RP and DUs in patients with CTDs should be coordinated by a multidisciplinary team and based on shared decisions with patients. Nifedipine should be used as first-line therapy for RP and/or DUs. Sildenafil, tadalafil, and/or iloprost IV are second-line options for severe and/or refractory patients with RP and/or DUs. Sildenafil, tadalafil and/or Iloprost IV, should be prescribed for healing and prevention (also including bosentan) of DUs.
In patients with RP and/or DUs, non-pharmacological interventions might be considered as add-ons, but there is limited quality and quantity of scientific evidence supporting their use.
Conclusions: These recommendations will inform rheumatologists, specialist nurses, other healthcare professionals, and patients about a comprehensive and personalized management of RP and DUs. A research agenda was developed to address unmet needs, particularly for non-pharmacologic interventions.

008 - INIBIÇÃO DA CINASE DE CÉLULA T INDUZÍVEL POR INTERLEUCINA-2 (ITK) COM SOQUELITINIB DEMONSTRA EFICÁCIA NA PREVENÇÃO DE DANOS PULMONARES EM MODELOS MURINOS DE ESCLEROSE SISTÉMICA

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Introdução: A ativação anormal de células T desempenha um papel crucial nas fases inflamatórias iniciais da esclerose sistémica (ES). A imunopatologia da ES é caracterizada por uma polarização predominante de Th2 e Th17. A cinase de célula T induzível por interleucina-2 (ITK) é uma tirosina cinase que promove a ativação, diferenciação e sinalização de receptores das células T. Estudos em ratos knockout ou ratos transgénicos indicam que a inativação ou deleção de ITK reduz não apenas as vias Th2, mas também as vias Th17, com mínima inibição das células Th1. O Soquelitinib (SQL) é um inibidor covalente altamente seletivo de ITK. Estudos in vitro demonstraram que o SQL suprime preferencialmente a produção de citocinas Th2 e Th17 e também inibe o crescimento in vivo de vários tumores murinos através do aumento da infiltração de

002 – TABLE 1. Overarching principles and recommendations for the management of Raynaud's phenomenon and digital ulcers in connective tissue diseases.

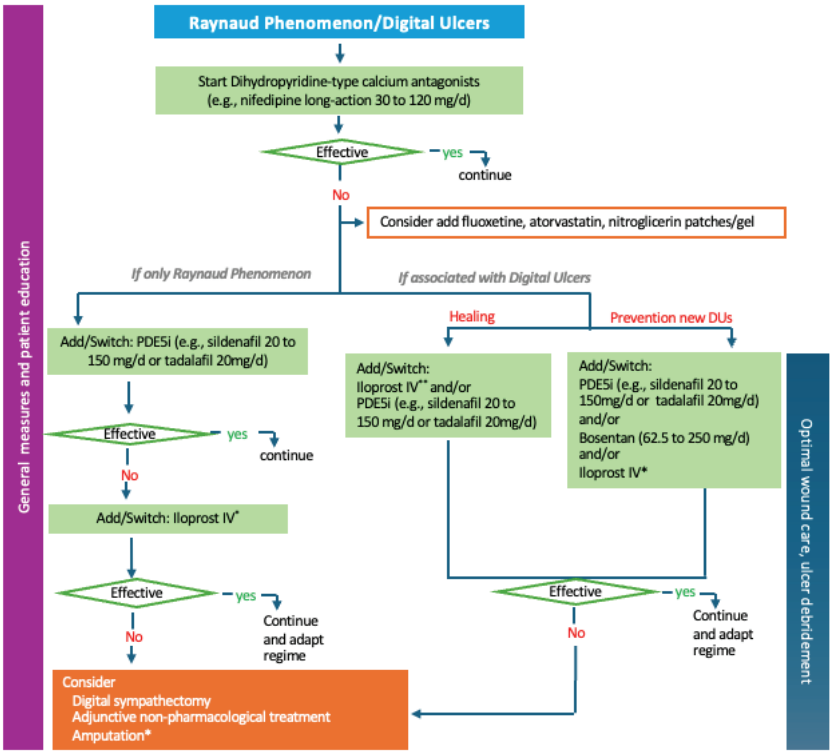
Overarching principles (A to E)	LoE	GoR	LoA (% LoA≥8)
A-Patient education and general measures, such as cold, trauma, and stress eviction, smoking cessation, and skin care, are the cornerstone of the management of RP and DUs and digital ulcers in patients with SSc and other CTDs.	n.a	n.a	9.61±0.50 (100%)
B-Rheumatologists should coordinate the care of patients with SSc/CTD-associated RP, and, particularly, digital ulcers, within a multidisciplinary team, including specialist nurses, vascular/plastic surgeons, physical/occupational therapists, and other health professionals.	n.a	n.a	9.74±0.54 (100%)
C-Early detection and optimal wound care, including debridement, are essential components in the management of DUs within the context of specialized DU clinics.	n.a	n.a	9.43±1.20 (91%)
D-A combination of non-pharmacological and pharmacological interventions should be adopted to treat RP and DUs in patients with SSc and other CTDs.	n.a	n.a	9.83±0.49 (100%)
E-Management of RP and DUs should be conducted on a shared-care basis, involving patients in decision-making.	n.a	n.a	9.78±0.52 (100%)
Recommendations (I to XIII)			
I-Dihydropyridine-type calcium antagonists, namely nifedipine, should be considered as first-line treatment to reduce the frequency and severity of RP.	LoE 1a	A	9.83±0.39 (100%)
II-PDE5i should be considered to reduce the frequency, severity, and duration of RP in patients refractory and/or intolerant to first-line therapy.	LoE 1a	A	9.70±0.47 (100%)
III- PDE5i should be considered for the healing and prevention of new DUs.	LoE 1a	A	9.65±0.71 (96%)
IV-IV prostacyclin analogues, namely iloprost, can be considered for reducing the frequency and severity of RP in patients refractory and/or intolerant to first-line therapy. IV prostacyclin analogues, namely iloprost, can be considered for the healing of DUs.	LoE 1a	A	9.48±1.16 (100%)
V-Oral prostacyclins analogues and prostacyclin receptor agonists* are not recommended for the treatment of RP and DUs. * Only for RP; no data on DUs.	LoE 1a	A	9.39±0.94 (91%)
VI-The ERA bosentan should be considered for the prevention of new DUs. ERA are not recommended for the treatment of RP or healing of DUs.	LoE 1b	B	9.65±0.71 (96%)
VII-Nitroglycerin patches can be considered for reducing the frequency and severity of RP and management of DUs.	LoE 2b	C	8.65±.1.77 (83%)
VIII-Angiotensin-converting-enzyme inhibitors and angiotensin receptor blockers are not recommended for the treatment of RP and DUs.	LoE 1b	B	9.43±0.73 (100%)
IX-Statins, namely atorvastatin, can be considered as a complement to standard vasodilator treatment for RP and DUs.	LoE 1b	C	8.96±1.15 (91%)
X- Selective serotonin reuptake inhibitors, namely fluoxetine, can be considered as a complement to standard vasodilator treatment for RP.	LoE 2b	C	8.39±1.90 (78%)
XI-Local oxygen-ozone therapy can be considered as an add-on therapy for the treatment of refractory DUs.	LoE 1b	B	8.48±1.70 (83%)
XII-Periarterial sympathectomy with or without concomitant vascular bypass can be considered for the treatment of refractory DUs in selected patients.	LoE 4	D	7.83±2.08 (74%)
XIII-Other non-pharmacological interventions might be considered as add-on treatments to improve RP and DUs in selected patients.	LoE 4	D	9.00±1.41 (87%)

Legend: RP – Raynaud phenomenon; DU – digital ulcer; SSc – systemic sclerosis; CTD – connective tissue disease; PDE5i - phosphodiesterase-5 inhibitors; IV – intravenous; ERA – endothelin receptor antagonist These recommendations should be interpreted in the light of the clarifications provided in the body of the text and by the supporting SLR. *Numbers in column 'LoA' indicate the mean and SD (in parentheses) of the LoA, as well as the percentage of task force members with an agreement ≥8. GoR, grade of recommendation; LoA, level of agreement; LoE, level of evidence; n.a, not applicable.

002 – TABLE 2. Research Agenda

Understanding the efficacy and safety of prophylactic treatment with iloprost in the management/prevention of DUs
Understanding the efficacy and safety of combination therapies management and prevention of DUs
Establishing a standardized protocol for the administration of intravenous iloprost
Understanding the efficacy and safety of non-pharmacological interventions in RP and DUs for which evidence is still scarce
Need for innovative and high-quality trials and designs that can provide insights into the effect of tailored interventions.

Legend: DU – digital ulcer; RP - Raynaud phenomenon



002 – Figure 1. This algorithm should be interpreted in the light of the clarifications provided in the body-of the text and by the supporting SLR.
*Protocols scheme attached in supplementary material; **In the case of irreversible ischemia; d, day; IV, Intravenous; PDE5i, Phosphodiesterase type 5 inhibitor.

células CD8+ normais nos tumores. Dada a imunopatologia da ES com polarização predominante de Th2 e Th17, o nosso objetivo foi investigar a eficácia do SQL em dois modelos murinos de fibrose pulmonar e hipertensão pulmonar (HTP), que reproduzem o envolvimento pulmonar na ES.

Métodos: O SQL foi avaliado no modelo murino de fibrose pulmonar induzida por bleomicina e no modelo murino transgénico Fra-2, caracterizado por doença pulmonar intersticial (DPI) e remodelamento vascular pulmonar que conduz a HTP. Duas doses do fármaco foram investigadas.

Resultados: No modelo de fibrose pulmonar induzida por bleomicina, o SQL reduziu significativamente o infiltrado leucocitário no líquido do lavado broncoalveolar (p=0,013) (Figura 1A) e reduziu o score histológico de Ashcroft (Figura 1B), indicativo de dano estrutural pulmonar, em comparação com ratos tratados com veículo (p<0,001). Neste modelo, o SQL reduziu a expressão do principal fator de transcrição que controla a expressão de citocinas Th2, GATA-3 (p=0,034), e o mRNA associado a fibrose, MMP2 (p=0,022).

No modelo Fra-2, os ratos tratados com SQL mostraram melhor evolução clínica (score clínico das manifestações da doença) em comparação com ratos Fra-2 não tratados (p<0,0001) (Figura 1C). O SQL aliviou a fibrose pulmonar; reduziu significativamente o score histológico de fibrose, avaliado pelo score de Ashcroft (p<0,05) (Figura 1D), embora não houvesse diferenças significativas nas lesões pulmonares quando avaliadas por micro-TC de tórax. As análises cardiovasculares revelaram uma redução significativa da pressão sistólica ventricular direita (23,9 mmHg vs. 26,7 mmHg, p=0,004) em ratos Fra-2 tratados com SQL em comparação com ratos Fra-2 não tratados (Figura 1E). A análise da espessura miocárdica não revelou diferenças significativas entre os ratos tratados com SQL e os de controle. Finalmente, o SQL reduziu a expressão de GATA3 dependente de Th2 e de RORγt dependente de Th17 nos pulmões dos ratos tratados com bleomicina e nos ratos Fra-2. Um efeito de dose foi observado nas várias análises.

Conclusões: Estes resultados sugerem que a inibição de ITK com SQL, ao diminuir a ativação de Th2 e Th17, oferece benefícios terapêuticos em dois modelos complementares de danos pulmonares semelhantes aos da ES. Dada a importância da ativação das células T nos estágios iniciais da doença, há um forte racional para o potencial benefício da terapia direcionada às células T na ES. O SQL representa uma nova estratégia promissora para o tratamento do envolvimento pulmonar na ES, justificando futuros ensaios clínicos.

032 - TIMING OF SURGERY FOR HIP FRAGILITY FRACTURES – SHOULD WE RACING AGAINST TIME?

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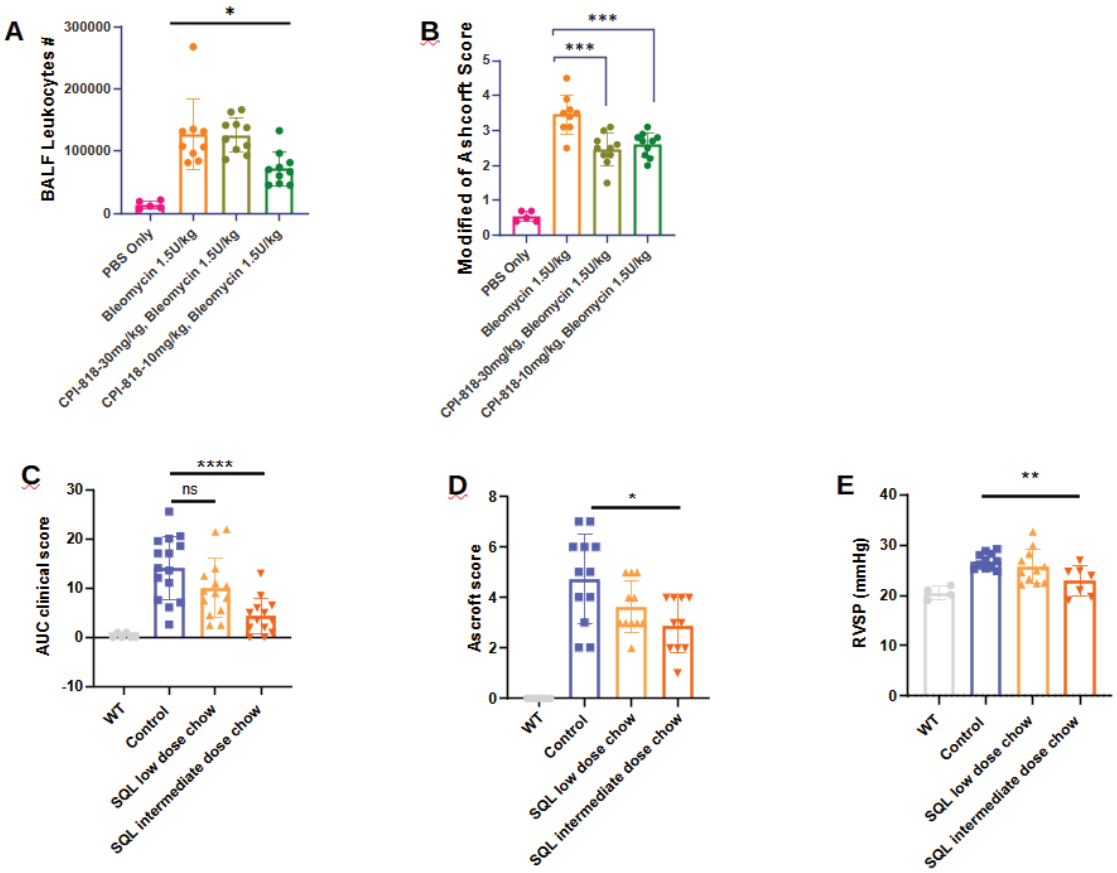

008 – Figure 1.

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Introduction: Managing hip fragility fractures surgically requires a delicate balance between prompt intervention and patient-specific considerations to optimize outcomes. While the ideal timing for surgery remains a topic of debate, early intervention is generally advocated for improved prognosis and functional recovery.
Objective: To evaluate the impact of surgical timing on clinical outcomes, complications, and mortality rates associated with hip fragility fractures.
Methods: A retrospective study was conducted involving patients aged ≥50 years old with fragility hip fractures admitted to our Fracture Liaison Service between 2019 and 2023. Lifestyle behaviours, demographic data, comorbidities, preoperative wait times, hospital stays, postoperative complications, including wound, urinary and respiratory infections, pulmonary embolism (PE), acute renal failure (ARF), acute heart failure (AHF), re-hospitalization at 1 and 3 months, and the need for re-operation, were assessed. The impact of surgical timing on one-year mortality was analysed. Data was analysed using RStudio.
Results: A total of 359 hip fracture patients were screened, with a mean age of 81.0 years (+/-9.2); the majority were women (85%). Patients were divided into two groups: Group 1 underwent surgical intervention within the first 48 hours (63%), while Group 2 experienced delayed surgical intervention (37%). The mean hospital stay was 6.8 days (+/-4.1) for Group 1 and 11.2 (+/-5.9) for Group 2. Nearly half (49%) of the patients had an ASA score of III, followed by II (26%), I (21%), and IV (4.2%). Post-operative complications were observed in 31 patients (8.7%), with respiratory tract infections being the most reported (3.6%), followed by urinary (2.5%) and wound infections (2.5%). 2 patients experienced Pulmonary Embolism, 1 Acute Renal Failure, and 6 Acute Heart Failure. Twenty-five patients required re-operation, while re-hospitalization was necessary for 7 and 3 patients at 1 and 3 months, respectively. The mortality rates were 3.4% and 5.3% at 6 and 12 months. Significant differences were noted

between patients regarding hospital stay and ASA score (p<0.005). However, no differences were observed between the two groups concerning postoperative complications and mortality rates.
Conclusion: Our findings suggest that while early surgical intervention within the first 48 hours is commonly advocated, delayed surgery remains a significant approach for many patients. No differences in postoperative complications and mortality rates between the early and delayed intervention groups were found. These findings highlight the need for further exploration into the factors influencing clinical outcomes beyond the temporal aspect of surgical timing.

050 - TYPE 2 LUPUS IS THE MAJOR PREDICTOR OF FATIGUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CROSS-SECTIONAL STUDY OF 200 PATIENTS

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Background: Fatigue is a major symptom in patients with systemic lupus erythematosus (SLE) significantly impacting health-related quality of life (HR-QoL). Causes of fatigue in SLE are multifactorial and not well understood. A novel framework categorizes SLE manifestations into type 1 and type 2. Type 1 manifestations can be ascribed to inflammation and captured in activity indexes, whereas type 2 symptoms (such as fatigue, pain, sleep, and mood disturbances) have no clear relation to disease activity. Type-2 SLE is defined using the polysymptomatic distress scale (PDSS).
Objective: To identify predictors of fatigue in SLE patients.
Methods: Cross-sectional study of SLE patients fulfilling ACR/EULAR 2019 and/or SLICC 2012 classification criteria followed in a Rheumatology outpatient clinic. Inclusion was from December 2023 to May 2024.

At inclusion, type 1 disease activity was scored with SLEDAI-2K and SLE-DAS, and organ damage with the SLICC/ACR Damage Index (SDI). HR-QoL was evaluated using FACIT-F, EQ5D-3L, EQ5D-3L VAS, and PDSS. Severe fatigue was defined as FACIT-F <30. Type 2 SLE was defined as a PDSS ≥12. An adjusted PDSS (aPDSS) excluding its fatigue component was calculated and a ROC curve was performed to determine the aPDSS cut-off for type 2 SLE definition. SLE low disease activity (LDA) was defined as SLE-DAS ≤2.48 with prednisolone ≤5 mg/day. Clinical diagnosis of fibromyalgia was retrieved from clinical records.

Differences in HR-QoL among patients with and without severe fatigue were compared with Mann-Whitney U tests. Logistic regression (LR) was used to identify predictors of severe fatigue through a two-step process: univariate LR identified variables with p<0.1, followed by multivariate LR to determine independent predictors and estimate adjusted odds ratios (OR) with 95% confidence interval (96%CI). Multicollinearity and overall fitness of the multivariate model were accessed through the Omnibus test, Hosmer and Lemeshow test, and R2 Nagerkerke. Significance was set at $\alpha \leq 0.05$.
Results: The study included 200 patients with SLE (female: 92.0%; mean age: 46.4±14.3 years; mean age at diagnosis: 30.2±12.7 years). Severe fatigue was present in 28.6%. In the study population, 87.5% fulfilled the LDA treatment target, 30.0% had type 2 SLE, 38.5% had organ damage, and 17.0% were diagnosed with fibromyalgia. Patients with severe fatigue had worse scores in EQ5D-3L (p<0.001), EQ5D-3L VAS (p<0.001), and both PDSS and aPDSS (p<0.0001). The aPDSS cut-off that better predicted SLE type 2 was ≥9.50 (sensitivity 96.9%, specificity 99.9%).

Univariate analysis showed significant variables for severe fatigue: female sex (p=0.071), age (p<0.05), disease duration (p<0.05), SLE-DAS (p<0.05), type 2 SLE (PDSS and aPDSS definitions) (p<0.001), and fibromyalgia (p<0.001), while LDA was protective (p<0.01). SLEDAI and SDI were not significant.

Multivariate analysis revealed type 2 SLE [OR 25.33; 95%CI(10.63-60.31); p<0.001) and diagnosis of fibromyalgia [OR 3.51; 95%CI(1.16-10.69); p<0.05] as independent predictors of severe fatigue. Similar findings were found when using aPDSS, [OR 16.16; 95%CI(7.22-36.13); p<0.001)] for type 2 SLE and [OR 4.44; 95%CI(1.51-12.26); p<0.05] for fibromyalgia.
Conclusion: In this cohort of SLE patients, type 2 lupus was the major predictor of severe fatigue. Physicians and patients should be careful not to attribute fatigue to inflammatory type 1 disease activity when the LDA treatment target is achieved. This should be taken into consideration for establishing the management strategy.

059 - SERUM C3 LEVELS AT DIAGNOSIS IN RENAL ANTINEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS: PREDICTORS OF LUNG DISEASE AND POORER RENAL SURVIVAL

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with the efficacy of Avacopan, a selective C5a receptor inhibitor used as a corticosteroids reduction strategy in the treatment of AAV.

Serum low complement factor 3 (sC3) levels without real hypocomplementemia are being increasingly recognized as predictors of prognosis in AAV. Serum low C4 (sC4) levels have not yet been associated with worst outcomes. We aim to evaluate the association between circulating sC3 and sC4 levels at diagnosis of AAV and outcomes.

Methods: Retrospective single-center study including 94 patients with AAV with renal involvement followed between 2003-2023, with sC3 and sC4 levels measurements at diagnosis. Patients were grouped according to the median sC3 and sC4 levels, as previously performed. We created a logistic regression model for the outcomes, adjusting for covariates. Patient and renal survival were compared between the groups using Kaplan-Meier with the log rank test and Cox regression.

Results: Mean age at diagnosis was 70±14.9 years old and most patients had ANCA MPO specificity (77.7%, n=73). Only 5 patients had real sC3 hypocomplementemia (< 83mg/dL) and sC4 hypocomplementemia (<12mg/dL) was present in 2 patients. Median sC3 levels were 125 mg/dL (106-142) and median sC4 levels were 30 mg/dL (24-38). Groups were defined according

059 – TABLE 1. Comparison of demographics, disease-related characteristics and histopathological features of patients with low or normal sC3 levels at diagnosis

	Low sC3 levels (n=45)	Normal/High sC3 levels (n=49)	p-value
Current age (years), mean (SD)	73.5 (60.8-83.0)	69.0 (59.0-78.0)	0.288
Age at diagnosis (years), mean (SD)	63 (56.5-71.5)	64 (49.0-72.0)	0.474
Gender			0.153
Female, n (%)	17 (37.8)	26 (53.1)	
Disease duration (years), median (IQR)	9 (4.5-12.3)	7 (3.0-10.0)	0.635
ANCA specificity, n (%)			0.205
MPO	36 (80)	37 (75.5)	
PR3	7 (15.6)	12 (24.5)	
Negative	2 (4.4)	0 (0)	
ANCA levels, median (IQR)	180 (110.5-200.0)	177 (123.5-200.0)	0.738
Anti-GBM positivity, n (%)	0	1 (2.3)	1.000
Histopathological confirmation, n (%)	34 (75.6)	41 (83.7)	0.403
ANCA Kidney Risk Score			0.337
Low	2 (8)	9 (24.3)	
Moderate	12 (48)	17 (45.9)	
High	9 (36)	8 (21.6)	
Very High	2 (8)	3 (8.1)	
Berden Scale			0.644
Crescentic	11 (42.3)	12 (31.6)	
Focal	10 (38.5)	17 (44.7)	
Sclerotic	2 (7.7)	6 (15.8)	
Mixed	3 (11.5)	3 (7.9)	
Complement levels at admission			
Median C4 (IQR)	27.0 (20.0-30.5)	34.0 (27.0-41.0)	**<0.001**
Low sC4 levels (<30 mg/dL), n (%)	28 (62.2)	17 (34.7)	**0.008**
Normal sC4 levels, n (%)	17 (37.8)	32 (65.3)	

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059 – TABLE 1. Continuation

Clinical Features, n (%)			
Extra-renal involvement	36 (80)	32 (65.3)	0.112
Lung involvement	32 (71.1)	17 (34.7)	**<0.001**
Alveolar hemorrhage	20 (44.4)	10 (20.8)	**0.015**
Relapse	9 (20.9)	12 (24.5)	0.685
Type of relapse (organ involved) (n=21)			0.173
Kidney	2 (22.2)	6 (50)	
Lung	1 (11.1)	3 (25)	
Kidney + Lung	5 (55.6)	1 (8.3)	
Cutaneous	0	1 (8.3)	
Other	1 (11.1)	1 (8.3)	
Acute dialysis requirement (first month), n (%)	21 (46.7)	9 (18.4)	**0.003**
Recovery from acute dialysis, n (%)	8 (38.1)	4 (44.4)	0.745
Dialysis, n (%)	28 (62.2)	16 (32.7)	**0.004**
Time to dialysis (months), median (IQR)	1.0 (1.0-12.0)	6.0 (1.0-48.0)	0.344
Death, n (%)	18 (40)	14 (28.6)	0.243
Time to death (months), median (IQR)	55 (24.0-99.0)	58.5 (112.0-86.3)	0.561
Urine analysis at baseline			
Hematuria, n (%)	38 (84.4)	42 (85.7)	0.863
Proteinuria, n (%)	38 (84.4)	43 (87.8)	0.642
Protein/Creatinine Ratio (mg/g), median (IQR)	1300.0 (413.8-2750.0)	1869.9 (974.2-3465.2)	0.783
Proteinuria g/24h, median (IQR)	2.4 (0.8-8.3)	1.7 (1.0-3.9)	0.744
Biochemistry			
Baseline GFR ml/min/1.73m2, median (IQR)	22.0 (10.5-35.0)	27.5 (16.8-42.8)	**0.019**
Current GFR ml/min/1.73m2, median (IQR)	44.0 (24.0-53.0)	42.5 (26.8-64.8)	0.528
Baseline sCr mg/dL, median (IQR)	2.9 (2.0-5.0)	2.2 (1.6-4.0)	**0.012**
Current sCr mg/dL, median (IQR)	1.4 (1.1-2.4)	1.4 (1.0-2.03)	0.650
Baseline Urea mg/dL, median (IQR)	122.0 (96.5-179.0)	114.5 (73.5-174.8)	0.368
Baseline Hemoglobin g/dL, median (IQR)	8.9 (8.0-9.8)	8.8 (7.8-10.4)	0.817
Baseline Platelets x10^9, median (IQR)	232 (188-307.5)	297 (244.8-376.3)	**0.002**
Baseline C-Reactive protein mg/L, median (IQR)	72.7 (16.1-165.6)	78.2 (18.2-130.8)	0.887

Footnote: sC3 – serum complement factor 3; SD – standard deviation; IQR – interquartile range; ANCA - antineutrophil cytoplasmic antibody; Anti-GBM – anti-glomerular basement membrane antibody; ENT – Ear-nose-throat; GFR – glomerular filtration rate; sCr – serum Creatinine.

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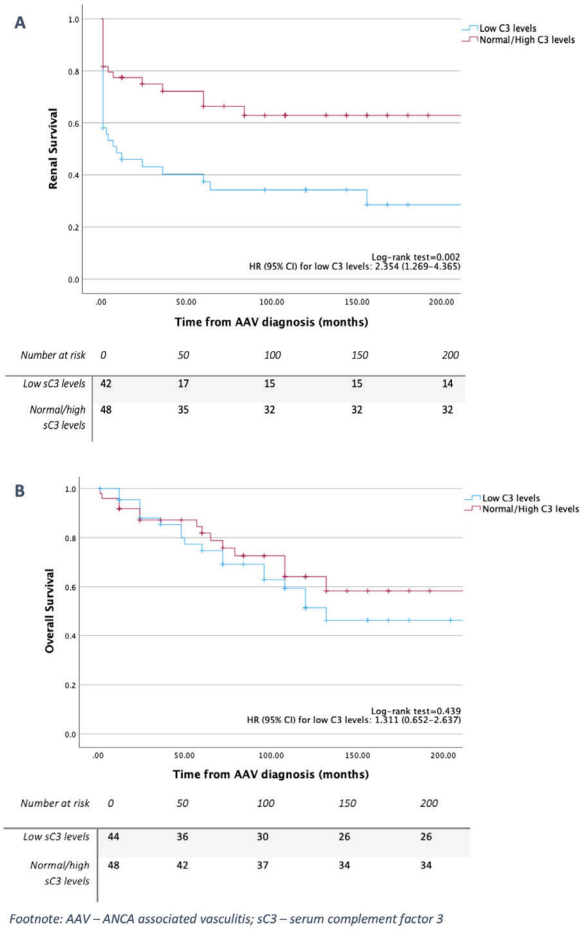
Background: Complement activation, specially the alternative pathway, has a role in the development of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). This was further corroborated



059 – Figure 1. Renal (A) and Overall (B) survival analysis according to median sC3 levels in AAV patients.

to these values: low sC3 levels (<125 mg/dL, n=45) and normal/high sC3 (n=49), low C4 levels (<30 mg/dL, n=45) and normal/high sC4 (n=49).

Patients with low sC3 levels had more frequent lung involvement than patients with higher sC3 levels (71.1% vs 34.7%, p=0.001, table 1), as well as alveolar hemorrhage (44.4% vs 20.8%, p=0.015). Regarding the outcomes, acute dialysis requirement (first month) was more prevalent in the low sC3 levels group (46.7% vs 18.4%, p=0.003). Furthermore, these patients also had a higher progression to dialysis anytime during follow-up (62.2% vs 32.7%, p=0.004).

After adjustment for baseline renal function, low sC3 levels independently predicted the odds of a patient requiring acute dialysis (OR 3.518, 95% CI 1.006-12.3, p=0.049), but the odds of progressing to dialysis anytime during follow-up was higher but not significant (OR 2.568, 95% CI 0.923-7.145, p=0.071). The group with low sC3 levels had an increase of 5 times the odds of lung disease after adjusting for baseline hemoglobin (OR=4.842 95% CI 1.948-12.031 p=<0.001, table 2) and of 2.6 times the odds of alveolar hemorrhage (OR = 2.649, 95% CI 1.026-6.849, p=0.044).

When looking at death and renal survival according to sC3 levels (figure 1), patients in the low sC3 levels group had significantly poorer long-term renal survival when compared with the normal sC3 levels group (p = 0.002). Patient survival was lower but not statistically different according to sC3 levels (p=0.439).

We did not find significant associations of sC4 values with the outcomes.

Conclusion: Complement activation in AAV has been associated to renal outcomes, but our results also highlight a possible role of complement in the pathophysiology of lung disease, with low sC3 levels as an independent predictor of lung involvement and of the occurrence of alveolar hemorrhage.

Patients with low sC3 levels without real hypocomplementemia had a higher risk of requiring acute dialysis and a poorer renal prognosis, expanding the existent evidence on the relevance of the alternative complement pathway activation in AAV patients.

075 - UNVEILING A RARE GENETIC ANOMALY: NEW MUTATION IN ACRO-DENTO-OSTEO DYSPLASIA LINKED TO HAJDU-CHENEY SYNDROME

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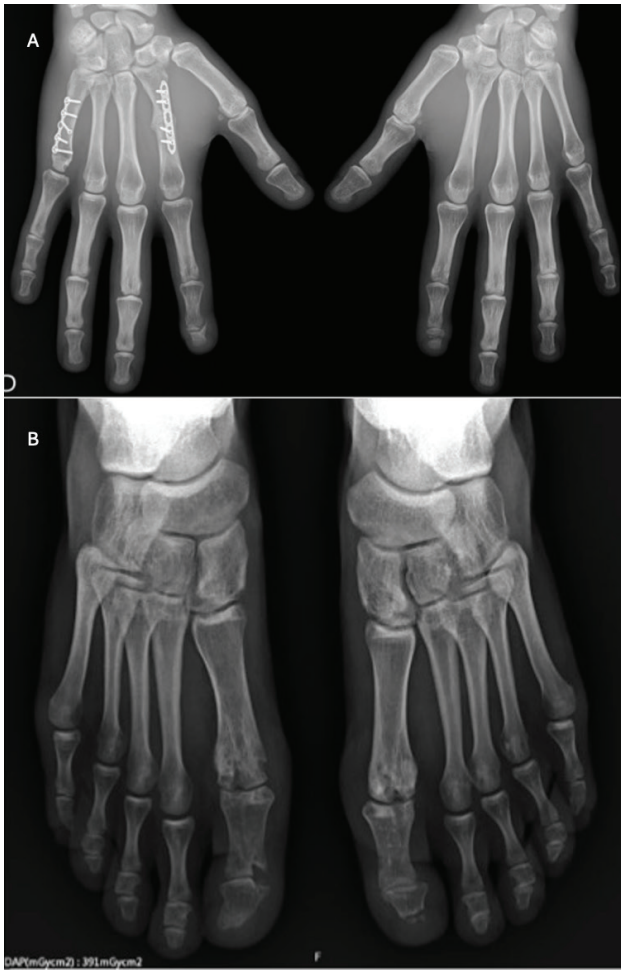
Introduction: Hajdu-Cheney syndrome, also known as acro-dento-osteo-dysplasia syndrome, is a rare genetic disorder whose prevalence is less than one person in one million. It is characterized by band osteolysis of distal phalanges and associated with facial dysmorphia, osteoporosis and other manifestations. Although there is no specific treatment, anti-resorptive treatment may offer a beneficial option.

Presentation: A 20-years-old handball man player presented to the rheumatology department with a 2-years history of bone fractures, both high and low impact, which required surgery treatment (right second and fifth metacarpals, second distal phalanges of both hands) and led him to stop playing sports. One day prior to the meeting, he underwent a fist premolar extraction and maxillary bone resorption was observed. He had no inflammatory back pain and anamnesis was negative for inflammatory rheumatic disease. Past medical history included amygdalotomy at age 3, hear surgery at age 3 due to hearing loss and chronic snoring with diagnosis of sleep apnea at the age of 11. It should be noted that from ages 11 to 13, the patient



059 – Figure 1. Hands (A) and feet (8) radiographic images showing band osteolysis in the 2nd distal phalanges of both hands, acroosteolysis of all distal phalanges in the hands and feet, erosions in :he first metatarsophalangeal joint and osteosynthesis material in 2nd and 5th metacarpals.

used a device to widen the palate, as it was vaulted and worsened the breathing difficulty. There was no family history of rheumatic or bone diseases. Physical examination revealed coarse voice, retrognathia, downslated palpebral fissures, long philtrum, full cheek, hypertelorism and digital pseudoclubbing. No peripheral arthritis was objectivated. Blood and urine tests, including acute phase reactants and autoimmune markers, were normal. Radiological examination showed band osteolysis in the 2nd distal phalanges of both hands, acroosteolysis of all distal phalanges in the hands and feet, erosions in the first metatarsophalangeal joint and osteosynthesis material in 2nd and 5th metacarpals (Fig. 1). Bone density scan (DXA) detected low vertebral bone mineral density (Z-Score: -2,85 SD). Given the patient history and these imaging tests, a congenital osteolysis syndrome was suspected. The genetic study detected a mutation in the NOTCH2 gene - variant c.6596dup, P.(Ser2200lefs*4 - and it was concluded that, although this variant had not yet been described, given its nature, it would be expected to have a deleterious impact. Considering the patient's phenotype and this pathogenic genetic mutation, the diagnosis of Hajdu-Cheney syndrome was made. Treatment with antiresorptive treatment (zoledronic acid; 5 mg intravenous, annually) was started, but before that, the patient has experienced two additional tooth losses with failure to place the respective dental implants. Currently, he has received one infusion of zoledronic acid and we did not observed new bone fractures.

Discussion: HCS is a rare genetic condition, characterized by generalized osteoporosis and focal bone loss (acro-osteolysis and dental). According to ORPHANET, less then 100 cases are registered. Patients have a variable clinical presentation (cranial, facial, musculoskeletal and, sometimes, cardiovascular alterations) that varies from early infancy to late adulthood, worsening over time because of its age-dependent evolution. Bone fragility is an important issue in management comorbidities. Chronic treatment with bisphosphonates is the main strategy for osteoporosis and to prevent new bone fractures. As this disease is particularly rare, the accumulation of clinical reports is extremely important. We report the second case of HCS in Portugal with a new mutation which has not been previously identified.

082 - VITAMIN D STATUS AND OSTEOPOROSIS IN PORTUGUESE PATIENTS WITH INFLAMMATORY BOWEL DISEASE: ASSOCIATION WITH CLINICAL FEATURES

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Background: Lower levels of vitamin D and total body mineral density have been found in patients with IBD which may increase OP and pathological bone fractures risk due to several mechanisms.

Objectives: To assess the prevalence of vitamin D deficiency in a Portuguese cohort of patients with inflammatory bowel disease (IBD). To evaluate the association of demographic, clinical and analytical features with vitamin D serum levels and differences between patients with and without osteoporosis (OP).

Material and Methods: Monocetric retrospective study. All patients included had IBD. Demographic, clinical and analytical data were collected at the time

082 – TABLE 1. Features related to vitamin D serum levels and osteoporosis (by DXA)

	25-HOVitD (ng/mL)	Osteoporosis (T-score ≤ 2.5 or Z-score ≤ 2.0)*		
		Yes (n=41)	No (n=194)	
Age at V1 - mean±SD	*r=-0.420; p=0.529*	48.73±14.75	42.78±12.84	***p=0.035***
BMI - mean±SD	*r=-0.136; p=0.590*	23.81±4.32	25.93±4.57	***p=0.008***
Duration of IBD - median (IQR)	*r=-0.850; p=0.201*	12.00 (14.00)	9.50 (9.30)	*p=0.104*
Hemoglobin - median (IQR)	***r=0.151; p=0.023***	14.00 (2.10)	14.00 (2.30)	*p=0.461*
Total proteins - mean±SD	*r=0.350; p=0.626*	72.00±5.48	73.28±5.33	*p=0.199*
Albumin - median (IQR)	*r=0.121; p=0.710*	41.70 (4.30)	42.80 (4.50)	*p=0.122*
Beta-CTX - median (IQR)	*r=-0.120; p=0.079*	0.38 (0.26)	0.36 (0.27)	*p=0.135*
Osteocalcin - median (IQR)	*r=-0.850; p=0.217*	23.20 (15.80)	19.00 (11.60)	***p=0.030***
Total calcium - median (IQR)	***r=0.135; p=0.045***	4.70 (0.30)	4.70 (0.20)	*p=0.730*
CRP - median (IQR)	*r=-0.119; p=0.073*	3.30 (7.20)	2.50 (5.30)	*p=0.303*
ESR - median (IQR)	***r=-0.232; p<0.001***	16.00 (29.00)	14.50 (19.00)	*p=0.132*
Ferritin - median (IQR)	*r=-0.30; p=0.671*	153.75 (240.30)	85.00 (130.80)	*p=0.061*
25-HVitD (ng/mL) - median (IQR)	---	15.00 (13.00)	19.00 (13.00)	***p=0.008***
25-HVitD deficency - n (%)	---	---	---	*p=0.054*
≤ 30 ng/mL (n=189)	---	38 (92.7)	151 (77.8)	---
> 30 ng/mL (n=36)	---	2 (4.9)	34 (17.5)	---
Sex, median - n (%)	---	---	---	*p=0.863*
Female	---	23 (56.1)	112 (57.7)	---
Male	---	18 (43.9)	82 (42.3)	---
Under VitD supplements – (n=15, %)	---	3 (7.3)	11 (5.7)	*p=0.842*

Footnote: Beta-CTX: beta-carboxy-terminal type-1 collagen crosslinks; BMI: body mass index; CRP – C reactive protein; DXA: Dual-energy X-ray absorptiometry; ESR: erythrocyte sedimentation rate; 25(HO)VitD: 25-hydroxy vitamin D; IBD: inflammatory bowel disease; IQR: interquartile range; SD: standard deviation; V1: first visit at rheumatology department; *considering age at V1 (≥40 or <40 years old, respectively)

of the first visit in the Rheumatology department (V1). Correlations between continuous variables were evaluated by Spearman rank test and Pearson's correlation coefficient; Mann-Whitney U and T-student tests were used in the comparison analysis between groups.

Results: Two hundred forty-four patients were included, mostly female (57.4%), with a mean age at V1 of 46.65 (±13.46) years. One hundred eighty-four (75.4%) patients had Crohn's disease (CD) and 60 (24.6%) had ulcerative colitis (UC). Forty-one patients (16.8%) had osteoporosis (T score ≤ -2.5 or Z score ≤ -2.0 in DXA, according to age ≥40 or <40 years, respectively) and 10 (4.1%) had previous fragility fractures. One hundred ninety-two (78.7%) patients exhibited low levels of 25-hydroxy vitamin D (25(HO)VitD; <30ng/mL), 17 (6.9%) were taking calcium and/or vitamin D supplements. Of all the parameters evaluated, serum levels of 25(HO)VitD correlated positively with hemoglobin (Hb; r=0.151, p=0.023) and total calcium (r=0.135, p=0.045) and negatively with erythrocyte sedimentation rate (ESR; r=-0.232, p<0.001). Among patients with osteoporosis, serum levels of 25(HO)VitD were lower (p=0.008) compared to non-osteoporotic patients; except for age at V1, body mass index and osteocalcin, no other statistically significant differences were observed (table 1).

Conclusions: This study reveals higher prevalence of OP in comparison with the general Portuguese population and an association of OP with vitamin D deficiency across patients with IBD. On the other hand, our results show significant correlations between clinical/analytical variables and vitamin D levels: positive correlation of 25(OH)VitD with Hb and negative correlation with ESR, suggesting a potential link to inflammatory state.

094 - PATIENTS WITH SERONEGATIVE SJÖGREN'S DISEASE HAVE COMPARABLE DISEASE ACTIVITY AND BURDEN TO ANTI-RO/LA-POSITIVE PATIENTS, BUT A LOWER FREQUENCY OF SKIN, HAEMATOLOGICAL AND BIOLOGICAL ACTIVITY:DATA FROM PORTRESS, THE PORTUGUESE REGISTRY OF SJÖGREN'S DISEASE

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Manuel Silvério-António[1, 2], Ana Rita Lopes[1, 2], Filipe Cunha Santos[3], Paulo Jorge Pereira[4], Diana Belchior Raimundo[5], Anita Cunha[6], C. Pinto Oliveira[7], Ana Catarina Duarte[8], João Madruga Dias[9], Mariana Emília Santos[10], Maria João Gonçalves[10, 11, 12], Ana Catarina Moniz[10], Ana Isabel Maduro[13], Mariana Luis[13], Ana Valido[14], Margarida Oliveira[15], Luísa Brites[16], Catarina Tenazinha[17], Nikita Khmelinskii[1], Filipe Barcelos[18, 19], JE Fonseca[1,2], Vasco C Romão[1, 2], PORTRESS Reuma.pt Task Force[2,3,8,10,16,20,21,22,23, 24,25,26,27,28,29,30,31]

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Background: Sjogren's disease (SjD) is a chronic systemic condition primarily characterized by reduced function of the lacrimal and salivary glands. B cell hyperreactivity and production of anti-Ro and/or anti-La antibodies are important features. Mechanisms and features of seronegative disease remain mostly understudied.

Objectives: To define the clinical characteristics of SjD patients with and without positivity of anti-Ro and/or anti-La antibodies.

Methods: This study is based on the Portuguese registry of SjD (PORTRESS) which included patients with a clinical diagnosis of SjD registered up to November 2023. Patients who had information regarding anti-Ro and/or anti-La status were included. Seropositivity was defined as the presence of anti-Ro and/or anti-La. Demographic, clinical and treatment data were collected. Variables were compared according to parametric or non-parametric tests, as applicable. Associations of seropositivity, adjusted for sex and age at diagnosis, were identified through binomial logistic regression modeling.

Results: We included 1288 patients, 94.3% female, mean age 61.7±14.3 years. The majority of patients (86.6%) were seropositive.

Seropositive patients were younger at symptom onset/diagnosis and had a higher prevalence of ANA and rheumatoid factor. Hypergammaglobulinemia, and risk factors for lymphoma, such as low C3 and C4, persistent salivary gland swelling, purpura / cutaneous vasculitis and lymphopenia were more common in these patients. Systemic disease was also more frequent in anti-Ro/La-positive patients, as evidenced by higher frequencies of constitutional, lymphadenopathic, glandular, cutaneous, haematologic and biologic involvements (ESSDAI definition). However, baseline ESSDAI and ESSPRI scores did not differ between groups. Hydroxychloroquine use was more common in patients with seropositivity, whereas methotrexate and pilocarpine use were numerically higher in anti-Ro/La-negative patients.

On multivariate analysis, a younger age at diagnosis (OR 1.02 [1.00-1.03], p=0.038), cutaneous (OR 2.45 [1.24-4.85], p=0.010), haematologic (OR 2.46 [1.48-4-10], p<0.001) and biologic involvement (OR 3.68

094 – TABLE 1. Demographic and clinical characteristics of seropositive and seronegative SjD patients.

	Seropositive SjD N=1115	Seronegative SjD N=173	p
Female	1047 (93.9)	167 (96.5)	0.218
Caucasian / White	864 (93.1)*	130 (93.5)**	0.854
Age at diagnosis	52.2±14.9*	58.8±12.7**	**<0.001**
Age at symptom onset	47.2±15.1*	52.3±12.1**	**<0.001**
Disease duration	11.0 [11.5]*	12.8±7.5**	0.615
Break up tear time <10s	223 (74.1)*	23 (74.2)**	0.990
Positive Schirmer's test	515 (74.3)*	59 (75.6)**	0.799
vB score ≥4 or OSS ≥5#	74 (13.2)*	11 (10.7)**	0.476
USF<0.1ml/min	138 (22.8)*	22 (21.6)**	0.788
Focus score ≥1	367 (47.4)*	75 (56.0)**	0.067
AECG 2002 or ACR/EULAR 2016	829 (73.5)	45 (26.0)	**<0.001**
ANA	979 (96.9)*	75 (51.4)**	**<0.001**
anti-Ro	1065 (96.1)*	0	NA
anti-La	785 (73.4)*	0	NA
Rheumatoid factor	499 (52.8)*	30 (21.1)**	**<0.001**
Cryoglobulin	40 (5.9)**	10 (9.4)**	0.163
Hypergammaglobulinemia	506 (53.0)*	31 (22.3)**	**<0.001**
Low C3	180 (18.7)*	13 (9.2)**	**0.005**
Low C4	95 (9.9)*	4 (2.8)**	**0.006**
Persistent salivary gland swelling	85 (8.7)*	4 (2.8)**	**0.016**
Purpura / cutaneous vasculitis	67 (6.9)*	1 (0.7)**	**0.004**
Lymphopenia	220 (22.5)*	9 (6.4)**	**<0.001**
Monoclonal gammopathy	58 (6.2)*	7 (5.2)**	0.647
Ectopic lymphoid structures on salivary glands	41 (6.8)*	4 (3.6)**	0.207
Lymphoma	16 (2.1)*	3 (3.6)**	0.428
Non Hodgkin lymphoma	3 (0.4)*	0**	NA
Baseline ESSDAI	2.0 [4.0]*	2.0 [4.0]**	0.597
Baseline ESSPRI	5.3 [4.7]*	5.8 [5.0]**	0.618
Involvements			
- Constitutional	209 (20.0)*	17 (9.9)**	**0.002**
- Lymphadenopathic	127 (12.1)*	10 (5.9)**	**0.017**
- Glandular	348 (33.2)*	34 (20.0)**	**<0.001**
- Articular	464 (44.2)*	71 (41.3)**	0.476
- Cutaneous	210 (20.1)*	11 (6.5)**	**<0.001**
- Pulmonary	94 (9.0)*	8 (4.7)**	0.065
- Renal	32 (3.1)*	2 (1.2)**	0.214

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094 – TABLE 1. Continuation

- Muscular	16 (1.5)*	2 (1.2)**	0.723
- Peripheral nervous system	39 (3.7)*	8 (4.7)**	0.540
- Central nervous system	19 (1.8)*	1 (0.6)**	0.342
- Haematologic	406 (38.6)*	21 (12.3)**	**<0.001**
- Biologic	607 (57.7)*	35 (20.5)**	**<0.001**
- Hepato/Gastrointestinal	34 (3.3)*	2 (1.2)**	0.138
- Other	154 (16.1)*	20 (13.6)**	0.444
Treatment			
- Corticosteroids	321 (39.8)*	32 (35.2)**	0.393
- Hydroxychloroquine	640 (79.3)*	64 (70.3)**	**0.049**
- Pilocarpine	207 (25.7)*	31 (34.1)**	0.085
- Methotrexate	126 (15.6)*	21 (23.1)**	0.068
- Azathioprine	91 (11.3)*	10 (11.0)**	0.934
- Leflunomide	32 (4.0)*	1 (1.1)**	0.241
- Rituximab	37 (4.6)*	2 (2.2)**	0.418
- Mycophenolate mofetil	25 (3.1)*	2 (2.2)**	1.000
- IVIG	5 (0.6)*	1 (1.1)**	0.474
- Cyclophosphamide	4 (0.5)*	0**	NA
Death	4 (0.6)*	1 (1.5)**	0.379

Results presented as mean±standard deviation or median [interquartile range] or n (%)
Positive ocular surface score van Bijsterveld score ≥4 or ocular staining score ≥5
* caucasian / white: N=928; age at diagnosis: N=1006; age at symptom onset: N=846; disease duration: N=846; ANA: N=1010; antiRo: N=1108; antiLa: N=1069; Rheumatoid factor: N=945; Cryoglobulin: N=680; Hypergammaglobulinemia: N=954; Low C3: N=961; Low C4: N=961; Persistent salivary gland swelling: N=982; Purpura / cutaneous vasculitis: N=976; Lymphopenia: N=978; Monoclonal gammopathy: N=937; Ectopic lymphoid structures on salivary glands: N=601; Lymphoma: N=749; Non Hodgkin lymphoma: N=749; Break up tear time<10s: N=301; Positive Schirmer's test: N=693; van Bijsterveld score ≥4 or ocular staining ≥5: N=559; USF<0.1ml/min: N=606; Focus score≥1: N=774; Baseline ESSDAI: N=915; Baseline ESSPRI: N=534; Constitutional: N=1044; Lymphadenopatic: N=1048; Glandular: N=1049; Articular: N=1050; Cutaneous: N=1047; Pulmonary: N=1048; Renal: N=1045; Muscular: N=1045; Peripheral nervous system: N=1046; Central nervous system: 1042; Haematologic: N=1051; Biological: N=1052; Hepato/gastrointestinal: N=1043; Other: N=958; Hydroxychloroquine: N=807; Corticosteroids: N=807; Pilocarpine: N=807; Methotrexate: N=807; Azathioprine: N=807; Rituximab: N=807; Leflunomide: N=807; Mycophenolate mofetil: N=807; IVIG: N=807; Cyclophosphamide: N=807; Death: N=662. ** caucasian / white: N=139; age at diagnosis: N=147; age at symptom onset: N=126; disease duration: N=126; ANA: N=145; Rheumatoid factor: N=142; Cryoglobulin: N=106; Hypergammaglobulinemia: N=139; Low C3: N=142; Low C4: N=142; Persistent salivary gland swelling: N=142; Purpura / cutaneous vasculitis: N=141; Lymphopenia: N=140; Monoclonal gammopathy: N=135; Ectopic lymphoid structures on salivary glands: N=110; Lymphoma: N=84; Non Hodgkin lymphoma: N=84; Break up tear time <10s: N=31; Positive Schirmer's test: N=78; van Bijsterveld score≥4 or ocular staining≥5: N=103; USF<0.1ml/min: N=102; Focus score≥1: N=134; Baseline ESSDAI: N=110; Baseline ESSPRI: N=64; Constitutional: N=171; Lymphadenopatic: N=170; Glandular: N=170; Articular: N=172; Cutaneous: N=170; Pulmonary: N=169; Renal: N=170; Muscular: N=170; Peripheral nervous system: N=170; Central nervous system: 170; Haematologic: N=171; Biological: N=171; Hepato/gastrointestinal: N=170; Other: N=147; Hydroxychloroquine: N=91; Corticosteroids: N=91; Pilocarpine: N=91; Methotrexate: N=91; Azathioprine: N=91; Rituximab: N=91; Leflunomide: N=91; Mycophenolate mofetil: N=91; IVIG: N=91; Cyclophosphamide: N=91; Death: N=66

[2.38-5.70], p<0.001) were associated with seropositivity, irrespective of sex and constitutional, glandular and lymphadenopathic involvement.

A sensitivity analysis including only seronegative patients with a positive minor salivary gland biopsy (n=75) showed similar findings except for comparable frequency of low C4 and hydroxychloroquine use.

Conclusions: Analysis of the PORTRESS cohort of SjD indicated that seropositive patients tend to exhibit more active serological and clinical disease. In particular, presence of anti-Ro and/or anti-La was associated with cutaneous, haematologic and biologic involvements. Nevertheless, seronegative patients, who may often be underdiagnosed, still experienced comparable disease activity, burden and need for immunosuppressive therapies.

102 - IS YOUR PATIENT'S DIAGNOSIS CORRECT? LESSONS FROM A SERIES OF CASES

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Background: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a chronic genetic autoinflammatory disease identified in adults, often misdiagnosed due to its varied clinical manifestations. The first case was reported in January 2021. Given the limited literature, we present two cases with differing outcomes to emphasize the crucial role of rheumatologists on its diagnosis.

Case 1: A 49-year-old male exhibited multiple inflammatory symptoms over four years, including erythema nodosum, orbital pseudotumor, and persistent anemia. Extensive diagnostic workups were inconclusive, apart from pancytopenia with persistently elevated inflammatory markers. He had a history of chronic corticosteroid treatments. At age 52, he was referred to the rheumatology department to evaluate due to one year of asymmetric oligoarthritis. He denied any past or present history of genital or oral ulceration, thrombotic events, or folliculitis. He started on methotrexate 15 mg weekly, folic acid 5 mg weekly, and calcium carbonate 1250 mg daily plus cholecalciferol 400 IU. Prednisolone was tapered to 12.5 mg daily At age 52 , he developed left inguinal swelling with a hardened center of 3 cm , with redness and pain and an excisional biopsy showed histiocytic necrotizing lymphadenitis. CT scans of the chest, abdomen and pelvis showed no significant abnormalities. He had monthly appointments for 19 months in rheumatology, but his macrocytic anemia worsened (despite normal values of folic acid and vitamin B12), developing into pancytopenia , leading to methotrexate titration and eventual suspension due concerns of myelotoxicity .Meanwhile, a new bone marrow biopsy revealed myelodysplasia with normal karyotype and FISH study. At age 53, he started infliximab 300 mg IV every 6 weeks but discontinued after 3 cycles due to several bacterial infections. Following the description of VEXAS syndrome in 2021, the patient was tested for the condition and the diagnosis was confirmed at age 55, just 3 months after the first case was described in the literature. Despite treatments with ruxolitinib, and azacitidine, the patient died due to transplant complications.

Case 2: An 76-year-old male followed in Hematology appointment due low risk to myelodysplastic syndrome with normal karyotype and FISH study and symptomatic anemia, responsive to epoetin (EPO) treatment. He was referred to the rheumatology department due to osteoporotic fractures. At the rheumatology appointment , the patient exhibited cauliflower ears. He referred a 2-year history of inflammatory pain and red swelling in both ear pinnae that resolved with corticosteroids and well as asymmetric oligoarthritis. He referred to multiple prolonged corticosteroid use in the past. Blood tests revealed persistent macrocytic anemia, elevated inflammatory markers, and moderate vitamin D. Genetic testing later confirmed VEXAS syndrome at age 80. The patient remains with stable hemoglobin values on EPO and does not require chronic corticosteroids. Osteoporosis with treated with teriparatide, but the patient suffers from severe mobility issues and requires third-party support.

Discussion/Conclusion: These cases highlight the diagnostic challenges and management complexities of VEXAS syndrome. Awareness of this syndrome is crucial for timely diagnosis and appropriate treatment. Multidisciplinary collaboration and further research are essential to improve outcomes and establish diagnostic and therapeutic guidelines.

118 - HOW EARLY IS EARLY? UNVEILING TIME TO DIAGNOSIS SINCE SYMPTOM ONSET AND ITS DETERMINANTS IN PATIENTS SUSPECTED OF EARLY AXIAL SPONDYLOARTHRITIS: DATA FROM THE SPONDYLOARTHRITIS CAUGHT EARLY (SPACE) COHORT

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Background: Patients with chronic back pain (CBP) of less than two-years (2y) duration suspected of axial spondyloarthritis (axSpA) referred to the rheumatologist can be reliably diagnosed (Marques ML, et al. 2024). However, the time to diagnosis from symptom onset and its determinants remain poorly studied in patients with recent-onset CBP. We aimed to investigate the time to diagnosis after symptom onset in patients with CBP suspected of axSpA referred to the rheumatologist and assess the main determinants for an early axSpA diagnosis.

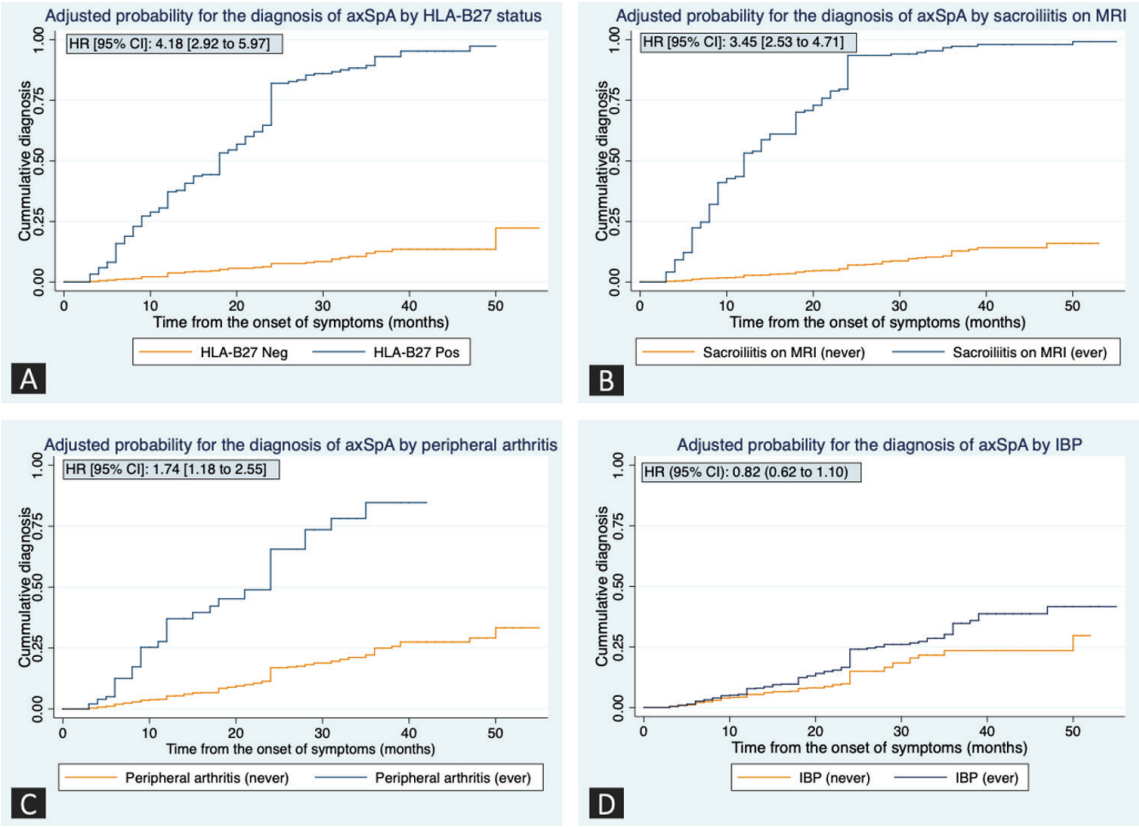
Methods: We analyzed the 2y-data from the SPondyloArthritis Caught Early (SPACE) multi-center cohort of patients (<45y) with CBP (≥3 months, ≤2y) of unknown origin. Clinical, laboratory, and imaging SpA features were collected over time. An event was defined as an axSpA diagnosis with level of confidence (LoC)≥7 at last observation or LoC< 7 in ≥2 last consecutive visits. Time to event (months) was computed from symptom onset to the first visit with the event. Patients without the event were censored at 2y or loss to follow-up. SpA features were considered at the time of diagnosis. Median survival times were computed overall and per SpA feature (un-/adjusted for covariates). Uni-/multivariable Cox-regression models identified determinants for the axSpA diagnosis. The final multivariable model allowed subgroup comparisons for time-to-event by SpA feature, adjusting for other SpA features (adjusted Kaplan-Meier curves).

Results: The SPACE cohort included 548 unknown-origin CBP patients with information on diagnosis, LoC and symptom duration. These were included in the survival analysis (mean [SD] age:31[8] years, symptom

118 – TABLE 1. Median survival times and Cox proportional hazard models for the axSpA diagnosis (event) in patients with chronic back pain symptom duration of ≥3 months but ≤2 years starting before the age of 45 years

Covariates at the time of diagnosis	With axSpA	Without axSpA	Median survival times [reference category] (months)	Univariable Cox regression	Multivariable Cox regression	
			Unadjusted	Adjusted	HR (95% CI)	Adj HR (95% CI)
Gender, male	50%	26%	24	39	2.00 (1.53-2.61)	1.36 (1.02-1.80)
HLA-B27, positive	76%	18%	21	18	5.30 (3.86-7.26)	4.18 (2.92-5.97)
Age, ≤31 years	60%	47%	24	NR	0.98 (0.96-0.99)	0.98 (0.96-0.99)
Family history of SpA, positive	51%	41%	35	NR	0.97 (0.74-1.27)	0.76 (0.56-1.03)
Inflammatory back pain, ever	60%	52%	36	NR	0.91 (0.69-1.20)	0.82 (0.62-1.10)
Good response to NSAIDs, ever	47%	34%	35	38	1.19 (0.91-1.56)	1.42 (1.07-1.89)
Peripheral arthritis, ever	17%	8%	24	24	1.99 (1.39-2.85)	1.74 (1.18-2.55)
Dactylitis, ever	7%	3%	24	35	1.76 (1.04-2.97)	1.19 (0.63-2.24)
Heel pain, ever	19%	9%	24	29	1.50 (1.07-2.12)	1.37 (0.95-1.97)
Anterior uveitis, ever	14%	4%	20	39	1.92 (1.30-2.82)	1.94 (1.27-2.97)
Inflammatory bowel disease, ever	7%	7%	29	12	1.06 (0.64-1.76)	1.21 (0.70-2.09)
Psoriasis, ever	11%	8%	24	NR	1.41 (0.92-2.15)	1.68 (1.02-2.75)
Elevated CRP (>5mg/l), ever	41%	29%	29	NR	1.26 (0.96-1.66)	1.25 (0.95-1.65)
Sacroiliitis on radiographs, ever	20%	1%	18	24	3.25 (2.32-4.54)	1.06 (0.72-1.56)
Sacroiliitis on MRI, ever	62%	9%	18	12	4.99 (3.79-6.58)	3.45 (2.52-4.71)

SpA features were considered at the time of diagnosis as 'once a feature, always a feature' using local reports and standardization according to the Assessment of SpondyloArthritis international Society (ASAS) definitions - Sieper J et al., Ann Rheum Dis. 2009;68 Suppl 2:ii1-44 (unless stated otherwise). #Categorized as ≤/> median age. $modified New York criteria according to local radiologists. §Inflammatory and/or structural changes compatible with sacroiliitis as reported by local radiologists. ^Elevated if >5mg/l. Adj – adjusted, axSpA – axial spondyloarthritis, CI – confidence interval, CRP – C-reactive protein, HR – Hazard ratio, NSAIDs – Nonsteroidal Anti-Inflammatory Drugs, MRI – magnetic resonance imaging. Colour-code: Blue – median survival times ≤ 24 months; Orange – median survival times > 24 months; Grey – median survival time not reached (NR). Significant results from the Cox proportional hazard models are highlighted in bold.



118 – Figure 1. Examples of Kaplan-Meier curves for the adjusted probability of axial Spondyloarthritis (axSpA) diagnosis since the onset of chronic back pain symptoms (in months) by A. HLA-B27 status (positive/negative), B. Sacroiliitis on MRI, i.e., inflammatory and/or structural changes compatible with sacroiliitis as reported by the local radiologist (ever/never), C. Peripheral arthritis (ever/never), and D. Inflammatory back pain (IBP) according to the ASAS definition (ever/never). Estimates derived from the Cox regression model including all SpA features: HLA-B27 status (except A), gender, age at diagnosis, family history of spondyloarthritis, inflammatory back pain (except D), good response to NSAIDs, peripheral arthritis (except C), dactylitis, heel pain, uveitis, inflammatory bowel disease, psoriasis, elevation of Creactive protein, sacroiliitis on radiographs (modified New York criteria) and sacroiliitis on MRI (except B).

duration:13[7] months, males:35%, HLA-B27 positivity:41%). Overall, 215 (39%) received a 2y diagnosis of axSpA (median time to diagnosis: 35 months). As expected, the axSpA group showed a higher prevalence of SpA features (Table 1). The lowest adjusted median survival times (up to 24 months) were observed for sacroiliitis on radiographs (8 months), sacroiliitis on MRI (12 months), inflammatory bowel disease (12 months), HLA-B27 positivity (18 months) and peripheral arthritis (24 months) (Table 1). Kaplan-Meier curves showed median survival times and diagnosis probability (Figure 1). A contrasting example of a SpA feature not determining the diagnosis (inflammatory back pain) is also shown. Multivariable Cox regression models emphasized HLA-B27 positivity and sacroiliitis on MRI as the strongest determinants implying a 4.2- and 3.5-times adjusted higher likelihood for the diagnosis of axSpA, respectively (Table 1). Peripheral arthritis, anterior uveitis or psoriasis implied each ~2-times higher risk for the axSpA diagnosis. Good response to NSAIDs, male sex and a younger age increased the probability for the diagnosis of axSpA slightly.

Conclusion: Half of the patients with CBP suspected of axSpA referred to the rheumatologist received the diagnosis within the first 35 months after symptom onset. HLA-B27 positivity, sacroiliitis on imaging and peripheral arthritis are the SpA features most contributing to an early (up to 2y after symptom onset) diagnosis of axSpA in these patients.

134 - UMA DÉCADA DE EPIDEMIOLOGIA DAS FRATURAS PROXIMAIS DO FÉMUR EM PORTUGAL

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Objetivos: Descrever a epidemiologia das Fraturas Proximais do Fémur (FPF) em Portugal, durante a última década, considerando também os dias de internamento e a taxa de mortalidade intra-hospitalar. Comparar os últimos 5 anos com o período homólogo de 2006-2010.

Métodos: Dados da Administração Central do Sistema de Saúde (ACSS), relativos aos registos totais de internamento nos hospitais do Serviço Nacional de Saúde de Portugal Continental, no período de 1 de janeiro de 2013 a 31 de dezembro de 2022, incluindo doentes com idade ≥40 anos e com os códigos de diagnóstico 820 (ICD-9-CM) até 2016, ou S720 (ICD-10-CM) a partir de 2017.

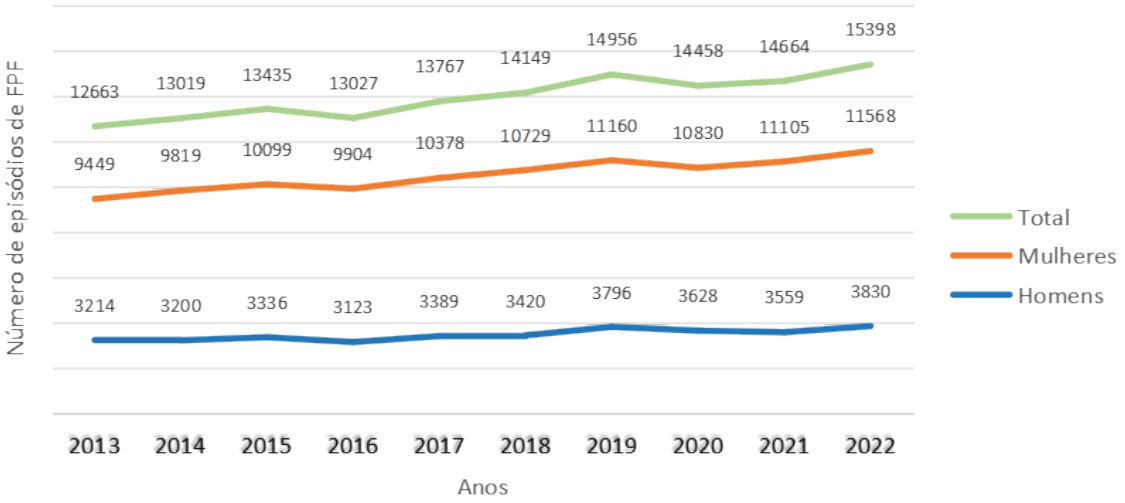
Resultados: Observou-se que o número de internamentos por FPF foi de 12.663 em 2013 e aumentou para 15.398 em 2022, com um acréscimo médio de 274 fraturas adicionais a cada ano (Imagem 1). A maioria dos doentes era do sexo feminino (74,3%), com idade média à admissão de 81,6 anos. O tempo médio de internamento foi de 15,4 dias. A taxa de mortalidade intra-hospitalar foi de 5,6%. A comparação do quinquénio 2006-2010 com o quinquénio 2018-2022, revela um aumento de FPF de 41,6% neste intervalo (51.701 vs 73.216), com uma aceleração do acréscimo médio (238 vs 245 casos adicionais por ano). A idade média à admissão aumentou de 81,3 para 82,9 anos no sexo feminino e 76,6 para 78,5 anos no masculino. A mortalidade intra-hospitalar aumentou de 5,1% para 5,8%, assim como o tempo médio de internamento para ambos os sexos (Mulheres: 14,2 vs 15,3 dias; Homens: 15,2 vs 17,1 dias). A população média anual portuguesa diminuiu neste intervalo (10.047.685 vs 9.908.283), mas a população com mais de 40 anos aumentou em percentagem (51,6% vs 59,5%) e em números absolutos (5,18 vs 5,89 milhões). A incidência média global de FPF aumentou de 200 para 261 fraturas/ano/100.000 habitantes ≥40 anos e a taxa de incidência por grupos etários de 5 anos, aumentou em todos os grupos entre os 40 e os 74 anos e diminuiu nos grupos etários entre os 75 e os 99 anos (Tabela 1). No geral, o número absoluto de FPF observado no período 2018-2022 foi maior do que o previsto com base nas taxas de incidência de 2006-2010, para a primeira faixa etária (≤74 anos) e menor do que o esperado para o grupo mais velho (>75 anos).

Conclusões: O estudo mostra que o número total de Fraturas Proximais do Fémur continua a aumentar em Portugal, assim como a idade média dos doentes, a mortalidade intra-hospitalar e a duração de internamento.

Os nossos dados sugerem que a prevenção em pessoas com idade inferior a 75 anos deve ser enfatizada, em paralelo com esforços mais profundos em idades acima deste limite.

134 – Table 1

	Incidência média anual de FPF por 100.000 habitantes			
	Homens		Mulheres	
Grupo etário (anos)	2006-2010	2018-2022	2006-2010	2018-2022
40-44	14,1	15,3	4	4,9
45-49	18,4	18,2	6,9	8,2
50-54	22,3	28,3	15,4	19,7
55-59	31,6	41,2	29,6	37,4
60-64	45,1	54,1	60,6	59,6
65-69	75,9	85	117	120
70-74	129	131	274	272
75-79	264	226	609	587
80-84	535	496	1190	1212
85-89	1006	843	2291	2072
90-94	1663	1693	2989	2806
95-99	2578	2360	3552	3113



134 – Figura 1. Número de episódios por Fratura Proximal do Fémur em Portugal Continental entre 2013 e 2022

Em termos globais, estes números demonstram o desafio notável que as fraturas de fragilidade representam para o sistema de saúde português, o que torna urgente uma política nacional integrada de combate à osteoporose, desde a prevenção primária até aos cuidados hospitalares após um evento crítico para prevenir a refratura.

140 - ADRENAL FAILURE: WHEN ANTIPHOSPHOLIPID SYNDROME LEAVES SCARS

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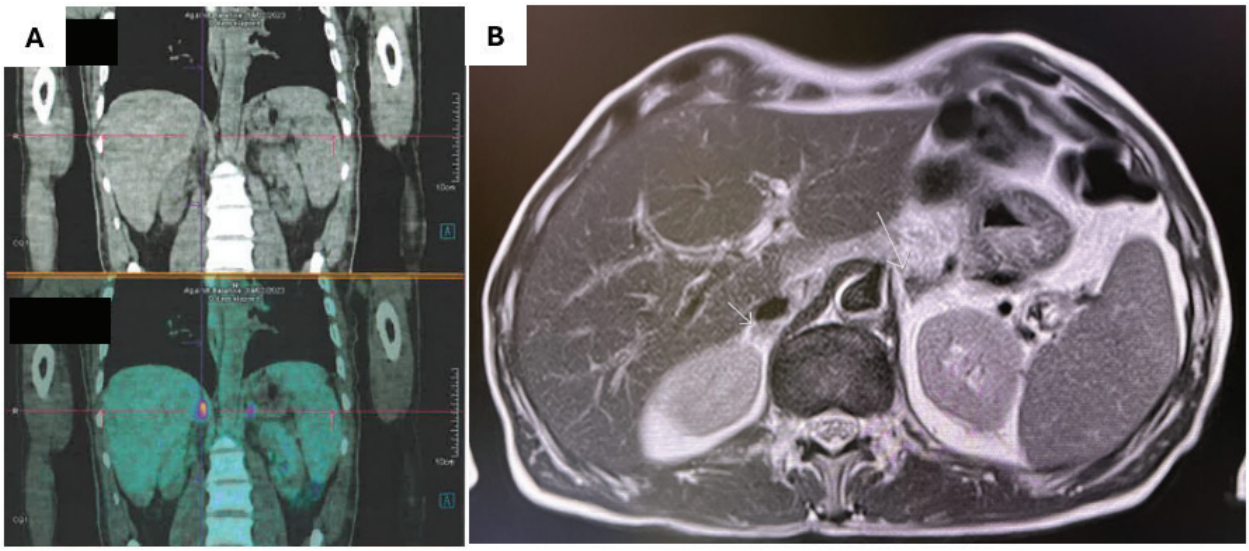
Introduction: Antiphospholipid syndrome (APS) is a multisystemic autoimmune disorder characterised by recurrent arterial, venous and/or microvascular thrombotic events. The disease rarely affects the endocrine system, especially at presentation. The involvement of the adrenal gland, although rare, can be severe. Possible mechanisms behind adrenal manifestations include multiple microthrombosis of the suprarenal vein leading to infarction and adrenal haemorrhage, atrophy and finally failure (primary adrenal insufficiency [PAI]). (1)(2)

Case Report: We report a case of a 56-year-old male with a previous history of chronic mild thrombocytopenia, assumed to be a consequence of alcohol consumption (despite the absence of other alcoholic stigmas). He was admitted to the Internal Medicine Department with a 3-month history of extreme fatigue, anorexia, and weight loss (20%). Upon admission, he was hypotensive (100/54mmHg). Blood tests revealed normocytic normochromic anaemia (Hb 9.9g/dL), thrombocytopenia (94 000x10^6/L), elevated activated partial thromboplastin time (76.4s, N 28-40), hyperkaliaemia (7.11mmol/L, N 3.5-5.2) (but normal sodium) and elevated inflammatory parameters (CRP 2.25 mg/dL, ESR 118 mm/h). An extensive workup study was conducted to exclude malignancy and infection. A PET-FDG showed intense uptake in both adrenal glands, with heterogeneity and areas of necrosis, especially in the right adrenal gland (Figure 1A). The endocrinology department was consulted, and hormonal assessments revealed a low serum cortisol (1.9 µg/dL; N 6.2-19.4) and a high adrenocorticotropic hormone (626.0pg/ml; N 7.2-63.3). PAI was assumed and intravenous hydrocortisone (200 mg/day) was started, with subsequent clinical (blood pressure, constitutional symptoms) and laboratory (blood cells count and inflammatory markers) improvement. The main causes for PAI, namely autoimmune Addison's disease, tuberculosis and human immunodeficiency virus infection, were excluded. At this moment, the Rheumatology department was consulted. Further workup revealed a positive lupus anticoagulant antibody (2 times in 12 weeks apart), ANAs 1/1280 (homogeneous nuclear pattern), anti-dsDNA antibodies elevation (517 UI/mL) and a weekly positive anti-nucleosome antibody. MRI scans showed atrophy of the adrenal glands (Figure 1B). The patient was di-



140 – Figure 1. A: PET-FOG at diagnosis moment, showing intense uptake in both adrenal glands; 8: abdominal MRI 6 months after the diagnosis, showing atrophy of both adrenal glands.

agnosed with SLE and APS, and after PAI control, he was discharged under glucocorticoid tapering (prednisolone 15 mg/day and fludrocortisone 0.05 mg/day), warfarin and hydroxychloroquine 400mg/day. Later on, azathioprine was also started (100mg/day) and the patient remained asymptomatic and with normal laboratory parameters.

Conclusions: This case illustrates one of the rarest and still most severe consequences of APS. Patients with APS and adrenal haemorrhage, typically have bilateral involvement and develop adrenal insufficiency, just like our patient. (3) The disease can be fatal, thus early diagnosis and treatment as well as a close follow-up and multidisciplinary approach is needed to improve the prognosis of this rare disease.

REFERENCES

1. Hochberg MC, et al. Rheumatology 8th Ed. Chapter 135: Clinical features of systemic lupus erythematosus. P1113. Elsevier, 2022.
2. Bouki K. Hormones (Athens). 2023;22(3):521-531
3. Meade-Aguilar JA, et al. Clin Immunol. 2024; 260:109906

178 - IMMUNE CHECKPOINT INHIBITORS-RELATED MYOSITIS: REAL-WORLD DATA FROM THE EUDRAVIGILANCE DATABASE

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Background: Immune checkpoint inhibitors (ICIs) have greatly improved the prognosis of cancer patients since their introduction. However, as ICIs block the immune checkpoints - cytotoxic T lymphocyte antigen 4 (CTLA-4) and programmed cell death protein 1 (PD-1)/programmed cell death ligand 1 (PD-L1) - they enhance T cell activation that contributes to autoreactivity. Consequently, by increasing the activity of the immune system, their use has been linked to a varied spectrum of adverse events, known as immune-related adverse events.

Myositis is a rare, yet potentially fatal immune-related adverse event linked to the use of ICIs.

Objectives: To evaluate the occurrence of myositis as a suspected adverse event of ICIs in a real-world pharmacovigilance database.

Methods: This study employed the EudraVigilance public version database to collect adverse events of six European Medicines Agency-approved ICIs – Atezolizumab, Avelumab, Cemiplimab, Durvalumab, Nivolumab and Pembrolizumab - between January 2021 and December 2023. The following MedDRA (Medical Dictionary for Regulatory Activities) Lowest Level Terms were considered as myositis SARs: "Myositis", "Dermatomyositis", "Polymyositis", "Autoimmune inflammatory myopathy", "Autoimmune myositis", "Idiopathic inflammatory myopathy", "Immune-mediated myositis", "Immune-mediated necrotizing myopathy",

178 – TABLE 1. Characteristics of myositis-related suspected adverse reactions (N = 279)

Characteristic	N (%)
Sex	
Male	191 (68.5)
Female	77 (27.6)
Not specified	11 (3.9)
Age group	
18 - 64 years-old	53 (19.0)
65 - 85 years-old	172 (61.7)
More than 85 years-old	16 (5.7)
Not specified	38 (13.6)
Reaction outcome at time of report	
Recovered/Resolved	33 (11.8)
Recovering/Resolving	84 (30.1)
Recovered with sequelae	2 (0.72)
Not recovered	40 (14.3)
Fatal	44 (15.8)
Unknown	76 (27.2)

"Necrotizing myositis". Only suspected adverse reactions (SARs) reported by healthcare professionals, occurring in the European Economic Area were included. SARs possibly related to other drugs and duplicated cases were excluded. Data including age group, sex, outcome, and action taken regarding the drug were retrieved from the public database. A descriptive analysis of the available data was performed, and the Reporting Odds Ratio (ROR) was calculated.

Results: A total of 279 myositis-related SARs were included (1.60% of all ICIs related SARs). Most cases concerned men (68.5%), aged between 65-85 years (61.7%). Among patients experiencing these SARs, 15.8 % (n=44) experienced a fatal outcome (Table 1). Among those who survived, the ICI was known to be withdrawn in 48.9% of the cases. Atezolizumab (ROR 0.35, 95% CI [0.18-0.66]) and Nivolumab (ROR 0.54, 95% CI [0.41-0.72]) were associated with a lower likelihood of reporting myositis-related SARs, whereas Avelumab (ROR 1.89, 95%CI [1.16-3.07], Durvalumab (ROR 1.77, 95%CI [1.15 -2.73]), and Pembrolizumab (ROR 1.56, 95% CI [1.23-1.98]) were associated with a higher likelihood of reporting myositis-related SARs.

Conclusions: Given the increasing use of ICIs in clinical practice, clinicians must be aware of their possible related immune adverse events. The onset of myositis is a potentially serious adverse reaction whose incidence should not be overlooked. In our study, Avelumab, Durvalumab, and Pembrolizumab were associated with a higher likelihood of developing myositis. Further studies are needed to identify predictors of myositis development and outcome in patients treated with ICIs.

205 - MICROVASCULAR IMAGING IS SUPERIOR TO POWER DOPPLER IN SYNOVITIS VASCULAR FLOW DETECTION IN RHEUMATOID ARTHRITIS

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Introduction: Superb Microvascular Imaging (SMI) uses an adaptive algorithm improving visualization of vessels with low-velocity blood flow. Power Doppler (PD) imaging is routinely used in clinical practice, but has a wall filter, resulting in signal loss of small blood vessels with low-velocity flow. A standardised EULAR-OMERACT scoring system that includes a semi-quantitative grey-scale grading (GS) and PD grading exists for rheumatoid arthritis (RA).

Objective: To compare SMI and PD in the hand and wrist joints of patients RA.

Methods: Consecutive patients with a RA diagnosis fulfilling the EULAR-ACR classification criteria and ultrasonographic synovitis in ≥1 joint were recruited. An ultrasonography assessment was performed using Canon Aplio i800 and i900 devices equipped with PLT-1005BT (4-14 MHz) and i22LH8 (8.8-22.0 MHz) linear transducers, for all metacarpophalangeal (MCP), proximal interphalangeal joints (PIP) joints and wrists (22 joints per patient), including GS, PD and SMI scoring. The EULAR-OMERACT score (synovitis combining GS and PD signal) was used, as well as an Adapted EULAR-OMERACT score (synovitis combining GS and SMI). A blinded live interrater agreement exercise between two ultrasonographers was performed beforehand.

Results: There was substantial agreement (squared-weighted k=0.729) between ultrasonographers. 58 RA patients were enrolled (1276 scanned joints), 74.1% female, average age 63.4±14.0 years. SMI detected intra-articular vascularization in 137/227 GS grade ≥1 joints (60.4%) while PD was detected in 58/227 GS grade ≥1 joints (25.6%) (p-value<0.001,Chi-square test). No joint had higher PD grade than corresponding SMI grade. SMI

significantly improved detection of vascular flow signal (χ2(9) 1020.35,p=0.001), with a large effect size (Cramer's V=0.52): 79 joints (57.7%) increased vascular flow grading from PD grade 0 to SMI grade ≥1; 29 joints (74.4% of PD grade 1) increased to SMI grade ≥2 and 9 joints (52.9% of PD grade 2) increased to SMI grade 3.
Comparing the EULAR-OMERACT score versus the Adapted EULAR-OMERACT score, SMI lead to an increase of the combined GS and vascular score and no joint had lower Adapted EULAR-OMERACT score than EULAR-OMERACT score (χ2 (9) 2076.09,p=0.001), with a large effect size (Cramer's V=0.86).
Conclusions: In RA patients SMI has a higher sensitivity for synovium vascular flow than PD, in all grades. Negative findings are reliable, as no vascular flow was found with PD in joints without SMI signal. This study is the first to adapt the EULAR-OMERACT scoring system to SMI, demonstrating that SMI determines a score change with statistical and ultrasonographic significance.

218 - COMORBIDITY PATTERNS IN ADULT JUVENILE IDIOPATHIC ARTHRITIS: A NATIONAL COHORT STUDY

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Introduction: Patients with Juvenile idiopathic arthritis (JIA) suffer considerable morbidity due to articular and extra-articular manifestations, including ocular, non-articular musculoskeletal, endocrine, cutaneous sequelae, and secondary amyloidosis, which can lead to serious impairment of their physical function and health-related quality of life (HRQoL). (1)
To date, little is known about the prevalence and incidence of comorbidities in adults with JIA.
Objectives: To identify key comorbidities and assess their incidence rate and prevalence and determine risk factors for comorbid conditions in adult JIA patients registered in the Rheumatic Diseases Portuguese Register (Reuma.pt).
Methods: National multicentric retrospective observational cohort study. Data on sociodemographic, clinical features and comorbidities were collected from patients with JIA according to the 2001 revised International League of Associations for Rheumatology (ILAR) criteria, registered in Reuma.pt, who at the time of data extraction were at least 18 years old. Comorbidities included cardiovascular disease, arterial hypertension, dyslipidaemia, diabetes, thyroid disease, amyloidosis, allergy and asthma, osteoporosis, autoimmune disease (multiple sclerosis, myasthenia gravis, autoimmune

hepatitis, autoimmune thyroiditis, type 1 diabetes, and vitiligo), and psychiatric disease. Incidence rates of comorbidities were calculated as the number of new events per 1000 person-years with 95% CIs.

Results: This study included 878 patients, of which 529 (60.3%) were female with a median age of 34.1 [26.9-47.1] years. Median age at disease onset was 11.6 [6.6-14.5] years, median disease duration was 20.4 [12.1-23.4] years and median diagnostic delay was 1.0 [0.1-5.5] year. The most frequent category of JIA was enthesitis-related JIA (n=304, 34.6%), followed by JIA categories with polyarticular involvement (n=246, 28%). Most patients were prescribed conventional synthetic DMARDs (csDMARDs; 868, 99%) and biologic DMARDs (490, 56%), and 43.7% (199/455) were in remission.

The comorbidity with the highest incidence rate was arterial hypertension with 4.5/1000 person-years, followed by dyslipidaemia (3.2/1000 person-years) and autoimmune diseases (2.4/100.00 person-years). The incidence of malignancy was 0.5/1000 person-years.

Biologic DMARD therapy in these patients was associated with a decreased risk of developing thyroid disease (OR 0.17, p=0.01), arterial hypertension (OR=0.3, p<0.001), amyloidosis (OR=0.06, p=0.01), inflammatory bowel disease (OR=0.3, p=0.01), autoimmune diseases (OR=0.35, p=0.003), osteoporosis (OR=0.18, p<0.001) and psychiatric comorbidities (OR=0.28, p=0.003). In contrast, bDMARD therapy was associated with an increased risk of infectious comorbidities (OR=2.15, p=0.04). There was no significant association between therapy with bDMARDs and development of malignancy.

Conclusion: Adult JIA patients commonly experience comorbidities, with hypertension being the most frequent. Biologic DMARD treatment seems to be associated with a decreased risk of developing comorbidities except for infections. These findings underscore the importance of careful management and monitoring of comorbidities in JIA patients.

REFERENCES

1. Ramos FO, Rodrigues A, Martins FM, Melo AT, Aguiar F, Brites L, et al. Health-related quality of life and disability in adults with juvenile idiopathic arthritis: comparison with adult-onset rheumatic diseases. RMD open. 2021;7(3):e001766.

226 - BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS SURVIVAL IN LATE-ONSET AXIAL SPONDYLOARTHRITIS – DATA FROM THE PORTUGUESE REGISTRY OF PATIENTS WITH RHEUMATIC DISEASES

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Background: Axial spondyloarthritis (axSpA) symptoms usually begin before the age of 45, but due to longer life expectancy and improved healthcare, late-onset axSpA (Lo-axSpA) is becoming more recognized. Previous studies have shown different clinical characteristics between the late and early onset (Eo) of the disease. However, there is limited data available on the efficacy of biological disease-modifying antirheumatic drugs (bDMARDs) in Lo-axSpA.

Objectives: Evaluate drug survival of bDMARDs in Lo-axSpA patients compared to those with Eo-axSpA.

Methods: We performed a retrospective multicenter national cohort study on patients with a diagnosis of axSpA, registered in Reuma.pt, the Portuguese registry of patients with rheumatic diseases. Adult patients who were clinically diagnosed with axSpA by their rheumatologist and had available information on the age of symptom onset were included. The patients were

226 – TABLE 1. Comparison of patient and disease characteristics between patients with late and early onset axSpA.

Variables	Early-onset SpA (n = 1703)	Late-onset SpA (n = 250)	*p*-value
Age of disease onset, med (min-max)	**28 (34-48)**	**56 (52-62)**	**<0.001**
Male gender, n (%)	925 (54)	123 (49)	0.13
BMI, med (min-max)	**25.6 (22.8-28.5)**	**28.2 (25.1-31.1)**	**<0.001**
Inflammatory back pain (ever), n (%)	1481 (87)	210 (84)	0.2
Peripheral arthritis (ever), n (%)	570 (33)	96 (38)	0.12
Dactylitis (ever), n (%)	90 (5.3)	18 (7.2)	0.2
Enthesitis (ever), n (%)	417 (24)	64 (26)	0.7
Acute anterior uveitis (ever), n (%)	**388 (23)**	**34 (14)**	**<0.001**
Psoriasis (ever), n (%)	75 (4.4)	14 (5.6)	0.4
Inflammatory bowel disease, n (%)	**135 (7.9)**	**30 (12)**	**0.031**
Radiographic sacroiliitis, n (%)	1522 (89)	219 (88)	0.4
HLA-B27 positivity, n (%)	**1141 (67)**	**140 (56)**	**<0.001**
SpA family history, n (%)	**228 (13)**	**14 (5.6)**	**<0.001**
Good response NSAIDs, n (%)	855 (50)	132 (53)	0.4
CRP elevated (≥0.5mg/dL) (ever), n (%)	1111 (65)	172 (69)	0.3
Age at 1st bDMARD, m (min-max)	**41 (34-48)**	**56 (52-62)**	**<0.001**
Disease duration, m (min-max)	**10 (5-18)**	**5 (3-8)**	**<0.001**
bDMARD, n (%)			0.9
Adalimumab	675 (40)	112 (45)	
Etanercept	427 (25)	59 (24)	
Infliximab	263 (15)	37 (15)	
Golimumab	257 (15)	34 (14)	
Certolizumab	49 (2.9)	2 (0.8)	
Secukinumab	32 (1.9)	4 (1.6)	
PGA, m (min-max)	**70 (50-80)**	**74 (54-83)**	**0.046**
BASDAI, m (min-max)	**6.00 (4.80-7.30)**	**6.30 (5.00-7.50)**	**0.043**
BASFI, m (min-max)	**5.80 (3.61-7.31)**	**6.35 (4.80-7.95)**	**<0.001**
BASMI, m (min-max)	**3.40 (2.40-4.60)**	**3.80 (2.80-4.80)**	**<0.001**
CRP, med (min-max)	1.08 (0.42-2.30)	1.03 (0.39-2.13)	0.5
ASDAS, med (min-max)	3.60 (3.10-4.10)	3.50 (3.10-4.00)	0.9
PGA 6 mon, m (min-max)	**30 (10-52)**	**40 (20-60)**	**0.002**
BASDAI 6 mon, m (min-max)	**3.30 (1.51-4.80)**	**3.63 (1.90-5.40)**	**0.006**
BASDAI50, n (%)	993 (58)	132 (53)	0.10
BASFI 6 mon, m (min-max)	**3.10 (1.30-5.40)**	**3.92 (1.71-6.00)**	**<0.001**
CRP 6 mon, m (min-max)	0.29 (0.10-0.75)	0.25 (0.08-0.62)	0.073
ASDAS 6 mon, m (min-max)	**1.90 (1.40-2.50)**	**2.10 (1.70-2.70)**	**0.002**
ASAS20 6mon, n (%)	**950 (56)**	**111 (44)**	**<0.001**
ASAS40 6 mon, n (%)	**841 (49)**	**97 (39)**	**0.002**
PGA 12 mon, m (min-max)	**27 (6-50)**	**31 (13-50)**	**0.004**
BASDAI 12 mon, m (min-max)	**2.78 (1.30-4.30)**	**3.35 (1.80-4.70)**	**<0.001**
BASDAI50 12 mon, n (%)	993 (58)	131 (52)	0.078
BASFI 12 mon, m (min-max)	**2.45 (0.92-4.40)**	**3.55 (1.65-5.30)**	**<0.001**
BASMI 12 mon, m (min-max)	**3.00 (2.00-4.40)**	**3.60 (2.60-4.80)**	**<0.001**
CRP 12 mon, m (min-max)	0.26 (0.10-0.67)	0.28 (0.11-0.81)	0.2
ASDAS 12 mon, m (min-max)	**1.80 (1.30-2.20)**	**1.90 (1.43-2.40)**	**0.005**
ASAS20 12 mon, n (%)	512 (30)	69 (28)	0.4
ASAS40 12 mon, n (%)	**661 (39)**	**165 (66)**	**<0.001**
Partial Remission 12 mon, n (%)	**719 (42)**	**78 (31)**	**<0.001**

ASAS - Assessment of SpondyloArthritis International Society; ASDAS - Ankylosing Spondylitis Disease Activity Score; BASDAI - Bath Ankylosing Spondylitis Activity Index; BASFI - Bath Ankylosing Spondylitis Functional Index; BASMI - Bath Ankylosing Spondylitis Metrology Index; bDMARD - Biologic disease-modifying antirheumatic drugs; CRP – C-reactive protein; BMI – body mass index; m – median; max – maximum; min – minimum; mon – months; n- number; NSAIDs - Non-steroidal anti-inflammatory drugs; PGA – patient global assessment; SpA - spondyloarthritis.

divided into 2 groups based on their age at symptom onset: Eo-axSpA (age <45 years) and Lo-axSpA (age ≥45 years). Non-parametric tests were used to evaluate the group differences. Drug survival was calculated as the time in months from the initiation of bDMARD until its discontinuation/switch and the log-rank test was used to calculate the persistence rate in biological treatment. R software version 4.3.2 was used, and a $p \leq 0.05$ was considered statistically significant.

Results: A total of 1953 patients (1703 with Eo-axSpA and 250 with Lo-axSpA) were included. The Lo-axSpA group had a higher body mass index (BMI), lower

prevalence of acute anterior uveitis, higher prevalence of inflammatory bowel disease, and lower HLA-B27 positivity and SpA family history. Lo-axSpA were more likely to have higher disease-associated parameters at baseline, 6, and 12 months of bDMARD therapy (table 1). The drug retention rate was lower in Lo-axSpA, and the survival analysis showed a higher probability of discontinuing treatment in this group (HR 1.50 (1.20-1.88), p<0.001). When adjusting for cofounders, the Lo-axSpA group had no significant differences in treatment persistence. However, a higher age of disease onset increased the risk of discontinuing therapy by 2% (HR 1.02 (1.01-1.04), p=0.001). Being male (HR 0.77 (0.65-0.92), p=0.004), having HLA-B27 positivity (HR 0.80 (0.67-0.95), p=0.01) and higher CRP levels (HR 0.80 (0.66-0.96), p=0.02) were associated with a lower risk of discontinuing therapy, while having a good response to NSAIDs (HR 1.22 (1.01-1.45), p=0.03) and higher BMI (1.02 (1.00-1.04), p=0.02) were associated with an increased risk. Regarding bDMARD therapy, patients who were on etanercept (HR 0.92 (0.50-0.78), p=<0.001), infliximab (HR 0.69 (0.53-0.90), p=0.006), and golimumab (HR 0.75 (0.58-0.97), p=0.03), had a lower risk of discontinuing therapy compared to the adalimumab reference group.

Conclusions: Based on real-world nationwide data, it was found that patients with Lo-axSpA who were treated with bDMARDs had a shorter drug retention time. Although Lo-axSpA itself was not a significant factor in predicting drug discontinuation, age at disease onset was associated with a higher risk of discontinuation. Additionally, HLA-B27 negativity, female gender and higher BMI were also linked to a higher risk of therapy discontinuation. Clinicians should be aware of this phenotype, even though it is a minority since it can be associated with a higher clinical burden and lower treatment efficacy.

281 - CLINICAL, LABORATORIAL AND IMMUNOLOGICAL RISK FACTORS OF VEDOSS PROGRESSION TO SYSTEMIC SCLEROSIS - A SINGLE-CENTRE STUDY

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Introduction: The very early diagnosis of systemic sclerosis (VEDOSS) identifies patients who don't meet the 2013 ACR/EULAR criteria for systemic sclerosis (SSc), but have Raynaud's phenomenon, puffy fingers, abnormalities in nailfold capillaroscopy and/or SSc-specific antibodies. Several studies have assessed the risk of VEDOSS progression to SSc based on the 2013 criteria, however they haven't considered other clinical, laboratory, and immunological factors.

Aims: To evaluate the predictive value of clinical, laboratory, and immunological features in VEDOSS progression to SSc, enhancing the understanding of the disease's early stages.

Methods: Clinical records of all patients with VEDOSS and SSc followed in our department were reviewed. SSc patients or overlap syndromes with VEDOSS were excluded. We collected demographic, clinical, laboratory and serological variables. T-test or Mann-Whitney test were used, as appropriate, for continuous variables, and chi-square or Fisher tests for categorical variables. A logistic regression analysis was performed to verify the independent association of relevant covariables with progression to SSc.

Results: From 129 patients with VEDOSS, 57 patients (44.2%) had progression to SSc (progressors) while 72 persisted with the initial diagnosis (pVEDOSS), after a mean follow-up period of 7.1 years. Raynaud's phenomenon was the main presenting symptom observed in 98.6% and 96.5% of pVEDOSS and progressors, respectively.

There were no differences between groups in the frequency of sex, body mass index, age of symptom onset or VEDOSS diagnosis, comorbidities, antinuclear antibodies (ANA), SSc-related antibodies (table 1). At VEDOSS diagnosis, progressors had more commonly puffy hands/fingers (77.2% vs. 22.2% in pVEDOSS, p=0.01) and capillaroscopic changes (89.3% vs. 57.4% in pVEDOSS, p=0.001). Active and late capillaroscopic patterns were also more common in progressors (p=0.001), and the mean EULAR/ACR SSc 2013 Criteria score was higher in this subpopulation (7.9±0.3 vs. 6.4±1.7 in pVEDOSS, p=0.001).

During follow-up, progressors had more commonly telangiectasias (47.4% vs. 8.3% in pVEDOSS, p=0.001), calcinosis (24.6% vs. 2.8% in pVEDOSS, p=0.001), and digital ulcers (38.6% vs. 12.5% in pVEDOSS, p=0.001). Notably, no association was found between any of the comorbidities at diagnosis of VEDOSS and progression to SSc.

On multivariate logistic regression, puffy hands/fingers [OR: 13.875 (3.676-52.374) p<0.001], telangiectasia [OR: 7.566 (1.701-33.656) p=0.008], and a higher score of EULAR/ACR 2013 SSc Criteria [OR: 13.897 (2.021-99.551) p=0.007] at VEDOSS diagnosis were

281 – Table 1 - Demographic, clinical and serological comparison of patients who progressed to Systemic Sclerosis with those who remained diagnosed with VEDOSS

Variables	Number of available data	VEDOSS patients (N = 72)	SSc patients (N = 57)	p value (univariate analysis)	p value (multivariate analysis)
Female, n/N (%)	129	67/72 (93.1%)	55/57 (96.5%)	0.651	-
Current age (years), mean ± sd (range)	129	59.2 ± 14.9 (26-89)	62.3 ± 14.4 (29-88)	0.659	-
Caucasians, n/N (%)	108	49/54 (90.7%)	52/54 (96.3%)	0.245	-
BMI (m2/Kg), mean ± sd (range)	73	26.0 ± 4.3 (18.3-37.7)	25.7 ± 5.2 (18.8-44.6)	0.791	-
First symptom: Raynaud's phenomenon, n (%) Puffy hands/fingers, n (%)	129	 71 (98.6%) 1 (1.4%	 55 (96.5%) 2 (3.5%)	0.562	-
First symptom age (years), mean ± sd (range)	127	45.7 ± 15.5 (17-81)	46.7 ± 16.7 (15-79)	0.848	-
First symptom onset before 30 years old, n/N (%)	127	15/71 (21.1%)	9/56 (16.7%)	0.474	-
First symptom onset before 50 years old, n/N (%)	127	44/71 (62.0%)	31/56 (55.4%)	0.456	-
VEDOSS age of diagnosis (years), mean ± sd (range)	129	52.9 ± 15.2 (20-83)	53.4 ± 14.7 (20-81)	0.421	-
VEDOSS age of diagnosis before 50 years old, n/N (%)	129	29/72 (40.3%)	22/57 (38.6%)	0.848	-
Time from first symptom to VEDOSS diagnosis (years), mean ± sd (range)	127	6.8 ± 7.9 (0-36)	6.2 ± 10.1 (0-50)	0.290	-
Time from first symptom to VEDOSS diagnosis lesser than 5 years, n/N (%)	127	41/71 (57.7%)	38/56 (67.9%)	0.185	-
Raynaud's phenomenon at VEDOSS diagnosis, n/N (%)	129	71/72 (98.6%)	57/57 (100%)	0.376	-
Raynaud's phenomenon age of onset (years), mean ± sd (range)	121	45.6 ± 15.6 (18-81)	47.6 ± 16.3 (15-79)	0.487	-
Puffy hands/fingers at VEDOSS diagnosis, n/N (%)	129	16/72 (22.2%)	44/57 (77.2%)	<0.001	<0.001
Puffy hands/fingers age of onset (years), mean ± sd (range)	58	48.4 ± 17.8 (23-71)	53.1 ± 14.3 (23-84)	0.310	-
Onset of telangiectasias during follow-up, n (%)	129	6/72 (8.3%)	27/57 (47.4%)	<0.001	0.008
Onset of calcinosis during follow-up, n (%)	129	2/72 (2.8%)	14/57 (24.6%)	<0.001	0.703
Onset of digital ulcers during follow-up, n (%)	129	9/72 (12.5%)	22/57 (38.6%)	0.001	0.813
Capillaroscopy changes at VEDOSS diagnosis, n/N (%)	124	39/68 (57.4%)	50/56 (89.3%)	0.001	1.000
Capillaroscopic pattern, n/N (%) No changes Non-specific changes Early pattern Active pattern Late pattern	122	 28 (41.8%) 6 (9.0%) 27 (40.2%) 6 (9.0%) 0	 6 (10.9%) 4 (7.3%) 25 (45.5%) 14 (25.4%) 6 (10.9%)	0.001	0.714
Age of identification of capillaroscopic changes (years), mean ± sd (range)	89	52.2 ± 14.4 (23-83)	54.4 ± 14.9 (23-81)	0.499	-
ANA positivity, n/N (%)	128	56/72 (77.8%)	48/56 (85.7%)	0.257	-
ANA positivity age of identification (years), mean ± sd (range)	93	54.7 ± 15.1 (22-83)	53.9 ± 14.4 (20-81)	0.793	-

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281 – Table 1 - Continuation

Variables	Number of available data	VEDOSS patients (N = 72)	SSc patients (N = 57)	p value (univariate analysis)	p value (multivariate analysis)
SSc-related antibodies positivity, n/N (%)	129	63/72 (87.5%)	53/57 (93.0%)	0.308	-
SSc-related antibodies positivity age of identification (years), mean ± sd (range)	101	55.2 ± 14.7 (22-83)	54.5 ± 14.4 (20-81)	0.803	-
SSc-related antibodies, n (%)	129			0.173	-
Anti-centromere		40 (55.5%)	30 (52.6%)		
Anti-centromere A		19/69 (27.5%)	9/56 (16.1%)		
Anti-centromere B		38/72 (52.8%)	30/57 (52.6%)		
Antitopoisomerase I		5 (6.9%)	16 (28.1%)		
Anti-Th/To		5 (6.9%)	0		
Anti-PM/Scl		4 (5.6%)	1 (1.8%)		
Anti-NOR90		4 (5.6%)	1 (1.8%)		
Anti-Ku		3 (4.2%)	0		
Anti-RNA polymerase III		1 (1.4%)	3 (5.3%)		
Anti-fibrillarin		1 (1.4%)	0		
Anti-Ro52		1 (1.4%)	3 (5.3%)		
Anti-Ro60		1 (1.4%)	0		
None		7 (9.7%)	3 (5.3%)		
Score in the 2013 EULAR/ACR SSc Criteria at VEDOSS diagnosis (points), mean ± sd (range)	129	6.4 ± 1.7 (3-8)	7.9 ± 0.3 (6-8)	<0.001	0.007
Comorbidities at diagnosis of VEDOSS, n/N (%)					-
Hypertension	129	22/72 (30.6%)	17/57 (29.8%)	0.929	
Diabetes mellitus	127	3/70 (4.3%)	4/57 (7.0%)	0.506	
Dyslipidemia	129	24/72 (33.3%)	19/57 (33.3%)	1.000	
Obesity	129	5/72 (6.9%)	7/57 (12.3%)	0.318	
Smoking status	111	60	51	0.496	
No		49 (81.7%)	39 (76.5%)		
Yes		4 (6.7%)	4 (7.8%)		
Former smoker		7 (11.7%)	8 (15.7%)		
Alcoholic habits	107	0	0	0.370	
Peripheral Venous Disease	129	13/72 (18.1%)	12/57 (21.1%)	0.672	
Asthma	129	4/72 (5.6%)	2/57 (3.5%)	0.587	
Chronic Obstructive Pulmonary Disease	129	1/72 (1.4%)	2/57 (3.5%)	0.432	
Osteoporosis	129	14/72 (19.4%)	9/57 (15.8%)	0.594	
Depressive Syndrome	129	12/72 (16.7%)	13/57 (22.8%)	0.385	
Metabolic Syndrome	129	4/72 (5.6%	6/56 (10.7%)	0.284	
Chronic liver Disease	128	1/72 (1.4%)	2/57 (3.5%)	0.432	
Chronic kidney Disease	129	3/72 (4.2%)	1/57 (1.8%)	0.436	
Ischemic heart Disease	129	6/72 (8.3%)	1/57 (1.8%)	0.080	
Constitutional involvement	129	1/72 (1.4%)	1/57 (1.8%)	0.869	
Neoplasia	128	6/71 (8.5%)	6/57 (10.5%)	0.489	
Type of neoplasia	129	6/72 (8.3%)	6/57 (10.5%)	0.183	
Breast		2 (33.3%)	5 (83.3%)		
Cervix		2 (33.3%)	0		
Colon		1 (16.7%)	1 (16.7%)		
Melanoma		1 (16.7%)	0		

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281 – Table 1 - Continuation

Variables	Number of available data	VEDOSS patients (N = 72)	SSc patients (N = 57)	p value (univariate analysis)	p value (multivariate analysis)
Laboratory tests at diagnosis of VEDOSS, n/N (%)					
Anaemia	125	8/69 (11.6%)	8/56 (14.3%)	0.657	-
Leukocytosis	125	5/69 (7.2%)	3/56 (5.4%)	0.671	-
Leukopenia	125	8/69 (11.6%)	4/56 (7.1%)	0.405	-
Lymphopenia	125	1/69 (1.5%)	2/56 (3.6%)	0.445	-
Thrombocytosis	125	0/69	1/56 (1.8%)	0.267	-
Thrombocytopenia	125	1/69 (1.5%)	0/56	0.370	-
Raised C-reactive protein	126	15/70 (21.4%)	15/56 (26.8%)	0.487	-
Raised erythrocyte sedimentation rate	127	14/71 (19.7%)	12/56 (21.4%)	0.814	-
Kidney function changes	74	8/42 (19.1%)	0/32	0.003	0.999
Raised uric acid	79	6/39 (15.4%)	3/40 (7.5%)	0.278	-
Raised blood glucose	123	5/68 (7.4%)	3/55 (5.4%)	0.674	-
Kidney function changes	88	5/42 (11.9%)	0/46	0.023	0.999
Ionogram changes	84	4/42 (9.5%)	2/42 (4.8%)	0.403	-
Thyroid function changes	92	6/47 (12.8%)	2/45 (4.4%)	0.157	-
Hypergammaglobulinemia	96	1/50 (2.0%)	1/46 (2.2%)	0.953	-
Hypoalbuminemia	55	17/30 (56.7%)	20/25 (80%)	0.063	-
Vitamin D deficit	124	10/68 (14.7%)	5/56 (8.9%)	0.320	-
Hepatic function changes					
Laboratory tests levels at diagnosis of VEDOSS:					
Hemoglobin (g/dL), mean ± sd (range)	125	13.2±1.2 (10.3-17.0)	13.2±1.1 (9.7-15.7)	0.980	-
Leucocytes (x10^9/mm), mean ± sd (range)	125	7.2±4.6 (3.0-33.0)	7.1±2.6 (2.0-18.5)	0.877	-
Lymphocytes (x10^9/mm), mean ± sd (range)	125	2.0±0.6 (0.9-3.5)	2.2±0.8 (0.7-4.3)	0.027	0.944
Platelets (x10^3/mm), mean ± sd (range)	125	250±46.9 (149-369)	253±65.9 (162-452)	0.800	-
CRP (mg/dL), mean ± sd (range)	126	0.39±0.52 (0.03-2.90)	0.41±0.54 (0.03-2.94)	0.831	-
ESR (mm3), mean ± sd (range)	127	23.0±15.1 (2-69)	22.9±15.3 (2-69)	0.971	-
Uric acid (mg/dL), mean ± sd (range)	73	4.7±1.6 (2-9.6)	3.9±0.8 (2.7-5.7)	0.012	0.385
Glucosis (mg/dL), mean ± sd (range)	77	96.7±13.5 (75-126)	93.0±12.8 (76-139)	0.224	-
HbA1c (%), mean ± sd (range)	16	5.5±0.5 (5.0-7.0)	6.0±1.5 (5.0-9.0)	0.306	-
Creatinine (mg/dl), mean ± sd (range)	123	0.8±0.3 (0.5-2.4)	0.7±0.2 (0.5-1.3)	0.276	-
Calcium (mg/dl), mean ± sd (range)	100	9.5±0.4 (8.5-10.8)	9.5±0.3 (9-10.3)	0.338	-
Phosphorus (mg/dl), mean ± sd (range)	74	3.3±0.6 (2.0-4.4)	3.5±0.4 (2.4-4.4)	0.211	-
TSH (µUI/ml), mean ± sd (range)	85	1.94±1.00 (0.05-4.74)	1.95±0.91 (0.30-4.76)	0.941	-
fT4 (µUI/ml), mean ± sd (range)	82	3.36±5.26 (0.82-17.5)	1.88±2.87 (0.76-17.5)	0.117	-
Gammaglobulinemia (g/dL), mean±sd (range)	91	1.1±0.3 (0.5-1.7)	1.0±0.2 (0.6-1.6)	0.362	-
Albumin (g/dl), mean ± sd (range)	96	4.2±0.3 (3.1-5.2)	4.2±0.3 (3.4-4.7)	0.756	-
Vitamin D (UI), mean ± sd (range)	55	33.1±23.9 (5.2-84.0)	21.2±9.1 (9.0-51.0)	0.022	-
NT-proBNP (pg/ml), median (IQR)	21	99.0 [42-163]	124.5 [51.3-251.8]	0.420	0.100
AST (UI), mean ± sd (range)	121	21.6±8.8 (11.0-63.0)	24.9±24.1 (12.0-196)	0.297	-
ALT (UI), mean ± sd (range)	121	22.5±15.8 (6.0-93.0)	27.0±50.2 (7.0-386)	0.489	-
GGT (UI), mean ± sd (range)	74	33.3±32.5 (6.0-129.0)	27.5±29.3 (8.0-161.0)	0.426	-
FA (UI), mean ± sd (range)	91	79.3±30.7 (41.0-171)	72.5±27.5 (40.0-169)	0.274	-
					-

associated with progression to SSc, adjusting for capillaroscopy changes, capillaroscopy pattern, calcinosis and digital ulcers. However, on multivariate logistic regression ajusted to raised uric acid, ionogram changes, lymphocytes level, uric acid level and vitamin D level no laboratory findings were associated with progression to SSc.

Conclusion: In patients with VEDOSS, the presence of puffy hands/fingers, telangiectasia and a higher score of EULAR/ACR 2013 SSc Criteria were associated with progression to SSc. These findings deserve further confirmation in larger cohorts.

285 - STILL'S DISEASE-ASSOCIATED LUNG DISEASE ACROSS LIFESPAN: A MULTICENTRIC STUDY

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Introduction: Still's disease (SD) is understood as a life course entity encompassing systemic-onset juvenile idiopathic arthritis (SoJIA) and adult-onset Still's disease (AOSD). SD-associated lung disease (LD) is an emerging severe complication that is apparently increasing in frequency.

Objectives: To describe and compare SoJIA and AOSD in a multicentric population emphasizing pulmonary involvement.

Methods: Clinical records of patients classified as SoJIA or AOSD, from 18 Portuguese centers, were reviewed. Patients with clinical or chest imaging objective findings were considered to have LD, including interstitial lung disease, pulmonary alveolar proteinosis and pulmonary arterial hypertension. Previous/concomitant known LD related to other causes was excluded. Data on demographic variables and clinical features were presented as frequencies and mean ± standard deviation for categorical and continuous variables, respectively. Linear regression was performed to assess the independent association of relevant covariables.

Results: We collected data from 175 patients, 104 with SoJIA, 67 with AOSD, 4 unknown age of symptoms onset. The mean age of symptoms onset was 8.2 years for SoJIA and 38.5 years for AOSD patients. LD developed in 14 patients (8%), 7 with SoJIA (6.7% of the total), and 7 with AOSD.

At SD onset 99% of the patients had fever, 89.1% arthritis, 81.3% rash, 43.5% odynophagia, 43% myalgia, 40.6% adenomegaly, 37.1% hepatomegaly/splenomegaly with no significant differences between SoJIA and AOSD except for lower reports of odynophagia and adenomegaly in SoJIA. Similar results were obtained in the subgroup of paediatric and adult patients that developed LD.

LD presented with tiredness in 57.1%, dyspnea in 42.9% and clubbed fingers in 15.4% of the cases. Low peripheral oxygen saturation was more frequent in AOSD than SoJIA (57.1% vs 14.3%).

The average time between SD symptoms onset and diagnosis of LD was 6.1 years for SoJIA and 7.3 years for AOSD, with a mean age at LD diagnosis of 9.0 and 39.2 years for SoJIA and AOSD, respectively. At LD di-

agnosis, all patients with AOSD and 57.1% with SoJIA had active SD. The most common radiological findings were ground glass (42.9%), peripheral consolidation (35.7%) and septal thickening (21.4%), while pulmonary hypertension was found in 21.4% of the patients, with similar frequencies in both subgroups.

Patients with LD had more pleuritis (42.9% vs 10.9%; p=0.024) and a higher frequency of macrophage activation syndrome (MAS) (35.7% vs 9.4%; p<0.001) independent of age of SD-onset. Half of the patients, all adults, had eosinophilia at LD diagnosis. After LD diagnosis, patients were treated with glucocorticoids (69.2%), tocilizumab (21.4%) and anakinra (7.1%), in similar proportions in both subgroups. After a mean of 1.8 years of follow-up after LD diagnosis, 6 patients (42.9%) needed intensive care (3 SoJIA), 4 (28.6%) died (1 SoJIA) and 9 (64.3%) had improvement or stabilization of the LD (all SoJIA).

Conclusion: LD is a significant and severe complication in patients with SD, affecting both paediatric and adult populations. Despite similar symptoms at onset in SoJIA and AOSD patients, those with LD may face a more severe prognosis, including higher rates of pleuritis and MAS.

285 – TABLE 1. Clinical, serologic and laboratory characterization of the Still's Disease patients

Variables	Data number available	All patients (N = 175)	Patients with lung involvement (N = 14)	Patients without lung involvement (N = 161)	p-value (univariate analysis)	p-value (multivariate analysis)
Female, n (%)	175	97 (55.4%)	8 (57.1%)	89 (52.1%)	0.894	-
Age of symptoms onset (years), mean ± standard deviation (range)	171	20.1 ± 17.6 (1 - 76)	18.7 ± 12.4 (4 - 41)	20.2 ± 18.0 (1 - 76)	0.762	-
Age of Still Disease diagnosis (years), mean ± standard deviation (range)	174	20.7 ± 17.6 (1 - 76)	20.6 ± 14.9 (4 - 58)	20.7 ± 17.8 (1 - 76)	0.988	-
Time between symptoms onset and Still Disease diagnosis (months), mean ± standard deviation (range)	171	8.4 ± 30.8 (0 - 252)	23.1 ± 58.4 (0 - 198)	7.1 ± 26.9 (0 - 252)	0.062	-
Age currently (years),mean ± standard deviation (range)	169	29.8 ± 18.9 (3 - 81)	30.1 ± 11.9 (17 - 58)	29.8 ± 19.3 (3 - 81)	0.960	-
Race, n (%)	175				< 0.001	0.996
Caucasian		159 (90.9%)	14 (100%)	145 (90.1%)		
Melanodermic		16 (9.1%)	0	16 (100%)		
Nationality, n (%)	175				< 0.001	0.996
Portugal;		157 (89.7%)	14 (100%)	143 (88.8%)		
Africa;		11 (6.3%)	0	11 (6.8%)		
Brazil;		3 (1.7%)	0	3 (1.9%)		
Other European country		4 (2.3%)	0	4 (2.5%)		
Course of Still's Disease, n (%)	174				0.921	-
Monophasic		65 (37.4%)	6 (42.9%)	59 (36.9)		
Intermittent/polycyclic		60 (34.5%)	3 (21.4%)	57 (35.6)		
Chronic/persistent		49 (28.1%)	5 (35.7%)	44 (27.5%)		

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285 – TABLE 1. Continuation

Variables	Data number available	All patients (N = 175)	Patients with lung involvement (N = 14)	Patients without lung involvement (N = 161)	p-value (univariate analysis)	p-value (multivariate analysis)
Symptoms, n/N (%)						0.136
Fever	103	102 (99.0%)	7/8 (87.5%)	95/95 (100%)	0.351	
Rash	171	139 (81.3%)	12/14 (85.7%)	127/157 (80.9%)	0.660	
Myalgia	172	74 (43.0%)	8/14 (57.1%)	66/158 (41.8%)	0.268	
Odynophagia	170	74 (43.5%)	10/14 (71.4%)	64/156 (41.0%)	0.035	
Abdominal pain	170	24 (14.1%)	4/14 (28.6%)	20/156 (12.8%)	0.239	
Dyspnea	14	6 (42.9%)	6/14 (42.9%)	-	-	
Tiredness	14	8 (57.1%)	8/14 (57.1%)	-	-	
Drumstick fingers	13	2 (15.4%)	2/13 (15.4%)	-	-	
Signs, n (%)						
Arthritis	174	155 (89.1%)	12/14 (85.7%)	143/160 (89.4%)	0.676	
Splenomegaly	171	51 (29.8%)	6/14 (42.9%)	45/157 (28.7%)	0.269	
Hepatomegaly	170	63 (37.1%)	7/14 (50%)	56/156 (35.9%)	0.298	
Adenomegaly	170	69 (40.6%)	9/14 (64.3%)	60/156 (38.5%)	0.060	0.024
Pleuritis	170	23 (13.5%)	6/14 (42.9%)	17/156 (10.9%)	0.038	
Pericarditis	170	26 (15.3%)	5/14 (35.7%)	21/156 (13.5%)	0.123	
Laboratory findings at diagnosis of Still's disease					0.479	
Eosinophilia, n/N (%)	162	6 (3.7%)	1/14 (7.1%)	5/148 (3.4%)	0.848	
Leukocytosis > 15x109, n/N (%)	71	47 (66.2%)	7/11 (63.6%)	40/60 (66.7%)	0.664	0.835
Leukocyte level, mean ± standard deviation (range)	71	17.6 ± 8.5	18.7 ± 11.5	17.4 ± 7.9		
CRP > 0.5 mg/dL, n/N (%)		(2.3 - 43.6)	(4.3 - 43.0)	(2.3 - 43.6)	0.305	
CRP level, mean ± standard deviation (range)	88	83 (94.3%)	11/13 (84.6%)	72/75 (96.0%)	0.853	
	88	15.4 ± 11.3	14.9 ± 14.1	15.5 ± 10.9		
High ESR, n/N (%)		(0.1 - 67.6)	(0.1 - 43.2)	(0.1 - 67.6)	0.123	
ESR level, mean ± standard deviation (range)	87	82 (94.3%)	10/13 (76.9%)	72/74 (97.3%)	0.046	
	87	86.2 ± 37.9	66.9 ± 48.6	89.6 ± 35.0		
High ferritin, n/N (%)		(5.0 - 214.0)	(5 - 135)	(18 - 214)	0.630	
Ferritin level (x103), mean ± standard deviation (range)	79	69 (87.3%)	11/12 (91.7%)	58/67 (86.6%)	0.854	
High LDH, n/N (%)	79	5.2 ± 8.3	5.6 ± 9.8	5.2 ± 8.1		
LDH level, mean ± standard deviation (range)		(0.01 - 44.4)	(0.44 - 33.7)	(0.01 - 44.4)	0.619	
	24	19 (79.2%)	1/1 (100%)	18/23 (78.3%)	0.914	
	24	525.5 ± 344.4 (165.0-1391.0)	318-	527.2 ± 352.0 (165 - 1391)		
Comorbidity						0.050
Prior MAS episode, n/N (%)	173	20 (11.6%)	5/14 (35.7%)	15/159 (9.4%)	< 0.001	
Age at MAS diagnosis, mean ± standard deviation (range)	20	16.1 ± 9.4 (2.0 - 38.0)	23.0 ± 8.0 (13.0 - 34.0)	13.8 ± 8.9 (2.0 - 38.0)	0.056	0.433
Number of MAS episodes, n/N (%)	20	1.3 ± 0.6 (1 - 3)	1.6 ± 0.9 (1 - 3)	1.2 ± 0.4 (1 - 2)	< 0.001	
Serological analysis						
ANA positivity, n/N (%)	167	24 (14.4%)	2/14 (14.3%)	22/153 (14.4%)	0.992	-
Autoantibodies detected, n/N (%)	168				0.132	-
Anticentromere		2 (1.2%)	0/14 (0%)	2/154 (1.3%)		
Lupus anticoagulant		2 (1.2%)	1/14 (7.1%)	1/154 (0.7%)		
Rheumatoid factor		3 (1.8%)	0/14 (0%)	3/154 (2.0%)		
Anti-dsDNA		3 (1.8%)	1/14 /7.1%)	2/154 (1.3%)		

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285 – TABLE 1. Continuation

Variables	Data number available	All patients (N = 175)	Patients with lung involvement (N = 14)	Patients without lung involvement (N = 161)	p-value (univariate analysis)	p-value (multivariate analysis)
Medical treatment						0.230
Under glucocorticoid, n/N (%)	166	96 (57.8%)	8/14 (57.1%)	88/152 (57.9%)	0.957	
Average prednisolone equivalent dose (mg), mean ± standard deviation (range)	100	13.0 ± 12.2 (2.5 - 60.0)	19.4 ± 11.5 (5.0 - 40.0)	14.0 ± 12.0 (2.5 - 60.0)	< 0.001	
Methotrexate, n/N (%)	166	80 (48.2%)	6/14 (42.9%)	74/152 (48.7%)	0.679	
Hydroxychloroquine, n/N (%)	165	6 (3.6%)	2/14 (14.3%)	4/151 (2.6%)	0.255	
Sulfasalazine, n/N (%)	165	7 (4.2%)	1/14 (7.1%)	6/151 (4.0%)	0.576	
Azathioprine, n/N (%)	165	3 (1.8%)	0/14	3/151 (2.0%)	0.597	
Anakinra, n/N (%)	165	49 (29.7%)	5/14 (35.7%)	44/151 (29.1%)	0.609	
Canakinumab, n/N (%)	165	9 (5.5%)	2/14 (14.3%)	7/151 (4.6%)	0.344	
Tocilizumab, n/N (%)	165	34 (20.6%)	4/14 (28.6%)	30/151 (19.9%)	0.444	
Rituximab, n/N (%)	165	2 (1.2%)	0/14	2/151 (1.3%)	0.667	
Adalimumab, n/N (%)	165	3 (1.8%)	0/14	3/151 (2.0%)	0.597	
Etanercept, n/N (%)	165	4 (2.4%)	0/14	4/151 (2.6%)	0.540	
Infliximab, n/N (%)	165	9 (5.5%)	1/14 (7.1%)	8/151 (5.3%)	0.773	
Identified adverse drug reaction, n/N (%)	166				0.569	-
Tocilizumab		6 (3.6%)	0/14	6/152 (4.0%)		
Anakinra		7 (4.2%)	2/14 (14.3%)	5/152 (3.3%)		
Methotrexate		5 (3.0%)	0/14	5/152 (3.3%)		
Infliximab		2 (1.2%)	0/14	2/152 (1.3%)		
Glucocorticoid		5 (3.0%)	1/14 (7.1%)	4/152 (2.6%)		
Adverse drug reaction age (years), n (%)	25	25.5 ± 18.4 (4.0 - 70.0)	28.7 ± 7.2 (24.0 - 37.0)	24.9 ± 19.9 (4.0 - 70.0)	< 0.001	0.753
Adverse drug reaction type, n/N (%)	175				0.427	-
Gastrointestinal intolerance		2 (1.1%)	0/14	2/161 (1.2%)		
Infection		1 (0.6%)	0/14	1/161 (0.6%)		
Osteoporotic fractures		2 (1.1%)	1/14 (7.1%)	1/161 (0.6%)		
Neutropenia		2 (1.1%)	0/14	2/161 (1.2%)		
Hidradenitis suppurativa		1 (0.6%)	0/14	1/161 (0.6%)		
Administration site reaction		6 (3.4%)	2/14 (14.3%)	4/161 (2.5%)		
Transaminase elevation		2 (1.1%)	0/14	2/161 (1.2%)		
Toxidermia		2 (1.1%)	0/14	2/161 (1.2%)		
Anaphylaxis		1 (0.6%)	0/14	1/161 (0.6%)		
Prostration and epistaxis		1 (0.6%)	0/14	1/161 (0.6%)		
Mucositis		1 (0.6%)	0/14	1/161 (0.6%)		
Secondary Diabetes mellitus		2 (1.1%)	0/14	2/161 (1.2%)		
Femoral head aseptic necrosis		2 (1.1%)	0/14	2/161 (1.2%)		
Loss of follow-up, n/N (%)	175	26 (14.9%)	4/14 (28.6%)	22/161 (13.7%)	0.264	-
Loss of follow-up reason, n/N (%)	26				0.006	0.077
Death		4/26	2/4 (50%)	2/22 (9.1%)		
Hospital reassignment		6/26	2/4 (50%)	4/22 ((18.2%)		
Discharge due to sustained remission without medication		4/26	-	4/22 (18.2%)		
Stopped attending appointments						
Change of country		11/26	-	11/22 (50%)		
		1/26	-	1/22 (4.5%)		
Outcome, n/N (%)						
Currently with a relapse with active disease	53	15 (28.3%)	1/14 (7.1%)	14/161 (8.7%)	0.497	-
Death	175	7 (4.0%)	4/14 (28.6%)	3/161 (1.9%)	0.700	-
Death by pulmonary involvement	14	1 (7.1%)	1/14 (7.1%)	-	-	-
Age of death (years), mean ± standard deviation (range)	7	61.7 ± 24.6 (27.0 - 91.0)	42.7 ± 18.5 (27.0 - 63.0)	80.7 ± 9.6 (72.0 - 91.0)	0.002	0.034

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285 – TABLE 2. Clinical, serologic and laboratory characterization of the Still's Disease patients by age

Variables	Data number available	All patients (N =175)	Still's Disease onset at pediatric age (N = 104)	Still's Disease onset at adulthood (N = 67)	p-value (univariate analysis)	p-value (multivariate analysis)
Female, n (%)	175	97 (55.4%)	51 (49.0%)	45 (71.6%)	0.018	0.033
Age of symptoms onset (years), mean ± standard deviation (range)	171	20.1 ± 17.6 (1 - 76)	8.2 ± 5.1 (1 - 17)	38.5 ± 13.8 (18 - 76)	-	-
Age of Still Disease diagnosis (years), mean ± standard deviation (range)	174	20.7 ± 17.6 (1 - 76)	9.0 ± 5.8 (1 - 29)	39.2 ± 13.9 (19.0 76.0)	-	-
Time between symptoms onset and Still Disease diagnosis (months), mean ± standard deviation (range)	171	8.4 ± 30.8 (0 - 252)	7.2 ± 30.3 (0 - 252.0	10.4 ± 31.6 (0 - 198.0)	0.001	0.670
Age currently (years),mean ± standard deviation (range)	169	29.8 ± 18.9 (3 - 81)	18.3 ± 10.5 (3.0 - 52.0)	48.5 ± 14.5 (22.0 - 81.0)	-	-
Race, n/N (%)	175				0.355	-
Caucasian		159 (90.9%)	96 (92.3%)	59 (88.1%)		
Melanodermic		16 (9.1%)	8 (7.7%)	8 (11.9%)		
Nationality, n/N (%)					0.219	-
Portugal;	175	157 (89.7%)	97 (93.4%)	56 (83.6%)		
Africa;		11 (6.3%)	3 (2.9%)	8 (11.9%)		
Brazil;		3 (1.7%)	2 (1.9%)	1 (1.5%)		
Other European country		4 (2.3%)	2 (1.9%)	2 (3.0%		
Course of Still's Disease, n/N (%)	174				0.117	-
Monophasic		65 (37.4%)	40	22		
Intermittent/polycyclic		60 (34.5%)	40	19		
Chronic/persistent		49 (28.1%)	24	25		
Symptoms, n/N (%)						-
Fever	103	102 (99.0%)	53/54	49/49	0.343	
Rash	171	139 (81.3%)	86/102	51/66		
Myalgia	172	74 (43.0%)	42/102	31/67		
Odynophagia	170	74 (43.5%)	35/101	37/66		
Abdominal pain	170	24 (14.1%)	16/101	8/66		
Dyspnea	14	6 (42.9%)	3/7	3/7		
Tiredness	14	8 (57.1%)	4/7	4/7		
Drumstick fingers	13	2 (15.4%)	1/6	1/7		
Signs, n/N (%)						
Arthritis	174	155 (89.1%)	92/104	60/67	0.826	
Splenomegaly	171	51 (29.8%)	31/102	19/66	0.826	
Hepatomegaly	170	63 (37.1%)	31/101	31/66	0.037	0.333
Adenomegaly	170	69 (40.6%)	31/101	38/66	0.001	0.011
Pleuritis	170	23 (13.5%)	16/101	6/66	0.340	
Pericarditis	170	26 (15.3%)	16/101	9/66	0.698	
Laboratory findings at diagnosis of Still's disease						
Eosinophilia, n/N (%)	162	6 (3.7%)	1/99	5/59	0.053	
Leukocytosis > 15x109, n/N (%)	71	47 (66.2%)	20/29	27/42	0.687	
Leukocyte level, mean ± standard deviation (range)	71	17.6 ± 8.5 (2.3 - 43.6)	17.5 ± 11.5 (4.3 - 30.1)	20.5 ± 10.9 (11.7 - 32.7)	0.198	
CRP > 0.5 mg/dL, n/N (%)	88	83 (94.3%)	44/47	39/41	0.764	
CRP level, mean ± standard deviation (range)	88	15.4 ± 11.3 (0.1 - 67.6)	13.4 ± 6.2 (5.9 - 22.3)	26.7 ± 2.1 (24.7 - 28.7)	<0.001	0.022
High ESR, n/N (%)	87	82 (94.3%)	44/46	38/41	0.558	
ESR level, mean ± standard deviation (range)	87	86.2 ± 37.9 (5.0 - 214.0)	81.3 ± 43.9 (18.0 - 120.0)	113.0 ± 12.1 (99 - 120)	<0.001	0.381
High ferritin, n/N (%)	79	69 (87.3%)	33/40	36/39	0.193	
Ferritin level (x103), mean ± standard deviation (range)	79	5.2 ± 8.3 (0.01 - 44.4)	9.2 ± 17.6 (0.039 - 44.4)	4.7 ± 3.6 (1.9- 8.8)	<0.001	0.223
High LDH, n/N (%)						
LDH level, mean ± standard deviation (range)	24	19 (79.2%)	16/21	3/3	0.021	0.138
	24	525.5 ± 344.4 (165.0-1391.0)	503.5 ± 464.8 (204.0 - 1391.0)	306.7 ± 24.9 (278.0 - 322.0)	<0.001	0.030

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285 – TABLE 2. Continuation

Variables	Data number available	All patients (N =175)	Still's Disease onset at pediatric age (N = 104)	Still's Disease onset at adulthood (N = 67)	p-value (univariate analysis)	p-value (multivariate analysis)
Comorbidity						
Prior MAS episode, n/N (%)	173	20 (11.6%)	14/104	6/65	0.410	
Age at MAS diagnosis, mean ± standard deviation (range)	20	16.1 ± 9.4	11.1 ± 4.9	27.7 ± 6.8	-	-
Number of MAS episodes, n/N (%)		(2.0 - 38.0)	(12.0 - 18.0)	(20.0 - 38.0)		
	20	1.3 ± 0.6 (1 - 3)	1.2 ± 0.4 (1 - 2)	1.5 ± 0.8 (1 - 3)	0.004	0.318
Serological analysis						
ANA positivity, n/N (%)	167	24 (14.4%)	16/98	8/65	0.481	-
Autoantibodies detected, n/N (%)	168				0.330	-
Anticentromere		2 (1.2%)	0	2		
Lupus anticoagulant		2 (1.2%)	2	0		
Rheumatoid factor		3 (1.8%)	0	3		
Anti-dsDNA		3 (1.8%)	2	1		
Medical treatment						
Under glucocorticoid, n/N (%)	162	94 (58.0%)	55/99	39/63	0.867	
Average prednisolone equivalent dose (mg), mean ± standard deviation (range)	104	13.0 ± 12.2	17.2 ± 13.3	11.5 ± 9.8	< 0.001	0.050
Methotrexate, n/N (%)		(2.5 - 60.0)	(3.8 - 60.0)	(2.5 - 40.0)		
Hydroxychloroquine, n/N (%)	162	76 (46.9%)	40/99	36/63	0.038	0.114
Sulfasalazine, n/N (%)	162	5 (3.1%)	0/99	5/63	0.024	0.005
Azathioprine, n/N (%)	162	6 (3.7%)	2/99	4/63	0.207	
Anakinra, n/N (%)	162	3 (1.9%)	1/99	2/63	0.378	
Canakinumab, n/N (%)	162	49 (30.2%)	34/99	15/63	0.157	
Tocilizumab, n/N (%)	162	9 (5.6%)	4/99	5/63	0.328	
Rituximab, n/N (%)	162	33 (20.4%)	24/99	9/63	0.111	
Adalimumab, n/N (%)	162	2 (1.2%)	0/99	2/63	0.159	
Etanercept, n/N (%)	162	3 (1.9%)	2/99	1/63	0.843	
Infliximab, n/N (%)	162	9 (5.6%)	7/99	2/63	0.256	
	162	4 (2.5%)	1/99	3/63	0.198	
Identified adverse drug reaction, n/N (%)	161				0.382	-
Tocilizumab		6 (3.7%)	5	1		
Anakinra		7 (4.3%)	2	5		
Methotrexate		4 (2.5%)	2	2		
Infliximab		2 (1.2%)	1	1		
Glucocorticoid		5 (3.1%)	2	3		
Adverse drug reaction age, n/N (%)	24	25.3 ± 18.6	13.8 ± 11.9	38.4 ± 15.4	-	
		(4.0 - 70.0)	(4.0 - 37.0)	(24.0 - 70.0)		
Adverse drug reaction type, n/N (%)	162				0.123	-
Gastrointestinal intolerance		1 (0.6%)	0	1		
Infection		1 (0.6%)	0	1		
Osteoporotic fractures		2 (1.2%)	2	0		
Neutropenia		2 (1.2%)	2	0		
Hidradenitis suppurativa		1 (0.6%)	1	0		
Administration site reaction		6 (3.7%)	2	4		
Transaminase elevation		2 (1.2%)	2	0		
Toxidermia		2 (1.2%)	1	1		
Anaphylaxis		1 (0.6%)	1	0		
Prostration and epistaxis		1 (0.6%)	1	0		
Mucositis		1 (0.6%)	0	1		
Secondary Diabetes mellitus		1 (0.6%)	0	1		
Femoral head aseptic necrosis		2 (1.2%)	0	2		
Loss of follow-up, n/N (%)	171	26 (14.9%)	12	14		

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285 – TABLE 2. Continuation

Variables	Data number available	All patients (N =175)	Still's Disease onset at pediatric age (N = 104)	Still's Disease onset at adulthood (N = 67)	p-value (univariate analysis)	p-value (multivariate analysis)
Loss of follow-up reason, n/N (%)	26				0.077	-
Death		4/26	1	3		
Hospital reassignment		6/26	2	4		
Discharge due to sustained remission without medication		4/26	1	3		
Stopped attending appointments						
Change of country		11/26	7	4		
		1/26	1	0		
Outcome, n/N (%)						
Currently with a relapse with active disease	53	15 (28.3%)	11	4	0.028	0.032
Death	175	6 (4.0%)	1	5	0.478	
Death by pulmonary involvement	14	1 (7.1%)	0	1	-	
Age of death (years),mean ± standard deviation (range)	6	61.9 ± 24.9 (27.0 - 91.0)	38.0	66.4 ± 24.3 (27.0 - 91.0)	-	-

285 – TABLE 3. Clinical, serologic and laboratory characterization of the Still's Disease patients with lung involvement

Variables	Data number available	All patients with lung involvement (N = 14)	Diagnosis of Still Disease in pediatric age (N = 7)	Diagnosis of Still Disease in adulthood (N = 7)
Female, n (%)	14	8 (57.1%)	3	5
Age of symptoms onset (years), mean ± standard deviation (range)	14	18.7 ± 12.4 (4 - 41)	8.7 ± 4.8 (4 - 17)	28.7 ± 8.8 (19.0 - 41.0)
Age of Still Disease diagnosis (years), mean ± standard deviation (range)	14	20.6 ± 14.9 (4 - 58)	10.1 ± 5.9 (4.0 - 18.0)	31.1 ± 13.7 (19.0 - 58.0)
Time between symptoms onset and Still Disease diagnosis (months), mean ± standard deviation (range)	14	23.1 ± 58.4 (0 - 198)	16.7 ± 42.0 (0 - 112)	29.6 ± 74.2 (0 -198)
Time between symptoms onset and diagnosis of pulmonary involvement (years), mean ± standard deviation (range)	14	6.1 ± 9.6 (0.0 - 35.0)	7.3 ± 14.0 (-8.0 - 35.0)	4.3 ± 5.2 (0.0 - 14)
Time between lung symptoms onset and diagnosis of pulmonary involvement (months), mean ± standard deviation (range)	14	4.8 ± 10.3 (-2.0 - 35.0)	8.0 ± 12.8 (0.0 - 35.0)	2.3 ± 4.1 (-2.0 - 10.0)
Age at pulmonary involvement onset (years), mean ± standard deviation (range)	14	24.4 ± 14.2 (4.0 - 55.0)	15.7 ± 9.9 (4.0 - 36.0)	33.0 ± 12.8 (19.0 - 55.0)
Age at diagnosis of pulmonary involvement (years), mean ± standard deviation (range)	14	24.4 ± 14.2 (4.0 - 56.0)	16.3 ± 9.9 (4.0 - 36.0)	33.4 ± 13.4 (19.0 - 56.0)
Active Still's disease at diagnosis of pulmonary involvement, n/N (%)	13	11 (84.6%)	4	7
Age currently (years),mean ± standard deviation (range)	10	30.1 ± 11.9 (17 - 58)	24.5 ± 8.0 (17.0 - 40.0)	36.8 ± 13.1 (22.0 - 58.0)
Race, n (%)	14		7 (100%)	7 (100%)
Caucasian		14 (100%)		
Melanodermic		0		

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285 – TABLE 3. Continuation

Variables	Data number available	All patients with lung involvement (N = 14)	Diagnosis of Still Disease in pediatric age (N = 7)	Diagnosis of Still Disease in adulthood (N = 7)
Nationality, n (%)	14		7 (100%)	7 (100%)
Portugal;		14 (100%)		
Africa;		0		
Brazil;		0		
Other European country		0		
Course of Still's Disease, n (%)	14			
Monophasic		6 (42.9%)	3	3
Intermittent/polycyclic		3 (21.4%)	3	0
Chronic/persistent		5 (35.7%)	1	4
Symptoms, n (%)				
Fever	8	7 (87.5%)	3	4
Rash	14	12 (85.7%)	6	6
Myalgia	14	8 (57.1%)	3	5
Odynophagia	14	10 (71.4%)	3	7
Abdominal pain	14	4 (28.6%)	2	2
Dyspnea	14	6 (42.9%)	3	3
Tiredness	14	8 (57.1%)	4	4
Drumstick fingers	13	2 (15.4%)	1	1
Signs, n (%)	14			
Arthritis		12 (85.7%)	5	7
Splenomegaly		6 (42.9%)	2	4
Hepatomegaly		7 (50%)	1	6
Adenomegaly		9 (64.3%)	4	5
Pleuritis		6 (42.9%)	3	3
Pericarditis		5 (35.7%)	2	3
Laboratory findings at diagnosis of Still's disease				
Eosinophilia, n/N (%)	14	1 (7.1%)	0	1
Leukocytosis > 15x109, n/N (%)	11	7 (63.6%)	3	4
Leukocyte level, mean ± standard deviation (range)		18.7 ± 11.5 (4.3 - 43.0)	18.7 ± 10.8 (7.1 - 33.1)	18.6 ± 12.7 (4.3 - 43.0)
CRP > 0.5 mg/dL, n/N (%)	13	11 (84.6%)	4	7
CRP level, mean ± standard deviation (range)		14.9 ± 14.1 (0.1 - 43.2)	13.6 ± 12.9 (0.1 - 28.6)	16.0 ± 15.9 (1.7 - 43.2)
High ESR, n/N (%)	10	10 (76.9%)	4	6
ESR level, mean ± standard deviation (range)		66.9 ± 48.6 (5 - 135)	50.0 ± 47.3 (5 - 135)	81.3 ± 48.3 (21 - 120)
High ferritin, n/N (%)	12	11 (91.7%)	4	7
Ferritin level (x103), mean ± standard deviation (range)		5.6 ± 9.8 (0.44 - 33.7)	4.0 ± 5.1 (0.44 - 13.5)	6.8 ± 12.3 (0.4 - 33.7)
High LDH, n/N (%)	1	1 (100%)	1	0
LDH level, mean ± standard deviation (range)		318 (-)	318 (-)	-
Eosinophilia at pulmonary involvement diagnosis, n (%)	12	6 (50%)	0	6 (85.7%)

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285 – TABLE 3. Continuation

Variables	Data number available	All patients with lung involvement (N = 14)	Diagnosis of Still Disease in pediatric age (N = 7)	Diagnosis of Still Disease in adulthood (N = 7)
Type of lung involvement in Still's Disease, n (%)	14			
Septal thickening		3 (21.4%)	1	2
Crazy-paving		1 (7.1%)	0	1
Peripheral consolidation		5 (35.7%)	3	2
Peribronchovascular consolidation		0	0	0
Ground-glass		6 (42.9%)	2	4
Honeycomb pattern		2 (14.3%)	1	1
Traction bronchiectasis		2 (14.3%)	1	1
Interstitial lung disease		2 (14.3%)	1	1
Pulmonary alveolar proteinolysis		0	0	0
Pulmonary alveolar hypertension		0	0	0
Hypoxemia		5 (35.7%)	1	4
Low peripheral oxygen saturation		5 (35.7%	1	4
Pulmonary hypertension		3 (21.4%)	1	2
Bronchoalveolar Lavage, n (%)	5			
No pathological findings		1	1	0
Nonspecific inflammatory findings		2	0	2
Bacterial identification		0	0	0
Alveolar macrophages, multinucleated giant cells, polymorphonuclear cells and lymphocytes observed		2	1	1
Medications used to treat lung involvement	13			
Glucocorticoid, n (%)		9 (69.2%)	4	5
Oxygen therapy, n (%)		4 (30.8%)	2	2
Tocilizumab, n (%)		3 (23.1%)	2	1
Anakinra, n (%)		1 (7.7%)	0	1
Sildenafil, n (%)		0	0	0
Tadalafil, n (%)		2 (14.3%)	1	1
Macitentan, n (%)		1 (7.7%)	0	1
Need for admission to Intensive Care Unit, n (%)		6	3	3
Pulmonary outcomes, n/N (%)	12			
Improvement of lung involvement		7 (58.3%)	3	4
Stabilization of lung involvement		2 (16.7%)	2	0
Worsening of lung involvement		3 (25.0%)	0	3
Survival outcomes, n/N (%)	13			
Death due to Still's Disease lung involvement		1	0	1
Death		3	1	2
Age of death (years), mean ± standard deviation (range)	3	42.7 ± 18.5 (27.0 - 63.0)	38 -	45 -

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