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How do you sleep?

OP0361-HPR SLEEPING PROBLEMS AND ANXIETY IS ASSOCIATED TO CHRONIC MULTISITE MUSCULOSKELETAL PAIN IN SWEDISH HIGH SCHOOL STUDENTS

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Background: The relationship between chronic multisite musculoskeletal pain (CMP) and sleep is complex, where pain can lead to sleeping problems and lack of sleep can intensify the pain perception. Most previous studies relates to adults, but adolescents may also suffer from CMP, and there is a need for more knowledge regarding the relationships between CMP and sleeping problems, stress, anxiety, depression, and health status.

Objectives: To study background factors associated to CMP in first year Swedish high school students.

Methods: First year Swedish high school students (n=296) were invited to complete questionnaires on chronic pain (mannequin with 18 body regions), sleeping problems (Uppsala Sleep Inventory, four items scored from 1–5), stress (ELO questions, scored from 1–5), anxiety and depression (Hospital Anxiety and Depression Scale, scored from 0–21), health status (EQ-5D, scored from 0 to 1, worst to best) and physical activity (International Physical Activity Questionnaire, categorised into low, moderate and high levels). Stress and sleeping items were dichotomized into 1–3 points (best) vs 4–5 points (worst). Individuals scoring at least severe problems (4 points) at one or more sleeping items were classified as having severe sleeping problems. HADS were categorised as non-cases (0–7), possible^{7–10} and probable cases (11–21 points). Students were grouped as having CMP (pain present in ≥3 regions) or not (no chronic pain or chronic pain in 1–2 regions). Multiple logistic regression analyses (adjusted for sex) with CMP as dependent variable were performed in SPSS, version 24.

Results: 254 students (86% of total sample, 87 boys and 167 girls) with a mean age of 16.1 (SD 0.6) years participated in the study. CMP was present in 25 (9.8%) students with no differences between boys and girls (8.0% vs 10.8%; p=0.488). Having CMP was associated with reporting severe sleeping problems (OR 2.49, 95% CI: 1.06 to 5.81, p=0.035) with initiating sleep, maintaining sleep, early morning awakenings and/or not feeling restored after sleep in comparison to the other students. Students with CMP were more likely to be categorised as probable cases for anxiety (OR 3.06, 95% CI: 1.09 to 8.61, p=0.034), but there were no associations for possible cases for anxiety (OR 1.15, 95% CI: 0.38 to 3.51, p=0.800), possible cases (OR 2.03, 95% CI: 0.63 to 6.54), or probable cases for depression (OR 3.35, 95% CI: 0.33 to 33.83). There was a nearly significant association between stress and belonging to the CMP group (OR 2.31, 95% CI: 0.97 to 5.53, p=0.059). A higher self-reported health status was associated to a lower likelihood for CMP (OR 0.04, 95% CI: 0.01 to 0.27, p=0.001). Distribution of physical activity levels of low, moderate and high was not significantly associated to having CMP in comparison with not having it.

Conclusions: One in ten high school students fulfilled criteria for having chronic multisite musculoskeletal pain. CMP was associated to sleeping problems, anxiety, and a worse health status. The results from this study may be used by school health-care professionals in their preventive work to promote student's health.

Disclosure of Interest: None declared

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Stratifying connective tissue diseases

OP0362 NOVEL GENE VARIANTS ASSOCIATED WITH CARDIOVASCULAR DISEASE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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Background: Patients with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA) have increased risk of cardiovascular disease (CVD).

Objectives: We investigated whether single nucleotide polymorphisms (SNPs) at autoimmunity risk loci were associated with CVD in SLE and RA.

Methods: SLE patients (n=1045) were genotyped using the 200K Immunochip SNP array (Illumina). The allele frequency was compared between patients with and without different manifestations of CVD. Results were replicated in a second SLE cohort (n=1043) and in an RA cohort (n=824). We analysed publicly available genetic data from the general population, performed electrophoretic mobility shift assays and measured cytokine levels and occurrence of anti-phospholipid antibodies (aPLs).

Results: We identified two new putative risk loci associated with increased risk for CVD in two SLE populations, which remained after adjustment for traditional CVD risk factors. An *IL19* risk allele was associated with stroke/myocardial infarction in SLE (OR 2.3 (1.5–3.4), p=8.5×10⁻⁵) and RA (OR 2.8 (1.4–5.6), p=3.8×10⁻³), meta-analysis (OR 2.5 (2.0–2.9), p=3.5×10⁻⁷), but not in population controls. The *IL19* risk allele affected protein binding and SLE patients with the risk allele had increased levels of plasma-IL10 (p=0.004) and aPL (p=0.01). An *SRP54-AS1* risk allele was associated with stroke/transient ischaemic attack in SLE (OR 1.7 (1.3–2.2), p=2.5×10⁻⁵) but not in RA. The *SRP54-AS1* risk allele is an expression quantitative trait locus for four genes.

Conclusions: The *IL19* risk allele was associated with stroke/myocardial infarction in SLE and RA, but not in the general population, indicating that shared immune pathways may be involved in the CVD pathogenesis in inflammatory rheumatic diseases.

Disclosure of Interest: None declared

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OP0363 OPTIMISINGPRECISION MEDICINE BY USING GENETICS TO ASSIGN DIAGNOSTIC PRIOR PROBABILITIES TO PATIENTS WITH SYNOVITIS – PROOF OF PRINCIPLE

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Background: In patients with synovitis, the question is 'Which disease does this patient have?' However, traditional tests often only inform us about disease presence yes/no and disease discriminating symptoms often take a while to arise. Time independent information, such as genetics, might accelerate the diagnostic process. As increasing number of patients have genotyping data available in medical records prior to their visit, the question emerges: can genetic data facilitate disease differentiation in early disease?

Objectives: Proof of principle study to test the differentiating ability of genetic profiles in patients with synovitis.

Methods: We studied the most common rheumatologic diseases: rheumatoid and psoriatic arthritis, SLE, spondyloarthropathy and Gout. The population level

disease probability for each disease comprised a sex adjusted disease prevalence and a weighted genetic risk score comprised of risk SNPs' odds ratio from literature. Within case genetic probabilities (GProb) were obtained through normalisation of the population risk assuring a patient's total disease probability of 1. So, each patient got a probability for each disease. GProb was developed in a simulated dataset and tested in

- Validation dataset of 1,211 rheumatology cases identified with ICD codes from 62,512 patients
- Replication dataset of 248 rheumatology cases identified by chart-review from 15,047 patients
- Clinical setting of prospective selected patients that presented with synovitis at the rheumatology outpatient clinic (n=242). Here, GProb was calculated for the five diseases plus the category 'Other'.

Having multiple GProbs for each patient, we tested whether the GProbs referring to the patient's real disease were higher than those that referred to the other phenotypes.

We used multinomial logistic regression with the six diseases as the dependent variables to test the additive value of GProb on top of clinical information.

Results:

- There was a strong significant correlation between GProb and the disease status ($r=0.27$ $P<0.0001$) with an AUC of 0.68.
- We observed a higher correlation with disease status in the more precisely identified cases ($r=0.49$ $P<0.0001$) and a high AUC 0.82
- Also in a prospective setting, the GProb performed well ($P<0.0001$ AUC 0.74 figure 1) especially in ruling out diseases (table 1).

The clinical information alone explained 41% of the variance in the final diagnosis. Adding GProb significantly improved the predictive value (expl. variance increased to 51% $p=0.0008$).

Sensitivity analysis showed that the results were not driven by one disease.

Abstract OP0363 – Table 1 Performance of G-Prob in ruling out diseases in the prospective dataset (n=242)

Selection	% of total G-Probs	% of G-Prob that correctly rejected disease
G-Prob < 0.05	14%	97%
G-Prob < 0.20	70%	89%

Abstract OP0363 – Figure 1 Ability of GProb to differentiate six disease outcomes (RA, PsA, SLE, SpA, Gout, Other) in a prospective selection of patients with synovitis.

The graph depicts the mean GProb (with range) of each quintile of GProbs on the x-axis and the corresponding proportion of those GProbs that matched with the patient's real disease on the y-axis. The graph demonstrates that the genetic probability of the disease highly resembles the real disease risk. In case of a perfect test performance, the dots would lie exactly on the diagonal (dashed) line.

Conclusions: This study developed methodology for disease-discriminating tests.

In patients with synovitis, genetic data can facilitate decision making in early disease by ruling out and pointing towards the most likely phenotype. Seeing the increasing importance of an early diagnosis in patients with synovitis, genetics can be considered as part of a patient's medical history.

Additional prospective studies will further need to validate this proof of principle study.

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Work and rehabilitation – key priorities for people with RMDs

OP0364-PARE WORK STATUS AND WORK BARRIERS IN PATIENTS RECEIVING bDMARDs AS INFUSIONS IN RHEUMATOLOGY HOSPITAL CLINICS IN NORWAY. A CROSS-SECTIONAL STUDY

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Background: Preventing work disability is an important treatment goal for people with rheumatic diseases. New treatment modalities with introduction of bDMARDs have led to better control of disease activity, symptoms and improvement of functional capacity. Still, sick leave and forced retirement is common, and studies have shown that work status at start of therapy is a predictor of work ability later in the disease course.

Objectives: The objective of this study was to explore work status, concerns about future work capacity and work barriers in a group of patients receiving bDMARDs as infusions in rheumatology hospitals in Norway.

Methods: This is a cross-sectional study. In March and April 2017, patients at two rheumatology hospitals were invited to participate in a survey. Participation was voluntary with anonymous response. Information about background, disease, and start of bDMARD infusions was self-reported in a questionnaire. Further, respondents who were working or on sick leave (full- or part time), answered questions about work capacity and degree of concern about future work capacity on NRS-scales from 1–10 (10=best capacity and high degree of concern). They also scored their experienced barriers related to seven different topics selected from the Work Experience Survey-Rheumatic Conditions (WES-RC) on 5 point Likert scales (5=severe problems).

Results: Of 343 eligible patients, 317 responded (92%). Mean (SD) age were 52.3 (14.9) years, 81% were under 67 (age of retirement in Norway). The largest diagnostic groups were rheumatoid arthritis (47%) and spondylarthritis (26%). Mean (SD) disease duration was 13.8 (10.6) years. Half of the respondents aged <67 years reported reduced work ability, of these 27% were on sick leave and 23% were on disability pension. The proportion of patients on sick leave was highest among those who started with bDMARD infusions within the last 3 months (42.3%), and lowest in the group who had started 25 to 36 months earlier (21.4%). For disability pension the numbers were opposite, with the largest amount in the group that received treatment for more than 36 months (29.7%).

There were significant differences in ratings of work capacity and concerns about future work capacity among respondents working full time and those on sick-leave. Mean (SD) scores of work capacity were 8.0 (1.7) and 5.5 (3.0) ($p<0.001$) in full time workers and participants on sick-leave, respectively. Corresponding scores for concerns about future work capacity were 5.2 (2.5) and 7.0 (2.7), ($p<0.001$). Thirty percent of respondents in full-time work scored 7 or higher on degree of concern about future work capacity. Regardless of work status, 'physical work demands', 'mental work demands' and 'balance between work and private life' was rated as the most severe barriers for work ability.

Conclusions: This cross-sectional study shows that approximately half of the patients receiving bDMARD infusions at two hospitals in Norway report reduced work ability, and nearly one third was concerned about future work capacity. Early identification of patients who, despite optimal treatment, experience work barriers is important. Activity regulation, ergonomic advice and self-management strategies for managing work demands and imbalance between work and private life should be further tested.

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