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ASSOCIATION OF GENETIC MARKERS WITH CLINICAL CHARACTERISTICS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Rheumatoid arthritis (RA) is a multifactorial disease caused by environmental and hereditary factors. RA contributes to an increased risk of developing osteopenia and osteoporosis (OP), especially due to the use of certain antirheumatic drugs. Identification of individual genetic predictors of an increased risk of RA complications will allow timely adjustment of treatment and avoidance of adverse effects.

Objective: To identify the most significant polymorphic variants in genes associated with clinical and biochemical parameters in patients with RA.

Methods: The study included 262 people (128 controls and 176 patients with RA). Individuals included in the study underwent an outpatient examination at the 1st Minsk City Hospital (Belarus); all participants signed informed consent. Clinical examination of patients included collecting a history of the disease, measuring body length and mass, assessing the clinical picture of the disease, including the presence of systemic manifestations, filling out patient cards with counting the number of swollen (SJ) and painful joints (PJ). The BMD was evaluated using DXA. Genetic studies were carried out using real-time PCR of the following polymorphic variants of the genes *IL19* rs587776843, *ATIC* rs4673993 and rs2372536, *ABCB1* rs1128503 and rs1045642, *ABCG2* rs2231142, *AMPD1* rs17602729, *ITPA* rs1127354, *ADORA2A* rs 5760410 and rs2236624, *TLR4* rs4986790, *HLA-E* rs1264457, *NR3C1* rs258751, *ATP5F1E* rs1059150, *KLRD1* rs2302489, *GLCCI1* rs37973, *CRHR1* rs1876828, *ESR1* rs1801132, *PRL* rs7739889, IL6 rs1800795, CALCR rs1801197.

Results: Based on genotyping results, we found that in carriers of the C/C genotype for rs1801132 of the *ESR1* gene, the level of BMD of the femoral neck was statistically significantly lower in the group of patients (0.76±0.01) compared to the control (1.02±0.01, p=0.048). An association was also established between the A/A genotype of the rs7739889 PRL gene variant and reduced femoral neck BMD in the patient group (0.77±0.02) relative to the control group (1.12±0.13, p=0.033). A similar association was revealed for the A/A genotype of the rs1801197 variant of the *CALCR* gene and the rs1800795 C/C genotype of the *IL6* gene - they are also statistically significantly associated with a decrease in BMD of the femoral neck (0.76±0.01 and 0.77±0.02 in patients against 1.03±0.02 in the control group, p=0.025 and p=0.038, respectively). In addition, a statistically significant association with the likelihood of RA was established for the TLR4 rs4986790, HLA-E rs1264457, IL19 rs587776843 loci.

Conclusion: Analysis of the results of genotyping of patients with RA allowed us to establish a significant association with the likelihood of decreased bone mass of loci *ESR1* rs1801132 C/C, *PRL* rs7739889 A/A, *CALCR* rs1801197 A/A, *IL6* rs1800795 C/C, with the likelihood of developing RA – loci *TLR4* rs4986790, *HLA-E* rs1264457, *IL19* rs587776843. Application of this approach in practice will improve the effectiveness of prevention of RA and its complications and accelerate the transition to personalized medicine.

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ROLE OF FRAILTY ON REHABILITATION SUCCESS IN AN ITALIAN ORTHOGERIATRICS UNIT

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Objective: To investigate the influence of frailty and delirium on rehabilitation outcomes in an Italian Orthogeriatric Unit.

Methods: All patients admitted to the Orthogeriatrics Unit at Sondrio Hospital (Italy) from 2011-2019, having ≥70 y and a femur fracture were prospectively enrolled. Among these, only patients who signed an informed consent form were included and formed the cohort study. The assessment included demographic information, functional and cognitive statuses, comorbidity, medications, and factors related to the fracture (type, timing, anesthesia, surgery). We calculated a frailty index (FI) based on 16 variables, and patients were classified in four categories according to frailty: fit (FI < 0.15; reference category), pre-frail (0.15 ≤ FI ≤ 0.24), mildly frail (0.25 < FI < 0.34) and moderate-to-severely frail (FI ≥ 0.35). Delirium was assessed according to the DSM-5 criteria.

Results: The study population included 818 subjects (mean age 85.6±5.7 y, 83.3% females). The most represented comorbid conditions were hypertension (55.8%), cardiac disorders (34.6%) and dementia (21.6%). The average time to surgery was 1.9±1.1 d, and 70.2% of patients were classified as ASA 3 (severe systemic disease) or higher, reflecting an overall high operative risk. The majority of patients experienced displaced fractures (89.7%) and underwent surgery (55.1% intramedullary nail, 38.3% hemiarthroplasty) in spinal anesthesia in 77.6% of cases. In terms of rehabilitation success, i.e., Rehabilitation Efficiency Index (REI) >0.5, it is expected that nonagenarians show the lowest rate compared to younger age groups (59.5% vs. 78.6% and 73.2% of 70-79 and 80-89 y, respectively). However, more than age per se, a frail phenotype represents a stronger risk factor for poor rehabilitation outcomes (OR 0.14, 95%CI 0.07-026 for mild frailty; OR 0.30, 95%CI 019-0.47 for moderate-to-severe frailty), with similar results among those who experienced delirium.

Conclusion: Frailty is a modifiable risk factor, thus we encourage the adoption of preventive strategies to counteract this syndrome. When caring for frail patients with hip fracture, it is advisable to direct the efforts towards early mobilization and physiotherapy, in order to make early rehabilitation as efficient as possible.

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