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SAT0122

EXPERIENCE OF MUSCULOSKELETAL ULTRASOUND SCANNING IMPROVES SKILL OF PHYSICAL EXAMINATION IN ASSESSMENT OF SYNOVITIS

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Background: Assessment of presence/absence of joint swelling is one of the most essential factors in the management of rheumatoid arthritis (RA) patients. Although physical examination by touch is the basic assessment, it often varies among physicians. In contrast, it has been reported that musculoskeletal ultrasound (US) assessment is more objective and sensitive than physical examination in detecting synovitis.

Objectives: We hypothesized accumulation of experience of physical examination by touch with checking results of simultaneous US assessment as right answers could improve the accuracy of physicians' physical examination by touch. This study aimed to compare the accuracy of physicians' physical examination by touch according to physicians' US experience when considering the results of US assessment as right answers.

Methods: Seventy RA patients who planned to take US in daily clinical practice were enrolled. Twenty three physicians affiliated with Department of Allergy and Clinical Immunology at Chiba University Hospital were also participated in this study. Written informed consent was obtained from all the patients and physicians. At first plural physicians touched wrists, metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints and assessed swelling/non-swelling ("Ph swelling/non-swelling") of the joints. Subsequently, US assessment was performed by another physician blinded to the results of physical examination. In this study, "US swelling" and "US non-swelling" were defined as gray-scale imaging score (GS) 2 and GS 1. The positive predictive value (PPV) of physical examination by touch was calculated ("Ph swelling" joint count/"US swelling" joint count). Negative predictive value (NPV) was also calculated ("Ph non-swelling" joint count/"US non-swelling" joint count). The associated factors for PPV and NPV were identified by the univariate and multivariate logistic regression analysis.

Results: The patients were median 65 years old with median 5 year history of RA. A majority of the patients was rheumatoid factor positive (59/70) and median DAS28-CRP was 2.63.

A total of 6116 joints per physician were evaluated by touch, and the numbers of "Ph swelling" and "Ph non-swelling" joints were 990 and 5126. A total of 1540 joints were examined by US, the numbers of "US swelling" and "US non-swelling" joints were 172 and 1368. Overall PPV and NPV were 51.7% and 88.3%.

Regarding PPV, multivariate analysis identified duration of physicians' attending to rheumatology clinic, wrists, tender joints, patients' gender, patients' age and Steinbrocker Stage as significant factors increasing the accuracy and patients' disease duration as a significant factor decreasing the accuracy. Regarding NPV, multivariate analysis identified duration of physicians' US experience and patients' disease duration as significant factors increasing the accuracy and wrists, tender joints, presence of osteophytes and DAS28-CRP as significant factors decreasing the accuracy.

Conclusions: Experience of US improved accuracy of physicians' physical examination by touch in non-swelling joints and prevented overestimation, while experience of attending to rheumatology clinic rather than US improved the accuracy in swelling joints.

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SAT0123

THE EFFECTS OF TRIMETHOPRIM-SULFAMETHOXAZOLE ON DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Some experimental models suggested bacterial infection, such as periodontal disease and gut microbiota, might be an inciting and aggravating factor in rheumatoid arthritis (RA)¹. Moreover, medications that have an antibacterial effect such as minocycline and sulfasalazine are used as DMARDs. However, the antibacterial effect itself on disease activity are unknown in patients with RA whereas trimethoprim-sulfamethoxazole (TMP-SMX) is often used for *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis because PCP is a prevalent and potentially life-threatening opportunistic infection among patients with RA, especially in Japan^{2,3}.

Objectives: To identify the effect of TMP-SMX on disease activity in patients with RA in a multi-center cohort study (ANSWER cohort study).

Methods: RA patients with a sampling interval of less than 1 year and at least two assessment of disease activity were enrolled. Disease activity was assessed using disease activity score 28-CRP (DAS28-CRP). Linear mixed effect models were used to evaluate the trajectories of disease activity in RA patients. Time from baseline, TMP-SMX administration, and their interaction were included as fixed effects while participant identification number and time from baseline were included as random factors. Age, sex, disease duration, RF, ACPA, HAQ, and DMARDs were included as covariates.

Results: A total of 49878 samples (mean sampling interval: 49 days) from 3255 patients was included. The median age at baseline was 64.0 years (interquartile range, 53.0 to 71.0 years) with 78.2 % of women (ACPA positivity, 79.2%; RF positivity, 70.8 %). The median DAS28-CRP was 2.83 with 33.8 % of patients taking TMP-SMX at baseline. Patients with taking TMP-SMX had a significantly but minimally better longitudinal trajectory on disease activity than patients without (-0.00012/month, $P=0.009$). This result was similar even when patients taking sulfasalazine were excluded from analysis.

Evolution of disease activity over time based on ST use

Conclusions: TMP-SMX has minimal impact on disease activity, and therefore clinical utility of TMP-SMX for controlling disease besides PCP prophylaxis is limited. These results did not support a theoretical effect of bacterial infection on

disease activity in RA, although the effect of the other antibiotics on disease activity should be examined.

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SAT0124

AORTIC STIFFNESS AND TIME TO WAVE REFLECTION ARE ASSOCIATED WITH LEFT VENTRICULAR DIASTOLIC DYSFUNCTION MEASURES IN RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) experience an increased frequency of heart failure with a preserved ejection fraction (HFpEF) (1). The treatment of HFpEF is currently suboptimal. Elucidation of the underlying pathophysiological mechanisms of HFpEF may provide potential targets for its management. Diastolic dysfunction often precedes the progression to HFpEF (2). Abnormalities in aortic function contribute to diastolic dysfunction in non-RA populations (3,4).

Objectives: The aim of this study was to determine whether impaired aortic function is associated with left ventricular diastolic dysfunction in RA.

Methods: Arterial function was determined by applanation tonometry using SphygmoCor software and left ventricular diastolic function was assessed by echocardiography in 176 patients with RA. Markers of arterial function included carotid femoral pulse wave velocity (PWV), central systolic and pulse pressure, pulse pressure amplification and the magnitude and timing of the forward and reflected waves. Markers of diastolic function included the ratio of early-to-late transmitral blood flow velocity (E/A), the ratio of E to the mean of the lateral and septal wall myocardial tissue lengthening at the mitral annulus (e')/(E/e') and the septal and lateral e'. Relationships of comprehensively evaluated arterial function with markers of LV diastolic function were determined in confounder adjusted multivariate regression models.

Results: The timing of the forward (Ft) and reflected (Rt) waves were each associated with E/A (Ft: partial $r=0.20$, $p=0.02$; Rt: partial $r=0.30$, $p=0.001$) and Rt was further associated with lateral e' (partial $r=0.36$, $p<0.0001$) and septal e' (partial $r=0.36$, $p<0.0001$); PWV was associated with E/e' (partial $r=0.18$; $p=0.03$). Reflected wave timing was associated with two indices of impaired relaxation (E/A<0.8: OR (95% CI)=0.51 (0.29-0.91), $p=0.01$; lateral e'<10: OR (95% CI)=0.43 (0.26-0.71), $p=0.001$); PWV was associated with an increased left ventricular filling pressure (E/e'>12: OR (95% CI)=1.58 (1.04-2.38), $p=0.03$).

Conclusions: Aortic stiffness and time to wave reflection are associated with increased filling pressure and impaired relaxation of the left ventricle, respectively. The development of diastolic dysfunction in RA may be partly mediated by changes in large artery function.

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SAT0125

THE IMPACT OF SELECTED COMORBIDITIES ON TREATMENT OUTCOME IN PATIENTS WITH RHEUMATOID ARTHRITIS: AN EXPLORATORY COHORT STUDY.

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Background: Patients with Rheumatoid Arthritis (RA) may present with various comorbidities resulting in worse treatment response.[1-2]

Objectives: To investigate the impact of selected comorbid diseases on RA outcome with the aim of Disease Activity Score in 28 joints-C-Reactive Protein (DAS28-CRP).

Methods: All our RA patients were included in this study. Patients' demographics, serology results and DAS28-CRP at the time of diagnosis and after 4 months of treatment initiation were collected. Patients' electronic hospital records were evaluated for a positive history of thyroid diseases, Diabetes Mellitus (DM), primary hyperparathyroidism, vitamin B12 deficiency and presence of other diagnosed autoimmune diseases.

Results: 1035 RA patients were included. 63.4% were female, mean of age 67.1 years, mean of disease duration 9.6 years, 58.6% rheumatoid factor positive and 51.3% anti-cyclic citrullinated peptide positive. The observed prevalence of thyroid diseases was 11.8%, DM 10.4%, primary hyperparathyroidism 2.8%, vitamin B12 deficiency 5.8%, and other diagnosed autoimmune diseases 1.6%. There were significant associations between presence of thyroid diseases and female gender ($p<0.001$); DM and greater age ($p<0.001$); primary hyperparathyroidism and longer disease duration ($p=0.002$); other diagnosed autoimmune diseases and antinuclear antibody positivity ($p<0.001$). RA patients with thyroid diseases ($p=0.001$) and other comorbid autoimmune diseases ($p<0.001$) had significantly poorer initial response to the RA treatment compared to patients with isolated RA. Univariate analyses revealed that age, presence of thyroid diseases, presence of other diagnosed autoimmune diseases and DAS28-CRP at the time of diagnosis were significantly associated with Δ DAS28-CRP. Additionally, multivariate analysis demonstrated that Δ DAS28-CRP deterioration was significantly correlated to the presence of thyroid diseases (unstandardized regression coefficient (standard error):-0.188(0.088), $p=0.030$) and presence of other diagnosed autoimmune diseases (-0.537(0.208), $p=0.010$). (table1)

Table 1. Univariate and multivariate analysis of risk factors for Δ DAS28-CRP.

	Variables	Univariate analysis	Multivariate analysis
Backward analysis	Gender	0.028 (0.066)	0.058 (0.056)
	Age	0.007 (0.002)**	- 0.003 (0.003)
IgM-rheumatoid factor	Disease duration	0.000 (0.003)	- 0.003 (0.003)
	Anti-cyclic citrullinated peptide antibody	-0.055 (0.065)	0.014 (0.068)
Anti-cyclic citrullinated peptide antibody	Antinuclear antibody	-0.098 (0.065)	-0.041 (0.068)
	Presence of Thyroid diseases	0.003 (0.086)	-0.042 (0.067)
0.160	Presence of Primary Hyperparathyroidism	-0.315 (0.098)**	-0.188 (0.088)*
	Presence of Diabetes Mellitus	0.059 (0.193)0.008 (0.159)	0.077 (0.104)-0.023 (0.086)

Presence of vitamin B12 deficiency0.102 (0.136)0.047 (0.112)Presence of other diagnosed autoimmune diseases-0.895 (0.249)**-0.537 (0.208)*-0.565 (0.204)*Thyroid stimulating hormone level0.013 (0.008)0.011 (0.007)DAS28-CRP at time of diagnosis0.724 (0.027)*0.711 (0.029)**0.715 (0.029)**P value <0.05, ** P value <0.005

Conclusions: RA patients are at increased risk of specific comorbidities with possible impact on the treatment outcome. The authors, therefore, recommend to do periodical assessment of comorbidities to diagnose concurrent comorbid diseases as early as possible.

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