



## Clinical, functional and neuropsychological status of joint replacement patients

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### Abstract

**Introduction** The number of hip and knee replacement surgeries is increasing annually in Russia and worldwide. The majority of patients receiving joint arthroplasties are elderly women.

The **objective** was to assess the clinical, functional and neuropsychological status of patients undergoing total knee or hip replacement.

**Material and methods** The study included 448 patients admitted for elective surgery of total knee or hip replacement at the Department of Traumatology and Orthopedics of the Federal Center for High Medical Technologies (CHMT, Kaliningrad Region). Anthropometric parameters of the patients were measured, the medical history and concomitant diseases recorded. Common blood count and biochemistry test were evaluated preoperatively. Neuropsychological examination included assessment of cognitive and executive functions, levels of distress, depression, anxiety and somatization.

**Results** Almost all patients studied were found to have varying degrees of obesity. A typical combination of concomitant pathology in volunteers was stage 2 hypertension, risk degree 2–3, and chronic gastritis in remission. Half of the volunteers showed moderate and high levels of distress, depression, anxiety and somatization. A significant number of volunteers showed moderate to high levels of cognitive decline. Age- and sex-related blood counts were slightly different from the normal ranges for a CBC and biochemistry. Changes in leukocyte count were detected.

**Discussion** Leukocyte counts indicated the osteoarthritis induced inflammatory process in most patients. Mitochondrial dysfunction and aging of the immune system contributed to the “proinflammatory status.” The high rate of cognitive impairment in volunteers was associated with age and comorbidity, cardiovascular conditions, in particular. Distress and anxiety were associated with emotional reactions to surgery.

**Conclusion** The factors reported can affect the duration and course of rehabilitation. The “pro-inflammatory status” of patients can complicate the healing of a postoperative wound. Neuropsychological disorders noted during postoperative rehabilitation can have a significant impact on physical recovery, social and professional adaptation.

**Keywords:** orthopedics, osteoarthritis, joint replacement, clinical, functional and neuropsychological status of patients

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## INTRODUCTION

Osteoarthritis (OA) is a group of heterogeneous polyetiological diseases of the joints and one of the major causes of disability in elderly. The prevalence of osteoarthritis (OA) increases with age and the disease is diagnosed in adults over the age of 85 years of age in 85–90 % [1]. As osteoporosis, OA is classified as an age-associated disease. OA primarily affects articular cartilage and involves the entire joint, including the subchondral bone, synovial membrane, menisci and periarticular structures. The pathogenesis of primary gonarthrosis/coxarthrosis is associated with chronic, age-associated inflammation, leading to the accumulated injury in organs and tissues [2]. Mitochondrial dysfunction developing with age and leading to caspase-1-dependent production of pro-inflammatory interleukins-1 $\beta$  (IL-1 $\beta$ ) and 18 (IL-18) contributes to the “pro-inflammatory status” of patients [3]. Anti-inflammatory therapy aimed at stabilizing the degenerative process can be practical in the early stages of OA [4, 5]. Surgical methods are used to treat patients with the condition when anti-inflammatory therapy for OA fails. Total replacement of the knee or hip joints is commonly used in the terminal stage of arthrosis. More than 2 million (in the Russian Federation about 150 thousand) operations are performed annually worldwide and the procedures are expected to increase in the future [6]. Joint replacement surgeries are normally performed for elderly and the majority are women. With the high social role of OA associated with disability, the projected increase in the number of joint replacement surgeries, and specific gender and age of patients, it is important to explore clinical, socio-psychological and cognitive status of candidates for surgical joint replacement. The data may improve management of the patients and rehabilitation.

The **objective** of the study was to evaluate clinical, functional and neuropsychological status of patients admitted for total knee or hip replacement.

## MATERIAL AND METHODS

*Cohort of patients*

The study included 448 patients diagnosed with post-traumatic or primary grade 3 gonarthrosis/coxarthrosis. The diagnosis was based on complaints, clinical manifestations and radiological findings. The surgical intervention was performed using a standard technique of TKA with PMMA-based bone cements. Hip joint implants fixation was dependent on age, bone density and individual structural features of the acetabulum and femoral canal and produced using three techniques. Smith & Nephew (USA), Zimmer (USA) TKA replacement systems were used for the patients. Smith & Nephew (USA), Zimmer (USA), Aesculap (Germany) replacement systems were employed for hip procedures. Surgeries were performed using combined epidural anesthesia (neuraxial anesthesia). The postoperative period was uneventful with no complications recorded. Patients were discharged from the hospital after 7 or 8 days.

The mean age of the patients was  $64.77 \pm 10.29$  years. There were 46.13 % of patients aged 65 years and younger and 53.87 % aged over 65. The examinees were volunteers aged from 50 to 70 years (59.73 %). There were 68.88 % female and 31.12 % male patients.

*Methods of investigation*

Patients were measured for height, weight, blood pressure, heart rate and respiration in the department, and the concomitant diseases and professional status recorded in the medical history. Muscle strength was measured using standard methods with a digital hand dynamometer MEGEON 34090 with 0.1 kg precision.

Preoperative laboratory findings included CBC and biochemistry blood count. Leukocyte count was additionally tested in the patients [7]:

- 1) SIRI (Systemic Inflammation Response Index) =  $\text{abs. number of neutrophils} \times \text{abs. monocyte count} \div \text{abs. lymphocyte count}$ ;
- 2) SII (Systemic Inflammation Index) =  $\text{neutrophil count} \times \text{platelet count} \div \text{lymphocyte count}$ ;
- 3) AISI (Aggregate Inflammation Systemic Index) =  $\text{neutrophil count} \times \text{monocyte count} \times \text{platelet count} \div \text{lymphocyte count}$ ;
- 4) IIR (Immunoreactivity Index). When using the immunoreactivity index (IIR Index), the sum of % eosinophils and % blood lymphocytes is measured and divided by the number of % monocytes;
- 5) Leukocyte intoxication index (LII) according to V.K. Ostrovsky =  $(\text{number of myelocytes in \%} + \text{young neutrophils in \%} + \text{band neutrophils in \%} + \text{segmented neutrophils in \%} + \text{plasma cells in \%}) / (\text{monocytes in \%} + \text{number of lymphocytes \%} + \text{eosinophils in \%} + \text{basophils in \%})$ ;
- 6) Allergy index (AI) =  $(\text{lymphocyte count in \%} + 10 \times (\text{eosinophil count in \%} + 1)) / (\text{neutrophil count in \%} + \text{monocyte count in \%} + \text{basophil count in \%})$ .

A neuropsychological study to explore cognitive function was produced after 4–6 days of surgery. The overall score of cognitive decline was verified in accordance with the Montreal Cognitive Assessment (MoCA). Episodic memory was examined by repetition of 10 words (Luria test). The word-color interference technique was used to assess executive function with the Stroop test. Language function was examined using MoCA subscales (tests for repetition of two syntactically complex sentences, verbal fluency) and assessment of semantic information processing (idiom comprehension). A test for studying subject gnosis (Boston Naming Test) was used to measure confrontation naming ability. Constructive praxis (test of drawing 4 geometric figures) and ideational praxis (performing complex movements including a series of simple actions) was performed to assess praxis. The Bourdon Test was used to explore the level of attention. To objectify cognitive function, the patients underwent a neurophysiological evaluation of the amplitude and latency of acoustic endogenous evoked potentials (EP), P300 from symmetrical areas of the left and right hemispheres of the cerebral cortex in the frontal and central leads.

Topical representation of P300 (hippocampus, parietal, superior temporal and lateral orbitofrontal cortex) facilitated assessment of the redistribution of attention, the amount of working memory involved, executive function, cognitive “flexibility” in the “stimulus-task-response” chain, control of motor response to external stimuli.

The Encephalan-131-03 hardware complex was used to amplify and average the EP. The level of distress, depression, anxiety and somatization was assessed using the Four-Dimensional Symptom Questionnaire (4DSQ).

### *Statistical analysis*

Statistical processing of the data was produced using the standard application package SPSS Statistics V23.0 for Windows, Pandas and SciPy libraries. Quantitative parameters were assessed for compliance with normal distribution using the Kolmogorov–Smirnov test. Quantitative parameters with a normal distribution were described using arithmetic means (M) and standard deviations (SD), variables with a non-normal distribution were described using median values, the 1st and 3rd quartiles (Q1, Q3). The Spearman rank correlation coefficient was used to assess relationships between leukocyte indices.

## RESULTS

*Social and psychological characteristics of the study group*

About 80 % of the volunteers were of retirement age and approximately 50 % continued their working career. In terms of the severity and intensity of working conditions, all types of professional activities of the volunteers were within the 1st (optimal) and 2nd (acceptable) classes of the labor process. Sixty-seven percent of the individuals were engaged in physical labor (earlier or at the time of the study), which implies an increased muscular load on the musculoskeletal system.

Persons engaged in physical labor could be structured as those preoccupied with mechanized labor (agricultural machine operators, drivers, welders, turners, equipment maintenance specialists) — 26 %, semi-automatic and automatic production (conveyor production workers) — 17 %, agricultural production workers (field farmers, greenhouse workers) — 24 %. Patients engaged in intellectual work (33 % of the study group) can be structured as: operators involved in managing technological processes and machines — 8 %, managers, teachers and university professors, accountants, salespeople — 12 %, creative workers (musicians, architects, designers, constructors) — 2 %, medical workers (doctors, nursing staff) — 11 %. Almost all subjects reported greater psycho-emotional stress during their working activities, which was confirmed by the results of neuropsychological testing in the present study. Analysis of the 4DSQ parameters revealed distress of high level in 16.67 % (> 20 points), moderate level (10–20 points) in 34.83 %, low level in the rest of the patients. A high level of depression (> 5 points) was identified in 13.22 % of patients, moderate level of depression (2–5 points) seen in 41.0 % of cases. Anxiety was registered in 51.32 % of patients and rated as a moderate level (8–12 points). Assessment of somatization revealed a high level (> 20 points) in 11.0 % of patients, and a moderate level (10–20 points) in 31.43 %.

*Assessment of cognitive functions in volunteers of the study group*

Cognitive impairment in the study cohort of patients was characterized by manifestations of moderate cognitive impairment (MoCA: 20–25 points) in 170 (37.91 %) patients. A cognitive function decreased to the level of dementia (MoCA < 20 points) was noted in 4.7 % of patients over the age of 65 years. Extensive neuropsychological testing demonstrated a predominant decrease in mnemonic, regulatory and neurodynamic functions. Diagnosis of auditory-verbal memory (repetition of 10 words without interference) revealed a decrease in memory in 201 (44.93 %) patients to ( $6.28 \pm 1.20$ ) points (normally 7–10 words). The Stroop test revealed a reduced low level of executive function in 301 (67.24 %) patients to ( $11.34 \pm 3.50$ ) points (maximum 20 points). Speech function, mainly affecting aspects of speech fluency, was reduced in 115 (25.74 %) patients to ( $2.32 \pm 2.6$ ) points (normal 3 points), mainly in the patients older 65 years. Decrease in the semantic information processing to ( $2.5 \pm 2.4$ ) points (normal — 3 points) in 11.8 % of cases and perception to ( $22.61 \pm 1.30$ ) points (maximum value — 24 points) 14.35 % of patients was observed in patients over 65 years of age with overall MoCA cognitive decline <22 points. Constructive praxis was reduced to 4.3 points in 116 (25.93 %) patients which corresponded to inadequate copying of one figure out of four on average. Ideation praxis was reduced to 4.4 points in 102 (22.82 %) patients, which reflected failure to comply with one of the five proposed instructions. Attention was reduced in 43.99 % of patients and corresponded to 4.05 points (normal 5 points). A greater increase in latency of the P300 cognitive evoked potential, beyond the normal range (> 450 ms) was observed in the central (C3–A1) and frontal (F4–A2) leads in 53.4 % of patients with cognitive decline.

*Concomitant diseases in volunteers of the study group*

Concomitant conditions were identified in volunteers. Concomitant diseases were not recorded in medical histories of 67 (14.96 %) individuals out of 448 in addition to the main diagnosis of the knee or hip arthrosis). Blood circulation conditions were most common to include hypertension of varying

degrees and risk (75 %), coronary heart disease (14 %), varicose veins of the lower extremities (56 %), etc. Cardiovascular pathologies were recorded in 243 (54.2 %) patients. The second common comorbidities (53.8 % of patients) were related to the digestive system identified in 240 (53.6 %) patients. Various forms of gastritis were common among the diagnoses of this group of conditions (all patients underwent gastroscopy was produced for all patients prior to admission to the clinic). Diseases of the endocrine system, nutritional disorders and metabolic disorders were noted in 68 (17.8 %) patients, of which 46 (12.1 %) patients suffered from type 2 diabetes mellitus, 9 (2.2 %) from type 1 diabetes mellitus, 13 (3.5 %) patients had other endocrine pathologies. 24 patients (5.36 %) had a history of neoplasms (breast tumors, gastrointestinal polyps, etc.). 4.69 % of volunteers had genitourinary diseases, musculoskeletal diseases were recorded in 16 patients (3.58 %). Isolated cases of infectious diseases were identified in 9 (2.4 %) patients with chronic infectious hepatitis and respiratory diseases in remission. Some patients had diseases of the nervous system, blood diseases and ophthalmological diseases. Stage 2 hypertension, risk degree 2–3, and chronic gastritis in remission was the most typical combination of concomitant pathology in the volunteers.

### *Anthropometry*

Almost all patients in the study group (more than 91.2 %) were diagnosed with varying degrees of obesity. The mean body mass index (BMI) measured  $32.66 \pm 2.54$ , which significantly exceeds the recommended normal values ( $N = 1.85\text{--}25.0$ ). The excess weight has an impact on the cardiovascular and the musculoskeletal systems (primarily the knee and hip joints). Adipose tissue is a source of pro-inflammatory cytokines and can aggravate the course of the underlying disease [8]. The mean muscle strength of volunteers measured ( $47.42 \pm 11.78$ ) kg for men and ( $23.15 \pm 7.29$ ) kg for women, which corresponded to the standard indicators for residents of Russia ( $43.4 \pm 11.1$ ) kg (M), ( $27.6 \pm 6.1$ ) kg (W). Patients aged over 65 years showed the mean measurements being within the range for men ( $41.41 \pm 10.57$ ) kg, and for women ( $20.99 \pm 6.67$ ) kg, that were within the age norm ( $37.8 \pm 10.0$ ) and ( $24.8 \pm 5.8$ ) (in men and women, respectively). Among elderly patients, 7.4 % of men and 23.95 % of women had muscle strength levels below the “threshold values” (24 kg for men, 17 kg for women) [9]. Blood pressure was higher by 7–8 % on admission in 24.5 % of patients and measured 140–155 mm Hg. The frequency of respiratory movements and heart contractions were within the physiological norm and amounted to 14–18 breaths per minute, respectively, and 68–82 heart beats per minute.

### *Blood groups and CBC*

The presence of one blood group or another in volunteers practically coincides with data on the distribution of blood groups among Russian citizens (<https://dop-mosreg.ru/rasprostranennost-gruppy-krovi-v-rossii>). In our series, 17.1 % had a negative Rh factor which was higher than the average statistical data for the Russian Federation (13.96 %). A note: 21.1 % residents of the Kaliningrad region have a negative Rh factor (data from the State Budgetary Healthcare Institution “Blood Transfusion Station of the Kaliningrad Region”).

CBC slightly deviated from the indicators generally accepted for the gender and the age. Therefore, we attempted to conduct a comparative assessment based on “new” markers of systemic inflammation, which were essentially indices, calculated indicators of systemic inflammation (SIRI, AISI, SII, IIR), as well as hematological markers based on leukocyte counts and the subtypes (IA, LII). These indices can be calculated as part of CBC with a leukocyte formula, which makes them financially accessible in routine clinical practice and they are easily feasible. In recent years, it has been shown that these indices can accurately predict poor prognosis in patients with a wide variety of pathologies compared to hematological markers based on leukocyte counts and the subtypes (neutrophils, lymphocytes and monocytes) [10–15].



The median value of the systemic inflammatory response index (SIRI) in the study group was 0.68 units (Q1 of 0.46, Q3 of 1.03). Only 28.34 % of the individuals had this index being within the normal limits of 0.4–0.6 units; 14.06 % had the index below 0.4 units, and all other patients (57.6 %) had the index significantly exceeding the recommended values. Calculation of the cumulative systemic inflammation index (AISI) showed median of 170.95, Q1 of 109.23 and Q3 of 280.81. AISI exceeded the normative values (51.10–125.57 units) in 67.05 % of volunteers. AISI was within the physiological norm in 28.8 % of patients and below it in 4.15 %. The systemic inflammation index (SII) in the study cohort showed median of 414.67, Q1 — 304.86, Q3 — 551.49. Standard values are 450–890 units and SII was within these limits in 28.11 % of volunteers. SII was above the normal values in 31.11 %, and the rest (40.76 %) had it below the lower limit of the norm. Normal values of the leukocyte intoxication index (LII), calculated as modified according to V.K. Ostrovsky, range from 1.0 to 1.6 units. A mild degree of endogenous intoxication corresponds to  $(2.8 \pm 0.64)$  units, a moderate degree of  $(4.3 \pm 1.5)$  units, a severe degree of  $(8.1 \pm 0.34)$  units. The majority of patients (82.2 %) had mild or moderate intoxication, and 13.6 % had severe intoxication.

The index of immunoreactivity (IIR) showed median of 5.56, Q1 of 4.07, Q3 of 7.23. An increased IIR can be interpreted as an increase in immunological activity. The immunoreactivity index is normally 18.1–37.4; it was significantly reduced in the majority of patients (75.35 %). IIR was normal in 21.89 %, increased values were seen in 2.76 % of volunteers. These results are comparable with data on the allergenic index (AI). Eosinophil and lymphocyte counts increase in 56–86 % of cases during allergic reactions. Analysis of the blood count will allow you to derive an index to identify an allergic reaction, AI. AI fluctuations range from 0.68 to 1.08 in normal people and increase to 2.37–2.97 in patients with various forms of allergic reactions. In our series, the majority of patients had a reduced AI (median of 1.08, Q1 of 0.85, Q3 of 1.45), which was clinically confirmed by rare complaints about manifestations of the allergic syndrome. The median ESR in the volunteers measured 11.00 (Q1 of 7.00, Q3 of 20.00) and was within the age-sex limits of normative values.

#### *Basic biochemical parameters in volunteers of the study group*

A blood biochemistry test was performed for all patients on admission to the clinic in addition to CBC to assess functioning of internal organs. The level of creatinine was within the age-sex norm in almost all patients and averaged to  $(81.41 \pm 21.82)$   $\mu\text{mol/l}$ . The normal level of total bilirubin in adults is 3.4–17.1  $\mu\text{mol/l}$  in women and 3.7–18.5  $\mu\text{mol/l}$  in men. The mean bilirubin level in the study group measured  $(13.65 \pm 6.69)$   $\mu\text{mol/l}$ . Bilirubin level was higher in 18.2 % of patients and measured 30.5–40.6  $\mu\text{mol/l}$  (median of 12.25, Q1 of 9.30, Q3 of 16.18). Similar results were obtained for transferases. The median of aspartate aminotransferase (AST) was 21.40 (Q1 of 17.10, Q3 of 27.95), the median of alanine aminotransferase (ALT) was 20.60 (Q1 of 16.00, Q3 of 28.85). Higher levels were observed in 10.7–14.84 % of volunteers. Some patients were diagnosed with type 2 diabetes mellitus and received therapy; only 15.5 % had elevated blood glucose levels measuring 10.0–12.5 mmol/l. The median was 5.65 mmol/l (Q1 of 5.20, Q3 of 6.39). The serum cholesterol level was mainly within the age norm measuring  $(5.80 \pm 1.40)$  mmol/l, but 8.52 % of volunteers had hypercholesterolemia of more than 8.0 mmol/l. In general, the patients had no significant deviations in biochemical analysis and, accordingly, had no contraindications to surgical treatment.

#### DISCUSSION

Muscle strength measured during dynamometry can be below threshold values in some patients and can be a diagnostic criterion for sarcopenia [16] and are associated with an increased risk of death, primarily from cardiovascular diseases [9, 17, 18, 19]. The biochemical panel is important

due to the fact that surgical intervention is preceded by a preparation period (sometimes a long period) to include courses of therapy, physiotherapy, rehabilitation measures aimed at remission of comorbid diseases to be followed by THA/TKA surgery. The question of using leukocyte counts as indicators of the severity and course of the inflammatory process in patients with OA remains controversial. On the one hand, the study demonstrated significance of the markers associated with reference values of CBC. On the other hand, leukocyte count can be influenced by a long-term, sometimes uncontrolled, use of NSAIDs and the concomitant diseases associated with chronic inflammation including diabetes mellitus, obesity and some gastrointestinal diseases. In the study group, a decrease in the immune reactivity index was associated with high intoxication index and low AI values, possibly, due to significant doses of NSAID used for pain relief. The parameters are closely related to each other and are directly or inversely related. The strength of the connection on the Chaddock scale ranges from “noticeable” to “very high” ( $p < 0.05$ ).

In general, the assessment of leukocyte indices indicated to a “pro-inflammatory status” in the volunteers and was characterized by increased production of pro-inflammatory cytokines. The levels of acute phase proteins, prostaglandins and coagulation factors increased to a lesser extent. At least three closely related groups of factors participate in the formation of the condition: mitochondrial dysfunction associated primarily with impaired mitophagy processes, chronic emotional stress, age-related inflammatory imbalance of the immune system. The age-related inflammatory status of the immune system can be explained by the fact that, the immune response with the inflammatory reaction as major protective mechanism becomes excessive during life. The changes are associated with chronic stimulation of the immune system, viruses and bacteria, altered microbiota, increased senescent cells, degradation products of the intercellular matrix and accumulation of adipose tissue with age leading to increased production of proinflammatory cytokines [20]. Age-associated mitochondrial dysfunction makes a significant contribution to the “proinflammatory status.” It results in a disruption in the mitophagy process, the utilization of defective mitochondria. Incomplete removal of damaged mitochondria leads to hyperactivation of inflammatory signaling pathways and to chronic systemic inflammation and inflammatory diseases [21]. Mitochondrial dysfunction was explored previously on a small sample of volunteers ( $n=48$  people) by the number of copies of the mitochondrial genome in postmitotic muscle cells.

Our series demonstrated that the critical threshold of mtDNA heteroplasmy was exceeded in a third of muscle samples, at which a pathological phenotype with noticeable biochemical abnormalities became dominant in the functioning of the oxidative phosphorylation system (OXPHOS) [22]. Chronic emotional stress, which is characterized by phase changes in the immune system contributes to the formation of a pro-inflammatory status. The production of anti-inflammatory cytokines (IL-10 and IL-13, TGF- $\beta$ ) increases at the initial stages due to decreased secretion of the pro-inflammatory group of cytokines (IL-1 $\beta$ , IL-6, TNF- $\alpha$  and IFN- $\gamma$ ). Then a mechanism of increased expression of inflammatory cytokine genes is launched after restructured activity of the nuclear cytoplasmic protein “kappa-B” (contained in T-lymphocytes, monocytes/macrophages) [23, 24]. Long-term (chronic) influence of stress factors leads to disruption of the homeostatic connection between the neuroendocrine and immune systems and to the development of a “pro-inflammatory status” [25, 26, 27]. In our case, impaired productivity due to significantly limited mobility and chronic pain was long-term stress factors. This was confirmed by manifestations of distress of varying severity diagnosed in the volunteers and was consistent with the studies reporting psycho-emotional disorders in patients with chronic pain of various etiologies [28, 29].

Cognitive deficit was characterized by moderate impairments in a third of patients and dementia in 4.7 % of cases, which corresponds to data from population studies demonstrating the prevalence of dementia of 6 % among people over 60 years of age and non-dementia disorders observed in 12 to 41 % [30, 31]. The wide representation of cognitive impairment in our series was associated with a number of reasons. First, the cognitive phenotype with predominantly impaired memory and regulatory functions is directly related to age (53.8 % of patients over 65 years of age) and is mediated by morphological and functional changes in the brain structures of elderly patients [32]. Secondly, comorbid pathology is important and was represented by endocrine (17.99 %) and cardiovascular (55.81 %) diseases as potential predictors of cognitive impairment, predominantly of a vascular nature with the manifestation of dysregulatory syndrome and decreased attention [33]. A psychoemotional disorder, characterized by a moderate level of affective disorders, somatization and distress was an important factor in the development and progression of cognitive deficits in half of the patients. Distress and anxiety are common in patients and associated with the preoperative emotional response and are reflected in the testing of cognitive flexibility and attention. The prevalence of speech, perceptual and semantic disorders, memory loss in elderly reflects the degenerative component of aging, characteristic of Alzheimer's disease and neurodegeneration [34, 35]. Larger cohort studies and standard neuroimaging examinations are needed to verify cognitive impairment of a degenerative or mixed nature. Lengthened P300 wave, along with the clinical phenotype of cognitive decline allows us to consider the parameters of P300 latency and amplitude as an objectifying method for assessing cognitive functions. Successful restoration of the function of the operated knee or hip joint relies on the quality of rehabilitation. Some factors reported may affect the duration and course of the recovery process. The factors include late adulthood and concomitant pathology, excess weight and greater weight on the operated joint, "pro-inflammatory status", characterized by the predominant serum pro-inflammatory cytokines, the presence of distress and cognitive impairment in some patients.

Rehabilitation for the volunteers should include preoperative preparation for rehabilitation and several stages of postoperative recovery. The main goal of the first (preoperative) stage is to improve blood circulation in the affected joint, increase muscle tone of the lower limbs, because many patients suffer from venous disorders of the lower limbs. Our patients spend an average of one day in the hospital before surgery and underwent appropriate physiotherapeutic procedures. Postoperative rehabilitation includes three stages with the duration of a year. At the first stage, the main task is to relieve pain and arrest infection. The new markers of systemic inflammation tested in this series were useful in predicting infection post surgery in individuals with surgical pathology [36, 37, 38, 39]. Their use requires further in-depth research, since the indices are calculated on the basis of CBC. The second and third stages of rehabilitation included postoperative physiotherapy, massage and kinesiotherapy aimed at restoration of the joint function motivating the patient to actively participate in the rehabilitation process in order to return to a normal lifestyle. In recent years numerous studies exploring the impact of cognitive and psycho-emotional disorders on the postoperative functional motivational status of the patient reported a negative impact of such outcomes as depression, decline in motivation, distress, regulatory and mnemonic dysfunction on the prognosis of restoration of the patient's physical condition, employment and social adaptation [40, 41, 42].

A high proportion of volunteers with impaired cognitive function and distress was observed in our series, and screening for cognitive and psycho-emotional disorders became an integral part of the preoperative preparation of patients and part of an elective surgical intervention. Neurophysiological and neuropsychological examination allowed us to assess the risk of persistent postoperative



cognitive disorders. The knowledge of the preoperative neuropsychological status can contribute to an accurate prediction of the risk of severe cognitive disorders at a short and long term. Verified cognitive and psychoemotional disorders upon admission of a patient for planned surgical treatment will allow optimizing postoperative rehabilitation methods and expanding the scope of recovery potential. The role of dynamometry and leukocyte counts revealed in the series is essential for planning studies aimed at verifying markers of systemic inflammation and muscle dysfunction in patients with osteoarthritis. The generated database will be further compared and analyzed with the results of assessing the level of heteroplasmy in mitochondrial DNA in the muscle tissue of our volunteers. The findings can be used to diagnose pathologies of elderly and for healthy aging.

## CONCLUSION

Selective assessment of the clinical, functional and neuropsychological aspects of patients admitted for total knee or hip replacement allowed for identifying the major indicators that can effect the success of the postoperative rehabilitation in elderly patients. Those were dynamometry parameters below threshold values, excess body weight, decreased neuropsychological functions and a “pro-inflammatory status”.

Verified markers of various modalities, along with comorbid pathology, will allow us to formulate optimal diagnostic and therapeutic strategies for managing patients post surgery. Identified factors such as depression, distress and cognitive deficits, which would narrow the scope of recovery potential require the services of neuropsychological specialists to be involved in rehabilitation to correct the patient’s psychosomatic condition post surgery.

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**Informed consent** Written informed consent was obtained from each subject or the subject's parent/legally acceptable representative on admission to the clinic.

**Ethical review** The study received a favourable opinion from the independent ethical committee of the Federal State Administrative Okrug of the Immanuel Kant Baltic Federal University (No. 25 dated 06/30/2021) and the Ethics Committee of the Federal State Budgetary Institution “FCVMT” of the Ministry of Health of the Russian Federation (No. 553 dated 07/07/2021).

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