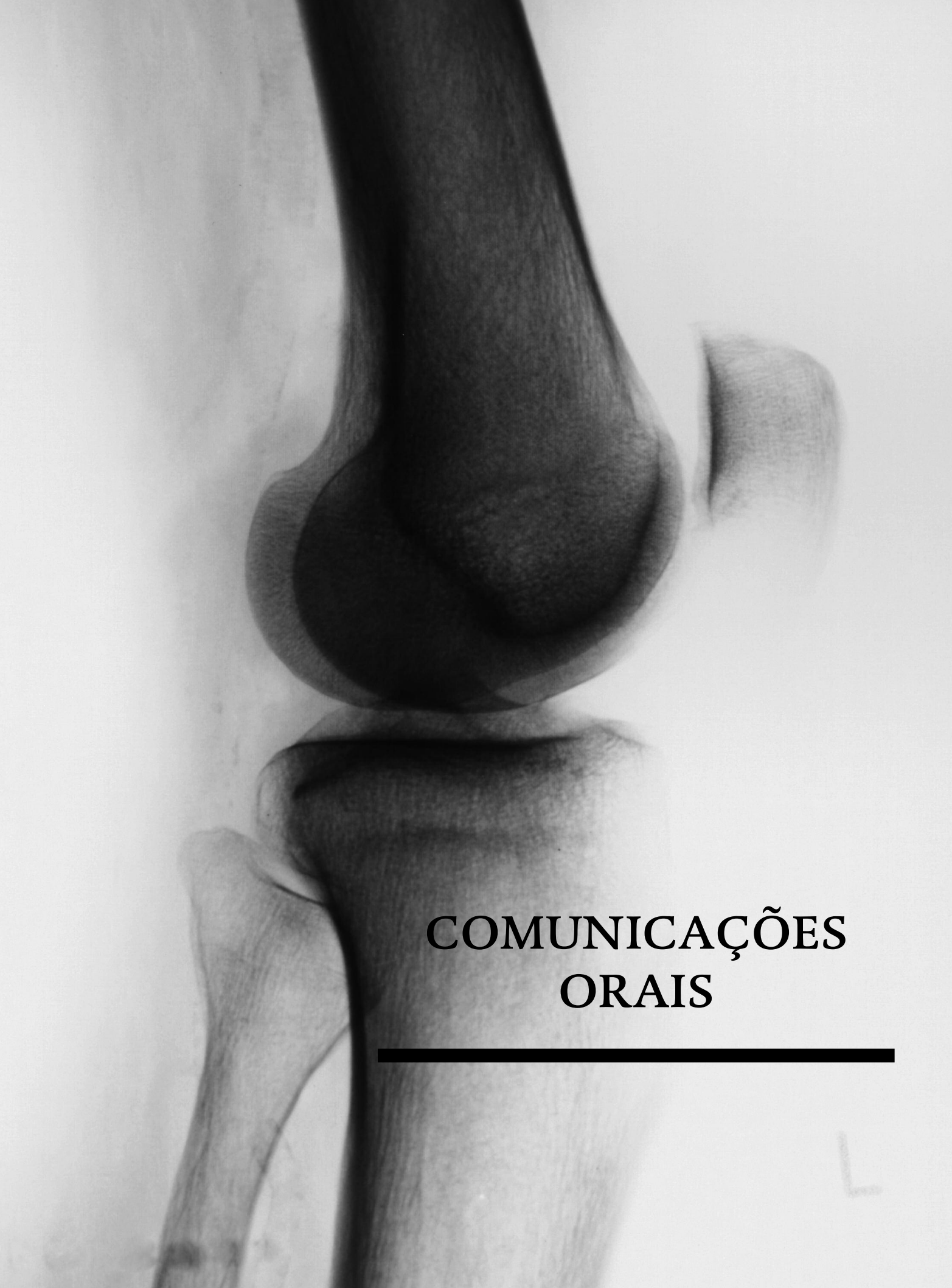

COMUNICAÇÕES ORAIS

Comunicações orais

ACTA REUMATOL PORT. 2012:37:55-69 (SUP)

MESA REDONDA 1: MESA EULAR

DIA 2 DE MAIO DE 2012

CO1 – EPIREUMAPT AFTER 3 MONTHS ON THE FIELD

Gouveia N, Canhão H, Ramiro S, Machado P, Mourão AF, Silva I, Laires P, Branco JC
EpiReumaPt – Estudo Epidemiológico das Doenças Reumáticas em Portugal

Introduction: In Portugal, data on prevalence and impact of Rheumatic Diseases (RDs) is scarce. EpiReumaPt is a national epidemiologic, cross-sectional study of RDs in the Portuguese population. The primary objective of the study is to estimate the prevalence of the different RDs in Portugal.
Objective: To describe the population participating in EpiReumaPt after the first 3 months on the field, including the proportion of subjects with RDs diagnosis.
Methods: EpiReumaPt involves a two-stage approach. The first phase is a survey randomly performed by trained interviewers at subjects' homes (selection by random route). Phase 2 consists of a clinical observation performed by a Rheumatologist, in order to confirm (or not) the RD diagnosis using a blinded methodology and to apply specific and validated questionnaires in case of a diagnosis of a RD.

Phase 2 began on 30 September 2011, in Lisbon and surroundings (Greater Lisbon area). For this analysis, data collected until 17 December was used (12 weeks, 24 assessment days, 22 collaborating Rheumatologists).

We performed a descriptive analysis of the initially surveyed population and an analysis of the subgroup with a rheumatological assessment.
Results: During the first phase of the study, the interviewers tried to contact 5014 subjects in 50 different locations of the Greater Lisbon area, having been successful in 1682 contact attempts (33.5%). Among those successfully contacted, 834 (49.6%) subjects accepted to be interviewed. Mean age of interviewed participants was 50 years-old (SD 18.5) and 534 (64.0%) were women.

The majority of participants were Caucasian (n=762, 91.4%). Regarding educational level, 275 (33.0%) had university education or equivalent (≥12 years of study), 181 (21.7%) had 10-12 years of education or technical courses, 179 (21.5 %) had four years of study and 43 (5.2%) primary school incomplete (1-2 years of school). The average number of years of education was 9.6 years (SD 6.7). All ranges of monthly income were represented (from <500€ to > 4000€), with 61.9% having an income ≤2000€ per month.

The average self-reported functional status/disability score (measured by HAQ) was 0.26 (SD 0.6).

The screening survey selected 554 cases (66.4%) of suspected RD or rheumatic complains associated with a RD. All positive screenings and 65 (23.2%) randomly recruited negative screenings were invited for phase 2 of the study. Of the total number of invited participants (n=619, table 2), 364 (58.8%) dropped-out (people who accepted but missed the phase 2 appointment + people who rejected the invitation) and 255 were observed by a Rheumatologist.

Among those observed by the Rheumatologist, 7.1% (18/255) were considered healthy regarding their musculoskeletal system. A RD diagnosis was established in 92.9% (237/255) of the subjects: 95 (11.4%) low back pain; 59 (7.1%) periarticular disease; 56 (6.7%) knee OA; 40 (4.8%) hand OA; 38 (4.6%) osteoporosis; 11 (1.3%) hip OA; 7 (0.8%) fibromyalgia; 5 (0.6%) gout; 4 (0.5%) rheumatoid arthritis; 2 (0.24%) spondyloarthritis; 2 (0.2%) lupus; 1 (0,1%) polymyalgia rheumatic; 1 (0.1%) childhood rheumatic disease.

232 (91.0%) subjects consented to donate blood to

		Women	Men	Average age (SD)
Invited participants for phase 2 (n=619)	Drop-outs (n=364, 58.8%)	262 (72.0%)	102 (28.0%)	50.9 (19.5)
	Observed by the Rheumatologist (n=255, 41.2%)	183 (71.8%)	72 (28.2%)	53.7 (16.2)

biobank donation and 246 (96.5%) accepted to be included in the cohort study.

Conclusions: After 3 months of enrollment, preliminary data obtained allows a demographic description of nearly 1000 individuals and begins to sketch the prevalence of RDs in Portugal.

CO2 – BIOLOGIC DRUG EFFICACY AND TREATMENT DISCONTINUATION IN RHEUMATOID ARTHRITIS PATIENTS FROM REUMA.PT

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2. HSM
3. HGO
4. HUC
5. IPR
6. CHAM
7. HEM-CHLO
8. CRL

Introduction: Large follow-up registries are irreplaceable tools for long term monitoring of chronic diseases in clinical practice.

Reuma.pt is the national register for rheumatic diseases from Portuguese Society of Rheumatology set up in 2008 to follow up distinct cohorts of rheumatic patients treated with synthetic and/or biological therapies.

The aim of this work was to assess treatment efficacy and drug discontinuation for rheumatoid arthritis (RA) patients registered in Reuma.pt.

Methods: We included RA first biological therapy users treated with adalimumab, etanercept, golimumab, infliximab and tocilizumab, starting biological treatment after 1 January 2008.

Our primary outcome was the proportion of patients achieving EULAR good response criteria at 6 months. Secondary outcomes were the proportion of patients in remission applying validated criteria (EULAR/ACR, DAS28, CDAI and SDAI). Groups were compared using a multivariate logistic model to adjust for potential confounders.

Our secondary analyses looked at treatment discontinuation rates and the reasons for discontinuation, which were analyzed upon 2 time frames: before and after one year of treatment for the 5 drugs above mentioned.

Results: 520 RA patients were included, 123 treated with adalimumab, 204 with etanercept, 31 with golimumab, 110 with infliximab and 52 with tocilizumab. Mean age at start of biological therapy was 54.4±12.5 years and disease duration was 11.2±9.6 years. 86.9% were females and 83.0% were either rheumatoid factor or ACPA positive. Baseline mean DAS28 was 5.3±1.2 for adalimumab, 5.6±1.2 for etanercept, 5.4±1.3 for golimumab, 5.6±1.3 for infliximab and 5.7±1.2 for tocilizumab groups (p=0.12 ANOVA). At 6 months, mean DAS28 was 3.7±1.3 for adalimumab, 3.8±1.3 for etanercept, 3.5±1.3 for golimumab, 3.7±1.4 for infliximab and 1.6±0.99 for tocilizumab groups (p<0.0001 ANOVA). The probability of achieving EULAR good response at 6 months was modeled adjusting for significant and clinically relevant covariates. A significantly higher rate of good response at 6 months was observed with tocilizumab compared to other groups with the exception of golimumab. Golimumab was excluded from the remission rate analyses due to small sample size. While DAS28 remission threshold was attained by a significantly higher number of patients treated with tocilizumab, remission rates assessed by CDAI and SDAI did not show significant differences between groups.

The mean duration of treatment was 22.3±13.4 months. 144 (27.7%) patients discontinued therapy over the period of follow-up (2008-2011), 88 (61.1%) of them in the first year of therapy. The reasons for drug suspension in the first year were adverse events in 36 cases (41%), inefficacy in 45 (51.1%) and other reasons in 13 (14.7%). The reasons for discontinuation for the 56 patients who stopped therapy after the first year of treatment were in 19 (33.9%) cases an adverse event, 37 (66%) inefficacy and 8 (14.2%) other reasons.

Conclusions: In this group of patients the proportion of good EULAR DAS28 response and DAS28 remission criteria at 6 months were higher for the tocilizumab group, but the significant difference was lost when other remission criteria were used. Inefficacy was the major determinant of drug discontinuation.

CO3 – ESTUDO PROSPECTIVO DE 42 MULHERES GRÁVIDAS COM ARTRITE REUMATÓIDE E ESPONDILITE ANQUILOSANTE: APLICAÇÃO DE PROTOCOLO DE AVALIAÇÃO DA DOENÇA

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Introdução: O efeito imunomodulador da gravidez nas artropatias inflamatórias há muito que é reconhecido, indutor de remissão na artrite reumatóide e inalterável na espondilite anquilosante. Nem todos os instrumentos clínicos que temos ao nosso dispor para avaliar a actividade inflamatória durante a gravidez são aplicáveis.
Objectivo: Aplicar um protocolo de avaliação da grávida com Artrite Reumatóide e Espondilite Anquilosante e estudar prospectivamente a actividade inflamatória destas doenças durante a gravidez e pós-parto.
Material e Métodos: Avaliou-se prospectivamente 42 mulheres, de idade média de 31.5±4.7 anos, com o diagnóstico de Artrite Reumatóide (18), Artrite Idiopática Juvenil (3), Espondilite Anquilosante (17) e Artrite Psoriática (4). As avaliações efectuaram-se antes da concepção, uma vez por trimestre e um mês após o parto. O protocolo consistia na avaliação dos seguintes parâmetros clínicos: n.º articulações dolorosas, n.º articulações tumefactas, lombalgia nocturna, lombalgia diurna e nocturna, rigidez matinal, entesite, dactilite, EVA-dor, EVA-global, uveíte, psoríase (PASI), interrupção temporária da actividade profissional.
Resultados: Não existe diferença estatisticamente significativa relativamente à idade ou duração média de doença entre os grupos AIJ/AR e EA/AP. No entanto, a duração média de doença é inferior no grupo EA/AP (5.3±4.4 anos) comparativamente ao grupo AR/AIJ (8.7±6.9 anos). Duas doentes com EA tiveram o início da doença durante o 1º trimestre da gravidez. Cinco doentes interromperam a terapêutica anti-TNFa (3 AR/AIJ e 2 EA/AP) antes da concepção, uma (AP) na 6ª semana de gestação.

Antes da concepção, a doença estava activa em 7/21 doentes com AR/AIJ e em 2/21 com EA/AP, existindo uma diferença estatisticamente significativa (p=0,037).

Durante a gravidez, observou-se uma redução da actividade da doença no grupo AR/AIJ desde a primeira avaliação até ao terceiro trimestre (p=0,014) e um aumento da actividade da doença no grupo EA/AP, que se manteve até ao 3º trimestre (p=0,005) e após o parto (p=0,025). A actividade da doença neste último grupo traduziu-se por lombalgia nocturna (12/21), rigidez matinal (12/21) entesite (8/21), coxite com comprovação ecográfica (6/21), dactilite (1/21), diagnóstico de colite ulcerosa (1/21), exacerbação da psoríase com necessidade de fototerapia (1/21) e necessidade de terapêutica com prednisona (9/21). Sete mulheres com EA interromperam a actividade profissional pelo quadro clínico, enquanto apenas uma com AR durante o último trimestre (por colestase gravítica).

O comportamento das doenças difere no 2º e 3º trimestre, com maior actividade da doença no grupo EA/AP (p<0,03) mas não no pós-parto (p=0,31).

Não existem diferenças estatisticamente significativas nos parametros inflamatórios entre os dois grupos ao longo da gravidez.
Conclusão: A actividade da doença durante a gravidez aumenta na EA/AP ao contrário da AR/AIJ, em que se reduz de forma gradual ao longo da gravidez. A aplicação de protocolos de seguimento é fundamental, pois os existentes apresentam itens não aplicáveis na grávida.

C04 – ENVOLVIMENTO DE ÓRGÃO NO LÚPUS ERITEMATOSO SISTÉMICO JUVENIL DE INÍCIO ANTES E DEPOIS DOS 10 ANOS

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Introdução: Vários estudos têm demonstrado que a idade de início tem um efeito modificador da expressão da doença no Lúpus Eritematoso Sistémico (LES) e que o envolvimento de determinados órgãos/sistemas, como nefrite ou compromisso do sistema nervoso central, se associa a maior gravidade e é mais frequente em doentes com início da doença em idades inferiores.
Objectivo: Definir o padrão de expressão do LESJ com início antes e depois dos 10 anos de idade.
Métodos: Estudo multicêntrico, retrospectivo, descritivo e analítico de 1987 a 2011 (24 anos), de todas as crianças e adolescentes (<18 anos) com diagnóstico definitivo de LESJ, de três centros com consulta diferenciada de Reumatologia pediátrica da área da Grande Lisboa. Analisaram-se dados demográficos, epidemiológicos, manifestações clínicas, complicações e actividade da doença, comparando dois grupos de doentes de acordo com a idade de início da doença: 1) ≤10 anos, 2) >10 anos.
Resultados: 56 doentes, 51 (91.1%) caucasianos e 46 (82.1%) do sexo feminino. Idade no início da doença de 12.6±4.04 (1-17) anos e um período médio de seguimento de 5.5±5.4 anos. O início da doença com

idade ≤10 anos verificou-se em 15 (26.8%). Não se verificou diferente incidência em relação ao género nos dois grupos (sexo feminino: 73.3% vs 85.4%, p=0.43). O tempo médio entre o início dos sintomas e o diagnóstico foi sobreponível entre os dois grupos (20.4±25.9 vs 10.1±16.1 meses, p=0.22). As principais manifestações clínicas dos doentes nos 2 grupos foram o envolvimento articular (86.7% vs 87.8%), cutâneo (80% vs 75.6%) e hematológico (73.3% vs 75.6%), sem se verificarem diferenças significativas. Úlceras orais e olho vermelho bilateral foram mais frequentes nos doentes com início ≤10 anos (50% vs 19% e 100% vs 22.6%, respectivamente; p<0.05). Não houve diferenças relativamente à incidência de envolvimento renal (40% vs 48.8%, p=0.763), serosite (20% vs 31.7%, p=0.513) ou manifestações neuropsiquiátricas (26.8% vs 19.5%, p=0.715). O SLEDAI médio na apresentação da doença foi 10.1±8.8 no grupo de início ≤10 anos e 11.4±9.3 no grupo de início >10 anos e não se observou diferença em relação ao SLEDAI máximo nos dois grupos (14.1±11.4 vs 14.6±10.4, p=0.88). Verificaram-se complicações em 35.7% dos doentes com início antes dos 10 anos e 30% nos de início mais tardio (p=0.745), sem diferenças no tipo de complicações observadas.

Comentários: O nosso estudo não demonstrou diferenças significativas no que respeita às manifestações clínicas, actividade da doença ou incidência de complicações entre os dois grupos definidos, não corroborando alguns resultados apresentados na literatura.

CO5 – ASSOCIATIONS BETWEEN A PRIORI DEFINED DIETARY PATTERNS AND LONGITUDINAL CHANGES IN BONE MINERAL DENSITY IN ADOLESCENTS

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Background: Maximizing the skeletal peak bone mass in early life is thought to predict a relatively higher bone mass and hence greater fracture risk reduction later in life. Accordingly, there has been considerable research aiming to understand in which extent modifiable environmental factors, such as nutrition, act on bone accrual during adolescence. Even though some isolated nutrients have been identified as determinants of bone accrual, it seems more interesting to assess the impact of overall diet in bone quality, in order to design realistic public health interventions. Assessing the compliance of an individual's diet with *a priori*-defined dietary patterns, i.e. patterns defined based on presumed health effects, allows to uncover potential associations between diet in its entirety and bone quality indices.

Objective: To quantify the association between forearm bone mineral density in early and late adolescence and adherence to *a priori* defined dietary patterns.

Methods: We analysed prospective data from 1180 adolescents (50.7% males) from the EPITeen cohort (adolescents born in 1990 and present at schools in Porto during the 2003/2004 school year) assessed at 13 and at 17 years old. In both evaluations, a physical examination including height, weight and forearm bone mineral density (BMD) using dual-energy X-ray absorptiometry was carried out. Dietary intake was assessed at 13 using a validated food frequency questionnaire and adherence to *a priori* defined dietary patterns was measured using a Mediterranean Diet Quality Index, a Dietary Approaches to Stop Hypertension Index and the Oslo Health Study (OHS) Dietary Index. Using tertiles of adherence to *a priori* patterns as the main exposure, associations were estimated cross-sectionally (with BMD at the age of 13) and prospectively (with BMD at 17 and bone gain between 13 and 17 years) using linear regression coefficients. All analyses were adjusted for BMI, total energy intake and, in girls, for menarche age.

Results: Mean (SD) forearm BMD increased from 0.368 (0.055) at 13 years-old to 0.440 (0.051) g/cm^2 at 17 years-old in girls and from 0.342 (0.050) to 0.452 (0.075) g/cm^2 in boys. We observed no significant differences in mean BMD at 13 and 17 years of age by tertiles of adherence to the different *a priori* dietary patterns. No associations were identified with adherence to any of the *a priori* dietary patterns and BMD at 13 or 17 or BMD gain in girls. However, among boys, a significant linear trend towards increased BMD at 17 with increasing adherence to the Mediterranean Diet pattern was observed, being the average BMD (mg/cm^2) significantly higher in boys in the highest tertile of adherence (1.08, 95%CI: 0.53; 2.68) when compared to those in the lowest tertile.

Conclusion: Significant relationships were not apparent between the *a priori* dietary patterns used and forearm BMD in early or late adolescence. The selected dietary patterns may not capture the elements of diet that are truly important in determining adolescent bone quality or, given the relative adequacy of nutrient

intake in high-income populations, dietary patterns may not add substantially to other determinants of BMD at this age.

MESA REDONDA 2: COMO PARAR A LESÃO ENDOTELIAL NAS DOENÇAS INFLAMATÓRIAS IMUNOMEDIADAS

DIA 2 DE MAIO DE 2012

C06 – EXERCÍCIO FÍSICO: QUEM PRATICA? QUE INFLUÊNCIA NA QUALIDADE DE VIDA? RESULTADOS PRELIMINARES DO ESTUDO EPIREUMAPT

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Objectivos: O exercício físico é apontado como um factor de melhoria da condição física e psicológica. Nesta análise pretende-se: 1- avaliar se existem diferenças na prática de exercício físico entre indivíduos saudáveis e doentes 2- identificar os factores que influenciam a pratica de exercício físico. 3- medir o impacto do exercício na qualidade de vida (QoL), nos componentes físico e mental.
Métodos: Os dados do EpiReumaPt, estudo epidemiológico cujo principal objectivo é o de estimar a prevalência das doenças reumáticas na população portuguesa, na primeira fase de forma auto-declarada, serviram de base para esta análise. Foram considerados os dados obtidos até 17 de Dezembro (12 semanas, 24 dias de avaliação, 22 Reumatologistas envolvidos) do grupo de inquiridos que declarou ter Artrite Reumatóide (AR), Espondilite Anquilosante (EA) e de Fibromialgia (FM) e da população saudável. Recolheram-se dados epidemiológicos, de diagnóstico e de QoL (EQ--5D, SF-36) através da aplicação de vários questionários por entrevistadores previamente treinados. A análise estatística envolveu análise descritiva univariada, modelos de regressão logística e modelos lineares generalizados.
Resultados: Foram analisados 834 indivíduos dos quais 225 (26.98%) declararam ser saudáveis, 454 (54.4%), ter doença crónica (não reumática), 29 (3.48%) ter EA ou AR ou FM e 126 (15.1%) ter outras doenças reumáticas. A prática de exercício físico foi referida por 42.7%, 38.1%, 10.3%, e 31.9%, indivíduos em cada grupo, respectivamente. Declaram fazer mais exercício físico, os indivíduos de sexo masculino ($p<0.001$), mais jovens ($p<0.007$), solteiros ($p=0.001$), com formação universitária ($p<0.001$), trabalhadores ou estudantes ($p<0.001$), com rendimentos mais altos (>2000 euro) ($p<0.057$). A prática de exercício físico associa-se a melhores *scores* de SF36 (componente saúde física e mental) e de EuroQoL-5D. Estima-se que os indivíduos que declaram ter EA, ou AR ou FM têm uma chance 76% inferior de fazer exercício físico quando comparados com indivíduos sem doença declarada. Estima-se que a prática de exercício físico esteja associada a um aumento de 10% e de 13% no score da função física e mental (SF-36), respectivamente. A identificação de EA, ou AR ou FM associou-se a uma redução de 50% e 33% nos scores supracitados.
Conclusões: O exercício físico está associado a melhor desempenho físico e mental. Quem declara ter EA, AR ou FM tem menor probabilidade de praticar exercício físico e apresenta maior compromisso na qualidade de vida.

C07 – CARDIAC INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: Cardiac disease is one of the major causes of mortality in SSc patients.
Objectives: We aimed to assess cardiac involvement in a cohort of Portuguese SSc patients followed up at our rheumatology department.
Patients and methods: Thirty patients were included

(18 limited SSc, 9 diffuse, 1 SSc sine escleroderma, 2 SSc overlap syndromes SSc/PM), including 27 females and 3 males, with a mean age of 56 (14) years and a mean disease duration of 6 (7) years. Patients were assessed for cardiac complaints according to the World Health Organization (WHO) functional class, electrocardiogram (EKG) abnormalities, echocardiogram (EchoCG) abnormalities [including right ventricular dysfunction (RVD), dilatation of cardiac chambers, pulmonary artery systolic pressure (PASP) estimation] and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, if available. Patients with elevated PASP were submitted to right heart catheterization (RHC).
Results: Only 9.6% of patients presented with functional class 3–4 according to the WHO classification. EKG abnormalities at rest were rare. EchoCG abnormalities were present in 55% of patients. The most common finding was left atrial enlargement (37.5%). Left heart dysfunction was frequent (12.5%), valve abnormities were present in 13% of patients, mostly tricuspid regurgitation (41%). No statistically significant difference was found in cardiac involvement between disease subsets. PASP was elevated in 23% of patients. RHC was performed in six patients. Two of these patients were classified as having pulmonary arterial hypertension (Group I of the Dana-Point Meeting 2008 classification). The other patients confirmed to have pulmonary hypertension came under the pulmonary disease and/or left heart involvement categories. Elevated NT-proBNP was present in 35% of patients. Anticentromere positivity was associated with lower NT-proBNP values (P¼0.003). NT-proBNP showed no correlation to PASP (P=0.084).
Conclusions: Despite the mild clinical complaints, cardiac abnormalities in EchoCG could be found in approximately half of the patients, not necessarily related to pulmonary vascular involvement. These findings reinforce the need to increase awareness of cardiac involvement in order to implement adequate prophylactic and therapeutic measures.

MESA REDONDA 4: CALEIDOSCÓPIO DE IMAGENS

DIA 3 DE MAIO DE 2012

C08 – SMOKING AND DRINKING IN EARLY ADOLESCENCE AS PREDICTORS OF LOWER FOREARM BONE MINERAL DENSITY IN LATE ADOLESCENCE: A COHORT STUDY IN GIRLS

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Introduction: Even though childhood and adolescence are the periods of highest bone mineral accrual, critical for peak bone mass attainment, there is comparative scarcity of research on the association between smoking and alcohol drinking and bone parameters in the early decades of life. Adolescence is a critical stage not only for bone accrual but also for the establishment of potentially deleterious health-related behaviors, such as smoking and drinking. Thus, it is relevant to assess whether precocity in these behaviors from early ages may reflect short- and long-term effects on bone status and acquisition up to peak bone strength.
Objective: To quantify the short- and long-term associations between early initiation of smoking and alcohol drinking and bone mineral density in girls.
Methods: We used prospective data from 731 girls identified in public and private schools in Porto, Portugal. Evaluations were conducted when participants were 13 and 17 years old. Bone mineral density (BMD) was measured at the forearm by dual-energy X-ray absorptiometry. Anthropometric measurements included weight, height and fat-free mass. Pubertal development status was estimated using menarche age. Self-administered questionnaires were used to collect data on smoking and alcohol drinking, physical exercise and calcium and vitamin D intakes. BMD in early and late adolescence was analyzed continuously or dichotomously (Z-score above or below -1). Associations were calculated using linear or logistic regression and estimates ore obtained crude and adjusted to menarche age and physical activity.
Results: Over one quarter of adolescents had tried smoking by 13 and almost 45% started drinking between 13 and 17 years old. One fifth had smoked and drank by 13 years old. After adjustment for menarche age and regular sports practice, bone mineral density at 13 years old was significantly lower with increasing precocity of drinking (4.1% lower mean BMD in girls who reported drinking at 13 years old than among those who reported not drinking by late adolescence), as well as among those who reported having tried both smoking and drinking at that age (2.8% lower than among the remaining girls). Regarding late adolescence, an association between bone mineral density and smoking emerged, with significantly lower mean

BMD at 17 being observed in girls who had ever tried smoking by age 13 (2.5% lower than among never smokers), as well as in those who reported drinking at that age (4.6% lower BMD than in non-drinkers). Concordantly, girls who reported having tried smoking and drinking by age 13 had a 3.6% lower mean forearm BMD than those who had tried one or neither of these. When late adolescence BMD was used dichotomously (z-score below or above -1), there were clear associations between lower z-score and having ever smoked by 13 years old (adjusted OR=1.92; 95% CI: 1.21, 3.05) as well as with ever smoking and drinking in the same period (adjusted OR=2.31; 95% CI: 1.45, 3.67). Lower BMD z-score was also more frequent with increasing drinking precocity.

Conclusion: Our study adds prospective evidence of early smoking and alcohol drinking as predictors of lower bone quality in late adolescence.

C09 – IL17 IS ASSOCIATED WITH DISTURBANCES IN THE WNT PATHWAY IN RHEUMATOID ARTHRITIS PATIENTS

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Objectives: Rheumatoid arthritis (RA) and primary osteoporosis (OP) are associated with bone fragility. In this study we aim to identify differences in bone gene expression between primary OP and rheumatoid arthritis bone samples.

Methods: RA patients submitted to hip replacement surgery were recruited. They were matched to a group of primary OP patients for bone mineral density (BMD) and major clinical fracture risk factors (age, gender, BMI and BMD). Trabecular bone microarchitecture was assessed by micro-computed tomography and bone mechanical behavior by compression tests. Wnt pathway, bone turnover and proinflammatory cytokines were analyzed by studying gene expression.

Results: Sixteen patients were included, ten with RA and six with primary OP. No differences were found between the two groups regarding age, gender, BMD or FRAX. RA patients reported disease duration of 4±3 years, a DAS 28 3V of 4.05±2.21 and Tscore was of -2.7±0.8. All RA patients were under low dose of corticotherapy and synthetic DMARDs. Bone microarchitecture and mechanical bone properties did not differ between RA and primary OP groups.

IL17 was significantly upregulated in RA patients bone (p=0.031), no significantly differences were found regarding other inflammatory cytokines when comparing to primary OP group. Wnt10b (p=0.015) and the receptor LRP6 (p=0.048), as well as SFRP1 (p=0.021) were upregulated in RA bone when compared with primary OP. In addition DC-STAMP (p=0.020), β3 integrin (p=0.001) were downregulated and osterix was upregulated in RA (p=0.035). In RA patients IL17 bone expression was significantly correlated with the expression of WNT10B (r=0.810, p=0.015), DKK2 (r=0.800, p=0.010), RANKL/OPG ratio (r=0.762, p=0.028) and cathepsin K (r=0.683, p=0.042). DKK2 gene expression was also correlated with the RANKL/OPG ratio of gene expression (r=0.870, p=0.002). These associations were not observed for the primary OP group.

Conclusion: Bone fragility in RA patients is induced by an unbalanced bone microenvironment different from the pathobiologic phenomena that occurs in primary OP. In RA, IL17 bone expression is associated with a specific pattern of gene expression, specifically with disturbances in the Wnt pathway, suggesting that its inhibition could prevent RA systemic bone loss.

C010 – CHALLENGES WITH THE APPLICABILITY OF THE EULAR RECOMMENDATIONS FOR RHEUMATOLOGY NURSING MANAGEMENT IN PORTUGAL

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Portuguese Rheumatology Nurse Practitioners Working Group

Background: Several studies have highlighted the added value of nurses in the management of patients

with chronic inflammatory arthritis, which led the EULAR Nursing Task Force to formulate a set of recommendations for the role of nurses in this particular context [1]. Rheumatology as a nursing specialty does not exist in Portugal, and this may constitute an important barrier for the implementation of these recommendations.

Objectives: We aimed to evaluate the level of agreement of Portuguese nurses working in rheumatology departments with the EULAR recommendations and the degree of their applicability in routine clinical practice.

Methods: During January 2012, a questionnaire was sent to all Portuguese Rheumatology centers, inviting practicing nurses to answer anonymously to a closed--type set of questions that addressed the level of agreement with each of the recommendations (1–total disagreement to 5–total agreement), the recommendations' application in practice (not applied (0), partly (1) or full applied (2)) and the level of confidence in the applicability of each of the recommendations (0-not at all confident to 5 totally confident). Chi2 and Mann--Whitney tests were used to plot the results.

Results: A total of 68 nurses (84% female; 4.0±4.2 years of practice) from 13 rheumatology centers were included. Forty (59%) worked at the outpatient clinic only, 18 at the inpatient clinic only and 10 at both places. Only 13 (19%) worked exclusively at rheumatology departments. Although all nurses (99%) stated to be interested in getting more training in rheumatology and 47% would like to have the formal specialty in rheumatology, only 21 (31%) had received some type of training. On average, the level of agreement with all the EULAR recommendations was 4.8±0.3 (with averages for the individual recommendations ranging from 4.6±0.7 to 5±0.2). In 51.6% of the cases these recommendations were partly applied in practice. The level of confidence in their full applicability was 3.6±0.8 (with averages for the individual recommendations ranging from 3.2±1.3 to 4.1±1.0). Comparing nurses with and without specific rheumatology training a significantly higher proportion of those who received training totally agreed with Recommendation 7 (86% vs 72%, p=0.04) - providing care based on protocols and guidelines - and with Recommendation 3 (95% vs 62% p=0.04) - patients should have access to nurse-led telephone services to enhance continuity of care and to provide ongoing support. The level of confidence in the applicability of Recommendation 7 was also significantly higher in these subgroups of nurses, and among those with a longer working experience in rheumatology and working at day-care units. The level of confidence in the applicability of Recommendations 3 and 10 (nurses should carry out interventions and monitoring as part of comprehensive disease management in order to achieve cost savings) was also higher in nurses with specific training in rheumatology.

Conclusions: There is a high level of agreement with the EULAR recommendations for rheumatology nursing management in Portugal, despite the fact that most of the nurses are working in partial dedication to rheumatology and without specific training. The highest level of agreement was verified among nurses with specific training, underlining the importance of specific training for future commitment.

C011 – DAS28, CDAI AND SDAI CUTOFFS DO NOT TRANSLATE THE SAME INFORMATION

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Introduction: DAS28, CDAI and SDAI are frequently used indexes to assess disease activity in rheumatoid arthritis (RA) patients. Cutoffs were defined to differentiate the states of disease activity that a patient can experience: remission or low, moderate and high disease activity. DAS28 intervals for these disease activity states are, respectively, [0, 2.6[, [2.6, 3.2],]3.2, 5.1] and]5.1, +∞[. CDAI intervals are [0, 2.8],]2.8, 10],]10, 22] and]22, +∞[, and SDAI intervals are [0, 3.3],]3.3, 11],]11, 26] and]26, +∞[. Taking into account the CDAI and SDAI cutoffs, new cutoffs for DAS28 have been proposed: [0, 2.4],]2.4, 3.6],]3.6, 5.5] and]5.5, +∞[.

Objective: To assess disease activity states classified by DAS28, CDAI and SDAI, and to analyze their concordance in a Portuguese population.

Methods: Patients with RA under biological therapy and followed up in the Reuma.pt were included in this analysis. A total of 1635 patients and 7316 visits were analyzed, 2285 of which were previous to the onset of biological agents, 2998 visits were within 2 years of starting biological treatment and 2033 visits occurred 2 or more years after initiation of biological treatment.

Overall Pearson's correlation coefficients (PCCs) were calculated for the 3 indexes. Chi-square tests were performed to analyze visits distributions for all disease activity states and indexes. PCCs were also calculated to test the concordance of DAS28 4v with both CDAI and SDAI indexes, varying each one of them along their scales with 0.1 intervals.

Results: A strong concordance was found between the 3 indexes throughout the 7316 visits: r=0.881 for DAS28/CDAI, r=0.876 for DAS28/SDAI and r=0.973 for the CDAI/SDAI correlation (all PCCs with p<0.001). However, when the different disease activity states were analyzed, both chi-square tests and PCCs revealed that the respective cutoffs were non-concordant. The hypothesis that the distributions were the same was rejected for all the compared cutoffs. For example, the correspondence between the new proposed cutoffs for DAS28 with CDAI (p=5.08966E-55) and SDAI (p=6.3064E-34) cutoffs was strongly rejected. For these DAS28 cutoffs (2.4, 3.6 and 5.5), the best correlation with CDAI was obtained at the cutoffs of 4, 10.1 and 26, and with SDAI at the cutoffs of 4.7, 11.1 and 28.1. The hypothesis that these 3 distributions are the same was not rejected (p = 0.991). For the original DAS28 cutoffs (2.6, 3.2 and 5.1), the best correlation with SDAI was obtained at the cutoffs of 5.6, 8.8 and 23.8. The hypothesis that these 2 distributions are the same was not rejected (p = 0.999). We also found that when considering all visits with DAS28 < 2.6, average patient global (PG) assessment score was 1.92 (on a scale of 0 to 10) and the average weight of PG was 11.16% for DAS28, 52.93% for CDAI and 45.61% for SDAI. According to the 2011 ACR/EULAR boolean definition of remission in RA, PG should not be higher than 1.

Conclusions: DAS28, CDAI and SDAI cutoffs do not translate the same clinical information for patients registered in the Reuma.pt. Since disease perception is influenced by several factors (e.g., culture) and PG weight in CDAI and SDAI indexes is considerably higher than in DAS28, established CDAI and SDAI cut-offs probably should not be universally applied.

C012 – FACTORS INFLUENCING THE DIAGNOSIS OF OSTEOPOROSIS – DATA FROM EPIREUMAPT

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Background: EpireumaPt is a cross-sectional study on the prevalence of rheumatic diseases (RDs) in Portugal. Osteoporosis (OP) is one of the diseases included in the study. Socio-demographic and clinical factors associated with this disease are well known. It is important to confirm if the same known factors are the ones associated with the diagnosis of OP in this study, in a setting when the rheumatologist is not aware of the DEXA results.

Objectives: To identify factors associated with the diagnosis of OP during the first months of EpiReumaPt.

Methods: Participants recruited for the EpiReumaPt survey and observed by a rheumatologist (December 2011 cutoff) were included in this analysis. The study population is a representative sample of the Portuguese population (random-route methodology) and first answers a questionnaire. In a second step, participants with a positive screening for RD (and 20% of the ones with a negative screening) are observed by a rheumatologist. A positive screening for OP (1st phase) is made in the event of a self-reported OP diagnosis, a history of non-traumatic fracture after the age of 40 or intake of anti-osteoporotic medication. The proportion of patients observed by a rheumatologist and with a final diagnosis of OP was calculated. Patients with and without OP were compared with respect to socio-demographic and clinical factors. The FRAX and wrist DEXA results (unknown to the rheumatologist at the time of the diagnosis) were compared between the two groups. Factors associated with OP were analysed by univariable logistic regression followed by multivariable regression. Forward selection was performed until the best-fit model was obtained.

Results: A total of 255 participants were included, 38 of which (15%) had a final diagnosis of OP. Participants with OP were older and had a higher probability for major and hip fractures (FRAX algorithm). The proportion of females and positive screening for OP were higher among OP sufferers and the T-score was lower. In the multivariable analysis, OP was in-dependently associated with older age and female gender (table). An alternative model additionally included the DEXA result, being a lower T-score in-dependently associated with OP. When included in the model, positive screening for OP was highly significant (OR 37.55).

Conclusion: FRAX and DEXA results were concor-

TABLE I. FACTORS ASSOCIATED WITH OSTEOPOROSIS

	Model 1 OR (95% CI) N = 255	Model 2 OR (95% CI) N = 235	Model 3 OR (95% CI) N = 255
Age (years)	1.05 (1.03; 1.08)	1.04 (1.01; 1.07)	1.05 (1.02; 1.10)
Gender (female vs male)	8.50 (1.95; 36.94)	9.31 (2.05; 42.32)	†
Positive OP screening (yes vs no)	‡	‡	37.55 (14.47; 97.47)
Active worker (yes vs no)	†	†	†
Retired (yes vs no)	†	†	†
Education level (years)	†	†	†
Major fracture probability	†	†	†
T-score	‡	0.59 (0.41; 0.86)	†
BMD	†	†	†
Alcohol intake			
Occasionally vs daily	*	*	*
Never vs daily	*	*	*
Physical activity (yes vs no)	*	*	*
Body mass index (kg/m2)	*	*	*
Coffee intake (yes vs no)	*	*	*
Smoking (yes vs no)	*	*	*
Ethnicity (white vs other)	*	*	*
Hip fracture probability	*	*	*

*Not selected in univariable analysis. †Not selected in multivariable analysis. ‡ Not included in the model

dant with expectations in patients with OP. A higher age and female gender were independently associated with OP. A lower T-score and a positive screening for OP (1st phase) were also independently associated with OP. The strong influence of the positive screening for OP on the diagnosis of OP shall be further analyzed in terms of its adequacy.

MESA REDONDA 8: EXAMES LABORATORIAIS EM REUMATOLOGIA: AINDA À PROCURA DE UM VERDADEIRO TESTE DIAGNÓSTICO

DIA 4 DE MAIO DE 2012

C013 – FACTORES PREDITIVOS DE RESPOSTA A TERAPÊUTICA BIOLÓGICA EM DOENTES COM ESPONDILITE ANQUILOSANTE – RESULTADOS DO REUMA.PT

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Introdução: A identificação de factores preditivos de resposta às terapêuticas biológicas em doentes com Espondilite Anquilosante (EA) é de extrema importância, especialmente tendo em conta os custos e os potenciais efeitos adversos associados a estas terapêuticas.
Objectivos: Determinar factores preditivos de resposta a terapêutica biológica às 12 semanas em doentes com EA, na prática clínica diária.
Métodos: Foram incluídos doentes com EA que iniciaram terapêutica biológica e foram registados no Reuma.pt. Foi utilizada a informação relativa ao início da terapêutica biológica e às 12 semanas de seguimento (n = 197). Realizaram-se análises de regressão

	ΔASDAS ≥ 1.1		ΔBASDAI ≥2 or ≥50%	
	OR (IC 95%) (n=166)	OR (IC 95%) (n=135)	OR (IC 95%) (n=174)	OR (IC 95%I) (n=193)
Idade no início do biológico (<40 vs ≥40)	**	4.04 (1.86; 8.78)	3.02 (1.56; 5.84)	3.43 (1.82; 6.44)
Sexo (masculino vs feminino)	3.01 (1.20; 7.57)	**	2.39 (1.21; 4.74)	2.73 (1.36; 5.45)
IMC (kg/m²)	**	**	**	**
Educação (anos)	1.11 (1.01; 1.21)	**	§	§
Dor (≥4 vs <4; 0-10)	0.27 (0.09; 0.84)	**	§	§
ASDAS inicial	3.98 (2.19; 7.21)	¤	1.47 (1.03; 2.10)	¤
BASDAI inicial (0-10)	§	§	§	1.20 (1.01; 1.43)
PCR (≥5mg/l vs <5mg/l)	¤	9.33 (3.89; 22.35)	§	§

§ Não incluída no modelo multivariado **Não seleccionada durante a regressão multivariada (p≥0.05).
¤ Excluída do modelo devido a colinearidade; o mesmo modelo foi repetido com esta variável incluída

logística univariadas de preditores de resposta ASDAS (melhoria ≥1.1) e de resposta BASDAI (melhoria ≥2 unidades ou ≥50%). As variáveis com um valor de p<0.1 foram testadas em modelos multivariados. Quando ambos o ASDAS e a PCR (ou ASDAS e BASDAI) foram significativos na análise univariada, foram incluídos em modelos multivariados separados, para evitar problemas de colinearidade. Utilizou-se o método de "forward selection" até se obter o melhor modelo, tomando os efeitos confundidores em consideração. Foram testadas interacções.

Resultados: Verificou-se uma resposta ASDAS em 64% dos doentes e uma resposta BASDAI em 58% dos doentes. A resposta ASDAS às 12 semanas ocorreu sobretudo em indivíduos do sexo masculino, com níveis mais elevados de educação, de dor lombar e de ASDAS inicial (tabela). Retirando o ASDAS do modelo, a idade mais jovem e a PCR mais elevada foram identificadas como preditores da resposta ASDAS. A resposta BASDAI teve como preditores a idade (<40), o sexo (masculino), o BASDAI ou ASDAS inicial (por unidade) (consoante a variável utilizada no modelo).

Conclusões: Uma melhor resposta à terapêutica biológica pode ser esperada em doentes com EA do sexo masculino e de idade mais jovem. A actividade de doença no início do biológico é também um factor preditor de resposta às 12 semanas. O ASDAS inicial é preditor de ambas as respostas ASDAS e BASDAI, mas o BASDAI é preditor apenas da resposta BASDAI. A PCR é um preditor importante de resposta ASDAS, mas não de resposta BASDAI. Os preditores identificados no Reuma.pt estão em linha com o observado em ensaios clínicos[1].

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C014 – PREDICTIVE FACTORS OF THE SIX MINUTES WALKING TEST IN OBESE INDIVIDUALS WITH KNEE OA

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Knee Osteoarthritis (KOA) is increasing, due in part to obesity making it one of the most common causes of disability. Knee loads related to obesity and joint weight-bearing plays an important role in the development and progression of KOA. Besides, knee pain is a common complaint among obese individuals compromising joint mobility and therefore physical function. One of the most important functional assessments for KOA individuals is walking capacity which might be done using the Six Minute Walk Test (6MWT). This test has been referred as a reliable test to predict functional capacity in individuals with symptomatic KOA.

Purpose: the purpose of this study was to determine which factors might predict the performance of the 6MWT in obese individuals with KOA.

Methods: From 80 obese volunteers with sympto-

matic KOA, 50 adults (35 women, 15 men) with radiographic KOA were included (age: 55.3±6.7yrs; Body Mass Index (BMI): 34.9±4.9Kg m^{-2}) in this study. Self-report measures were recorded by using the Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain and Other Symptoms subscales, the Beck Depression Inventory (BDI) and the International Physical Activity Questionnaire, short version (IPAQ) to control the amount of physical activity. Functional tests included the 6MWT, balance test (stand on foam with eyes closed) and Five-Times-Sit-to-Stand Test (FTSST). Pearson's coefficient was used to analyze the correlation between age, BMI, distance of 6MWT, impact of pain on activities of daily living, other knee symptoms, depression, balance, and lower extremity muscle performance. Multiple regression analyses (stepwise) were used to identify which factors best predict the 6MWT.
Results: Pearson's correlation showed that 6MWT was inversely correlated with knee pain (r=-.535, *p*<.001), with BMI (r=-.421, *p*=.002), and with BDI score (r-.455, *p*=.001), and positively correlated with the FTSST (r=.413, *p*=.003). The Stepwise multiples regression analysis revealed that the significant predictors of 6MWT were KOOS pain subscale, BDI score, and FTSST (adjusted R^2=0.421, *p*<.001). Additionally, separate analyses for sex were done showing that only one factor significantly predicted the 6MWT. For men the FTSST explained 64% of the variance obtained in the 6MWT (*p*<.001) and for women the unique predictor was the KOOS other symptoms subscale (adjusted R^2=0.245, *p*=.001).
Conclusions: Negative association between 6MWT and BMI was somehow expected, as obese individuals suffer higher joint stress showing poor walking ability. However, BMI in this regression model did not explain the walked distance, probably because all the subjects in this study were obese. Our findings suggest that higher knee pain and lower limb strength were associated with a lower functional capacity. Muscle weakness is considered part of the mechanical pathology of KOA and pain has mostly a mechanical pattern, affecting postural control required in walking. Depression state was also related to walking ability, showing that attitudes and beliefs negatively reflected in the capability of accomplishing this physical task. The lower limb strength explained the walking ability in men, but this finding should be considered cautiously due to the small number of individuals. Finally, the women's perceived knee health status moderately explains the performance in this walking test.

C015 – ASSOCIAÇÃO ENTRE ACTIVIDADE DE DOENÇA, NÍVEIS SÉRICOS DE ESCLEROSTINA E DENSIDADE MINERAL ÓSSEA (MÃO E FÉMUR) EM DOENTES COM ARTRITE REUMATÓIDE ESTABELECIDA

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Introdução: A artrite reumatóide (AR) está associada a perda localizada de massa óssea nas mãos, assim como a osteoporose generalizada. A *Dual energy X-ray Absorptiometry* (DXA) é um instrumento muito sensível para a medição de perda de massa óssea na AR.

As erosões articulares são características da AR e são causadas por aumento da reabsorção óssea. O sistema RANKL/OPG é o principal mecanismo regulador do recrutamento dos osteoclastos. Adicionalmente, na AR não se verifica um aumento da formação óssea que permita prevenir ou diminuir o aparecimento de erosões.

A via Wnt tem um papel fulcral no controlo da formação óssea através da regulação da actividade osteoblástica. A esclerostina e o Dkk-1 são reguladores importantes desta via.
Objectivo: Determinar o grau de associação da actividade de doença com os níveis dos biomarcadores ósseos e a densidade mineral óssea (DMO) nas diferentes localizações anatómicas avaliáveis em doentes com AR estabelecida, analisando as diferenças em função dos regimes terapêuticos instituídos (DMARDs convencionais exclusivamente versus agentes biológicos com ou sem associação de DMARDs convencionais).
Métodos: Em consulta de monitorização, foram obtidas as diferentes variáveis clínicas e as amostras sanguíneas. Foi aplicada a versão portuguesa do Standford Health Assessment Questionnaire (HAQ) e obtidos os Disease Activity Score quatro variáveis (DAS28(4v)), contagem das 68 articulações dolorosas (TJC) e 66 articulações tumefactas (SJC). A DMO foi avaliada por DXA (Lunar Expert 1320®) na coluna lombar, anca, colo femoral, triângulo de Wards, mãos e segundas falanges proximais.

Efectuaram-se doseamentos séricos de VSG, PCR, β-C-telopeptide of collagen1 cross-links (β-CTX1), osteocalcina, Dkk-1 (ELISA, Biomedica), esclerostina (ELISA, TECOmedical), RANKL (ELISA, Cusabio), osteoprotogerina (ELISA, Biomedica) e serotonina (ELISA, Labor Diagnostika Nord). Para análise estatística dos dados, utilizou-se o PASW Statistics 18.

Resultados: Foram avaliados 110 doentes com AR, 88 (80%) mulheres, 56 (51%) sob agentes biológicos, com 54±11 anos de idade, 14±10 anos de duração de doença, DAS28(4v) médio de 4.25±1.31 e um HAQ médio de 1.215±0.651. Num modelo de análise multivariada (ajustando para a idade, IMC, duração de doença, dose média diária de prednisolona, anos de corticoterapia e anos de terapêutica anti-reabsortiva) e em doentes com AR exclusivamente sob DMARDs convencionais, a actividade de doença moderada, segundo o DAS28(4v), associou-se a níveis de esclerostina mais elevados ($p<0.05$). Verificou-se uma tendência para níveis de RANKL mais altos em pacientes com doença severamente activa. O DAS28(4v) associou-se negativamente com a DMO no colo femoral ($p<0.05$), mãos ($p<0.001$) e segundas falanges proximais ($p<0.005$). Usando o mesmo modelo e ajustando também para anos de terapêutica com agentes biológicos, no grupo de doentes sob agentes biológicos, os níveis de esclerostina associaram-se positivamente com a actividade de doença ($p<0.05$). Níveis superiores de DAS28(4v) associaram-se a valores inferiores de DMO na anca, colo femoral, mãos e segundas falanges proximais ($p<0.001$).

Conclusões: Na nossa população de doentes com AR, verificou-se uma forte associação negativa entre actividade de doença e valores de DMO na mão e fémur. A ligação entre grande actividade de doença e níveis aumentados de esclerostina pode ser uma das causas para uma formação óssea diminuída na AR activa.

CO16 – THE IMPACT OF IMMUNOGENICITY ON DRUG SAFETY PROFILE

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Over the last years, an increasing body of evidence has highlighted the clinical significance of drug immunogenicity. Anti-drug antibodies (ADA), by forming immune complexes with the drug, promote its faster clearance from circulation, reducing therapeutic effectiveness. However, ADA have also been associated with increased incidence of drug-related adverse events (AE), particularly infusion-related AE during infliximab therapy, despite severe thromboembolic phenomena associated with antibodies against adalimumab have also been reported in the literature.

We assessed the association between ADA and infusion-related AE in patients with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA) and Inflammatory Bowel Disease (IBD), receiving infliximab therapy.

We conducted a prospective cohort study over 2--years evolving 84 consecutive patients (22 AR, 33 AS, 9 PsA and 30 IBD) receiving infliximab at 3-5 mg/Kg every 6 or 8 wks, at day care unit of Hospital Garcia de Orta, Almada. Seventy-six percent of patients were female, with mean (SD) age of 48 (10.2) years, disease duration of 8 (6.4) years, receiving biologic therapy by 2.9 (2.0) years. All RA patients and 89% of PsA were receiving concomitant MTX. IBD patients were receiving concomitant azathioprine and also hydrocortisone plus anti-histaminic prior to each infliximab infusion. ADA were detected by an optimized Bridging ELISA, just prior to next infliximab infusion. Clinicians were blind for the tests results. Therapeutic response and low disease activity were defined according to the EULAR guidelines (RA and RA-like PsA), ASAS group guidelines (AS and AS-like PsA) and by an expert clinician (IBD patients).

During the follow-up period, a total of 25 patients (30%) had detectable ADA (41% of RA, 33% of PsA, 18% of AS and 23% of IBD patients). Of those, 44% developed an infusion-related AE (4 RA patients, 2 PsA, 2 AS and 4 IBD patients). In all of those cases, ADA detection occurred prior to the AE. All patients with RA, PsA and AS who developed infusion-related AE were unable to maintain therapeutic response over time, while 2 out of 4 patients with IBD were still considered responders during the follow-up period. All the reactions were mild-moderate requiring hydrocortisone and anti-histaminic administration.

We verified that 100% of patients with infusion-related AE had detectable ADA, while 44% of patients with detectable ADA developed such AE. Those patients were not able to sustain therapeutic responses and the maintenance of therapy in such cases may have serious deleterious effects with no additional therapeutic benefits. Our results are in agreement with other studies published in the literature. However,

more robust studies are warranted to better evaluate safety aspects related with immunogenicity.

CO17 – ZOLEDRONATE EFFICACY AND SAFETY IN ACTIVE PAGET'S DISEASE LONG-TERM FOLLOW-UP AND RETREATMENT IN CLINICAL PRACTICE

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Introduction: Zoledronate, a third generation bisphosphonate, has showed high efficacy in the inhibition of bone resorption and it is nowadays considered first line therapy in the treatment of Paget Disease (PD). The objective of this observational study was to assess the efficacy and safety of zoledronate in clinical practice in short and long-term follow-up.

Mehods: Patients with active PD treated with zoledronate 5 mg were consecutively recruited between 2006 and 2011 and followed prospectively. Clinical (bone and joint pain attributed to PD) and laboratory parameters (alkaline phosphatase (ALP), bone specific alkaline phosphatase (BSALP), procollagen type 1 N-terminal propeptide (P1NP), collagen type 1 beta C-terminal telopeptide (b-CTX), seric and urinary calcium and phosphorus and parathormone levels) were determined before, at 3 and then every 6 months after treatment, up to a maximum of 60 months of follow-up. Adverse events were registered according to clinical protocol.

Results: 60 patients (60% males), with a mean age of 68±11 years and a mean disease duration of 11±9 years were included. 69% had polyostotic disease and the mean percentage of skeletal involvement (Howarth table) was of 10.8±7.6%. 68% were symptomatic: 71% of those referring bone and 54% joint pain attributed to PD. 54% were receiving analgesic or non steroidal anti-inflammatory drugs. 48.3% had been previously treated with parental pamidronate, with a cumulative dose of 234±209mg. The mean follow-up period after zoledronate infusion was of 37±13 months (minimum of 12 and maximum of 60). Only 4 patients (6.6%) required retreatment, on average 30 months after the first zoledronate infusion. A marked reduction of ALP (261,6±152,5 U/L at baseline) was observed at 3 (70%;79,6±42,6) and 6 months (74%;67,0±22,1) after zoledronate administration, being maximal at 12 months (75%;66,3±22,2) ($p<0.001$). The difference of the mean values of ALP between 3 and 6 months was also significant ($p<0.05$). At 3 and 6 months, 95% and 96% of patients respectively, achieved remission defined as a normalization of ALP levels. Maximum effect was obtained at 12 months after treatment with 98% of patients being in remission. Significant reductions of the mean levels of BSALP, P1NP, and b-CTX ($p<0.001$) were also verified at 3, 6 and 12 months after treatment. 47% of patients reported pain improvement: 89% at 3 months, 7% at 6 months and 4% at 12 months. Transitory side effects were registered in 15 patients, 18% referred flu-like symptoms, 10% showed asymptomatic hypocalcaemia and 30% asymptomatic hypophosphoremia.

Conclusions: This study confirms the efficacy and safety of zoledronate in a Portuguese population of patients with active Paget's disease. Biochemical remission was achieved in 98% of patients at 12 months and improvement of pain in 47%, the majority 3 months after treatment. Furthermore these benefits were long-term sustained with only 6.6% of patients requiring retreatment during an average follow-up of 37 months.