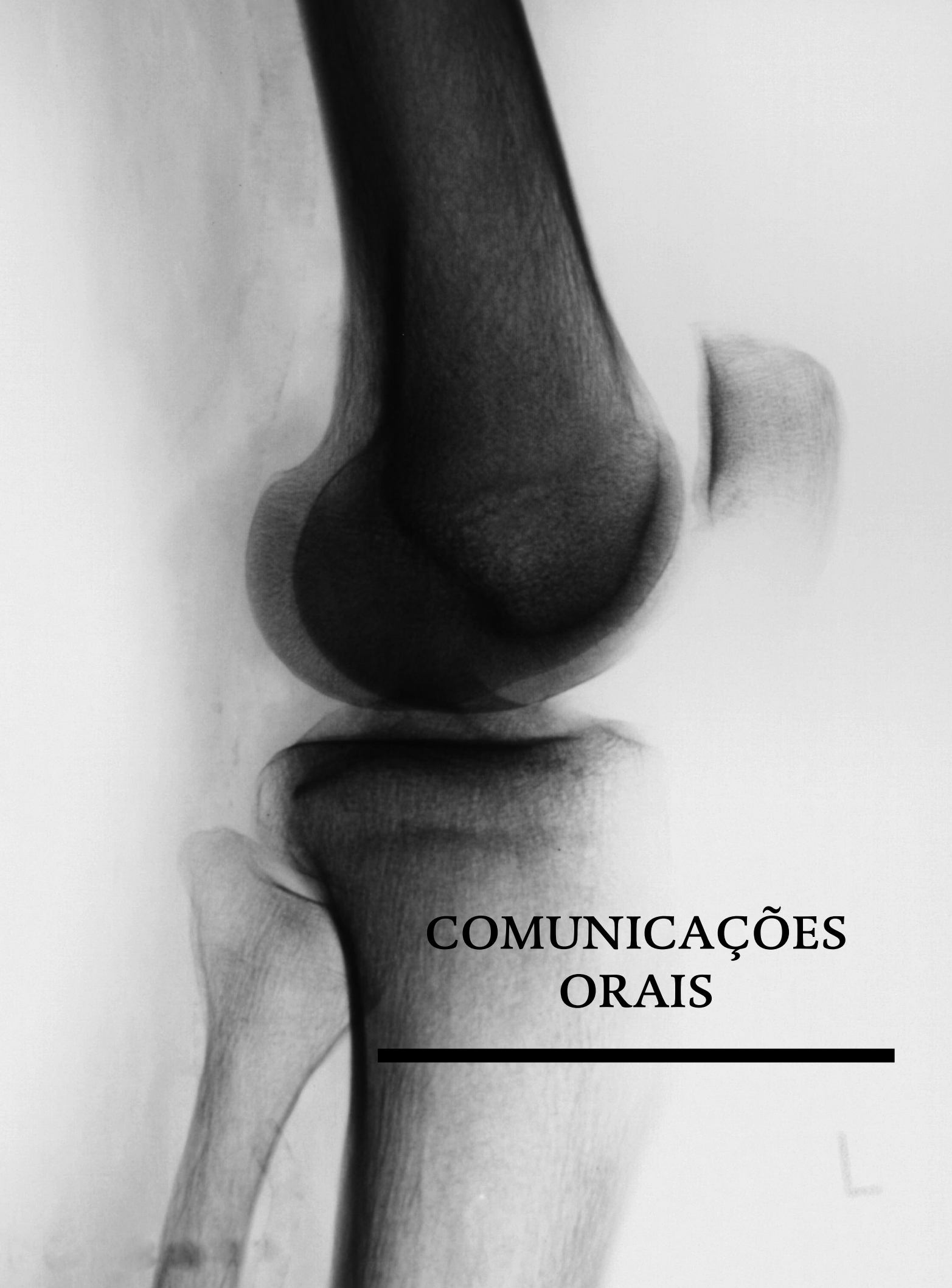

COMUNICAÇÕES ORAIS

Comunicações orais

ACTA REUMATOL PORT. 2015:40:21-29 (SUP)

CO1 – ASSOCIATION BETWEEN SOCIODEMOGRAPHIC AND CLINICAL FEATURES WITH RADIOGRAPHIC SEVERITY IN KNEE OSTEOARTHRITIS – RESULTS FROM EPIREUMAPT

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Objective: To assess patient characteristics associated with radiographic severity in knee osteoarthritis (KOA) in a population-based study.

Methods: EpiReumaPt is a national epidemiologic, cross-sectional study of rheumatic diseases (RD) in the Portuguese population conducted from September 2011 to December 2013. From the 3877 patients assessed by a rheumatologist on the second phase of the study, we included all cases of KOA defined according to the American College of Rheumatology clinical and /or radiographic classification criteria. Knee x-rays were acquired using a standardized protocol and centrally scored according to the Kellgren-Lawrence (KL) scale. The knee osteoarthritis outcome score (KOOS) was used to assess KOA clinical features. Weighted stepwise multivariate logistic regression was used to assess which features associated with radiographic severity, after stratifying the disease in mild (grade 0 to 2) and severe (grade 3 and 4) KOA according to the KL scale.

Results: A total of 981 (weighted prevalence: 12.4%) patients were classified as KOA patients. Knee radiographs were available for 553 patients. From those, 318 (63.7%) had mild disease and 235 (36.3%) had severe disease. On the multivariate analysis, several patient's features were significantly and independently associated to radiographic severity: age (OR: 1.08; p<0.001), obesity (OR: 2.7; p=0.014); dyslipidemia (OR: 2.73; p=0.002), the total number of non-rheumatic comorbidities (OR: 0.63; p<0.001); Country region (OR: 0.61; p<0.001); orthopaedic intervention of the knee (OR: 4.71; p=0.004); KOOS symptoms subscale (OR: 0.96; p=0.001; higher KOOS, less symptoms). Alentejo region had the higher proportion of severe disease [56.0% (36.2-75.7)], whereas Lisbon area had the lowest [36.4% (26.9-45.8)].

Conclusions: We found several clinical and sociodemographic features associated with radiographic severity in KOA patients. Our findings contribute to the understanding of disease progression mediators. A longitudinal evaluation is needed to validate these results.

CO2 – RANDOM SPOT URINE PROTEIN/CREATININE RATIO IS A SUBOPTIMAL PREDICTOR OF 24H PROTEINURIA IN LUPUS NEPHRITIS

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Background: The gold standard to assess proteinuria is the protein content of 24h urine collection. Random spot urine protein/creatinine (P/C) ratio seems to have a good correlation with 24h protein and has been used to simplify urine collection. However, it has been reported that it is unreliable for monitoring proteinuria in lupus nephritis (LN) patients.
Objectives: To evaluate the agreement between random spot urine P/C ratio (mg/g) and protein measured by 24h urine collection (g/24h) in LN patients.
Methods: Cross-sectional study was performed. Patients with biopsy proven LN underwent 24h urine collection (for P and C) and random urine (for P/C ratio), sequentially. Correlation (Spearman rank correlation analysis) and limits of agreement between the two methods (Bland-Altman plot analysis) were evaluated. The discriminant cut-off values for spot urine P/C ratio in predicting 24h protein threshold excretion >300, 500, 1000 and 1500 mg were determined using receiver operating characteristics curve (ROC).
Results: Sixty-one paired (total 122) spot and 24h urine collection were evaluated. The mean glomerular filtration rate (assessed by CKD-E equation) was 97mL/min/1.73m2 (SD 10.9). Strong correlation (r=0.921, p<0.001) was found between the two measures. Stratifying by protein degrees, less strong correlation was found between the two methods (r=0.722, p<0.001 when 24h protein <500mg and r=0.699, p<0,001 when 24h protein was between 500 and 1000 mg). Bland-Altman analysis showed wide limits of agreement (-496.1 to 891.3 mg) and the limits became wider as the protein excretion increased. In low level of protein excretion (<500mg) the two tests had acceptable limits of agreement (-122.3 to 194.7 mg) but in subnephrotic range (500- 3400mg), Bland-Altman plot showed clinically inacceptable wide limits of concordance (-438.1 to 1198.8 mg). Using ROC curves, the spot urine P/C ratio discriminant values of 270.3 mg/g (sensitivity (S) 89.2%, specificity (E) 91.7%, area under the curve (AUC) 0.976), 336.5 mg/g (S 93.8%, E 96.6%, AUC 0.990), 655 mg/g (S 87%, E 92.1%, AUC 0.953) and 931 mg/g (S 100%, E 91.7%, AUC 0.958) predicted 24h protein equivalent "thresholds" of >300, 500, 1000 and 1500mg, respectively.
Conclusions: Spot urine P/C ratio and 24h protein have good agreement in low protein levels (<500 mg). In subnephrotic protein range (500-3400), even though we found a good correlation between the two methods, the P/C ratio seems to be a weak predictor of 24h protein showing unacceptable limits of agreement.

C03 – VITAMIN D DEFICIENCY AND DISEASE ACTIVITY/SEVERITY IN SPONDYLOARTHRITIS: RESULTS OF THE ASAS-COMOSPA INTERNATIONAL STUDY

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Introduction: Vitamin D deficiency has been associated with several chronic inflammatory diseases. However, only few studies have evaluated the vitamin D levels in spondyloarthritis (SpA) patients, with some controversial results.
Objectives: a) To describe vitamin D status in a worldwide SpA population and b) to evaluate the association between vitamin D deficiency and demographic/geographic/season/SpA phenotype/disease activity and severity, and comorbidities.
Methods: ASAS-COMOSPA is an international cross-sectional study, conducted in more than 15 countries representing the 4 continents. From a total of 3984 SpA patients included in the study, 1558 (39.1%) patients had available data on vitamin D level. Patients currently on vitamin D supplementation (528 patients) were excluded. The remaining 1030 SpA patients were included for this analysis.

Demographics, patients' phenotype, disease activity/severity measures (ASDAS-CRP, BASDAI, 44 swollen/tender joint index, physicians' global assessment, hip articular replacement, bamboo spine) and SpA patient's comorbidities (cardiovascular disease, osteoporosis, cancer, infections) were assessed. Vitamin D deficiency was defined as < 20 ng/ml (50 nmol/L).

Statistical analysis: The mean +/-SD of the available Vitamin D levels in the COMOSPA population and per country was calculated. Univariate and Multivariate analysis using logistic regression was performed to explain the variation in vitamin D deficiency in the COMOSPA cohort.

Results: Mean vitamin D was 22.2 (±13.4) ng/ml, and vitamin D deficiency was observed in 527(51.2%) patients.

In the univariate analysis, patients with vitamin D deficiency had higher body mass index (26.3±5.3 vs. 25.7±5.3, p=0.0251); were more frequently living in Europe (55.5% vs. 44.5%; p=0.0037), and in latitudes above 37º (53.0%vs 47.0%, p <0.008), were dosed for Vitamin D levels in winter-spring (56.8%vs 43.2%; p <0.0001), presented more frequently with radiographic sacroiliitis (80.5% vs 66.2%; p=<0.0001), and positive HLA B-27 (81.8% vs. 76.2%; p=0.0422). Patients with vitamin D deficiency had also higher mean ASDAS-CRP (3.0±1.3 vs. 2.7±1.2; p=0.0015), BASDAI (3.9±2.3 vs. 3.5±2.3; p=0.0142), and there were more patients with hip articular replacement (22 vs. 6; p=0.0033). After adjusting for age, gender and variables with p<0.1 in the univariate analysis, vitamin D deficiency remained significantly associated with season winter/spring (odds ratio (OR) 1.88 [95%CI= 1.24; 2.85], p=0.0029) and radiographic sacroiliitis (OR 2.07[95%CI= 1.29; 3.31], p=0.0026).

No independent association between vitamin D deficiency and comorbidities in this worldwide SpA population was found.

Conclusion: As expected, vitamin D deficiency primarily occurs during less sunny seasons of the year. Moreover, this study suggests that: 1) vitamin D deficiency in SpA is frequent worldwide and 2) such vitamin D deficiency might be associated with both disease activity and (potentially more importantly) disease severity.

ACKNOWLEDGEMENTS
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C04 – LONG-TERM RETENTION AND PREDICTORS OF ANTI-TNF TREATMENT RESPONSE IN JUVENILE IDIOPATHIC ARTHRITIS: DATA FROM REUMA.PT, A NATION-WIDE REGISTER

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Objectives: To assess the effectiveness and safety of biological therapy as well as predictors of response at 1 year of therapy, the retention rate in biological treatment and predictors of drug discontinuation in JIA patients registered in the Portuguese register of rheumatic diseases, Reuma.pt.
Methods: We collected prospectively patient and disease characteristics from patients with JIA who started biological disease modifying antirheumatic drugs. Adverse events were collected during the overall follow-up period. The predictors of response at 1 year were assessed and drug retention rates were calculated at 4 years of treatment for the first biologic agent using the Kaplan-Meier method.
Results: Of the 812 JIA patients registered in Reuma.pt, 227 received biological therapy. The mean age at disease onset was 7.5 ± 4.9 years and the mean age at the beginning of biological therapy was 16.2 ± 9.4 years. The most common JIA category on biologics was polyarticular rheumatoid factor (RF) negative (23.3%). Most patients (90.3%) were treated with an anti-TNF as first biologic (etanercept, 69.2%). Disease activity decreased significantly at 6 months and 1 year of treatment. Fourteen patients discontinued biological therapies during the follow-up period due to adverse events. Baseline JADAS10 was the strongest predictor of treatment response at 1 year of biological therapy, with a 0.73 decrease for each unit increase at baseline (95% CI 0.45-1.10, p<0.001). Retention rates for the first biological agent were: 92.9% at 1 year, 85.5% at 2 years, 78.4% at 3 years and 68.1% at 4 years of treatment. Among all JIA subtypes, only concomitant therapy with corticosteroids was found to be univariately associated with withdrawal of biological treatment (p=0.016).
Conclusion: Data from Reuma.pt confirm that biological therapies are effective and safe in patients with JIA. Additionally, baseline disease activity was the strongest predictor of treatment response and the retention rates for the first biological agent are high throughout 4 years.

C05 – GREATER ORGAN INVOLVEMENT AND DISEASE ACTIVITY IN CHILDHOOD-ONSET THAN ADULT-ONSET WITH SLE (DATA FROM REUMA.PT/LES)

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Background: Systemic lupus erythematosus (SLE) is a multi-organ immune-mediated disease that affects predominantly women at reproductive age but may present itself at any age. Age at disease onset has a strong modulating effect on clinical presentation and

course of disease. Although young patients may have a more aggressive disease, controversies persist regarding the impact of age at disease onset on SLE outcome.

Objectives: Characterize childhood-onset, adult-onset and late-onset SLE and assess whether disease outcome differs in these three patient groups.

Methods: Patients with childhood-onset (diagnosis ≤ 18 years) SLE fulfilling ACR 1997 criteria were identified in the Portuguese registry Reuma.pt/SLE and compared with adult-onset (≥19y and ≤49 years) and late-onset (≥50 years) SLE patients paired for disease duration.

Results: Two hundred and sixty seven SLE patients with mean disease duration of 11.9 ± 9.3 years were analyzed (Table 1). The number of fulfilled ACR criteria was significantly higher in childhood-onset SLE. A greater proportion of women, higher prevalence of arthritis and anti-SSA antibodies were noted in the adult-onset group. Hypertension, diabetes and thyroid disease were significantly more prevalent in late-onset SLE.

Disease activity at last visit evaluated using the SLEDAI-2K was significantly higher in childhood-onset group than in the late-onset counterparts.

SLICC/ACR damage index was numerically higher in late-onset SLE and significantly more patients in this group had irreversible damage.

Cyclophosphamide and mycophenolate mophetil were used more frequently in childhood-onset SLE patients.

Conclusions: The skin, kidney and neurological involvement are most common in childhood-onset, as well as the use of immunosuppressants, supporting the concept of a more severe disease. In contrast, patients with late-onset SLE have more comorbidities and irreversible damage. The age of SLE onset has a significant impact not only on the clinical characteristics and disease activity, but is also important for disease outcome.

C06 – NEGATIVE GAENSLEN'S ("SQUEEZE") TEST PREDICTS THE ABSENCE OF SIGNIFICANT METATARSOPHALANGEAL INVOLVEMENT IN EARLY ARTHRITIS

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Background: Gaenslen's test (GT) positivity is characterized by tenderness upon lateral compression (squeezing) of the metacarpophalangeal (MCP) or metatarsophalangeal (MTP) joints. Joint ultrasonography (US) is a useful clinical tool that has increasingly been applied in routine practice in Rheumatology, given its sensitivity over clinical examination for detection of inflammation.

Objective: The aim of this work was to evaluate the agreement between Gaenslen's test (GT) and MTP US findings.

Methods: Consecutive patients referred to the Early Arthritis (EA) Clinic in the Rheumatology Unit, in whom arthritis was identified and a feet ultrasound performed, were included. The following parameters were assessed at the first EA consultation: (1) spontaneous pain reported by the patient; (2) squeeze test of the MTFs joints; (3) ultrasound synovitis defined as ≥ grade 2 synovial hypertrophy and/or ≥ grade 1 power-Doppler, identified by an experienced sonographer. Chi-square test and Cohen's kappa were used to analyse concordance between both methods.

Results: 55 patients (110 feet) were included, with half of the patients referring forefoot symptoms spontaneously. None of them presented Morton disease in US, and significant hallux valgus was identified in three feet (2.7%). The GT was positive in 45.6% cases at the right side and 41.2% at the left. Among patients with negative GT, 90.0% were free of US changes at the right side and 87.5% at the left. The agreement proportion was lower when GT was positive, with 56.0% having normal US at the right side and 52.2% at the left. This difference of proportions was statistically significant (Chi2=8.307; p=0.005; Kappa=0.353 (right side) and Chi2 =8.419; p=0.006; Kappa=0.371 (left side)).

Conclusion: In this study a negative GT of MTP corresponded to a normal ultrasonography in 90% of the cases. Thus, GT has a high negative predictive value, and can be used to exclude MTP involvement in patients with EA, without the need for US examination.

Positive GT is not regularly related with US abnormalities and may, therefore, justify US examination. Further studies with larger samples to test are warranted.

CO7 – RUMO À MEDICINA PERSONALIZADA NA ARTRITE REUMATÓIDE: POLIMORFISMOS NO GENE ATIC COMO PREDITORES FARMACOGENÉTICOS DA RESPOSTA CLÍNICA AO METOTREXATO

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Objetivos: A identificação de preditores genéticos do perfil de resposta clínica ao metotrexato (MTX) em doentes com artrite reumatoide (AR) poderá ser determinante na personalização da medicina. Assim, este trabalho tem por objetivo avaliar a influência de polimorfismos genéticos em genes intervenientes na síntese de novo de purinas no perfil de resposta clínica ao MTX em doentes Portugueses com AR.
Metodologia: 233 doentes com AR tratados com MTX foram genotipados para 8 Single Nucleotide Polymorphisms (SNPs): 1) aminoimidazole-4-carboxiamida ribonucleotídio transformilase (ATIC) rs2372536 C>G, rs3821353 G>T, rs4673993 T>C, rs7563206 T>C, rs12995526 T>C and rs16853834 C>T; 2) glicinamida ribonucleotídeo formiltransferase (GART) rs8971 A>G; e, 3) fosforribosil pirofosfato amidotransferase (PPAT) rs3796548 C>T. Análises univariadas e regressões logísticas binárias (RLB) foram realizadas, seguindo abordagens genotípica e haplotípica. Indexes de risco genético para não-resposta (IRG) e toxicidade (IRT) foram criados.
Resultados: Da RLB verificou-se um risco acrescido para não resposta associado a 4 SNPs no ATIC: alelo G para rs2372536; e alelos T para rs4673993, rs7563206 e rs12995526. O IRG demonstrou que a presença das 4 variantes de risco conferia um risco acrescido em cerca de 2 vezes para um perfil de não resposta.

O haplótipo CGTTT (rs2372536, rs3821353, rs4673993, rs7563206 e rs12995526) demonstrou-se associado a um risco acrescido para não-resposta. Quanto à toxicidade relacionada com o MTX, e após a RLB, um risco acrescido demonstrou-se associado aos homozigóticos CC para rs7563206 e rs12995526, portadores do alelo G para rs2372536 e portadores do alelo T para rs3821353. O IRT revelou que a presença das 4 variantes de risco conferia um risco acrescido em cerca de 16 vezes para um perfil de toxicidade. O haplótipo CTTCC (rs2372536, rs3821353, rs4673993, rs7563206 e rs12995526) demonstrou-se associado a um risco acrescido para toxicidade. Não foram encontradas diferenças estatisticamente significativas para os polimorfismos estudados nos genes GART e PPAT.
Discussão/Conclusões: Polimorfismos no gene ATIC poderão ser úteis na predição dos doentes com AR que não beneficiarão do tratamento com MTX. No entanto, mais estudos são necessários para suportar os resultados obtidos. A possível previsão da resposta clínica no momento do diagnóstico oferecerá uma ferramenta poderosa para o papel da translação dos polimorfismos genéticos na prática clínica e será essencial para sustentar um avanço no campo da medicina personalizada.

CO8 – REPORT OF A 6 MONTHS EXPERIENCE WITH THE USE OF ULTRASOUND IN THE DIAGNOSIS AND MANAGEMENT OF PATIENTS WITH GIANT CELL ARTERITIS

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Backgroung/Aims: Giant cell arteritis (GCA), the most common primary vasculitis, can cause irreversible blindness in 20-30% of untreated cases, but glucocorticoid therapy leads to significant toxicity in >80% of patients. Ultrasound has proven to be effective in diagnosing GCA and has shown advantages in monitoring disease activity.

All patients with suspected GCA or GCA flare referred to the Nuffield Orthopaedic Centre, Oxford, are rapidly evaluated by a combination of ultrasound (to the temporal, axillary and carotid arteries) and stan-

dard clinical assessment to reduce the risk of misdiagnosis or instituting unnecessary treatment.

We aim to report our experience between August 2014 and January 2015 with this "fast-track" approach in GCA.

Methods: We performed a retrospective analysis and comparison of the ultrasound findings with the clinical features, temporal artery biopsy (TAB) results and decision to treat patients with suspected or established GCA. Ultrasound was considered positive when a dark halo around the temporal artery wall or a homogeneous hypoechoic wall thickness>1.5mm in the carotid or axillary arteries was found.

Results: There were 110 ultrasound exams performed in 99 patients (67% females) with a mean age of 71±10years. In 75 cases patients were referred for suspected GCA: 66% were already on high-doses of steroids (mean of 12±10days), 75% had headache; 64% high inflammatory-markers; 48% abnormal vascular examination; 31% previous diagnosis of polymyalgia rheumatica; 28% jaw-claudication and 24% visual symptoms. In 27 cases the ultrasound was positive: 7 performed TAB (3 positive) and all were treated as GCA. In 42 cases the ultrasound was negative: 18 performed TAB (1 positive) and 5 were treated as GCA. In 6 cases the ultrasound was inconclusive requiring further investigations (e.g. TAB or PET).

In 35 cases patients with an established diagnosis of GCA were scanned to assess flare or monitor disease-activity: 18 had a positive ultrasound (16 increased medication; 2 were follow-ups with improvement from baseline). The 17 negative ultrasounds allowed a safer tapering or withdrawal of glucocorticoids.

Conclusions: The combination of a rapid clinical evaluation and ultrasound proved to be a key element in the diagnosis and monitoring of GCA. It allowed a safer management of treatment and reduced the number of TABs needed. The only negative ultrasound with a positive TAB was seen in a patient who was already on 20 days of glucocorticoids, suggesting that in selected cases ultrasound may safely replace TAB if performed early in disease treatment.

C09 – INCIDENCE AND PREDICTORS OF CARDIOVASCULAR EVENTS OVER A PERIOD OF 5 YEARS IN A COHORT OF WOMEN WITH RHEUMATOID ARTHRITIS

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Background: An excess in cardiovascular (CV) morbidity and mortality has been recognized in Rheumatoid Arthritis (RA) patients when compared to the general population.

Objectives: Given the paucity of prospective data, our aim was to estimate the incidence of CV events and the contribution of traditional CVD risk factors and RA-related parameters to future events.

Methods: Incident fatal and non-fatal CV events (hospitalizations due to unstable angina, myocardial infarction, coronary artery revascularization procedures, stroke, or CV death) were assessed in a prospective cohort of RA women followed since 2007 and without CV events at cohort entry. The presence of traditional CV risk factors, disease characteristics, medication, carotid ultrasound, and biomarkers of inflammation and endothelial activation were evaluated at baseline. Univariate Cox proportional hazard models were used to identify risk factors for CV events.

Results: Among 106 women followed over 565 patient-years we identified 4 CV events (1 fatal stroke, 2 myocardial infarction and 1 unstable angina), which contributed to an incidence rate of 7 per 1000 person-years (95%CI 2.0-13.9). Patients who developed CV events were older, but the distribution of other traditional CV risk factors was otherwise similar in both groups. Also, corticosteroid dosage and proportion of patients with carotid atherosclerotic plaques was higher in those with CV events (Table 1). Erythrocyte sedimentation rate (ESR) (HR 1.036; 95%CI 1.005-1.067) and soluble intercellular adhesion molecule-1 (sICAM-1) serum levels (HR 1.002; 95%CI 1.000-1.003) significantly contributed to CV events. These results remained significant after adjusting for patients' age.

Conclusions: We found an incidence of cardiovascular events in women with RA of 7 per 1000 patent-years. This value is similar to that found in other Portuguese cohort of RA patients[1] and much higher than the incidence reported for the general Portuguese population[2,3]. Markers of inflammation and endothelial activation contributed significantly to CV events, but the limited number of events prevents further analysis.

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