

THU0118 WHAT IS THE ROLE OF STEROIDS IN INDUCING DIABETES MELLITUS IN PATIENTS WITH RHEUMATOID ARTHRITIS? AN OBSERVATIONAL COHORT STUDY

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Background: Patients with Rheumatoid Arthritis (RA) are at increased risk of Diabetes Mellitus (DM) probably due to immune system activation or RA treatment with steroids.[1] However the pathology of DM in RA is not fully understood.

Objectives: To define the prevalence of DM in our RA patients population. Furthermore, to clarify the role of steroid treatment to induce DM in the RA patients.

Methods: All patients with diagnosis of RA who were registered in Danish Danbio Registry at time of study, Nov 2016, were included. To find the concurrent DM, patients' medical records including past medical history and lab tests (Hemoglobin A1c and Blood Sugar) were reviewed. In addition, year of DM as well as RA diagnoses were extracted from Fyns Diabetes Database and Danbio respectively to the extent that data were available. Patients' drug histories were searched for information about steroid treatment if diagnosis of RA was made prior to diagnosis of DM.

Results: Of 1035 patients with diagnosis of RA, 104 (10%) patients had DM. Of 104 RA patients with DM, data regarding the year of diagnosis for both RA and DM was found in 55 patients which of them 15 patients were diagnosed with RA before DM, one patient was diagnosed with both DM and RA at the same year and 39 patients were diagnosed with RA after DM. However, only one patient, of those who were firstly diagnosed with RA, was prescribed prednisolone during the time period between diagnoses of RA and thereafter DM. Of 15 patients with prior diagnosis of RA to DM, 13 patients were diagnosed according to 1987 classification criteria (Old) for RA and 2 patients were diagnosed according to 2010 classification criteria (New). Out of 39 patients where DM was diagnosed before RA, 10 patients was diagnosed based on the old criteria and 29 patients was diagnosed based on the new RA criteria [Fig 1A and 1B]. Patients with firstly diagnosed DM were more often diagnosed according to the new RA criteria and, on the contrary, patients with latterly diagnosed DM were more often diagnosed with old RA criteria ($p < 0.001$).

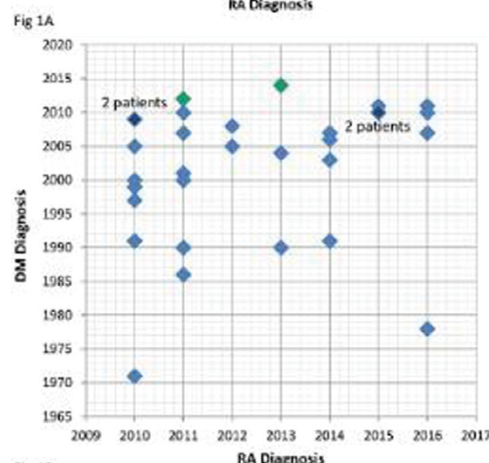
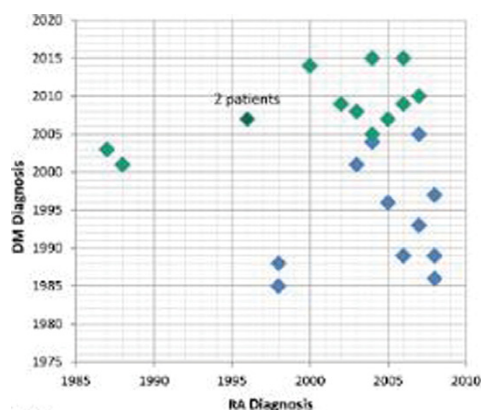


Figure 1A: In 13 Rheumatoid Arthritis (RA) patients who were diagnosed according to 1987 classification criteria for RA, diagnosis of RA was made earlier than Diabetes Mellitus and **Figure 1B:** In 2 Rheumatoid Arthritis (RA) patients who were diagnosed according to 2010 classification criteria for RA, diagnosis of RA was made earlier than Diabetes Mellitus.

Conclusions: The prevalence of DM in this RA population (10%) was about twice of Danish population (5.7%). The role of steroid treatment in which to what extent

increases the risk of DM is not clear, however in this study it was negligible, why we propose that the pathology of DM in RA patients most importantly deals with the role of immune system activation namely Tumor Necrosis Factor alpha and not the treatment modality i.e. steroids.

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THU0119 ASSESSMENT OF RHEUMATOID CACHEXIA AND ITS ASSOCIATION WITH CLINICAL, FUNCTIONAL AND THERAPEUTIC OUTCOMES

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Background: Rheumatoid arthritis (RA) is a chronic and inflammatory disease that besides articular symptoms leads to loss of muscle mass in presence of stable or increased fat mass (FM), condition defined as rheumatoid cachexia (RC). RC is associated with a worse prognosis, but it is still overlooked in clinical practice.

Objectives: To evaluate the prevalence of rheumatoid cachexia (RC) in patients with rheumatoid arthritis (RA) and determine its correlation with the features of RA, the level of physical activity and with the current therapy.

Methods: Ninety one RA patients in a cross-sectional study underwent total body dual-energy x-ray absorptiometry (DXA) for measurement of total and regional fat mass index (FMI; Kg/m²), lean mass index (LMI; Kg/m²), bone mineral content (BMC; Kg/m²) and fat free mass index (FFMI; Kg/m²) to assess the prevalence of RC. The associations of measures of body composition with RA features - age, diagnosis time, Health Assessment Questionnaire (HAQ), Disease Activity Score in 28 joints (DAS 28), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) -, level of physical activity (measured by International Physical Activity Questionnaire - IPAQ) and current therapy were explored.

Results: Mean age was 56.8±7.3, disease duration 9 years (3 – 18), DAS28 3.65±1.32, HAQ 1.12 (0.25 – 1.87) and use duration of biological agents was 25 months (17.8 – 52.5). 17% of the patients had FFMI below the 10th percentile and FMI above the 25th percentile of a reference population and 33% of the patients had FFMI below the 25th percentile and FMI above the 50th percentile, condition known as RC, according to the more recently used definitions. FFMI correlated negatively only with age ($r = -0.219$; $p = 0.037$) and disease duration ($r_s = -0.214$; $p = 0.042$). FMI correlated positively with CRP ($r_s = 0.229$; $p = 0.029$), ESR ($r_s = 0.235$; $p = 0.025$), DAS 28 ($r_s = 0.273$; $p = 0.009$) and HAQ ($r_s = 0.297$; $p = 0.004$). Among patients under biologics, 3.8% (n=1) had RC versus 23% (n=15) of those not taking biologics ($p = 0.033$), according to the stricter definition.

Conclusions: The prevalence of RC was considerable and deserves additional research. Besides that, patients under biological therapy had lower prevalence of RC, suggesting a protective effect of biological agents.

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THU0120 PREVALENCE OF CHRONIC KIDNEY DISEASE IN RHEUMATOID ARTHRITIS PATIENTS AND ITS ASSOCIATION WITH MULTIMORBIDITY

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Background: RA pts commonly present with multiple concurrent chronic disease. The great importance is attached to cardiovascular diseases due to their proven association with high frequency of morbidity and death. Much attention has been paid to the potential role of high-grade systemic inflammation and classical modifiable CVD risk factors – such as hypertension, dyslipidaemia, insulin resistance/metabolic syndrome, obesity, physical inactivity and smoking. A recent meta-analysis has shown that renal impairment is a strong independent cardiovascular risk factor in the general population [1].

Objectives: To assess the prevalence and associations of CKD in RA pts (ACR/EULAR 2010y.) and relate with pts multimorbid background, RA activity and duration.

Methods: 209 RA pts (F-70,6%, mean age 67,0±11,3y), admitted to rheumatology division from 1999 to 2015, were included into analysis. RA duration was 19

[6;93] mo, average disease activity (DAS28) 5.2 ± 1.7 . CKD was defined as the presence of markers of renal impairment (proteinuria $\geq 1+$, hematuria $\geq 2+$ or leucocyturia $\geq 2+$) and/or eGFR < 60 ml/min/1.73m² (using CKD-EPI formula) persistent beyond 3 months. The extent of multi-morbid environment was rated using Cumulative Illness Rating Score (CIRS) [2]. CIRS was calculated using the 5 score scale (0–4) to assess 14 major organ systems of the body (0–56).

Results: The prevalence of CKD was 82,3% (172), and 30,1% (63) had eGFR < 60 ml/min/1.73m², and 50,2% pts had CKD stage 2. The range of proteinuria was 12,4%. In group of pts with CKD 3–5 stage the prevalence of arterial hypertension (AH) was 84%, ischemic heart disease (IHD) - 63,5%, diabetes militants 2 22%, oncology 12,7%. Mean CIRS value in RA pts was 15 [10;19] scores. The eGFR was independent of the RA duration ($r = -0,01$, $p = 0,86$) and RA activity ($r = 0,09$, $p = 0,17$). There was found the strongest correlation of eGFR with CIRS ($r = -0,61$, $p < 0,01$), age ($r = 0,58$; $p < 0,05$), AH ($r = -0,34$, $p < 0,01$), IHD ($r = -0,28$, $p < 0,05$), BMI ($r = -0,17$; $r = 0,35$), uric acid levels ($r = -0,37$), as well as with hemoglobin level ($r = 0,19$) and HAQ scores ($r = 0,31$; $r = 0,32$). No correlation was found between eGFR and oncology, gender, VAS score, and ESR, CRP, cholesterol ($p > 0,05$).

Conclusions: CKD is a serious condition associated with premature mortality, decreased quality of life, and increased health-care expenditures, but it doesn't consider as comorbid disorder of RA. The CKD prevalence is greater among aged RA pts than in general population and it has a stronger correlation with multimorbid burden than traditional factors. Compromised renal function, apart from the age, is of dominant importance in pts management issues, limiting the range of available effective therapies, thus, aggravating RA natural course on one side, and inducing and catalyzing the severity of dysmetabolic syndrome, AH and anemia – on the other.

References:

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THU0121 ULTRASOUND IN THE ASSESSMENT OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Carpal tunnel syndrome (CTS) is one of the most frequent extra-articular manifestations of rheumatoid arthritis (RA). Ultrasound (US) has proven to represent a reliable tool for the diagnosis of CTS [1]. However, its role in the diagnosis of CTS in patients with RA has been poorly investigated.

Objectives: The aim of this study is to evaluate the US findings at carpal tunnel level in a cohort of patients with RA, focusing on those with a clinical diagnosis of CTS.

Methods: Patients with RA fulfilling the ACR/EULAR 2010 classification criteria were consecutively enrolled. The diagnosis of CTS was made according to the American Academy of Neurology practice parameter for CTS [2]. The MSUS assessment was carried out using a MyLab Twice (Esaote SPA) US system working with a 18–22 MHz linear probe. The power Doppler (PD) frequency was set between 7.5 and 11.3 MHz. The following grey scale (GS) US parameters were assessed at the carpal tunnel level: cross-sectional area (CSA) of the median nerve at the carpal tunnel inlet (at the level of the pisiform and scaphoid bones), presence of flexor tenosynovitis and palmar radio-carpal synovitis (both in GS and PD), presence of crystal macro-aggregates and marked bone profile irregularities. The median nerve was considered enlarged if its CSA was more than 12 mm². We evaluated the presence of intra-neural PD signals at the carpal inlet and scored its entity (0=no PD signal, 1=one single vessel within median nerve, 2=two or three single or two confluent vessels and 3=more than three single or more than two confluent vessels). PD was considered "positive" if grade 1 or more was found.

Results: We included 40 RA patients. CTS was diagnosed in 19 out of 80 wrists (23.8%) and in 13 out of 40 RA patients (32.5%). Enlarged median nerve was found in 3 out of 19 wrists with CTS (15.8%) and in 6 out of 61 wrists without CTS (9.8%). Flexor tenosynovitis was found in 7 out of 19 wrists with CTS (36.8%) and in 5 out of 61 wrists without CTS (8.2%). Palmar radio-carpal synovitis was found in 2 out of 19 wrists with CTS (10.5%) and in 3 out of 61 wrists without CTS (4.9%). Crystal macro-aggregates were not detected in any of the scanned wrists. Marked bone profile irregularities were found in 2 out of 19 wrists with CTS (10.5%) and in 14 out of 61 wrists without CTS (23%). Positive intra-neural PD was found in 9 out of 19 wrists with CTS (47.4%) and in 9 out of 61 wrists without CTS (14.7%).

Conclusions: These preliminary results suggest that MSUS could be a useful tool in the diagnosis of CTS also in patients with RA. Intra-neural PD and flexor tenosynovitis were the most frequently MSUS abnormalities detected in RA patients with CTS. The inflammatory involvement of the tendinous and joint structures which are part of the carpal tunnel could lead to median nerve compression and CTS symptoms and should be considered in the MSUS assessment of CTS.

References:

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THU0122 QUANTITATIVE ASSESSMENT AND ANALYSIS OF HAND MUSCLE VOLUME

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by bone, cartilage and muscle loss. While bone and cartilage damage have been extensively studied in the past, the effects of RA on volume and composition of hand muscles have not yet been studied. This situation is surprising, since visible hand muscle atrophy is a hallmark of RA and quantification of muscle composition is of growing interest.

Objectives: Quantitative assessment of hand muscle volume and fat using MRI.

Methods: A random forest based method was used to segment hand muscle in T1 weighted MR scans of 76 RA patients (37 males, 26–87 years, mean 61 years). The segmentation procedure is fully automated but allows for manual corrections of wrongly segmented areas. Multimodal registration of the muscle segmentation masks to MR Dixon Fat Fraction images was used for fat quantification.

Outcome parameters were absolute hand and muscle volume (V_H^{abs} resp. V_M^{abs}), relative muscle volume $V_M^{rel} = V_M^{abs}/V_H^{abs}$ and absolute and relative fat content (V_F^{abs} resp. V_F^{rel}).

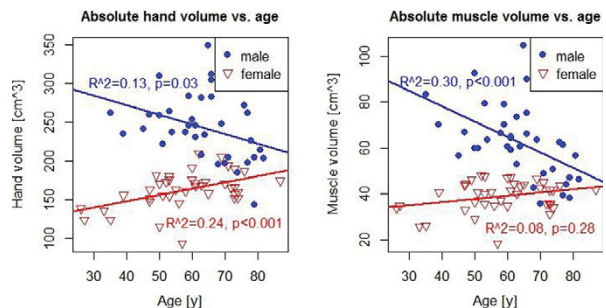
Student's t-tests were performed for gender discrimination. Linear regression was used to model age dependency. Further a multivariate regression was used to model dependence on predictors BMI, RA disease duration, DMARD treatment duration, HAQ, DAS28, RF, ESR and CRP after age adjustment. Dixon sequences were not available for all patients, therefore fat analysis could only be done in 17 females.

Results: V_H^{abs} in males was significantly higher than in females ($p < 0.001$, means: 63 cm³ vs. 29 cm³). Similar results were observed for V_H^{abs} ($p < 0.001$, means: 243 cm³ vs. 163 cm³) and V_M^{rel} ($p = 0.02$, means: 0.256 vs. 0.239).

The table shows the results of the linear regression analysis for significant predictors of males and females, respectively. The figure shows age dependence of V_M^{abs} and V_H^{abs} .

	Age	BMI (age adj.)	Disease duration (age adj.)
Males			
V_M^{abs}	$p < 0.001$, $R^2 = 0.25$	$p < 0.001$, $R^2 = 0.61$	ns.
V_H^{abs}	$p = 0.03$, $R^2 = 0.13$	$p < 0.001$, $R^2 = 0.50$	ns.
V_M^{rel}	$p < 0.001$, $R^2 = 0.30$	$p = 0.04$, $R^2 = 0.35$	$p = 0.02$, $R^2 = 0.36$
Females			
V_M^{abs}	ns.	ns.	$p = 0.07$, $R^2 = 0.16$
V_H^{abs}	$p < 0.001$, $R^2 = 0.24$	ns.	ns.
V_M^{rel}	ns.	ns.	$p = 0.06$, $R^2 = 0.12$

V_H^{abs} and V_F^{rel} showed no dependence on age or disease duration. V_F^{abs} but not V_F^{rel} was highly correlated with V_M^{abs} and V_H^{abs} (both: $p < 0.001$, $R^2 = 0.75$). V_F^{rel} was positively correlated with BMI ($p = 0.03$, $R^2 = 0.32$), a weaker but not significant effect was observed for V_F^{abs} .



Conclusions: Results for muscle volume were highly sex specific. Males showed higher V_M^{abs} , V_H^{abs} and V_M^{rel} . Nevertheless V_M^{abs} and V_H^{abs} in males showed significant decrease with age while the opposite but weaker effects were observed in females. Relative fat volume depends on BMI but is independent of muscle volume.

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