THU0401

IMPACT OF BODY COMPOSITION MEASURES ON THE RESPONSE TO BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Data on the impact of body weight and body mass index (BMI) on the response to biological disease-modifying anti-rheumatic drugs (bDMARDs) in axial spondyloarthritis (axSpA) including ankylosing spondylitis (AS) are still contradictory. Data on the impact of different components of the body composition on the treatment response are lacking.

Objectives: To investigate the impact of body composition on the response to biological disease-modifying anti-rheumatic drugs (bDMARD) in patients with AS after 6 months of treatment.

Methods: Patients with AS (radiographic axSpA), fulfilling the modified New York criteria and starting a bDMARD therapy were recruited between 2015 and 2019 in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC-AS). All patients were required to be candidates for bDMARD therapy at baseline with high disease activity (BASDAI ≥ 4 and/or ASDAS ≥ 2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs. Disease activity measures (BASDAI, CRP, ASDAS), as well as body composition parameters were assessed at baseline and after 6 months of bDMARD treatment. Body composition was assessed by the bioelectrical impedance analysis (BIA). Weight, body mass index (BMI), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle mass value (SMM), visceral adipose tissue (VAT), total body water (TBW), and extracellular water (ECW) values were collected. The primary measure of the treatment response was ASDAS change at month 6 as compared to baseline.

Results: A total of 129 patients with AS were included in this cohort. BIA was performed in 77 patients. There were 71.4% males, and 85.7% were HLA-B27 positive. At baseline, BASDAI was 5.4 ± 1.4 , CRP was 12.8 ± 16.5 mg/L, and ASDAS -3.0 ± 1.0 . The baseline BMI was 25.0 ± 4.3 kg/m². A total of 75 patients were treated with TNFi, 2 patients received an IL-17 inhibitor.

A higher BMI at baseline was associated with a worse response to bDMARD therapy that was attributable to both, the fat mass as reflected by FMI and to the fat-free mass reflected by FFMI, but not to SMM or VAT or water components – Table. This effect was independent of age, sex, symptom duration, HLA-B27 status and ASDAS at baseline.

Conclusion: Both fat mass and fat free mass have an impact on the response to bDMARDs after 6 months of treatment in patients with AS. Interestingly, skeletal muscle mass, visceral fat as well as water components showed no association with treatment response.

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THU0402

SERUM MARKERS OF BONE RESORPTION, FORMATION, AND MINERALIZATION DURING 8 YEARS OF TNF- α BLOCKING THERAPY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease, characterized by both excessive bone formation and bone loss. The bone turnover marker (BTM) bone-specific alkaline phosphatase (BALP) plays a central role in bone mineralization. Our previous study demonstrated that 3 years of TNF- α blocking therapy results in a significant increase in BALP.¹ However, longer follow-up is needed to investigate whether BALP stays elevated during TNF- α blocking therapy and also to explore the course of other BTM, osteocalcin (OC), procollagen type 1 N-terminal peptide (PINP) and serum type 1 collagen C-telopeptide (sCTX) in AS.

Objectives: To evaluate serum markers of bone resorption, formation, and mineralization during 8 years of TNF- α blocking therapy in AS patients.

Methods: Included were consecutive AS outpatients from the University Medical Center Groningen (UMCG) attending the Groningen-Leeuwarden Axial SpA (GLAS) cohort and who were treated with a maximum of 2 TNF- α blockers for at least 8 years. Patients were excluded when they used bisphosphonates at baseline or during follow-up. Data for a specific visit was coded as missing when patients either had experienced a fracture or received systemic corticosteroids within 1 year of that particular visit. Clinical and laboratory measurements were performed at baseline (before start of TNF- α blocking therapy), 3 and 6 months as well as 1, 2, 4, 6 and 8 years. Markers of bone formation OC, PINP and BALP, and marker of bone resorption sCTX were measured in serum. Z-scores of BTM were calculated using matched 10-years-cohorts of a Dutch reference group to correct for the normal influence that age and gender have on bone turnover. Serum levels of 25-hydroxyvitamin D (25(OH)D3) were assessed yearly. Generalized estimating equations were used to analyze BTM Z-scores over time within patients. Simple contrast was used to compare follow-up visits to baseline. P-values < 0.05 were considered statistically significant.

Results: In total, 37 AS patients were analyzed; 62% were male, 86% HLA-B27+, mean age was 38.6 ± 10.4 years, median symptom duration 14 years (IQR 10-25), median CRP 13 mg/L (IQR 6-25), and 30% had low vitamin 25(OH)D3 status (< 50) at baseline. 35% of patients switched to a second TNF- α inhibitor during follow-up. ASDAS_{CRP} improved significantly during treatment, from mean 3.8 ± 0.9 at baseline to 1.9 ± 0.9 after 8 years of follow-up ($P < 0.001$). 25(OH)D3 levels were stable at group level, median 58 nmol/L (IQR 45-70) at baseline and 60 nmol/L (IQR 50-70) after 8 years. Bone regulation marker OC Z-score was

Table. Univariable and multivariable linear regression analysis of the association between response to bDMARD treatment (change in the ASDAS score after 6 months) and body composition parameters in patients with AS (n=77)

Variables	Univariable	Multivariable analysis*						
	Analysis B (95%CI)	Model 1 B (95%CI)	Model 2 B (95%CI)	Model 3 B (95%CI)	Model 4 B (95%CI)	Model 5 B (95%CI)	Model 6 B (95%CI)	Model 7 B (95%CI)
BMI, kg/m ²	-0.016 (-0.063; 0.031)	-0.043 (-0.079; -0.006)	-	-	-	-	-	-
FMI, kg/m ²	-0.024 (-0.103; 0.054)	-	-0.065 (-0.128; -0.003)	-	-	-	-	-
FFMI, kg/m ²	-0.010 (-0.133; 0.112)	-	-	-0.138 (-0.253; -0.022)	-	-	-	-
SMM, kg	0.026 (-0.020; -0.071)	-	-	-	0.012 (-0.044; 0.069)	-	-	-
VAT, liters	0.069 (-0.099; 0.238)	-	-	-	-	-0.095 (-0.248; 0.057)	-	-
TBW, liters	0.020 (-0.016; 0.056)	-	-	-	-	-	0.007 (-0.036; 0.051)	-
ECW, liters	0.054 (-0.43; 0.150)	-	-	-	-	-	-	0.005 (-0.98; 0.107)

*Adjusted for age, sex, HLA-B27 status, symptom duration, and ASDAS at baseline.

BMI: Body Mass Index; FMI: Fat Mass Index; SMM: Skeletal Muscle mass; VAT: Visceral Adipose Tissue; AS: ankylosing spondylitis; bDMARD: biological disease-modifying anti-rheumatic drug; CI: 95% confidence interval.

found to be significantly increased only after 3 months of TNF- α blocking therapy compared to baseline. No significant changes during follow-up were found for collagen resorption marker sCTX Z-score. Collagen formation marker PINP Z-score was significantly increased after 3 and 6 months as well as 2 years of TNF- α blocking therapy. Bone mineralization marker BALP Z-score was significantly increased at all time points up to and including 2 years and returned to baseline levels during 4 to 8 years of TNF- α blocking therapy (Figure 1).

Conclusion: In this subgroup of AS patients with established and active disease responding to TNF- α blocking therapy, we observed that the bone turnover balance favored bone formation during the first years of TNF- α blocking therapy, which corresponds to previously reported improvement in bone mineral density, especially at the lumbar spine.¹ New finding of our study is that after 8 years of treatment, markers of bone resorption, formation, and mineralization were all comparable to baseline values.

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Figure 1. The effect of 8 years of TNF- α blocking therapy on bone formation markers OC (A), sCTX (B), PINP (C) and BALP (D) in patients with AS (n=37). Z-scores were calculated to correct for the effect of age and gender on bone turnover. Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, • indicates mean; whiskers indicate 1.5 times interquartile distances; * indicate outliers. * indicate p-value of <0.05 and ** indicate p-value of <0.01.

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THU0403 THE EFFECT OF SPINAL STABILIZATION EXERCISES ON SPINAL CURVES DIAGNOSED WITH ANKYLOSING SPONDYLITIS

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Background: Postural deformities can cause changes in spinal curvatures patients with ankylosing spondylitis. In these patients, preventive and therapeutic approaches are needed for spinal deformities (1). Positive effects of the spinal stabilization exercises are manifested in reducing pain, maintaining mobility, improving posture, increasing aerobic capacity and improving quality of life (2).

Objectives: The aim of this study is to investigate the effect of stabilization exercises on spinal curvatures in s ankylosing spondylitis patients.

Methods: Twenty-eight ankylosing spondylitis patients (25 females, 3 males) with a mean age of 30.87 $\pm$ 9.13 years were included in the stabilization exercises program. The patients performed spinal stabilization exercises two days a week for six weeks. Stabilization training includes training of deep muscles providing diaphragmatic breathing, neutral spine position control training and local motor control, and motor control training of global muscles, dynamic stabilization exercises and

strengthening training. Thoracic kyphosis and lumbar lordosis curvature of patients in an upright position were evaluated with Spinal Mouse (SM) device before and after therapy program. The SM device is a reliable, valid, safe, quick method that can be used in the clinics and researches of the adults with no side effects.

Results: At the end of 6 weeks of treatment, there was a decrease in the total curvature degree of the thoracic vertebrae in the sagittal axis ($p=0.026$). No significant difference was found in the lumbar region ($p=0.109$).

Table 1. Differences of Total Curve Degrees

	Pre-Exercises Program Mean $\pm$ SD	Post-Exercises Program Mean $\pm$ SD	z	p
Thoracic Total Curve Degrees	43.50 $\pm$ 8.11	42.57 $\pm$ 7.70	-2.232	*0.026
Lumbar Total Curve Degrees	-26.42 $\pm$ 8.46	-23.77 $\pm$ 7.15	-1.604	0.109

*p<0.05, SD: Standart Deviation

Conclusion: Stabilization exercises are effective in reducing thoracic kyphosis in patients with ankylosing spondylitis patients. The use of these exercises in treatment programs will contribute significantly to improving spinal alignment and preventing postural deformities.

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Crystal diseases, metabolic bone diseases other than osteoporosis

THU0404 INFLUENCE OF URATE TRANSPORTOSOME FOR HYPERURICEMIA AND GOUT

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Background: Gouty arthritis, caused by a persistent increase in serum uric acid level, can be caused by underexcretion of uric acid by uric transporters; however, the effects of allelic variants of urate transportosome are yet to be fully determined.

Objectives: In this study we investigated the effects of 10 genes of urate transportosome in a cohort of patients with primary hyperuricemia and gout.

Methods: The cohort consisted of 114 hyperuricemic individuals; 207 gout patients; and 274 normouricemic controls.

Results: We identified 39 non-synonymous allelic variants in the 10 genes of urate transportosome in hyperuricemia/gout cohort. For 22 variants, a European MAF <0.0001 is documented. From the total of 39 identified variants we selected 23 variants for functional characterization based on a) finding of a newly identified variant, b) MAF variant was significantly different in the group of patients with hyperuricemia/gout, c) with high probability, in silico predictions showed devastating influence of variant on protein function.

Conclusion: Although further analyzes are needed to elucidate the contribution of urate transportosome to urate homeostasis, our results clearly show that ABCG2 transporter analysis has significant clinical potential. Of the identified non-synonymous allelic variants of the urate transportosome, rs2231142 (p.Q141K) in the ABCG2 gene, proved to be the most clinically significant on the age onset ($P < 0.0002$, Kruskal-Wallis test).

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