01 – SEVENTH SESSION: Spondyloarthriris and Psoriatic Arthritis

S7:1

SPONDYLOARTHRITIS: EPIDEMIOLOGY, NUTRITIONAL-ASPECTS AND ENVIRONMENTAL FACTORS

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Spondyloarthritis refers to a group of distinct diagnostic entities with overlapping clinical, radiological, genetic and pathophysiological features. These diseases are considered at the cross-roads of inflammation and biomechanics, both factors contributing to the clinical picture and to the pathophysiology.Although genetic factors have a strong impact, environmental factors also play a role. Among these, factors that affect the homeostasis of the skin and the gut may play important roles, *e.g.* changes in the microbiome leading to gut inflammation. Whether nutritional interventions can affect the disease however remains unclear. Other environmental factors of particular interest include smoking and the effects of exercise and labor.

S7:2

SPONDYLOARTHRITIS: THE EARLY DISEASE AND DIAGNOSTIC TOOLS

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Early diagnosis and treatment are important for Axial Spondyloarthritis, as new insights were gained recently that early treatment with Non Steroidal anti-inflammatory drugs (NSAID's), physical therapy, and biologicals (TNF inhibitors) might delay radiographic changes (1).
Important tools to identify patients at an early stage of the disease are inflammatory back pain ≥3 months and age at onset <45 years, but also a positive family history of SpA, HLA-B27 positivity and the presence of extra-articular manifestations, such as anterior uveitis, psoriasis and inflammatory bowel disease (IBD) (2). In addition, it is important to realize that often in women the diagnosis is delayed because in the past axial SpA was considered as predominantly male disease, whereas recent studies have shown that the number women with AS has increased (3).
Diagnostic tools that can be helpful, in addition to history and physical examination, are the effect of NSAID's (which substantially decrease the inflammatory symptoms such as night pain and morning stiffness), CRP levels and imaging. Acute phase reactants, such as ESR and CRP, can be raised in axial SpA and if so, are predictors of a good response to TNFi. The problem is that in most cases the acute phase reactants are normal, despite the clinical symptoms of an active disease. According to imaging, the fact that radiographic changes of the sacro-iliac (SI) joints take several years before they are clearly visible is another challenge but in this case MRI of the SI-joints can be useful.
However, despite the high expectations, many patients with active non-radiographic axial SpA do not fulfill the ASAS criteria of a positive MRI. MRI of the spine does not provide any additional information next to the MRI of the SI joints (4).
However, PET-CT scanning with bone markers, shows some promising results, but these technique still has to be refined (5).

References

1. VAN DER HEIJDE D, BARALIAKOS X, HERMANN KA, LANDEWÉ RBM, MACHADO PM, MAKSYMOWYCH WP, DAVIES OR, DE PEYRECAVE N, HOEPKEN B, BAUER L, NURMINEN T, BRAUN J: Limited radiographic progression and sustained reductions in MRI inflammation in patients with axial spondyloarthritis: 4-year imaging outcomes from the RAPID-axSpA phase III randomised trial. *Ann Rheum Dis* 2018 Jan 17. pii: annrheumdis-2017-212377.
2. VAN DER HORST-BRUINSMA IE, NURMOHAMED MT: Management and evaluation of extra-articular manifestations in spondyloarthritis. *Ther Adv Musculoskelet Dis* 2012 Dec; 4(6): 413-22.
3. HAROON NN, PATERSON JM, LI P, HAROON N: Increasing proportion of female patients with ankylosing spondylitis: a population-based study of trends in the incidence and prevalence of AS. *BMJ Open* 2014 Dec 15; 4 (12).
4. EZ-ZAITOUNI Z, BAKKER PA, VAN LUNTEREN M, DE HOOGE M, VAN DEN BERG R, REIJNIERSE M, FAGERLI KM, LANDEWÉ RB, RAMONDA R, JACOBSSON LT, SARAUX A, LENCZNER G, FEYDY A, PIALAT JB, THÉVENIN F, VAN GAALEN FA, VAN DER HEIJDE D: The yield of a positive MRI of the spine as imaging criterion in the ASAS classification criteria for axial spondyloarthritis: results from the SPACE and DESIR cohorts. *Ann Rheum Dis* 2017 Oct; 76(10): 1731-1736.
5. BRUIJNEN STG, VERWEIJ NJF, VAN DUIVENVOORDE LM, BRAVENBOER N, BAETEN DLP, VAN DENDEREN CJ, VAN DER HORST-BRUINSMA IE, VOSKUYL AE, CUSTERS M, VAN DE VEN PM, BOT JCJ, BODEN BJH, LAMMERTSMA AA, HOEKSTRA OSH, RAIJMAKERS PGHM, VAN DER LAKEN CJ: Bone formation in ankylosing spondylitis during anti-tumour necrosis factor therapy imaged by 18F-fluoride positron emission tomography. *Rheumatology* (Oxford). 2018 Feb 3. doi: 10.1093/rheumatology/key034. [Epub ahead of print] PubMed PMID: 29415219.

S7:3

MANAGEMENT: FROM GUIDELINES UP TO THE LAST TREATMENT ISSUES

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Purpose. Seronegative spondyloarthritis (SpA) are recurrent chronic diseases with a huge impact on patients' quality of life, but also with a significant socio-economic burden. Many drugs have been approved for the management of these diseases with a dramatic improvement in patients' outcomes. A non-pharmacological approach aiming to educate patients to a correct and healthy lifestyle is nevertheless always recommended. As diet is a considered in the non-pharmacological approach, we set out to review the literature to assess the impact of diet on SpA.
Methods. A comprehensive electronic search in Pubmed was performed.
Results. The selected articles are listed in Table I. The 2016 ASAS/EULAR recommendations stressed the importance of physical exercise and patient education, but without details on the type of interventions, especially regarding dietary reg imes. National and international guidelines for Psoriatic Arthritis (PsA) (GRAPPA, EULAR, SIR) also stressed the importance of PsA comorbidities, but did not recommended specific lifestyle modifications. In 2013, Feldtkeller et al. proposed a core set of recommendations for ankylosi ng spondylitis (AS) that focused exclusively on behavioral and environmental interventions, including adopting a dietary regime with a low meat intake (arachidonic acid) and rich in omega-3 fatty acid.
Many of the other articles confirmed the beneficial role of a fiber-rich diet with low starch and red meat intake on SpA disease activity. The rationale is based on the evidence that levels of arachidonic acid levels in plasmatic phospholipids correlate with SA disease activity, while PsA patients frequently present an abnormal fatty acid pattern and low selenium levels. An association between total saturated fatty acid and PsA duration, articular symptoms and acute phase reactants has also been reported. A fiber-rich diet could also be beneficial for microbiome, promoting short chain fatty acids production with anti-inflammatory effects, while animal-derived proteins and starch could favor gut inflammation, which is frequently observed in SpA patients with gastrointestinal (GI) symptoms. Indeed, modifying the microbiome with probiotics seems to be an appealing strategy in SpA management, even if existing RCTs have failed to show disease improvement. There is also some convincing evidence that a weight loss in overweight Ps/PsA patients not only reduces cardiovascular risk, but also helps to achieve the minimal disease activity (MDA), irrespective of treatment.
The role of diet in SpA activity is controversial, as some observational studies have demonstrated that there is no significant correlation between diet and disease activity indexes, while some case reports (strength of evidence: very low) have shown SpA improvement or remission after drastic dietary changes (fasting or vegan diet). Furthermore, Chatfield SM *et al*. 2013 observed that SpA patients frequently requested a dietary consultation (61/75 pts).
Conclusions. Scientific literature supports the importance of a correct lifestyle in SpA patients, however it is still being debated if it could have any real effect on comorbidities prevention and disease activity. This review highlights that behavioral changes are still an important unmet need for physicians and patients and deserved to be studied in depth.
The authors declare no financial support or potential conflict of interest in this study

Table I. Literature review: principal guidelines or expert recommendations are reported in the upper rows.

n°	Year	Author	Topic	diagnosis	type of study	n° pz	Conclusion
1	2017	van der Heijde D *et al*.	-	AS	2016 ASAS/EULAR recommendation s	-	Regular exercises may improve several outcomes. No recommendation about dietary regime.
2	2016	Coates LC *et al*.	-	PsA	GRAPPA recommendation	-	Pharmacological treatment recommendation
3	2016	Ramiro S *et al*.	-	PsA	EULAR recommendation	-	Pharmacological treatment recommendation
4	2015	Roubille C *et al*.	-	PsA	Evidence based recommendations Expert Opinion	-	Healthcare providers should be aware that higher BMI is associated with a reduced treatment response in RA, PsA, and PsO. TNF may be associated with a mild increase in weight in RA, PsA, and PsO, but the clinical relevance is unknown (level 3b, 4, 5, B) BMI should be determined in all patients with RA, PsA, and PsO (5D) Healthcare providers should encourage healthy BMI (5D).
5	2013	Feldtkeller E *et al*.	-	AS	Expert recommendations	-	Two meals with red meat and two fish meals per week are recommended in AS patients. Correct Vitamin D and calcium intake are recommended to prevent osteoporosis. Be aware of individual food intolerance or sensitivity.
6	2017	Brenner M *et al*.	diet	Murine model	Case-control	-	Rats on low-magnesium diet had significant reduction in synovial tissue expression genes required for the development of Th17 T cells. Dietary magnesium could regulate autoimmune arthritis; this opens new possibilities for the treatment of autoimmune of PsA with short courses of dietary or drug-induced modulations of magnesium levels
7	2017	Nakamizo S *et al*.	diet	Murine model	Case-control	-	High fat diet induces exacerbation of psoriatic dermatitis.
8	2017	Afifi L *et al*.	diet	PsO	Case-control	-	The most common dietary reductions associated with patient-reported positive skin response were alcohol (53.8%), gluten, nightshades, junk foods, and white flour products. A positive skin response was also reported by respondents when adding fish oil/omega-3, vegetables, oral vitamin D, probiotics, organic foods, and fruits
9	2016	Kristensen S *et al*.	diet	PsA	RCT	145	No significant differences were noted with control group (olive oil). In marine n-3 polyunsaturated fatty acids group, it was noted a significant heart rate reduction after their introduction (p=0.01)
10	2014	Di Minno MN *et al*.	diet	PsA	Prospective	126	≥5% of weight loss was a predictor of MDA achievement (OR=4.20, 95% CI 1.82 to 9.66, p<0.001) after 6 months of anti TNFα drugs An higher weight loss was significantly associated with higher MDA rate.
11	2013	Sundström B *et al*.	diet	AS	Case-control	88	No significant differences between AS and HC in hypertension, body mass index, physical activity, diet, or smoking. AS showed significantly lower levels of serum triglycerides and cholesterol that correlated inversely with the intake of total fat and monounsaturated fats and positively correlated to the intake of carbohydrates.
12	2013	Di Minno MN *et al*.	diet	PsA	Observational	270	135 obese PsA patients vs 135 normal weight PsA during anti TNFα treatment Not achieving MDA rate at 12 months was higher in obese PsA patients (64.0% vs 25.5%; p<0.001). Obesity was a predictor of not achieving MDA at 12 months ([HR] 4.90, 95% [95% CI] 3.04-7.87; p<0.001)
13	2012	Solis MY *et al*.	diet	PsO/PsA	Cross-sectional	34	PsO/PsA male patients presented a higher incidence of overweight/obesity and excessive caloric intake, especially lipids, fatty acids and cholesterol.
14	2012	Sundström B *et al*.	diet	AS	Cross-sectional	66	Significant correlation between disease activity (BASDAI score) and levels of arachidonic acid in plasmatic phospholipids but not diet. Negative correlation between long-chain omega-3 fatty acids and ESR. No significant correlation between diet and BASDAI and BASFI.
15	2011	Sundström B *et al*.	diet	AS	Cross-sectional	165	High prevalence of bowel pain (30%) irrespectively to NSAID treatment. AS patients with GI pain have significantly higher BASDAI (<0.01) and BASFI (0.01), higher consumption of vegetables (<0.01) and lower consumption of milk and soured milk (0.04).
16	2011	Ge R. *et al*.	diet	AS B27+	Case-only cross-sectional	150	Significant differences in SNPs rs3811047 of IF-1F7 was significantly associated with alcohol consumption and the use of half plants–half animal fats cooking oil. No significant associations related to smoking habits, salt consumption, meat and vegetable dietary in- take.
17	2010	Jenks K *et al*.	diet	SpA	RCT	63	No significant improvement of SpA disease activity after probiotics treatment.
18	2009	Chatfield SM *et al*.	diet	AS	Cross-sectional	75	94.7% AS patients resorted to dietary complementary and alternative medicine: 61/75 dietary modification, 51/75 behavioral change and 28/75 magnetic or copper products.
19	2008	Brophy S *et al*.	diet	SpA	Internet based RCT	147	No significant modification in SpA disease activity, bowel symptoms and PROs after probiotics introduction.
20	2006	Sundström B *et al*.	diet	AS	Clinical trial	24	High dose supplementation omega-3 fatty acids was significantly associated with BASDAI reduction
21	2001	Huber R *et al*.	diet	AS	Case report	1	clinical remission in AS patient after introducing vegan diet
22	1995	Azzini M *et al*.	diet	PsA	Case control	25	PsA patients present significantly higher total saturated fatty acids (SFA) and lower omega-6 polyunsaturated fatty acids (PUFA) and selenium levels. SFA levels directly correlated with ESR, disease duration and morning stiffness.
23	1994	Appelboom T *et al*.	diet	AS/RA	Case-only	25/10	AS presented a higher compliance to a lactose free diet than RA patients. Lactose free diet determined a significantly higher improvement of SA, but not RA.
24	1990	Lassus A. *et al*.	diet	PsO/PsA	Case only	80	80 Ps patients (34/80 with PsA) underwent dietary supplementation of poly-unsaturated ethyl ester lipids. After 8 weeks, a significant reduction of PASI score was observed (p<0.001). PsA patients reported a subjective improvement of articular disease.

PsA: Psoriatic arthritis, PsO psoriasis, AS ankylosing spondylitis, SpA spondyloarthritis, RA Rheumatoid Arthritis, HC Health Control, EULAR European League Against Rheumatism, GRAPPA Group for Research and Assessment of Psoriasis and Psoriatic Arthritis, ASAS Assessment of SpondyloArthritis, RCT Randomized Controlled Trial, BMI Body Mass Index, MDA minimal disease activity, TNFα Tumor Necrosis Factor alpha, GI Gastrointestinal, OR Odds Ratio, HR Hazard Ratio, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, BASFI Bath Ankylosing Spondylitis Functional Index, PASI Psoriasis Area and Severity Index, ESR erythrocyte sedimentation rate, NSAID Nonsteroidal anti-inflammatory drugs, SNPs single nucleotide polymorphisms, PROs patients reported outcomes.

S7:4

SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS. MANAGEMENT: NON-PHARMACOLOGICAL ASPECTS AND UNMET NEEDS

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Spondyloarthritis (SpA) are a group of related disorders sharing common genetic bases and clinical and extra-articular clinical manifestations. The pathogenesis of SpA is still elusive although the activation of innate immune system in genetically predisposed subjects seems to play a major role in driving the disease. Different pharmacological approach designed to target pro-inflammatory cytokines such as TNF-α, IL-23 and IL-17 have been demonstrated to be effective in SpA even though the achievement of a disease remission in a significantly high proportion of patients still remains an unmet need. The efficacy of non-pharmacological interventions such as exercises, education and physiotherapy is confirmed by a series of clinical studies. Regular exercises may improve disease activity, function, spinal mobility and pain in patients with axSpA.
The correlation between specific diets and intestinal microbial composition and systemic markers of inflammation like high-sensitivity C-reactive protein (HS-CRP), interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF-α) has been demonstrated in humans and mice. A traditional Mediterranean dietary pattern, characterized by a high ratio of monounsaturated (MUFA) to saturated (SFA) fats and ω-3 to ω-6 polyunsaturated fatty acid (PUFAs) and an abundance of fruits, vegetables, legumes, and grains, has shown anti-inflammatory effects compared with typical North American and Northern European diets and might be considered the diet of choice for diminishing chronic inflammation in clinical practice. In SpA, alterations of microbiome have been demonstrated and recent evidences suggest the diet pattern might influence the activation of innate immune pathways such as inflammasome and autophagy directly involved in the production of pro-inflammatory cytokines such as IL-1b and IL-18. Although probiotic use has been demonstrated to be not effective in modulating systemic inflammation in SpA, modification of dietary patterns and/or use of probiotics might be considered in patients with high risk of development of SpA.

02 – Spondyloarthritis and Psoriatic Arthritis

OC7:1

METABOLIC SYNDROME, NON ALCOHOLIC FATTY LIVER DISEASE AND LIVER STIFFNESS IN PSORIATIC ARTHRITIS AND PSORIASIS PATIENTS: A CROSS-SECTIONAL STUDY

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Objective. Metabolic syndrome (MetS) and non-alcoholic fatty liver disease (NAFLD, potentially evolving into liver fibrosis-LF), are frequent in patient with psoriasis (PsO), but data about psoriatic arthritis (PsA) are lacking. Aims of the study were: 1) investigating if the presence of arthritis, other than PsO, could determine any difference with respect to the prevalence of these comorbidities 2) assess the presence of NALFD and LF and their determinants in PsO/PsA.
Design and Method. PsA patients with concomitant PsO and PsO patients without history or manifestation of arthritis were consecutively enrolled in the period October 2015-June 2016. Exclusion criteria were: liver diseases potentially causing LF except for NAFLD, alcohol consumption>=20 g/day, daily use of non-steroidal anti-inflammatory drugs, use of methotrexate currently/in the previous year. Anamnestic, biochemical, metrological data were collected, thus defining insulin-resistance index HOMA (Homeostatic Model Assessement) and the presence of MetS. All patients underwent 1) liver ultrasound to assess the presence of steatosis (therefore NAFLD) 2) transient elastography, which measures liver stiffness, to evaluate presence and grading of LF (stiffness>=7 kPa=fibrosis). Statistical analysis included Mann-Whitney and Chi-square test to evaluate differences between PsA/PsO patients, regression analysis to identify predictors of NAFLD and liver stiffness, Spearman's coefficient to examine correlations; p<=0.05 was considered as significant.

Table (OC7:1). Logistic and linear regression models to identify predictors of NAFLD and liver Stiffness grading

	NAFLD				Liver stiffness (kPa)			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	RRR (95% CI)	p	RRR (95% CI)	p	Beta (95% CI)	p	Beta (95% CI)	p
Female sex	1.34 (0.42, 4.22)	0.609	-	-	0.15 (0.68, 3.31)	0.193	0.15 (-0.23, 3.43)	0.169
Age	1.00(0.96, 1.05)	0.707	-	-	0.06 (-0.05, 0.09)	0.587	-	-
Arthritis (yes/no)	0.32 (0.10, 1)	0.050	0.27 (0.04, 1.52)	0.140	0.05 (-1.45, 2.35)	0.639	-	-
PASI	1.14 (-0.01, 0.26)	0.034	1.03 (0.87, 1.22)	0.673	-0.02 (-0.24, 0.20)	0.870	-	-
BMI	1.21 (1.07, 1.36)	0.002	*	-	0.11 (-0.10, 0.29)	0.338	-	-
Waist circumference	1.06 (1.01, 1.12)	<0.001	1.04 (-0.97, 1.11)	0.464	0.16 (0.02, 0.12)	0.176	-0.02 (-0.8, 0.07)	0.858
Smoking (current)	1.74 (0.51, 5.92)	0.372	-	-	-0.06 (-2.5, 1.59)	0.656	-	-
CRP	1.18 (0.64, 2.17)	0.577	-	-	-0.06 (-1.3, 0.78)	0.578	-	-
Total cholesterol	0.99 (0.98, 1.01)	0.873	-	-	-0.26 (-0.04, -0.01)	0.027	*	
HDL cholesterol	0.`97 (0.93, 1.02)	0.303	-	-	-0.09 (-0.08, 0.03)	0.461	-	-
LDL cholesterol	1.00 (0.98, 1.01)	0.879	-	-	-0.28 (-0.05, -0.01)	0.018	-0.19 (-0.04, -0.24)	0.088
Tryglicerides	1.00 (0.99, 1.01)	0.123	1.00 (0.98, 1.01)	0.715	0.10 (-0.009, -0.02)	0.407	-	-
HOMA	1.32 (1.07, 1.63)	0.009	-0.75 (-0.49, 1.14)	0.188	0.51 (0.45, 1.08)	0.000	0.33 (0.24, 1.09)	0.046
Glycosylated hemoglobin	4.61 (1.55, 13.63)	0.006	8.34 (1.48, 46.96)	0.016	0.42 (0.83, 2.6)	0.000	0,17 (-0.42, 1.83)	0.218
Diabetes mellitus (yes/no)	7.85 (2.19, 28.03)	0.002	*		.59 (4.17, 8.33)	0.000	*	
Uric acid	1.68 (1.14, 2.49)	0.009	1.19 (0.68, 2.08)	0.531	0.22 (-0.03, 1.36)	0.062	-0.01 (-0.71, 0.77)	0.896
Hypertension (yes/no)	3.57 (1.15, 11.08)	0.027	4.86 (0.97, 24.16)	0.053	0.25 (1.14, 3.88)	0.035	0.12 (-0.95, 2.60)	0.279
Past use of methotrexate (yes/no)	-1.01 (-3.34, 1.31)	0.161	-0.12 (0.01, 1.53)	0.104	-1.01 (-3.34, 1.31)	0.388	-	-

Legend: NAFLD (Non Alcoholic fatty Liver Disease); PASI: Psoriasis Area Severity Index; BMI: Body Mass Index; CRP: C Reactive Protein; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; HOMA: Homeostatic Model Assessment; RRR: Relative Risk Ratio; *: not included in the model because of correlation with other parameters.

Results. PsA/PsO patients (43/33 individuals) had similar characteristics: age 60.2±8.4/54.5±19.6 years, male 74.4/63%, PsA/PsO duration 12.6±8.5/18.2±14.2 years. Significant differences were found in: Body Mass Index (BMI) (25.7±3.4/29.1±6.3, p=0.0092), PASI (1.5±2.5/5±4, p=0.03556), uric acid (4.9±1.5/5.7±1.4 mg/dL, p=0.0001), all higher in PsO. MetS and LS prevalence was similar between AP/PsO: 34.9%/33.3% and 30.8%/27.6% (p=ns). NAFLD was significantly higher in PsO (64.7% vs 35.3% in PsA, p=0.044). Multivariate regression analysis identified glycosylated haemoglobin as independent predictor of NAFLD (RRR 8.34, p=0.016) and HOMA of liver stiffness grading (beta 0.33, p=0.046) (Table). A strong correlation emerged between uric acid and HOMA (p=0.0001, r=0.80) and uric acid- liver stiffness (p<0.0001, r=0.73) in PsO.
Conclusions. MetS and LF were equally prevalent in PsA/PsO, while NAFLD was more frequent in PsO. Insuline resistance seems the main determinants to liver disease (in terms of NAFLD and LF) in PsA/Ps. In this scenario hyperuricemia could be a relevant co-factor.

Keywords: liver stiffness, metabolic syndrome, NAFLD.

OC7:2

DO NOT DO RECOMMENDATIONS IN THE MANAGEMENT OF COMORBIDITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS. GECOAX PROJECT

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Objective. To recognize what prescriptions, risk assessments, or preventive strategies are wrong practices and should thus be avoided in clinical practice. To establish not to do recommendations in the management of the comorbidity of axial spondyloarthritis (ax-SpA).
Design and Method. A multidisciplinary group was selected including 10 rheumatologists, 1 internist, 1 cardiologist, 1 gastroenterologist, 1 psychologist and 2 family physicians. With the support of 3 methodologists, and after interactions aimed to edit a document for the management of comorbidity launched by the same panel, a list of Not to do recommendations was issued. In a discussion meeting, evidence was provided to support the recommendations, items without sufficient basis were removed, and the final list was produced.
Results. A summary list of Not To Do recommendations was issued:
- DO NOT prescribe NSAIDs to patients with CKD, heart failure or liver cirrhosis and, if necessary, exert caution.
- DO NOT use CV risk scores in patients who already suffered a CV event or those with multiple risk factors (smoking, obesity, sedentary lifestyle, DM, hypertension, dyslipidemia) or a family history of premature CV disease; All should be considered high CV risk.
- DO NOT base renal disease screening on a single glomerular filtration test and / or albuminuria (ALWAYS should be confirmed); serum creatinine should not be used as the only test to evaluate renal function.
- DO NOT administer biological therapy in case of active, serious and uncontrolled infection, sepsis or risk of sepsis or tuberculosis or without a previous screening of chronic HBV, HCV, HIV and TB.
- DO NOT repeat HBV vaccination unless HBV antibody levels are not achieved.
- DO NOT vaccinate a patient in therapy with biological agents or in immunosuppressive treatment with live viruses

Conclusions. These recommendations aim to avoid making common mistakes in clinical practice and to help better management of frequent comorbidity in patients with ax-SpA.

Keywords: comorbidity, recommendations, spondyloarthritis.

OC7:3

EFFECT OF FOOD INTAKE AND AMBIENT PARTICULATE AIR POLLUTION ON ANKYLOSING SPONDYLITIS DISEASE ACTIVITY

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Objective. Ankylosing spondylitis (AS) is a chronic inflammatory disease characterized by axial arthritis. The genetic and environmental factors seem to be involved in the pathogenesis of the disease and the disease debilitates patients during the most productive stages of their lives. The aim of this study was to examine the relationships between two environmental factors, food intake and ambient particulate air pollution with disease activity and functional impairment in AS.
Design and Method. A case-control study was carried out. Thirty patients with AS and 30 age and sex-matched healthy controls were included. Disease scores including BASMI, BASDAI, BASFI, and BASG were calculated by means of the international Ankylosing Spondylitis Assessment working group consensus recommendations. The food intake was evaluated by semi-quantitative food frequency questionnaire (147 items FFQ). Level of air pollution indices, PM10 and PM2.5 was obtained from the Tehran air quality control network.
Results. Total energy and fat intake, some vitamins (A, B1, B2, C) and mineral intake (potassium, calcium, iron, phosphorus, magnesium, zinc, copper and selenium) were significantly higher in patients with AS compared to controls. Fat component consumption especially saturated fat of food was moderately correlated with BASFI score. PM2.5 long-term exposure was strongly correlated with BASMI, BASFI and BASDAI scores of patients.
Conclusions. High-fat diet and long-term exposure to air pollution are associated with worse disease outcomes reported in patients with AS. This is an interesting area of investigation in AS pathogenesis and management.

Keywords: ankylosing spondylitis, food intake, air pollution.

OC7:4

BONE DENSITY IN ALGERIAN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Objective. Ankylosing spondylitis (AS) is deemed by inflammation of the entheses and paravertebral structures.Osteoporosis can be one of complication of AS, but diagnosing spinal osteoporosis can be difficult since pathologic new bone formation interferes with the measurement of the bone mineral density (BMD). The aims of our study is to explore prevalence of bone loss in a group of AS and to deduct risk factors for reduced BMD in this population.
Design and Method. A monocentric cross-sectional study was conducted, including patients with AS naive for all biotherapy. A demographic checklist was completed and the disease activity was evaluated using BASDAI and ASDAS indexes. Serum levels of vitamin D, calcium, phosphorus were measured in all participants. Dual-energy X-ray absorptiometry was done to evaluate the bone density in the spine and femoral neck for each patient.
Results. Sixty-four patients were included, the mean age of patients was 28.62 (±9.28) years. The BMD for twenty-five (39.6%) of them were normal, 13 (18.8%) were osteopenic, 26 (41.6%) were osteoporotic. There was no relationship between the different groups (AS patients with osteopenia or osteoporosis and those with normal BMD) and the use of steroids. Statistically significant differences among the three groups were found for body mass index (BMI), age and disease duration (p=0.001, p<0.0001 and p=0.02 respectively). Multivariate analysis revealed that the most significant factors associated with BMD were advanced age and low BMI (p<0.0001- p=0,015). A slight but statistically significant correlation was also found for long disease duration (p=0.03).
Conclusions. Our study has showed that the prevalence of osteopenia and osteoporosis is high in the Algerian population with AS. Major risk factors for low BMD values were: a low BMI, advanced age and long disease duration.

Keywords: ankylosing spondylitis, osteoporosis, bone density.

OC7:5

EFFICACY AND SAFETY OF USING ETANERCEPT IN TREATMENT OF SPONDYLOARTHROPATHIES, EXPERIENCE OF MONTENEGRO

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Objective. The efficacy and safety of etanercept have been proven in several studies. Etanercept represents anti-TNF drug used in primary healthcare. We used retrospective analysis to determine the efficacy and safety of the drug in Montenegro.
Design and Method. We retrospectively analysed the data of all patients suffering from spondyloarthropathies, who were treated with etanercept in the period from December 2014. till December 2016. We evaluated the efficacy of the drug by analysing the measured values of BASDAI at the first specialist check-up and the final BASDAI in the examined period. The safety of the drug was evaluated based on the number of reported adverse reactions for the period. Also, data about age, sex, disease duration and etanercept usage duration were collected and data about concomitant therapy and anti-drug antibodies tests results.
Results. According to available data from the reports of the internal medicine clinic concilium in examined period, etanercept therapy was used by 39 patients. Ankylosing spondylitis had 28 (71.79%) patients, 9 (21.51%) had psoriatic arthritis and 3 (7.9%) had juvenile idiopathic arthritis with ankylosing spondylitis. Total of 28 patients (71.79%) were men and 11 (28.2%) were women. The average patient age was 42 years 4 months and average duration of the disease was 10 years 7 months years. Average duration of the taking etanercept was 2 years 9 months. The average BASDAI score at first check-up during the period was 5.9. At last check, average BASDAI was 2.49. Only 1(2.56%) patient had last BASDAI score above cutoff point (4.1). Adverse reactions to the drug were found in 2 patients, of whom 1 patient had elevated ALT level and cholesterol and 1 patient had pruritus. In the patient with pruritus therapy regime was changed, but pruritus still persisted, so etanercept was discontinued.
Conclusions. Based on analysed data, we can conclude that etanercept is highly efficient in spondyloarthropathies treatment, with almost 100% (97.46%) of patients having a good response to therapy in examined period. The average value of BASDAI score at last check-up was to 2.49. Number of reported adverse reactions was 3 and 1 patient had to discontinue etanercept therapy.

Keywords: efficacy, spondiloarthropathies, etanercept.

OC7:6

A SUSTAINABLE RELIEF OF CHRONIC LOW BACK PAIN IMMEDIATELY AFTER ONE SESSION OF LOW-LEVEL LASER ACUPUNCTURE THERAPY

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Objective. Low-level Laser acupuncture therapy (LLLAT) is defined as the stimulation of acupuncture points with low-intensity, laser irradiation and is widely used in treating musculoskeletal pain. The purpose of this study was to determine whether the use of a single session of LLLAT for Chronic Low Back Pain (CLBP) will result in a better outcome than using acupuncture alone.
Design and Method. 40 patients with CLBP were randomly assigned to two groups: G1 (Acupuncture; 20) and G2 (laser acupuncture; 20 patients). All received a single session only. The Acupuncturists inserted a stainless steel needle in local low back, distal and auricular points. laser-acupuncture treatment with a 20Hz 200mW 820 nm Gallium Aluminium Arsenide diode laser was used the same previous points. Pain intensity was assessed on a 100mm visual analogue scale (VAS). The lumbar range of motion was measured by fingertip-to-floor method. A physiotherapist, who was blinded to treatment assignment, evaluated the patients immediately before and after treatment as well as 4, 12 and 24 weeks later.
Results. Immediately after the completion of treatment, the mean VAS dropped from 78 to 66 mm in the acupuncture group (G1) but increased at the follow-up visits to 76 mm after 24 weeks. In contrast, VAS scores decreased from 80 to 48 mm in the laser acupuncture group. Although it increased in the follow-up visits 60 mm after 24 weeks, it remained significantly better than at the initial assessment. The mean of fingertips and floor distance decreased significantly in G2 from 41 cm to 15 cm immediately after the completion of the first session (the difference from baseline was 26 cm) compared to a decrease from 44 to 35 after the first session in G1. Forward flexion of the lumbar spine improvement remained stable between the first assessment and the other four assessments in patients exposed to prayers with the difference between the baseline and 24-week assessments highly significant ($p<0.0001$) compared to G1 ($p>0.05$).
Conclusions. Both measures were decreased in both groups but laser acupuncture resulted in a significant improvement in functional and symptomatic outcomes in this group of patients with CLBP even after 24 weeks follow-up.

Keywords: back pain, acupuncture, laser.

03 – SPECIAL ULTRASOUND SESSION: what about pitfalls and misinterpretations related to the nutritional status in Rheumatic Diseases

US1:1

ULTRASOUND IN RHEUMATOLOGY: WHAT, WHY, WHEN DO WE ASSESS MUSCULOSKELETAL TISSUES AND OTHER ORGANS?

A. Iagnocco

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In recent years ultrasound (US) has become a relevant tool in the hands of the rheumatologists for its capacity of detecting a relevant part of abnormalities that occur in rheumatic and musculoskeletal diseases (RMDs). Thanks to its feasibility, limited costs and non-invasiveness, it can be used as a bedside modality in rheumatology practice in order to evaluate joint and peri-articular pathologies in a wide set of RMDs.
In addition, recent developments in research have demonstrated that US is a valid and reliable imaging technique for the assessment of different abnormalities and that it can be a support for evaluating responsiveness to local and systemic treatments (1, 2).
Basic requirements for developing expertise in US in rheumatology are the followings (3): Anatomy: detailed knowledge of US-orientated anatomy.
B-mode: basic knowledge of the physics and main findings of US in rheumatology.
Clinical setting: ability to evaluate the US findings in the clinical setting. Doppler: basic knowledge of colour and/or power Doppler technique. Equipment: basic technical knowledge of the US equipment.
At the level of the musculoskeletal system, US is able to visualise the following tissues (3):

Soft tissue	Shape		Texture	
Synovial tissue Synovial fluid Articular cartilage	Not visualised in normal joints The shape of the cavity it fills Curved layer with sharp and continuous hyperechoic margins		Not visualised in normal joints Anechoic Anechoic or homogeneously hypoechoic	
Tendon	*Longitudinal*	*Transverse*	*Longitudinal*	*Transverse*
	Band with sharp and continuous hyperechoic margins	Oval or rounded areas	Fibrillar	Densely packed hyperechoic spots
Bone profile	Thin band		Hyperechoic	
Peripheral nerve	*Longitudinal*	*Transverse*	*Longitudinal*	*Transverse*
	Band	Oval or rounded areas	Fascicular	Scattered hyperechoic tracts

Moreover, several other tissues and organs involved in RMDs are easily accessible for evaluation by US, such as the lung, the salivary glands and the skin, thus spreading the applications of this tool to a wide spectrum of pathologies in which organ involvement is prevalent (*i.e.* scleroderma, SLE, Sjogren Syndrome) (4).
US technique includes grayscale imaging of anatomic structures and blood flow detection with the usage of Doppler modalities.
By using those two modes, US shows different pathologic changes in RMDs.

The most commonly detected musculoskeletal abnormalities are the following:
Joints: joint effusion, synovial hypertrophy and active synovitis.
Tendons: tenosynovitis, tendinosis, tears and damage, dislocation and fibrosis; enthesitis and enthesopathy.
Bursae: bursitis.
Bony cortex: erosion, osteoproliferation.
US should be performed when it is expected to add valuable information to history and physical examination of rheumatic patients. Moreover, US is able to monitor disease activity and progression (3). US as the initial diagnostic tool can replace other invasive and expensive tests, shorten examination times and improve efficiency at rheumatology units (3).
However, currently US is not yet included in the diagnostic classification/criteria for the most important rheumatic diseases and in many cases it is not recommended as the principal tool for the assessment and follow-up of patients (2).
In expert' hands, US can be considered the new millennium stethoscope of the rheumatologist. Its capacity to be complementary to clinic and to recognize subclinical inflammation makes it a useful instrument that can help the rheumatologist in taking therapeutic decisions and in monitoring response to therapy. It is expected that its use in clinical practice will further increase in the coming years (3).

References

1. WAKEFIELD RJ *et al*.: The OMERACT Ultrasound Group: status of current activities and research directions. *J Rheumatol* 2007 Apr; 34(4): 848-51
2. FILIPPOU G *et al*.: The big misunderstanding in rheumatology: Ultrasound is just equipment it cannot replace a doctor! *Med Ultrason* 2016; Vol. 18, no. 3, 273-274.
3. FILIPPUCCI E *et al*.: Ultrasound imaging for the rheumatologist. *Clin Exp Rheumatol* 2006; 24: 1-5.
4. RUARO B *et al*.: Well-trained sonographers are worth their weight in gold: ultrasound in systemic sclerosis. *Rheumatology* (Oxford). 2018 Jan 31.

US1:2

TIPS AND TRICKS FOR PITFALLS AND MISINTERPRETATIONS RELATED TO THE NUTRITIONAL STATUS IN RHEUMATIC DISEASES

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Rheumatic disorders require appropriate and suitable nutrition of patients, the aim of which is to strengthen the therapeutic response. Besides the importance of evaluating the subcutaneous tissue, muscle mass in overweight patients has been widely studied with ultrasound (US) showing a greater tendency to sarcopenia, related to fatty infiltration of peripheral skeletal muscles. Ultrasound (US) can give accurate estimation of the volume of individual muscles or muscle groups as it has been assessed in a variety of specialized settings. Estimation of the muscle volume is a complex task which requires stereological methods based on systematic sectioning the muscle with equidistant parallel planes along a know distance and the application of a mathematical formula. Using these methods, recent studies performed with current generation machines concluded that US can provide accurate and reproducible measurements of muscle volume. Using unrestrained free-hand technique, however, US is not unbiased, requires external markers and has certain disadvantages compared with MR imaging-based measurements. Main limitations include: some underestimation of the muscle volume, dependency upon the orientation of the probe and restricted use to superficial and relatively small muscles only. With introduction of 3D systems, the validity and reliability of US-based volume measurements is expected to improve, even if some limitation related to the attenuation of the US beam for evaluating deep-seated structures and a too small acquisition field-of-view seems to be difficult to overcome. Given the complexity of volume calculation with US, a widely used alternative and quicker way to estimate the muscle bulk and compare it with the opposite side relies on measuring either the muscle thickness or the cross-sectional area (CSA) by the ellipse formula. Thickness measurements are also used to estimate the amount of subcutaneous fat. These methods are more practical but are also more subjective and, in themselves, do not perfectly correlate with true volume assessment. They serve as indicators of either muscle disuse/atrophy or hypertrophy when values are compared with the opposite side. On the other hand, these methods have several potential sources of errors, such as the need to match scan landmarks precisely, to use identical probe orientation when comparing the two sides and to avoid any pressure on the underlying tissues. As regard this latter point, the flattening-related error related to probe pressure would be greater for thickness measurements than for CSA measurements, since the reduction in one dimension would be presumably compensated by bulging in another dimension and the volume of the muscle would remain constant. Apart from these considerations, US has proved to be a reliable means to measure both muscle thickness and CSA with a test-retest correlation of 0.98-0.99 and a 0.90-0.99 correlation with MR imaging. Regarding healthy subjects, the established normal values are dependent on site of measurement, subject's position, activity and body mass. In addition, the influence of age and gender is different for each muscle group and should be taken into account when evaluating US images of muscles of individual patients.

US1:3

CLINICAL CASES: ULTRASOUND EXAMINATIONS IN PATIENTS WITH NUTRITIONAL STATUS ABNORMALITIES

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As technology progresses, definite indications where ultrasound would be the primary consideration are growing up and more and more this technique is now viewed as one that competes with MR imaging rather than a complementary tool. In this interactive session, some patients with rheumatological disorders who have normal and abnormal nutritional status abnormalities will be examined live with ultrasound as examples to evaluate muscles and subcutaneous tissue planes. The aim is to offer an opportunity to improve theoretical background together with practical skills to perform an appropriate ultrasound examination of the musculoskeletal system. A combined presentation using two screens (one connected to the ultrasound equipment, the other to the laptop) will be used simultaneously. After a short clinical introduction, in each patient the live demo will highlight the value of ultrasound in depicting nutritional abnormalities of the musculoskeletal tissues in the upper and lower extremity. A special focus will be given to the ultrasound scanning techniques and the most common pitfalls and interpretation errors the examiners can encounter during the study. Finally, a case quiz session with correlative imaging will be presented.

04 – EIGHTH SESSION: Osteoporosis and life style

S8:1

EPIDEMIOLOGY, NUTRITIONAL ASPECTS AND ENVIRONMENTAL FACTORS

L. Carmona

Osteoporosis and associated fractures are an important cause of mortality and morbidity. The female-to-male ratio of osteoporotic fractures is 1.6, and incidence rates increase exponentially with age, especially in women. The combined lifetime risk for hip, forearm and vertebral fractures coming to clinical attention is around 40%, equivalent to the risk for cardiovascular disease, and it varies widely across European countries. Apparently, there is a gradient North-South that is turning around with time, in likely relation with lifestyle changes and use of antiosteoporotic medication.
Bone health has many determinants, two of which are diet, basically vitamin D and calcium intake, and sun exposure – this latter due to its involvement in maintaining adequate levels of vitamin D levels. Variations in sun exposure due to latitude, season, time of day, atmospheric components, clothing, sunscreen use and skin pigmentation, as well as age, obesity and the incidence of several chronic illnesses, may lead to different prevalence estimates. Basically, the environment is less favourable in Northern countries, with less sun exposure and higher risk of falls in the winter, but diet is healthier for bone in non-Mediterranean countries.
A new known determinant is pollution. Long-term exposure to traffic particles has been found to be an independent risk factor for bone fractures, possibly involving changes in parathyroid hormone concentrations.

S8:3

MANAGEMENT: FROM GUIDELINES TO THE LAST TREATMENT ISSUES

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The osteoporosis is a growing healthcare problem, as fragility fractures are around the world.
Guidelines on the management of osteoporosis and fragility fractures are available worldwide. Guidelines may be appropriate for many patients, especially those managed in primary care settings, there are some limitations to guidelines particularly for patients with special circumstances. Moreover, even if the guidelines do not differ among themselves, the management of osteoporosis somewhat varies around the world and certainly it does in the European countries.
Therapies for osteoporosis are easily recognizable in the compounds anti-fracture compounds in controlled clinical trials. Drugs recommended today by guidelines with different levels of evidence are: antiresorptives (alendronate, risedronate, zoledronate, ibandronate, raloxifene, bazedoxifene, denosumab) and anabolics (teriparatide). We need more anabolics and this could potentially be satisfied by the registration of two new compounds, abaloparatide and romosuzumab. The future of osteoporosis treatment is open to innovation.

S8:4

MANAGEMENT: NON PHARMACOLOGICAL ASPECTS AND UNMET NEEDS

J.A.P. da Silva

Despite the remarkable progress observed in the efficacy of medications used to treat osteoporosis and prevent fractures, non-pharmacological interventions and correction of modifiable risk factors are universally recommended for all subjects Non-pharmacological interventions include diet, physical activity, adequate calcium intake and sun exposure. Risk factors that may and should be corrected are exemplified by cigarette smoking, alcohol abuse, and environmental risk factors for falls.
The recommendation of an “adequate” diet, with a “correct” intake of vitamin D and a “balanced” intake of proteins, carbohydrates and fats is common to almost all current guidelines for the treatment of osteoporosis.
However, the exact definition of “adequate” and “balanced is far from clear, the best way to convey the concept to patients is left to the clinician and the potential risks associated with some of these suggestions have not fully cleared: the cardiovascular risk attributed to oral calcium, skin cancer and kidney stones related to vitamin D are just some examples. The actual relevance of these measures in addition to medication has raised controversy and is still poorly established.
This presentation will explore and discuss the evidence underlying the common views referred above and try to generate a practical algorithm for use in practice.

05 – Osteoporosis and life style

OC8:1

CHARACTERIZATION OF A NOVEL VITAMIN D RECEPTOR (VDR) POLYMORPHISM BY SEQUENCE-BASE TYPING

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Objective. The vitamin D endocrine system is involved in several biological processes, including the bone metabolism, the immune response modulation and the regulation of cell proliferation and differentiation. The vitamin D role is mediated by the vitamin D receptor (VDR), a member of the steroid/thyroid hormone receptor family. VDR gene (RefSeq: NG_008731.1) is located on the chromosome 12 at position 12q13.11 and contains 11 exons. Several common VDR polymorphisms have been documented in recent genetic studies. Three restriction fragment lenght polymorphisms (RFLPs), BsmI, ApaI and TaqI, were identified at VDR 3’ end. Their effects on VDR protein function are still unknown and the presence of other VDR functional polymorphisms was supposed. The aim of this study was to genotype the mutational hot spot VDR 3’ end searching for additional polymorphisms.
Design and Method. We integrated a bioinformatics and a molecular approach in order to characterize the 3’ end of VDR gene. Specific primer pairs were designed for the coverage of the region. Genomic DNA was extracted from the whole blood of 40 subjects (age range: 30–76 years old). Primer-specific polymerase chain reaction (PCR) was carried out. PCR products were sequenced and bioinformatics tools (BlastN and Mutation Surveyor) were queried for the mutational analysis.
Results. We identified a de novo adenine to thymine heterozygous substitution at 65042 position of VDR nucleotide sequence (NG_00873.1:g.65042A>T; HGSV nomenclature). The polymorphism is a missense variation responsible for the substitution Arg to Lys at 347 amino acid position (NP_00367.1:p.Arg347Lys; HGSV nomenclature). Interestingly, the substitution was found in a hot-spot mutational region and it was associated with the TaqI polymorphism (homozygous state) and with hypovitaminosis D.
Conclusions. Here we reported a de novo missense polymorphism across the coding region of VDR gene. It could contribute to better characterize the VDR variability. The novel haplotype needs to be analysed in future genetic association studies including a larger series of patients and healthy controls.

Keywords: vitamin D, vitamin D receptor, polymorphism.

OC8:2

ANKYLOSING SPONDYLITIS BONE: “ STIFF AND BRITTLE AS A CRISTAL GOBLET”

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Objective: Bone loss in ankylosing spondylitis (AS) is related to both inflammation and immobility. It is not easy in these patients to evaluate risk fracture on lumbar spine due to the presence of sindesmophytes that overestimate bone mineral density (BMD). Trabecular bone score (TBS) is a new tool to assess bone quality. The aim of the study was to investigate the relationship among skeletal microarchitecture, bone density and disease activity in AS patients.
Design and Method. 9 male pts fulfilling ASAS criteria for AS (mean age 42±9.2 years, disease duration 8±2.5 years, BASFI 5.8±1.9, BASDAI 6.3±1.4) and 6 controls were enrolled. The BMD (g/cm2) of the lumbar spine (L1-L4) was analyzed by dual-energy X-ray absorptiometry scan (Lunar Prodigy) and using the same machine were performed anteroposterior spine analysis to evaluate TBS for L1-L4 using TBS iNsight Medimaps software. TBS> 1.350 units was considered normal. Lateral X-rays of lumbar and dorsal spine were taken in order to show the presence of vertebral fractures. Disease activity was measure by Bath Ankylosing Spondylitis Disease Activity (BASDAI) and functional status using Bath Ankylosing Spondylitis Functional Index (BASFI). Vitamin D (25OH)D was tested by immunofluorescence
Results. The mean BMD resulted significantly highest in patients with AS than in the control group [1.231±0.16 gr/cm2 vs 1.152±0.17 gr/cm2; $p<0.04$ but TBS lower 1.070±0.18 units vs 1.332±0.13 units; $p<0.05$. Interestingly, a positive correlation was found between TBS and BASFI (r=0.6, $p=0.005$). and a negative correlation was found between TBS values and BMD (r= -0,5 $p<0.02$). No correlation was found between TBS and BASDAI. After division of patients according to the presence or not of vertebral fractures and highest BMD (1.257±0.04 gr/cm^2 vs 1.207±0.05 gr/cm^2; $p=0.02$) and a lower TBS value (1.055±0.01 units vs 1.084±0.02 units; $p<0.01$) was reported in the fracturated group (26%). Blood sample revealed vitamin D insufficiency in all patients.
Conclusions. This study showed a higher BMD value in AS but a poor quality of bone microarchitecture. TBS is a novel instrument that reflects the trabecular bone structure and could provide skeletal information, that is not captured from the standard BMD measurement at least in AS with vertebral fractures.

Keywords: osteoporosis, ankylosing spondylitis, trabecular bone score.

OC8:3

VERTEBRAL BONE MINERAL DENSITY EVALUATION USING A QUANTITATIVE ULTRASOUND METHOD (ECHOLIGHT) IN A GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS

R. Decianu[1], M. Bojinca[2,3], I.A. Badea[2], A. Balanescu[1,3], S. Daia-Iliescu[1,3], M.M. Negru[1,3], R. Ionescu[1,3], V.C. Bojinca[1,3]

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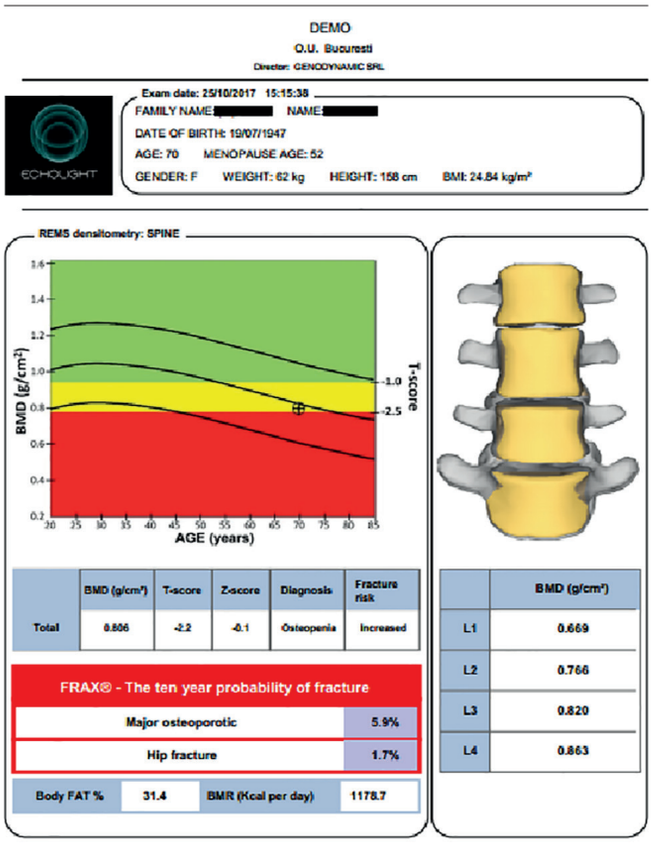
Objective. Applying a recently introduced echosound approach for the diagnosing ostheoporosis. This new method integrates ultrasound imaging with radiofrequency signals from an echographic scan.
We evaluated the bone mineral density (BMD) in patients with rheumatoid arthritis (RA), using a new, ultrasound based technique, instead of dual X-ray absorptiometry (DXA). Also, we set ourselves to contribute to the related literature with data from our clinic.
Design and Method. We evaluated 45 women with RA and 40 age matched controls, without an inflammatory disease and with no history of corticotherapy. All women in both studies were in menopause.
The patients with RA were under monotherapy with a conventional synthetic DMARD: methotrexate or leflunomide. All evaluations were done using a quantitative ultrasound Echolight machine. There were only two evaluators for both groups, so there would be little inter-operator variations.
Results. All patients in the study group are (12%) or have been (88%) under corticotherapy during the evolution of RA. The medium dose followed for more than 2 weeks was 8.2 (5–10) mg prednisone/day. The corticotherapy was followed over an average period of 2.2 (0.5–14) months.
The average T score in the study group was -1.8 (0.8 – -3.5), closer to the osteoporosis cut-off than the control group, which had a T score of -1.16 (1.0 – -3.1).
Conclusions. Although both groups had an average T score included in the osteopenia interval, the difference of 0.64 is significant with regard to the fracture risk and also to the treatment duration.

	Study group	Control group
Age distribution (yrs)	64,8 (51–85)	63,12(41–85)
Menopause age (yrs)	47,8 (35–60)	45,38 (30–53)
BMI (kg/m^2)	25.68 (15.63–34.67)	27.09 (19.0–33.33)
Period since dg of RA (yrs)	7.14 (5–12.5)	–



Currently, DXA is considered the gold standard for diagnosing osteoporosis, but there are several limits to this technique: ionising radiation, massive machine, needing dedicated spaces, specialized operators and all in all, high costs. These limitations prevent DXA from becoming a screening technique, in spite of the need of a screening programme for osteoporosis.
This is a preliminary study for evaluating the BMD. Using this new, portable, radiation-free technique, that implies less time and space for the evaluation, we plan to prove the cost-effective superiority of this method, which would make it suitable for a screening programme. In order to do so, further studies are necessary.

Keywords: osteoporosis, bone mineral density, ultrasonography.

OC8:4

FEMORAL NECK BONE MINERAL DENSITY EVALUATION USING A QUANTITATIVE ULTRASOUND METHOD (ECHOLIGHT) IN A GROUP OF PATIENTS WITH RHEUMATOID ARTHRITIS

R. Decianu[1], M. Bojinca[2,3], I.A. Badea[2], A. Balanescu[1,3], S. Daia-Iliescu[1,3], M.M. Negru[1,3], D. Opris-Belinski[1,3], R. Ionescu[1,3], V.C. Bojinca[1,3]

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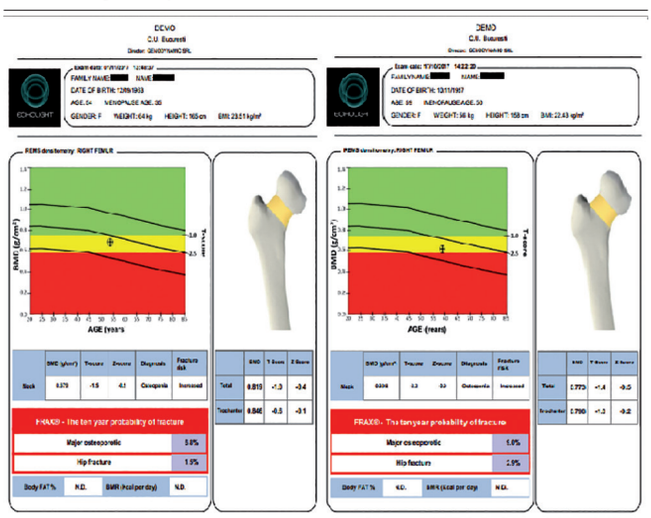
Objective. Applying a recently introduced echosound approach for the diagnosing ostheoporosis. This new method integrates ultrasound imaging with radiofrequency signals from an echographic scan.
We evaluated the bone mineral density (BMD) in patients with rheumatoid arthritis (RA), using a new, ultrasound based technique, instead of dual X-ray absorptiometry (DXA). Also, we set ourselves to contribute to the related literature with data from our clinic.
Design and Method. We evaluated 45 women with RA and 40 age-matched controls, without an inflammatory disease and with no history of corticotherapy. All women in both studies were in menopause.
The patients with RA were under monotherapy with a conventional synthetic DMARD: methotrexate or leflunomide.
All evaluations were done using a quantitative ultrasound Echolight machine.
There were only two evaluators for both groups, so there would be little inter-operator variations.
Results. All patients in the study group are (12%) or have been (88%) under corticotherapy during the evolution of RA. The medium dose followed for more than 2 weeks was 8.2 (5–10) mg prednisone/day. The corticotherapy was followed over an average period of 2.2 (0.5–14) months.
The average T score in the study group was -1.76 (0.8 – -3.8) for the left hip and -1.85 (0.9 – -3.9) for the right hip. The control group had a T score of -0.82 (1.0 – -2.4) for the left hip and -1.11 (1.0 – -2.5) for the right hip. The average T score is -1.8 for the study group and -0.96 for the controls.

	Study group	Control group
Age distribution (yrs)	64,8 (51–85)	63,12(41–85)
Menopause age (yrs)	47,8 (35–60)	45,38 (30–53)
BMI (kg/m^2)	25.68 (15.63–34.67)	27.09 (19.0–33.33)
Period since dg of RA (yrs)	7.14 (5–12.5)	–



Conclusions. The difference of almost 1 point places the control group in normal range, while the study group is in the osteopenia range.
DXA is considered the gold standard for diagnosing osteoporosis, but there are limits to this technique: ionising radiation, massive machine, dedicated spaces and specialized operators.
This is a preliminary study for evaluating the BMD. Using this new, portable, radiation-free technique, that implies less time and space for the evaluation, we plan to prove the cost-effective superiority of this method, which would make it suitable for a screening programme. In order to do so, further studies are necessary.

Keywords: osteoporosis, bone mineral density, ultrasonography.

OC8:5

COMPARISON OF THE EFFECT OF DENOSUMAB ON BONE MINERAL DENSITY OF LUMBAR SPINE AND FEMORAL NECK IN POSTEMENOPAUSAL WOMEN WITH OSTEOPOROSIS, WHEN ADMINISTERED AS FIRST-LINE THERAPY OR AFTER BISPHOSPHONATE

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Objective. To clarify the two-year efficacy of Denosumab (DNS), in terms of bone mineral density (BMD) of lumbar spine (LS) and femoral neck (FN), in postmenopausal women with osteoporosis, when given as first-line therapy or after bisphosphonates (BIS).
Design and Method. Retrospective study of 155 postmenopausal women, aged 66.6±9 years and postmenopausal years 19±10, with osteoporosis (t-score < -2.5), who received DNS (60mgSC/6months) for 1-2 years and Ca^{++}1000mg^{+}Vitamin D 400-800IU/day. Patients were further subdivided into group A (n: 49) BIS naïve and group B (n: 106) with previous BIS uptake for 1-13 years (mean: 5.8±3.3 years). Patients in group A and B aged 66±9 and 66.7±9 respectively (ns, p: 0.12) and their postmenopausal years were 17±9 and 19±10 respectively (p<0.05). Bone densitometry of LS and FN was performed at 0, 1 and 2 years.
Results. Significantly greater increases in BMD were observed at all measured skeletal sites in both groups at the end of the second year (FN-BMD group A: 0.667±0.01 to 0.772±0.017, p: 0.002, FN-BMD group B: 0.673±0.008 to 0.734±0.017, p: 0.006, LS-BMD group A: 0.815±0.009 to 0.908±0.01, p: 0.007, LS-BMD group B: 0.840±0.09 to 0.898±0.01, p: 0.003). DNS administration in BIS naïve patients resulted in higher increase from baseline compared to those with prior BIS administration (group A vs B LS: +10.24% vs +6.9%, p<0.0001, group A vs B FN: +13.6% vs +8.31%, p<0.0001). Finally, three patients (2%), who had previously received BIS for at least 8 years, developed osteonecrosis of jaw, while four patients (2.5%) discontinued because of BMD deterioration and one because of a new vertebral fracture.
Conclusions. Both groups increased BMD at all evaluated skeletal sites after 2 years of therapy; however the effect of DNS on BMD, when administered in BIS naïve patients was superior. The incidence of side effects was relatively low and previous BIS administration seems that should be counted in.

Keywords: osteoporosis, denosumab, bisphosphonates.

OC8:6

CASE REPORT - CALCIUM INTAKE IN RHEUMATIC DISEASES: "EST MODUS IN REBUS"

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Objective. Sarcoidosis is a chronic inflammatory disease that can affect almost all the organs characterized by noncaseating and giant cell granulomas, which macrophages that induces disorders of bone and calcium metabolism.
A 49-year-old female patient was admitted to our hospital with chest pain, dyspnea and asthenia in the last two months she was hospitalized in the last year for schizophrenia. She did not smoke or use alcohol and she did not declare fever, or pathological weight loss. A chest X-ray revealed bilateral parenchymal thickets with shaded margins of interstitial appearance. Chest tomography showed mediastinal lymphadenopathy. Blood cell counts, liver function test and blood sugar were normal. Creatinine revealing an acute renal failure, calcemia correct for albumin serum was 14.1 mg/dL (normal 8.5–11.0 mg/dL), angiotensin converting enzyme (ACE) level was high. Parathyroid glands were normal and both infectious either oncological screenings were negative. Venous hemogas analysis revealed metabolic alkalosis. A more in-depth anamnesis from the family of the schizophrenic patient revealed a non-existent supply of water in the last year, replaced by the intake of milk, on average one liter per day, with any sun exposure due to her prolonged hospitalization. The patient refused any biopsy assessment and a pharmacological treatment was started with intravenous physiological saline, furosemide and metilprednisone with a fast improvement of renal function and calcemia.
Design and Method. It was made a diagnosis of milk-alkali syndrome in sarcoidosis. Kidney involvement is rare in course of sarcoidosis. A granulomatous tubulointerstitial nephritis or a glomerular disease are the most frequent histological findings
Results. In patients affected by sarcoidosis, hypercalcemia is usually related to macrophage production of 1,25-dihydroxyvitamin D [1,25(OH)2D] and impaired degradation of 1,25(OH)2D but other causes have to be excluded (3). Limiting sunlight exposure, vitamin D and calcium intakes and ensuring an adequate water intake are easy non-pharmacological approaches that limit peak of calcemia in these patients. Milk-alkali syndrome (or calcium-alkali syndrome) is a rare condition, but it could be evaluated in all the patients with acute renal failure, hypercalcemia and metabolic alkalosis, especially if there are conditions predisposing to an increased intestinal absorption of calcium, such granulomatous diseases

Keywords: hypercalcemia, vitamin D, inflammatory diseases.

06 – PATIENT SESSION: The cold hand: from symptom to diagnosis

PS3:1

THE COLD HAND: THE SYMPTOM

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Purpose. to describe different clinical aspects of Raynaud's phenomenon. It is a vasospastic response of the extremities in response to changes in temperature and emotional stress that results in a visible cutaneous color changes and sensory symptoms in the digits. Community-based studies showed that Raynaud's phenomenon is a common problem in women, with a prevalence ranging from 4 to 21% in the population.
Methods. some examples of Raynaud's phenomenon will be provided to show colour changes of the digits. Color changes of the fingers when exposed to cold become turning white (ischaemia), then blue (cyanosis), and then
red (reperfusion). Unusual sensitivity of the fingers to cold, manifesting as pain or paresthesia (eg, tingling, pricking, numbness) can be frequent.
Results. Raynaud's phenomenon frequently presents to physicians because of concerns about the possibility of an underlying disorder that can be associated with severe morbidity. The stratification of patients with Raynaud's phenomenon is currently underpinned by the medical history, examination and investigation (*i.e.*, capillaroscopy and antibodies) Raynaud's phenomenon can be idiopathic (primary) or secondary to another condition potentially leading to ischemic complications such as digital ulceration and even loss of digits. These two different forms are characterized by different severity in terms of pain and number of fingers involved, and impact on quality of life.
Raynaud's phenomenon can also occur in other areas of the body that have thermoregulatory vessels, such as the toes, ears, nipples, tongue, and nose.
Symptoms related to Raynaud's phenomenon often mimic sensory changes including paresthesias, numbness, aching, and clumsiness of the hand.
Conclusions. Raynaud's phenomenon is bilateral in the majority of patients, and the middle finger is more frequently involved.
A decreasing frequency of Raynaud's phenomenon from the middle finger to the thumb is generally present. Young patients with mild Raynaud phenomenon, normal nailfold capillaries, and no additional symptoms or signs to suggest a rheumatic or other underlying disease should be reassured.

PS3:2

COLD HANDS: DIAGNOSIS AND MANAGEMENT

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Background. Cold hands can be "primary". This denotes a patient with cold hands but without any underlying disease. Most of the patients with cold hands have uncomplicated "primary" cold hands (= primary Raynaud's phenomenon [RP]). Cold hands can also be associated to a disease. This is called "secondary" cold hands.
Purpose. In this lecture the differential diagnosis between "primary" and "secondary" cold hands will be explained as well as its management.
Results. There are several reasons for secondary cold hands. There are for example diseases that damage blood vessels, or alter their nervous control, or are associated with abnormal circulating factors. Secondary cold hands are most frequently caused by rheumatic diseases, especially systemic sclerosis, mixed connective tissue disease, systemic lupus erythematosus, Sjogren syndrome and dermatomyositis. Other causes of secondary cold hands are use of vibration tools, certain medicines, certain chemo-therapeutics, external compression or "intravascular" diseases.
The "cold hands" phenomenon is a clinical diagnosis. Patients with cold hands will have a complete anamnesis by their medical doctor and some investigations. In this way the medical doctor will for example ask whether the attacks occur in one hand only or in both hands. If the cold hands occur in only one hand then the patient will be referred to the vascular surgeon and examination of larger vessels will be performed. Blood tests will be performed, more specifically autoantibodies will be searched for. Diseases that belong to the scleroderma spectrum can be detected easily by evaluation of the nailfold of the patient with cold hands, with nailfold capillaroscopy.
Nailfold capillaroscopy is a safe and non-invasive tool to look at the microcirculation. The microcirculation is evaluated at the nailfold because the capillaries lie parallel to the skin surface. In a patient with a primary RP the capillaries have the shape of a hairpin and lie on equal distances to each other (like the teeth of a hair comb), with an average of about 9 capillaries per linear mm. In patients with diseases of the scleroderma spectrum there are characteristic changes: giants, capillary loss, hemorrhages and abnormal shapes: "(neo)angiogenesis". According to the different proportions of the hallmark changes of the scleroderma pattern the capillaroscopic images are classified as "early", "active" and "late" scleroderma pattern according to the school of Cutolo.
Besides playing a paramount role in distinguishing a primary from secondary RP, capillaroscopy has an additional role. It can inform the rheumatologist dealing with a patient population with merely the RP and no other signs of a connective tissue disease, who will futurely develop systemic sclerosis. No large-scale prospective cohorts exist describing capillaroscopic morphology in connective tissue diseases other than systemic sclerosis. Moreover, several morphologic definitions exist across literature of different schools. The management of the cold hands consists of tackling the cause of the RP. Cold prevention is primordial. In a second step vasodilating therapies may be administered.
Conclusions. Cold hands can be primary and secondary. Nailfold capillaroscopy is paramount in making the differential diagnosis.

02 – Spondyloarthritis and Psoriatic Arthritis

S9:1

"NEW NUTRITIONAL ASPECTS AS POSSIBLE RISK FACTORS: THE ROLE OF SALT"

S. Colafrancesco, G. Valesini

Data on the role of nutrition in Sjögren Syndrome (SS) are scarce and controversial. Nonetheless, several studies support a role of fatty acids, salt, and vitamin D intake in the regulation of immune cells and the modulation of autoimmune response. Considering the degree of xerostomia, it is likely that patients with SS may avoid foods which aggravate their oral symptoms causing a different nutrient intake and possibly determining nutritional deficiencies. Nowadays, only few studies evaluated this aspect demonstrating in SS patients a major glutamate, carbohydrates, lactose, unsupplemental thiamin and riboflavin intake possibly related to a greater assumption of nutrients behaving as saliva substitute (e.g milk). Moreover, a higher caffeine intake, probably aimed at attenuating dry mouth, thanks to its theoretical ability to amplify cholinergic transmission, has been demonstrated. On the other hand, own to their property to aggravate xerostomia, a lower consumption of unsupplemental vitamin C foods (such as citrus fruits and juices) has been demonstrated as well. It has been recently proposed how supplementation with oral omega-3 and omega-6 fatty acids may be a useful tool to improve inflammation on the ocular surface and relieve dry eye symptoms. A possible influence of Mediterranean diet and vitamin D supplementation on xerophtalmia has been also investigated but without evidence of efficacy. Concerning the metabolic pattern, SS patients seem to present with a higher prevalence of dyslipidemia, DM, and hyperuricemia. In this setting, metabolic alterations are apparently associated with a different clinical and immunological disease phenotype. Despite this association, the clinical significance of free fatty acids in the pathogenesis of SS is still unclear. A possible negative contribution of an excessive fat acids intake is likely to occur own to the ability of adipocytes in producing mediators (interleukin (IL)-6, Tumor Necrosis Factor alpha (TNF?), leptin and adiponectin) responsible for a pro inflammatory state and a deregulation of Th17/Treg balance. Not only fat tissue but also the excessive salt intake may be called in cause in this specific imbalance. Indeed, in vitro studies performed in hypertonic saline concentration, demonstrate an overexpression of IL-17A and IL-23R by T helper cells accompanied by a Th17 cell differentiation and loss of regulatory T cells properties.
Talking about diet, we cannot finally forget the possible role of microbiome in SS. The majority of studies focused on the effect of hyposalivation on the oral microorganisms underlining how hyposalivation is associated with a higher number of Candida species and increased acidogenic and aciduric microorganisms on tooth surfaces. Next to the oral microbiome, dysbiosis in the gut can also drive an increased peripheral migration of local TH17 cells, leading to a possible salivary glands colonization.

S9:2

BIOMARKERS IN SJÖGREN'S SYNDROME: DISCOVERY, VALIDATION AND CLINICAL APPLICATIONS

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Sjögren's syndrome is a slowly progressing autoimmune disease, seen in 0.2-0.5% of the population, which predominantly affects middle-aged women, although it can occur at any age. Sjögren's syndrome is characterized by lymphocytic infiltration of the exocrine glands, mainly the lacrimal and salivary glands resulting in impaired secretory function. Simultaneously, systemic features of cutaneous, respiratory, renal, hepatic, neurologic, and vascular nature often occur. The syndrome can present either alone (as primary Sjögren's syndrome) or in the context of underlying connective tissue disease (as secondary Sjögren's syndrome). Prognosis and appropriate treatment planning are important issues, because of the complexity and varying nature of the disease. During the past few years, clinicians have come to appreciate and distinguish between two types of Sjögren's syndrome: a localized disease that affects quality of life, and a systemic syndrome, which is associated with increased morbidity and mortality due to the high risk of malignant transformation. Systemic Sjögren's syndrome is defined by the presence of palpable purpura, mixed monoclonal cryoglobulinemia, and low complement C4 levels at presentation. The phenotypic expression of the disease plays a vital role for both follow up and treatment. However, the need of biomarkers, aiming to define the different types of the disease, mirror the pathogenetic mechanisms and utilized as indices for the outcome and response to treatment are certainly needed. Biomarkers can derived from sera, saliva and tissue of patients and validated in large harmonized patient populations. In the present lecture, potentially clinically useful biomarkers in SS will be discussed.

S9:3

MANAGEMENT OF SJÖGREN'S SYNDROME TODAY: FROM GUIDELINES UP TO THE LAST TREATMENT ISSUES

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The management of patients suffering from primary Sjögren's syndrome (pSS) has long been mainly symptomatic and demonstration of effectiveness of systemic drugs was lacking. Consensual indexes have been developed in recent years allowing assessment of disease activity and symptoms in pSS patients and thus setting-up of clinical trials. In the same time, progresses made in the understanding of pSS pathogenesis have allowed moving into a more targeted approach to therapeutic intervention. Given the key role of chronic B cell activation, B cells target therapies were the first candidates. But despite promising results from open trials and retrospective studies, rituximab failed to demonstrate efficacy in pSS in 2 randomized controlled studies. Belimumab appears promising in an open study.

New means of targeting B cells are currently investigated including co-stimulation and ectopic germinal centre. For the first time, a positive randomized clinical trial was presented at the 2017 ACR meeting with a monoclonal anti-CD40 antibody. New pathways are being also investigated including co-stimulation of T cells and interleukin-6. In this talk, we will summarize the current evidence regarding targeted therapies in pSS and will do an overview of the promising drugs in the pipeline.

S9:4

MANAGEMENT: NON PHARMACOLOGICAL ASPECTS AND UNMET NEEDS

L. Quartuccio

Sjögren's syndrome (SS) is autoimmune disease mainly affecting of the exocrine glands with associated inflammatory lymphocytic infiltrates of the affected glands. The main symptoms include the dryness of the mouth and eyes deriving from involvement of the salivary and lacrimal glands. Different therapeutic strategies have been proposed for SS; systemic therapy includes steroidal and non-steroidal anti- inflammatory agents, disease-modifying agents, and cytotoxic agents to address the extraglandular manifestations.
Many issues are still open to a deep research by many scientists: a) the issue of disease definition, since the new classification criteria are now available but the diagnosis is still in the hands of the expert clinician, b) the definition of the disease activity, as data from large cohort studies and therapeutic trials suggested that the ESSPRI, more than the ESSDAI, significantly correlated with health status and health-related quality of life measures in SS patients, and different studies demonstrated that systemic and patient scores are, poorly correlated, suggesting that these measures are complementary in the assessment of the disease and should be separately evaluated in clinical trials and practice, c) the usefulness of the ultrasounds in classification and diagnosis of SS, d) the standardization of the histopathological assessment of the salivary gland biopsy, e) the discovery of new biomarkers to be use in prognosis and prediction of treatment effect, f) possible treatments of the disease; in fact, three biologics, *i.e.*, rituximab, belimumab and abatacept, proved their effectiveness in open studies for some extraglandular features of SS, but not for dryness up to now, even if morphological and biological changes under drugs were clearly documented. Also, patient inclusion criteria, disease duration, concomitant treatments, study endpoints, treatment duration and other parameters markedly differed among studies with biologics in SS. Many additional international phase II and III studies are now ongoing with new drugs in SS. Besides pharmacological interventions, nutritional immunology might play an adiuvant role in calorie restriction on transforming growth factor beta 1 and proinflammatory cytokines in murine Sjögren's syndrome
Finally, a better stratification of SS patients represents the first step to improve future treatment studies.

08 – NINTH SESSION: Sjögren syndrome today

OC9:1

ERDJ5 FUNCTION IS INVOLVED IN INFLAMMATORY MANIFESTATIONS OF SJÖGREN'S SYNDROME IN THE SALIVARY GLAND

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Objective. Sjögren's Syndrome (SS) is a chronic autoimmune disease that mainly affects the exocrine glands. The initiation and causative agents are still unknown. Endoplasmic Reticulum (ER) stress proteins have been suggested to participate in autoimmune and inflammatory responses, either by acting as autoantigens themselves, or by modulating factors of inflammation. ERdj5 is an ER-resident chaperone protein with a disulfide reductase activity, required for the translocation of misfolded proteins across the ER for proteasomal degradation. In this study we sought to investigate the role of ERdj5 in the salivary glands, in association with inflammation and autoimmunity.
Design and Method. Sjögren's Syndrome (SS) is a chronic autoimmune disease that mainly affects the exocrine glands. The initiation and causative agents are still unknown. Endoplasmic Reticulum (ER) stress proteins have been suggested to participate in autoimmune and inflammatory responses, either by acting as autoantigens themselves, or by modulating factors of inflammation. ERdj5 is an ER-resident chaperone protein with a disulfide reductase activity, required for the translocation of misfolded proteins across the ER for proteasomal degradation. In this study we sought to investigate the role of ERdj5 in the salivary glands, in association with inflammation and autoimmunity.
Results. Human MSGs expressed ERdj5 with higher intensity in MSGs of SS patients with severe inflammatory lesions. Mice deficient in ERdj5 spontaneously developed SS-like inflammation in submaxillary glands and presented ANAs systemically. Inflammation was characterized by T and B infiltrating lymphocytes. Notably, female ERdj5-knockout mice developed severe chronic periductal inflammation in contrast to the much milder phenotype found in male littermates. The cytokine profile in the sera and SGs of ERdj5-knockout mice was characterized by the altered IL-23 and IL-17 axis. Saliva production was significantly reduced in female ERdj5-/- mice when compared to wild type controls. The described phenotype was accompanied by increased cell death prevalence within the SGs of ERdj5-knockout animals.
Conclusions. Salivary glands of ERdj5-knockout mice resemble the pathologic lesions of human Sjögren's Syndrome whereas ERdj5 was induced in MSGs of SS patients. Our findings suggest a critical connection between the function of the ER stress chaperone protein ERdj5 and autoimmune inflammatory responses in the salivary glands.

Keywords: ERdj5, salivary glands, inflammation.

OC9:2

LOW MIR200B-5P LEVELS IN MINOR SALIVARY GLANDS ASSOCIATE WITH LYMPHOMA DEVELOPMENT IN PATIENTS WITH SJÖGREN'S SYNDROME (SS)

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Objective. The miRNAs of the miR-200 family are critical regulators of oncogenesis. Preliminary evidence suggested that, although not deregulated compared to sicca-controls, miR200b-5p levels are decreased in the minor salivary glands (MSGs) of SS patients with non-Hodgkin's lymphomas (NHL). Herein, we studied the expression of miR200b-5p in the MSGs of SS-associated NHLs and its predictive value for the identification of SS-patients susceptible to develop NHL.
Design and Method. miR200b-5p expression was investigated in MSG-tissues of SS-patients who were at (a) low-risk and didn't develop NHL during follow-up (SSwo, n=27; median follow-up time upon biopsy performance, range: 8.9-yrs, 1.33-14-yrs), (b) high-risk and diagnosed with NHL during follow-up (pre-lymphoma, SSpL, n=17; median follow-up to till lymphoma diagnosis, range: 3.67-yrs, 0.42-8.5-yrs) and (c) had NHL (n=35), as well as non-SS sialadenitis-controls (sarcoidosis and HCV-infection, 4-each). The differential miR200b-5p expression, correlations with disease features and its discriminative/predictive value were evaluated by appropriate statistical approaches.
Results. The MSG levels of miR200b-5p were significantly downregulated in SS patients who will develop or have NHL (mean relative expression±SD: 0.31±0.33 and 0.21±0.25 vs 0.72±0.37 and 0.95±0.84 in SSwo and sialadenitis controls, respectively). Analysis of 14 sequential paired samples from SS patients before and on lymphoma diagnosis revealed that miR200b-5p levels were reduced long before clinical onset of lymphoma and did not significantly change upon transition to lymphoma. They also correlated with several clinical, laboratory and histological features indicative of adverse outcome and lymphoma development, as well as with worst lymphoma prognosis. Furthermore, ROC analysis revealed that strongly discriminated SSpL and SSL patients from SSwo with AUC-values 0.863 and 0.986 (p<0.0001), respectively, and cut-off values 0.4156 (sensitivity=0.765, specificity=0.926) and 0.3164 (sensitivity=0.952, specificity=1), respectively. Kaplan-Meier analysis of patients split into two groups according to miR200b-5p expression levels of 0.4156 (as defined by the specificity-sensitivity analysis) revealed that patients with miR200b-5p levels lower/equal to 0.4156 had a 4.8-fold (HR:4.81, 95%-CI:3.15-6.47, p<0.0001) higher risk to develop lymphoma compared to patients with miR200b-5p levels >0.4156.
Conclusions. These findings support that miR200b-5p levels in MSGs represent a novel predictive, and possibly pathogenetic mechanism-related, factor for the development of SS-associated NHL, since its expression is impaired years before lymphoma clinical onset.

Keywords: miRNAs, lymphoma, minor salivary glands.

OC9:3

SCORING SYSTEMS IN ULTRASOUND OF SALIVARY GLANDS IN SJÖGREN SYNDROME - A VIEW OVER TIME

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Objective. To standardize the assessment of B mode US of salivary glands (SG), different semi-quantitative scores were proposed. Our objective is to apply and compare 9 ultrasonographic (US) semi-quatitative scoring systems in B mode scanning of salivary glands in Sjögren Syndrome.
Design and Method. A research using keywords "salivary glands", "ultrasonograpy", "Sjögren Syndrome", "semi-quantitative score" in Medline/Pubmed was performed. There was a selection of most relevant articles. There were not considered relevant publications with impact factor <1. We performed the examination on SG in B mode US and applied these scores (De Vita, Niemela, Hocevar, Salaffi, Yukinori, Cornec,Theander) to our patients (primary and secondary SS).
Results. Eighty four SG in patients diagnosed with primary and secondary (57.15%) SS were assessed. In the group of patients with SSA/SSB presence (85.7%), mean score was De Vita 1.78±1.21, Niemela 2.56±2.17, Hocevar and Wernicke 2.39±2.14, Salaffi 2.83±2.52, Yukinori 2.39±2.14, Milic 3.39±2.14, Cornec 1.78±1.215, Theander 1.28±0.752. Schirmer test and the need for using the artificial tears was correlated to SG alterations in scoring systems proposed by Niemela (r 0.465, $p<0.05$) and Salaffi (r 0.496, $p<0.02$). All scoring systems were strongly correlated between them ($r>0.8$, $p<0.01$).
Conclusions. Inhomogeneity of parenchyma was considered in all scoring systems. Others considered relevant glandular dimension and margins regularity. There was no difference between the scoring systems. Xeroftalmia valided through Schirmer test is correlated to SG parenchymal alterations. Our data is an update about semiquantitative scoring systems in US of SG in Sjögren Syndrome.

Keywords: ultrasound, salivary glands, semiquantitative scoring.

OC9:4

ULTRASONOGRAPHIC SCORING OF THE MAJOR SALIVARY GLANDS: IS THERE A RELATIONSHIP WITH DISEASE ACTIVITY AND FUNCTIONAL STATUS OF GLANDS

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Objective. Ultrasonography (USG) of major salivary glands (SG-USG) is a non-invasive tool that has been used to evaluate salivary glands in primary and secondary Sjögren's syndrome (SjS). In this study, we aimed to investigate relation between the ultrasonographic scoring of major salivary glands and systemic disease activity or salivary secretion in patients with primary SjS.
Design and Method. Fifty-eight primary SjS patients (F/M:57/1) with the mean age of 53±11 fulfilling ACR-EULAR classification criteria (2002) were included. Disease activity indexes (Sjögren's Syndrome Patients Reported Index (ESSPRI), Visual Analogue Scale (VAS), EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI)] were recorded. Simultaneously, stimulated whole saliva production was obtained from all patients into a preweighed tube after chewing on a piece of paraffin for a total of 10 minutes. Major salivary glands (bilateral parotis and submandibular glands) were scored according to two different scoring systems [Hocevar A. (0-48) and Milic VD. (0-12)].
Results. Eighty percent of patients were positive for ANA and 48% were positive for Anti-Ro/La. ESSPRI-total and ESSDAI-total scores were 15.4±5.9 and 0.7±0.9 respectively. The mean score of VAS was 54±21. Thirty-three (57%) and 37 (64%) patients had the cut-off values of >17 (Hocevar) and >6 (Milic USG). The patients with the scores of >17 (Hocevar) were found to have higher scores of ESSPRI-total (17±6 vs 14±5, $p=0.037$) and lower sialometry (4.8±5.2 vs 7.4±3.5 ml, $p=0.005$). Scores of Hocevar and Milic-USG were negatively correlated with sialometry (r=-0.351, $p=0.018$ and r=-0.334, $p=0.025$). Hocevar and Milic USG scores were shown to be higher in patients with sialometry of <1.5 ml (n=7)(28±3 vs 18±10, $p=0.038$ and 8±1 vs 5±3, $p=0.004$) and anti-Ro positivity (n=24) (24±10 vs 14±8 and 7±3 vs 4±2, $p<0.001$).
Conclusions. Hocevar scoring system of major salivary glands was found to be related to patient reported activity in SjS. USG scores were associated with reduced saliva secretion and anti-Ro positivity. Evaluation of SG-USG might reflect disease activity and function of the salivary glands.

Keywords: Sjögren's syndrome, ultrasonography.

OC9:5

SJÖGREN SYNDROME: EVALUATION OF THE DISEASE ACTIVITY USING THE ESSDAI IN 70 PATIENTS

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Objective. Primary Sjögren Syndrome (PSS) is a chronic systemic inflammatory disease characterized by lymphocytic infiltration of the exocrine glands. The main manifestations are xerostomia and xerophthalmia. However, its clinical spectrum ranges from local involvement of exocrine glands to a wide range of organ and system involvement. As in other diseases of the connective tissue also for SSP, instruments for assessing disease activity have been developed. Since 2009 the ESSDAI, a validated instrument, composed of 12 domains, has been used as Gold Standard for evaluation of disease activity in this pathology. This study aimed to analyze the demographic characteristics, clinical spectrum, therapeutics and to evaluate the disease activity of patients with SSP, followed in a Rheumatology Service.
Design and Method. We obtained data from clinical records and discharge letters of patients followed in our service with PSS according to the classification criteria of the American-European Consensus (AECG) of 2002. The information collected included demographic data, clinical and serological manifestations, immunosuppressive therapy and disease activity, applying ESSDAI.
Results. The study included 70 patients who met the 2002 AECG criteria, 1 of whom was male and 69 were female. The mean age was 56.49 years ± 13.20 DP. The most frequently observed systemic manifestations were lymphopenia (37.1%), arthritis (35.7%), neutropenia (20.0%), anemia (14.3%), thrombocytopenia (10.0%), livedo reticularis (4.5%), interstitial pulmonary disease (3.0%), interstitial nephritis (3.0%) and autoimmune hepatitis (2.9%).
As an immunosuppressive therapy, 22 patients were under Hydroxyloquine, 17 with cortocosteoids, 3 with Methotrexate, 2 with Mycophenolate Mofetil, 2 with Azathioprine and 1 with Dapsone. Most of the patients (55.7%) had no disease activity (ESSDAI=0), 32.9% presented with mild activity (ESSDAI=1-4), 10.0% with moderate activity (ESSDAI=5-13) and 1.4% with high activity (ESSDAI>14).
Conclusions. PSS has a wide variety of presentations, ranging from the local involvement of exocrine glands to the systemic, extraglandular involvement of multiple organs, with variable prognosis. The application of ESSDAI, in the daily clinical practice allows an standardized assessment of the disease activity and facilitates the follow-up of these patients by providing a set of evaluation parameters, contributing for compliance in clinical attitudes and decisions among physicians.

Keywords: Sjögren syndrome, essdai, disease activity.

OC9:6

CLINICAL, BIOLOGICAL AND IMMUNOLOGICAL FEATURES OF SJÖGREN SYNDROME: A RETROSPECTIVE MONOCENTRIC TUNISIAN COHORT

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Objective. Sjögren syndrome (SjS) is an autoimmune disease (AID) characterized with sicca syndrome. It can be primary (PSjD) or secondary (SSjD) associated with another AID. We aimed to describe clinical, biological and immunological features of SjS
Design and Method. A retrospective descriptive study of patients with SjS diagnosed according to the American European Consensus Criteria, followed in the Internal Medicine Department of Fattouma Bourguiba University Hospital between 2002 and 2016.
Results. There were 83 patients with SjS. SSJS was diagnosed in 45.8% of cases. Mean age was 50.37 years with sexe ratio F/M= 9.3. history of AID was found in 10.8% of patients with history of SjS in 1.2%. clinical manifestations were : xerophtalmia (98.8%) confirmed with Break Up Test in 76.5% and Shirmer test in 25.9%, xerostomia (100%), pulmonary involvement (66.3%), arterial involvement (50.6%), neurologic manifestations (32.5%), renal (4.8%), psychiatric (2.4%) and cardiac (3.6%). Biological findings were: accelerated sedimentation rate (70%), high C- reactive protein (60.2%) and hyper gammaglobulinemia (56.6%). Anti Nuclear antibodies were positive in 53% of patients as following: anti SSA in 47%, anti SSB in 57.8%, anti DNA in 6%, anti SM in 3.6% and rheumatoid factor in 10.8%. Associated AID were rheumatoid arthritis in 33.2%, systemic lupus erythematosus in 26.5%, systemic sclerosis in 6.7%, myositis in 2.2% and Hashimoto thyroiditis in 53.2%. Lymphomatic transformation was diagnosed in 2 cases.

Conclusions. SjS is a connective tissue disease characterized with glandular and extra glandular manifestations. The latter need thorough investigations as they hamper the prognosis of the disease

Keywords: Sjögren syndrome, sicca syndrome, clinical manifestations.

09 – PATIENT SESSION: Balneotherapy explained

PS4:1

BALNEOTHERAPY EXPLAINED

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Objective. Balneotherapy means the use of natural mineral waters, natural peloids, which are muds, and other natural resources of different gases for medical purposes: prevention, treatment and rehabilitation. It is an ancient, traditional treatment modality used for mainly musculoskeletal disorders, but gynaecological, and dermatological conditions and vascular diseases too. Main regions being the south of Europe, and the east countries. Most of the articles have been published by French, Italian, Hungarian, Turkish, Japanese and Israelian authors; namely in these countries balnoetherapy is an accepted form of treatment.
Design and Method. Although the mechanism of action of balneotherapy in still not clear, its efficacy seems to be proven by recent RTC studies, reviews and metaanalyses. Spa therapy may have beneficial effects on muscle tone, joint mobility and pain intensity. As for the chemical effect, it was presumed that most mineral ingredients would be absorbed through the skin, which is an active immune organ and may play an important role in the mechanism, but to date this has not been confirmed. The new studies confirmed the potential effect of balneotherapy on the immune system, especially by using in sulphurous spa waters.
Results. Until now the main objection against balneotherapy was the lack of scientific evidence. This fact was indeed true for several years, but nowadays it can be easy to deny. If somebody searches in the medical database, he or she can find more and more evidence (including reviews and metaanalysis) that proves the effect of balneotherapy in some locomotor (especially in OA, which has now been entered into guidelines for OA therapy), and other diseases (for instance dermatological, gynaecological and vascular diseases, cancer rehabilitation). In spite of the growing number of evidence there are also some problems (limitation) in balneology, since most of these studies included heterogeneous patient populations, and the type, intensity, and duration of treatments, the methods used, and the time of assessments were not uniform.
Conclusions. Balneotherapy is not a new Panacea, which will heal all forms of diseases. Nowadays, on the basis of exisiting evidence, this kind of therapy is to be considered more than an alternative or complimentary therapy; it has a place among the non-pharmocological interventions.

Keywords: balneotherapy, mechanism, evidence based medicine.

PS4:2

PATIENT SESSION: BALNEOTHERAPY EXPLAINED

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Over the last three decades there has been a resurge in the use of medical therapies that are not considered mainstream/conventional Western medicine.
Balneotherapy (BT) is one of the most commonly used non-pharmacological approaches for different rheumatic diseases (RDs) in many European countries, as well as in Turkey, Israel and Japan. BT is classified under the label of traditional medicine (TRM) as clearly specified in WHO's (WHO, *General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine available on line at http://whqlibdoc.who.int/hq/2000/WHO_EDM_TRM_2000)* and it is considered as a complementary medicine. The term of "complementary" generally refers to using a non-conventional approach **together with** mainstream Western medicine.
The words of Balneotherapy, Hydrotherapy (HT) and Spa therapy are frequently confused and tend to be used interchangeably. However, HT generally employs normal tap water for medical treatment; BT traditionally involves immersion in mineral and/or thermal waters from natural springs, or treatment with mud. BT is usually practiced in health resorts with their special therapeutic atmosphere as part of a complex therapy program, which is why the term is often used synonymously for spa therapy. Spa therapy employs a number of different treatment modalities, including HT and BT, often combined with massage, exercise, physical therapy and/or rehabilitation.
The precise mechanisms by which BT alleviates symptoms in RMDs are not fully understood; the net benefit probably is the result of a combination of mechanical (hydrostatic force), thermal (temperature of mineral water) and chemical (chemical composition of mineral water or mud) effects. Thermal stress alleviates pain and decrease muscle tension, increases the secretion of ACTH, cortisol, prolactin, growth hormone and β-endorphin. Mud-bath therapy decrease serum levels of many important factors which are involved in inflammation and in cartilage degradation. Furthermore, it has been also shown a positive action of mineral waters on the oxidant/antioxidant system.
Various studies support the beneficial effects on pain, function and quality of life of BT in various RDs and in particular, in lower limb of osteoarthritis, chronic low-back pain, fibromyalgia syndrome, ankylosing spondylitis and psoriatic arthritis. On the contrary, doubts persisting about the use of BT in rheumatoid arthritis. New evidence demonstrated a significant reduction in analgesic consumption (acetaminophen and non steroidal inflammatory drugs) after BT; this is particularly important, considering the toxicity of these drugs, as well as their cost. Surprisingly, the improvement induced by BT lasts over time, until 3–6 months after the treatment.
Finally, tolerability of BT seemed to be good, with light and transitory side effects also in patients who presented different co-morbidities.