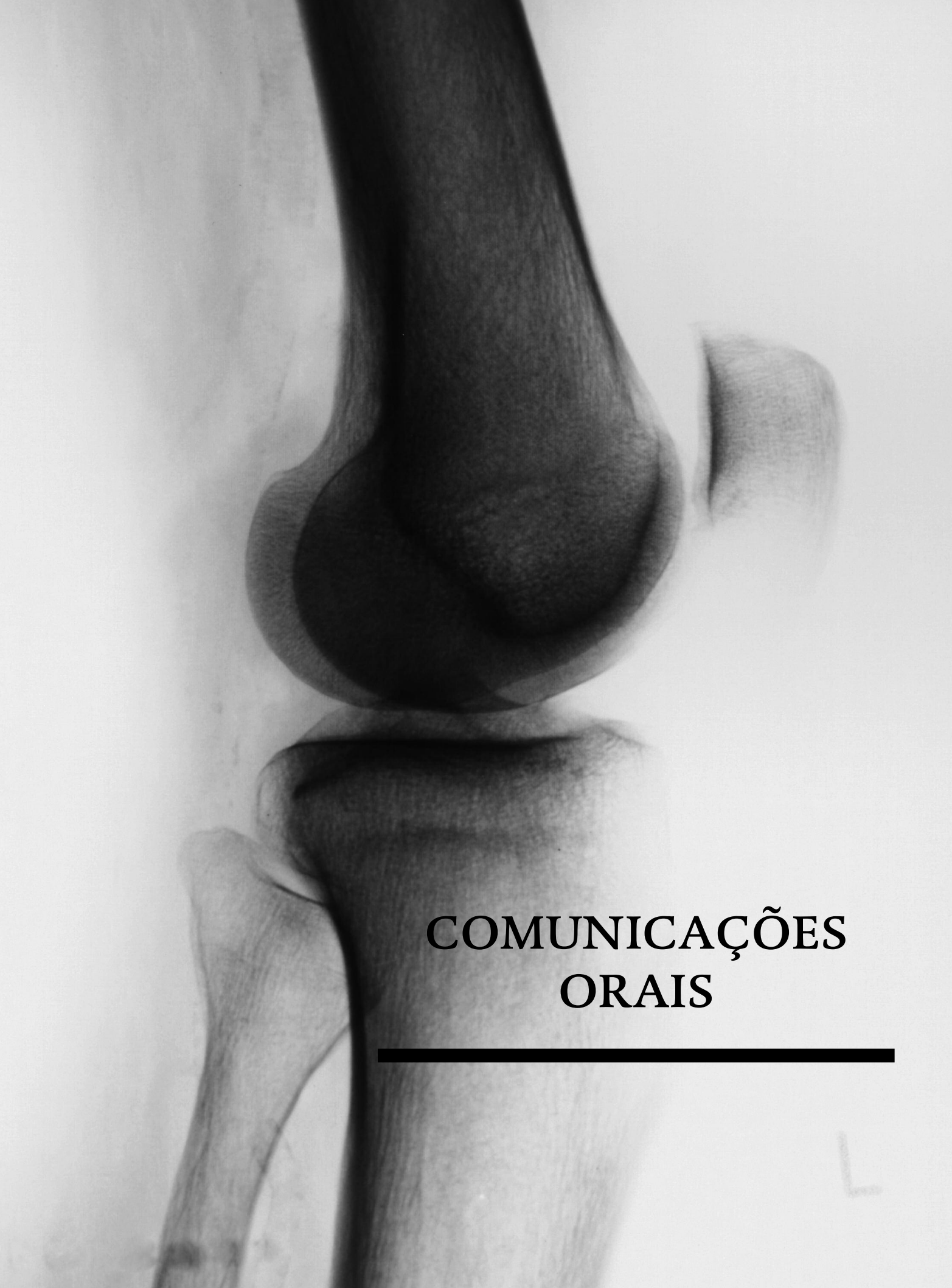

COMUNICAÇÕES ORAIS

Comunicações orais

ACTA REUMATOL PORT. 2013:38:25-32 (SUP)

CO1 – INFLUÊNCIA DE VARIÁVEIS CLÍNICAS E POLIMORFISMOS GENÉTICOS NA EFETIVIDADE DO TRATAMENTO COM METOTREXATO NUMA POPULAÇÃO PORTUGUESA COM ARTRITE REUMATÓIDE

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Introdução: O MTX é, dos fármacos modificadores de evolução da artrite reumatoide, o mais usado no seu tratamento. Todavia, a grande variabilidade na resposta clínica apresentada pelos doentes é uma realidade. Vários estudos têm sido realizados no sentido de averiguar o papel de potenciais biomarcadores na previsão da inefetividade do MTX. Não obstante, existe pouca informação no que respeita à população Portuguesa. Este trabalho pretende determinar possíveis associações entre a inefetividade do MTX em doentes com AR e um conjunto de variáveis clínicas e polimorfismos genéticos, numa amostra populacional portuguesa.

Material e Métodos: Desde 2009 foram monitorizados 233 doentes com AR ativa tratados com MTX de acordo com as "guidelines" de referência para o tratamento. Foram analisadas 26 variáveis clínicas que potencialmente influenciam o estado da doença e a resposta ao tratamento, bem como 6 polimorfismos genéticos relacionados com o mecanismo de ação do MTX (rs1801133, rs4673993, rs34743033, rs2853542, rs34489327 e rs1051266).

As variáveis foram comparadas entre doentes com uma resposta inefetiva (nResp) vs doentes em que o fármaco foi efetivo (Resp). Os doentes nResp foram definidos como aqueles que apresentaram um DAS28>5,1 em duas avaliações consecutivas apesar de doses elevadas, máximas e toleradas, de MTX.

A análise estatística (nível de significância: P<0,05) foi realizada recorrendo aos testes t-Student, Mann--Whitney U e/ou 2. As diferenças na distribuição dos grupos genotípicos foram testadas por tabelas de contingência 2x2 para portadores vs não portadores e, posteriormente, pela análise do teste de 2 bicaudal.

Resultados: Os resultados obtidos apresentam-se a seguir, optando-se pelo agrupamento das variáveis analisadas. Variáveis clínicas: os fumadores apresentaram maior probabilidade de serem Resp (P=0,009); uma menor idade ao diagnóstico e uma maior duração da doença revelaram estar associados com nResp (P=0,046 e 0,008, respet.);a positividade para anti--CCP e/ou ANAs demonstrou-se associada a nResp (P=0,005 e 0,007, respet.);um maior DAS28 revelou--se associado a nResp (P=0,001 e 0,029; usando PCR ou VS, respet.);maior número de articulações tumefactas e dolorosas demonstraram-se relacionados com nResp enquanto que valores mais altos de PCR revelaram-se associados a Resp (P=0,002; 0,001 e 0,035; respet.);uma maior pontuação no HAQ relacionou-se com nResp (P=0,005) e os utilizadores de AINEs apresentaram maior probabilidade de serem nResp (P=0,002). Variáveis genéticas: homozigóticos TT para MTHFRC677T e 3R3R para TYMS28bpVNTR, portadores do alelo T para ATIC C675T e do alelo 6pb- para TYMS1494 de l6 revelaram-se associados a nResp (P=0,049; 0,007; 0,025 e 0,023; respet.); portadores do alelo C para MTHFRC677T e do alelo 2R para TYMS28bpVNTR, homozigóticos CC para ATICC675T e 6bp+6bp+ para TYMS 1494del6 apresentaram maior probabilidade de serem Resp (P=0,049; 0,007; 0,025 e 0,023; respet.).

Conclusão: Os polimorfismos genéticos rs1801133, rs4673993 e rs34489327, combinados com a idade precoce ao diagnóstico; o maior tempo de evolução da doença; a positividade para anti-CCP e ANAs; a utilização de AINEs e o maior valor de DAS28, articulações tumefactas, articulações dolorosas e HAQ, poderão constituir indicadores de inefetividade ao MTX no tratamento da AR e, consequentemente, poderão constituir ferramentas práticas de auxílio na atividade clínica diária.

C02 – A COMPARISON OF DAS28(4V)-CRP AND ACR/EULAR REMISSION CRITERIA IN AN ANTI-TNF-TREATED RHEUMATOID ARTHRITIS PATIENT COHORT

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that is potentially disabling. Early diagnosis and remission-oriented treatment are essential to achieve good outcomes. Early management ensures a better response and higher rates of remission. New RA remission criteria have been developed by American College of Rheumatology/The European League Against Rheumatism (ACR/EULAR) in 2011. In this study we compare remission rates of anti-tumor necrosis factor (anti-TNF) treated RA patients using ACR/EULAR versus disease activity score 28 - 4 variable (DAS28(4v)-CRP) remission criteria.
Methods: Demographic, clinical and laboratory data were collected prospectively from a cohort of 273 biologic naive RA patients commencing biological therapy at baseline and following 3, 6 and 12 months of therapy. Remission status was calculated at all timepoints using both DAS28(4v)-CRP (<2.6) and 2011--ACR/EULAR Boolean remission criteria. Response was scored using EULAR response criteria (good, moderate and no response).
Results: Mean (range) patient age was 59.9 (7.2-85.4) years with disease duration of 13.4 (1.0-52.0) years. In total 87% of patients were responders (37% good vs 50% moderate) at 3 months and maintained at 12 months, with a further increase towards good versus moderate response (51% good vs 32% moderate). Laboratory and clinical parameters (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), patient global health (PGH), DAS28(4v)-CRP showed significant sustained improvement at 3 and 12 months of therapy ($p<0.05$). Over half of patients (54.9%) had disease activity of DAS28(4v) CRP<3.2 at 12 months. All patients in Boolean remission were in DAS28 remission at all timepoints. 102 patients (37%) were in any remission at 12 months: 75 (27%) in DAS28 remission alone and 27 (10%) in both Boolean and DAS28 remission. All patients in remission were significantly younger ($p=0.041$) with lower baseline tender joint count 28 (TJC28) and patient global health (PGH) scores than those who did not meet either remission criteria ($p=0.001$, $p=0.047$). Boolean-remission patients were younger ($p=0.026$) and had lower 12 months DAS28 and PGH values than only DAS28 remission patients (all $p<0.0001$). Disease activity of the most active Boolean remission patient was found to be 1.97 calculating by DAS28(4v)-CRP. Patients not achieving Boolean remission due to one Boolean subcriteria being 1 (30.8 %) most frequently missed PGH 1 criteria (76.2 %).
Conclusion: Boolean remission was achieved by 10% of patients at 12 months compared to only DAS28 remission in 37%; 58% had low disease activity or remission and 83% had sustained good or moderate response. Boolean remission criteria sets lower disease activity state for remission (defined as DAS28(4v)-CRP 1.97), therefore less patients are considered to be in remission than according to DAS28(4v)-CRP based criteria. Patients often miss PGH 1 criteria and remain omitted from Boolean remission. New remission criteria are more stringent and exclude residual disease activity due to PGH. Diminished disease activity cut--off for remission may offer an opportunity for slower radiographic progression.

C03 – REUMA.PT/LES: THE EXPERIENCE OF TWO CENTRAL HOSPITALS IN LISBON

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Background: Reuma.pt, the Rheumatic Diseases Register from the Portuguese Society of Rheumatology has recently expanded its coverage to Systemic Lupus Erythematous (SLE) patients, the Reuma.pt/LES. Reuma.pt/LES is a web-based platform launched in September 2012 that simultaneously serves as a nationwide registry and as an electronic medical record. Its aim is to register all patients with SLE and follow them up in a standard manner in order to improve the monitoring and clinical care for patients with SLE while simultaneously increase the knowledge of this disease.
Methods: The authors present the structure and the functioning of this national project, giving as an example the subpopulation of patients with SLE from two centres in Lisbon (Hospital Santa Maria and Hospital Garcia de Orta) included in Reuma.pt/LES.
Results: 878 patients from all the country with the clinical diagnosis of SLE were registered in the database Reuma.pt/LES until January 2013. Recorded information includes demographics, work status, life-styles, ACR and SLICC 2012 classification criteria, thrombotic and obstetric manifestations, SLE disease activity at each visit, fatigue scale, health related quality of life measures (SF-36 and EQD5), irreversible damage, comorbid conditions, medication and adverse events. Hospital Santa Maria (Lisbon) and the Hospital Garcia de Orta (Almada) contributed to Reuma.pt/LES with 305 patients, 95.1% females, 80% Caucasians with a mean age of 45.5 ±14.9y. The mean age at diagnosis was 35.9 ±14.9y and the mean disease duration was 10.3 ± 7.3y. SLE Disease Activity Index (SLEDAI) at the first evaluation was 3.4 ± 3.9 and current accrual damage assessed by the Systemic Lupus International Collaborating Clinics (SLICC) was 0.7 ± 1.1. Hypertension was reported in 27.2% of the patients, diabetes in 8.9% and cardiovascular diseases in 8.9%. The vast majority of patients were treated with hydroxychloroquine (93.9%) and corticosteroids (prednisolone 61.8%, prednisone 25.2%, deflazacort 17.1%). Immunosuppressive drugs were used in about half of the cases (azathioprine in 27%, methotrexate in 15.5%, cyclophosphamide in 7.4%, mycophenolate in 4.8%) and to a lesser extent biological therapies (rituximab in 5.9% and belimumab in 0.98% of the patients).
Conclusion: Reuma.pt is a very useful tool that allows a more efficient patient follow-up, and standardized data collection, storage and analysis, with the ultimate objective of improving patient care and simultaneously scientific research in the field of SLE.

CO4 – INCREASED FREQUENCY OF INTERLEUKIN-2 PRODUCTION BY TH17 AND TC17 LYMPHOCYTES IN PERIPHERAL BLOOD OF SYSTEMIC SCLEROSIS PATIENTS

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Background: The pathogenesis of systemic sclerosis (SSc) is largely unknown, although proinflammatory cytokines are considered to play a central role. We hypothesized that Th17 and/or Tc17 cell populations and cytokine expression may be altered in SSc.
Objectives: Our purpose was to investigate the pattern of expression of proinflammatory cytokines by peripheral blood (PB) IL-17+ T cell populations in SSc and to explore clinical associations.
Methods: This study included 41 SSc patients and 20 age- and sex-matched healthy controls (HC). All SSc patients fulfilled the American College of Rheumatology Criteria for the classification of SSc and were classified according to LeRoy *et al.* as having limited cutaneous SSc (lSSc, n=29) or diffuse cutaneous SSc (dSSc, n=12). A clinical evaluation was made, including disease duration, disease activity as measured by the European Scleroderma Study Group criteria, modified Rodnan skin score (mRSS), digital necrosis and target organs' involvement. The autoantibody profile was collected from medical records. Each participant was submitted to a blood sample collection, which was processed in order to separately analyze the intracellular expression of IL-2, TNF- and IFN- in IL-17+ T cell populations, within the CD4 and CD8 T cell subsets. Data was statistically analyzed using the SPSS® version 20.0 for windows. Mann-Whitney test was used to evaluate differences between groups. Correlations between continuous variables were assessed by Spearman's correlation coefficient. P values < 0.05 were considered statistically significant.
Results: The mean age was 56.1+11.8 and 52.0+9.9 years for SSc patients and HC respectively. Females represented 78% of the SSc group and 80% of the HC. The patients had a mean mRSS of 11.32+7.76 and mean disease activity of 2.76+2.44.

The frequency of PB Th17 and Tc17 cells was not statistically different in SSc patients when compared to

HC. The percentage of Th17 and Tc17 cells expressing IL-2 was significantly higher in SSc patients than in HC (p<0.001 and p=0.006, respectively). There were no differences in the frequency of Th17 and Tc17 cells expressing either TNF- or IFN- between patients and controls. There were no differences between lSSc and dSSc patients regarding the frequency of IL-2, TNF- and IFN- expression among Th17 or Tc17 cells populations. We had similar negative findings regarding disease duration and internal organs' involvement. The frequency of IL-2-producing Th17 cells showed a positive correlation with mRSS (p=0.002). Conversely, the frequency of IL-2-producting Tc17 cells presented a positive correlation with disease activity (p=0.021). SSc patients with history of digital ulcer presented higher frequencies of IL-2 expression among Tc17 cells (p=0.001).

Conclusions: IL-2-producing Th17 and Tc17 cells frequency is higher in SSc than in HC, no differences being found between the two clinical subtypes of the disease. The frequency of IL-2-producing Tc17 cells was correlated with disease activity whereas the frequency of IL-2-producing Th17 cells was correlated with the extension of skin involvement. These findings support the hypothesis that IL-2 produced by Th17 and Tc17 cells may be involved in the pathological process of SSc, regardless of the disease subset.

CO5 – SARCOPENIA NOS DOENTES COM ESPONDILARTRITES – UM ESTUDO CASO CONTROLO

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Introdução: A perda de massa muscular (MM) é um problema grave, podendo causar morte prematura. Vários estudos demonstram que cerca de 2/3 dos doentes com artrite reumatóide (AR) têm perda de MM. Alguns fatores foram identificados na patogénese deste processo: produção excessiva de TNF e outras citocinas inflamatórias que conduzem ao catabolismo muscular, baixa atividade física e redução da ação periférica da insulina. A elevação de citocinas pró-inflamatórias está também presente nas espondilartrites (Spa) e, tal como na AR, a perda de massa muscular poderá ocorrer. Os estudos sobre sarcopenia nas espondilartrites são escassos e revelam resultados discrepantes; como tal, o efeito da inflamação, atividade da doença e dano estrutural na composição corporal permanece desconhecido. Com o presente trabalho, os autores pretenderam: avaliar o índice de massa muscular (IMM) numa coorte de doentes com Spa; verificar se o risco de sarcopenia era superior em relação ao grupo controlo; analisar eventuais relações entre IMM, duração e atividade da doença, compromisso funcional e dano radiológico.

Material e Métodos: Estudo caso-controlo, numa população de doentes com Spa. O grupo controlo foi constituído por utilizadores de uma unidade de cuidados de saúde primários. As variáveis analisadas foram: sexo, idade, altura, peso, duração da doença, antecedentes patológicos, medicação crónica, MMI, atividade da doença compromisso funcional e, nos doentes com envolvimento axial, dano radiológico estrutural). O IMM foi determinado a partir do valor de MM usando a equação de Lee. Os dados foram tratados usando o sistema SPSS, tendo sido atribuído significado estatístico a valores p<0,05.

Resultados: Uma amostra de 60 doentes foi reunida; 52% do sexo feminino. A idade média foi de 45,5±13,4 anos e a duração média da doença foi de 10,9±11,6 anos; 40% tinham o diagnóstico de artrite psoriática (APs). De acordo com a classificação de IMM, 62% dos doentes apresentavam sarcopenia. Registou-se uma diferença estatisticamente significativa entre o IMM no grupo de doentes e no grupo controlo (7,12±0,99 vs 7,8±0,93; p<0,05). O *odds ratio* entre casos e controlos com e sem sarcopenia foi de 2,1. No grupo de doentes com espondilite anquilosante não se identificou associação entre MMI e BASFI, BASDAI ou duração da doença. Contudo, no subgrupo de doentes com APs e envolvimento axial, identificou-se forte correlação negativa entre MMI e BASFI (=-0,823; p<0,05). Na totalidade dos doentes com envolvimento axial, não se identificou diferença estatisticamente significativa entre os diferentes graus de sarcopenia. Apenas nos homens se identificou uma correlação negativa moderada entre o IMM e o mSASSS (=-0,384). O sexo, medicação concomitante e antecedentes patológicos não influenciaram o grau de sarcopenia.

Discussão: Este estudo demonstrou um risco de sarcopenia em doentes com Spa duas vezes superior em relação ao grupo controlo. Verificou-se ainda que uma maior limitação funcional se correlaciona, nos doentes com Aps e envolvimento axial, com um maior grau de sarcopenia. Nas Spa axiais, um maior valor de mSASSS

está relacionado com menor imm. Não se identificaram outros factores associados à diminuição da MM.

C06 – REFERENCE INTERVALS OF SPINAL MOBILITY MEASURES IN NORMAL INDIVIDUALS – THE MOBILITY STUDY

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Background: Spinal mobility is frequently assessed in the follow-up of patients with axial SpA, which is also in accordance with the recommendations by the Assessment of Spondyloarthritis international Society (ASAS). However, the interpretation of spinal mobility measures has been hampered by the absence of reference values.
Objective: To establish reference intervals (RIs) for spinal mobility measures.
Methods: A cross-sectional study ("MOBILITY-study") was conducted among healthy volunteers aged 20-69 years old. Recruitment was stratified by gender, age (10-year categories) and height (10 cm categories). Participants were Caucasian volunteering to be measured in the Netherlands and Portugal. Exclusion criteria were factors potentially influencing spinal mobility (eg. back surgery, low back pain). Several spinal mobility measures were assessed: tragus-to-wall distance (cm), occiput-to-wall distance (cm), lateral spinal flexion (LSF, cm), cervical rotation (degrees), intermalleolar distance (cm), chest expansion (cm), 10cm- and 15cm-Schober's test. The Bath Ankylosing Spondylitis Mobility Index (BASMI) was computed. Age-specific equations for percentiles of spinal mobility measures were derived by maximum likelihood. Each parameter of normal or exponential-normal density was modeled as a fractional polynomial function of age. The

TABLE. REFERENCE INTERVALS (2.5TH -97.5TH PERCENTILES) OF SPINAL MOBILITY MEASUREMENTS

		Percentiles		
Spinal mobility measure	**Age**	**2.5th**	**50th**	**97.5th**
Lateral spinal flexion (cm)	25	16.2	22.1	28.0
	35	14.7	20.6	26.5
	45	13.2	19.1	25.0
Cervical rotation (degrees)	25	62	81	99
	35	59	77	96
	45	55	74	92
Intermalleolar distance (cm)	25	94	119	144
	35	92	117	142
	45	88	113	138
10cm-Schober's test (cm)	25	3.4	5.2	7.4
	35	3.3	5.1	7.2
	45	3.2	5.0	7.1
15cm-Schober's test (cm)	25	4.5	6.7	8.9
	35	4.2	6.5	8.7
	45	4.0	6.3	8.5
Chest expansion (cm)	25	3.2	7.4	11.7
	35	2.9	7.1	11.4
	45	2.6	6.8	11.1
BASMI (0-10)	25	0.66	1.30	2.27
	35	0.65	1.42	2.60
	45	0.73	1.64	3.03

estimated 95% RI (2.5th and 97.5th percentiles), as well as the 50th percentile, are presented. RIs can be computed for any age, but examples were chosen for the ages of 25, 35 and 45, ages in which these assessments have particular clinical relevance for comparison purposes with mobility measurements of patients with axial SpA.

Results: 393 volunteers were included (only the category of 60-69 year-old women with height >1.80m was incomplete, due to difficulties in recruitment). RIs were derived and are presented in the Table. Percentiles graphs were also plotted for each of the measurements, with the best-fitting equation. An example is given in the Figure for LSF. The lower border of the RI for both Schober's 10cm and 15cm test lies below the "cut-off" of 5cm frequently used in clinical practice (see Table). No individual had a BASMI<0.15, being the median value of 1.3 for a patient of 25 years old and increasing with age.

Conclusion: Age-specific RIs and percentiles were derived for each of the spinal mobility measures for normal individuals. These RIs may guide clinicians when assessing the mobility of patients with axial SpA, and may serve as cut-off levels for 'normal' vs. 'abnormal'.

C07 – HIP FRACTURES IN PORTUGAL: 2006-2010 AN EPIDEMIOLOGIC ANALYSIS

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Background: Hip fractures are considered to be the most devastating consequence of osteoporosis. They require long hospitalizations and high health-care costs and represent an important cause of morbidity, disability, and mortality, especially in the elderly[1]. As patients are invariably hospitalized in most countries the epidemiology of hip fracture is well documented compared with other fracture outcomes and provides a surrogate for the total burden of osteoporosis[2]. Objectives: To carry out an epidemiologic analyses of hip fractures incidence rates in Portugal.

Methods: All cases of hip fracture occurred at 40 years of age or above from 2006 to 2010 were extracted from the Portuguese National Hospital Discharge Register. Age and gender-stratified population data was collected from the Institute for National Statistics. Average annual incidences were computed for age and gender groups along with the associated mortality, length of hospital stay and destination of the patient after discharge. Statistical differences between genders were assessed trough IBM SPSS® 20 with 0.05 as level of significance.

Results: A total of 51701 hip fractures occurred in the period under analysis. Hip fracture incidence rates were higher in women than in men and increased with age. The lowest incidence was observed in the 40-44 age group (14.1 and 4.0 per 100,000 inhabitants for men and women, respectively). The highest rate was observed among the 95-100 age-group (2,577.6 and3,551.8/100,000 inhabitants, for men and women, respectively). The mean length of hospital stay was13.4 days for men and 14.2 days for women [$t(19271.4)=6.731$; $p<0.05$], respectively. We also found statistically significant differences between genders on patient's destination after discharge (Chi Square(5)=253.099; $p<0.05$), the most frequent being: home 88.5% (men=85.3%; women=89.6%), mortality 5.1% (men=7.9%; women=4.3%), transferred for another hospital 3.9% (men=4.9%; women=3.7%), with homecare help 1.9% (men=1.2%; women=1.9%), discharge without medical consent 0.6%(men=0.7%; women=0.5%).

Conclusions: Compared to men Portuguese women have a higher incidence of hip fractures; are more likely to go home after discharge of the hospital instead of transferred for another hospital and have a lower mortality. Further studies are necessary for access the mortality rates after discharge.

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C08 – ULTRASONOGRAFIC CAROTID PLAQUE MORPHOLOGY IN WOMEN WITH RHEUMATOID ARTHRITIS WITHOUT PREVIOUS CARDIOVASCULAR EVENTS

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Introduction: Patients with inflammatory rheumatic diseases die prematurely, largely due to cardiovascular (CV) diseases. In Rheumatoid Arthritis (RA) patients subclinical atherosclerosis and cardiovascular events (CV) occur 2 to 3 times more frequently and earlier than in the general population. Atherosclerotic plaque vulnerability may be important for the occurrence of clinical events. High-resolution B-mode ultrasonography (US) of the carotid artery provides a noninvasive and reproducible method of identifying and characterizing atherosclerotic plaques. Previous data suggest that heterogeneous and echolucent plaques on US are more unstable and frequently contain a higher amount of lipids which make them hypoechoic. The aim of our work was to estimate the prevalence and ultrasonographic morphology of the carotid plaques in a cohort of RA patients without prevalent CV events.

Methods: 69 RA women who fulfilled the 1987 American College of Rheumatology (ACR) criteria and 44 controls, age matched, free of clinically evident CV disease underwent clinical evaluation (demographics, CV risk factors, RA characteristics and medication) and ultrasonographic assessment. RA patients with and without plaques were compared and plaque morphology and location was analyzed.

Results: The mean age of the RA women was 47.7 ± 13.5 years old, mean disease duration 7.7 ± 6.2 years, 26.1% had hypertension, 23.2% dyslipidemia, 1.4% diabetes, 20.3% were smokers and 37.7% were obese. The mean DAS28 and the mean HAQ score were 4.17 ± 1.41 and 1.01 ± 0.66, respectively. RA patients with plaques were older than RA patients without plaques (60.0 vs 46.5; p=0.013) and had a higher intima-media thickness (IMT) (0.084 vs. 0.035; p=0.001). Eleven RA women (15.9%) presented at least one carotid plaque, while in controls plaques were found in 5 cases (11.36%). In both groups the plaques were mainly found in common carotid bifurcation. Most RA patients had type 4 plaques (homogeneous, hyperechoic); in controls type 2 (heterogeneous hypoechoic, 50%) and 4 (50%) plaques were equally frequent.

Conclusion: In this group of young RA women with moderately active disease, subclinical atherosclerosis was mainly determined by traditional CV risk factors, in particular by age. No distinct disease characteristics could be identified among those with plaques.

Despite the limitations of our sample size, we found some differences regarding the US type of plaques in RA and controls. Surprisingly, atherosclerotic plaques of RA patients displayed ultrasonographic characteristics of less instability, with higher amount of calcium and lower amount of lipids than controls. This is an interesting finding that is in agreement with the higher content of coronary calcium previously documented by other authors in RA and stresses the need for a tight control of traditional CV risk factors in patients with arthritis.

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