Original Paper

Phenotypic Classification and Functional Assessment in Knee Osteoarthritis Patients

OVIDIU-FLORIN FUGARU[1], DUMITRU RĂDULESCU[2], MIRCEA-SEBASTIAN ȘERBĂNESCU[3,4], MAGDALENA RODICA TRĂISTARU[4,5]

[1]*PhD Student, University of Medicine and Pharmacy of Craiova, Romania*

[2]*Department of Surgery, The Military Emergency Clinical Hospital 'Dr. Stefan Odobleja' Craiova*

[3]*Department of Medical Informatics and Biostatistics, University of Medicine and Pharmacy of Craiova, Romania*

[4]*Filantropia Clinical Municipal Hospital Craiova*

[5]*Department of Physical and Rehabilitation Medicine, Nursing Faculty, University of Medicine and Pharmacy of Craiova, Romania*

ABSTRACT: The purpose of our study was the phenotypic classification of patients with osteoarthritis of the knee (KOA) and the dynamic assessment of functional status, monitored both numerically and in conformity with the International Classification of Functioning, Disability, and Health (ICF-basic set, shortened form). We conducted a prospective study in the Department of Physical Medicine and Rehabilitation, Filantropia Hospital, Craiova, from June of 2022 to November of 2023. In total, 100 patients with KOA were enlisted. Using data from the literature, physiotherapeutic examination, and results from paraclinical examinations, we classified studied patients into the five phenotypic categories: chronic pain (F1), local pathology with predominance of inflammatory mechanisms (F2), local pathology with predominance of metabolic mechanisms of bone and cartilage structures (F3), metabolic disorders (F4) and comorbidities (F5)-primarily chronic venous insufficiency in the lower limbs. We analyzed the values of generic qualifiers (at two evaluation time points) for the most significant elements of the core ICF set, abbreviated form, used in OAG, across each of the five phenotypes. Phenotypes F4 and F5 showed significant improvements across all evaluated functions, indicating increased efficacy in patients with comorbidities and metabolic diseases. Reduction in pain sensation, improvement in joint and muscle mobility, as well as enhancements in functions related to walking, dressing, and hand use, reflect an overall improvement in the quality of life for these patients.

KEYWORDS: *Knee, osteoarthritis, phenotypic categories, functional status.*

Introduction

Osteoarthritis (OA) is a chronic and progressive disorder widely accepted as a condition affecting the entire organ, with inflammatory, biochemical, and biomechanical components. Together, these systemic changes result in a significant burden on health and the economy [1].

OA is a common condition with notable consequences on functional status, significantly restricting daily activities and reducing quality of life [2].

One of the most frequent locations of osteoarthritic disease is the knee, the intermediate pivot of the lower limb, playing an essential biomechanical role in standing and walking.

It should be noted that the impact of knee osteoarthritis (KOA) on the overall functioning of the body is multidimensional, as described in the International Classification of Functioning, Disability, and Health (ICF), with high preponderance rates for pain (96.3%) and joint mobility limitation (94.9%), disturbance in changing basic body positions (90.1%), and walking (88.3%) [3].

Furthermore, due to extensive joint structural abnormalities, KOA is considered one of the most prevalent causes of global disability. Thus, the well-being and quality of life of the patient are significantly altered, with a direct economic impact. The economic burden of knee OA on patients and society is considerable [4].

The patient with KOA must be thoroughly evaluated by a multidisciplinary team that will subsequently implement an appropriate medical care program. After evaluation, an accurate diagnosis of KOA is possible, specifying the form of the disease and categorizing the patient into a correct phenotype. Identifying the most important phenotypes of KOA has been a medical focus of the last decade.

Functional evaluation must include the patient's social and environmental dimensions, aspects that currently receive relatively little attention [5].

With the approval of the new ICF, there is a globally accepted framework and classification system that defines the typical range of problems in the functioning of patients with OA. The patient is evaluated comprehensively, integrating clinical data into the complexity of information

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about activity limitations, participation restrictions, and the action of environmental factors [6].

A formal consensus process, which incorporates evidence and expert opinions rooted in the ICF framework and classification, has evolved in the establishment of the Comprehensive ICF Core Sets for osteoarthritis.

The comprehensive ICF Core Set includes 55 categories-6 from the body structures component, 13 from the body functions component, 17 from the environmental factors component and 19 from the activities and participation component [7].

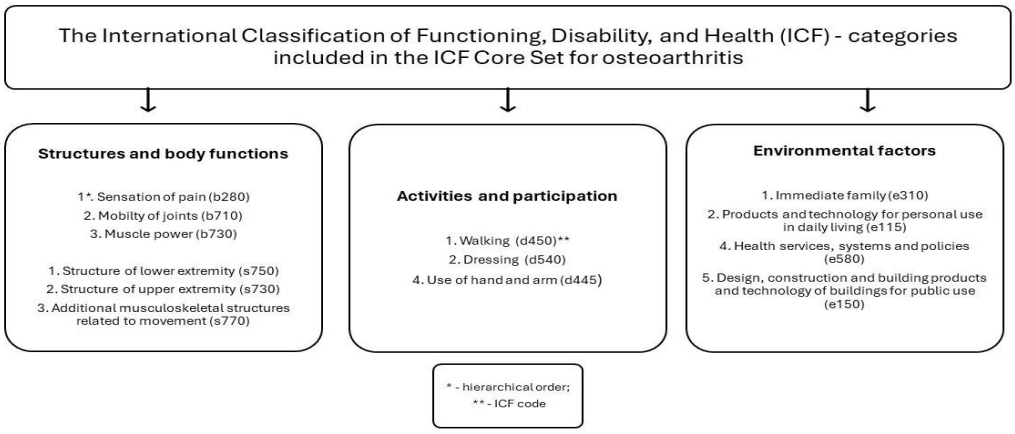

Figure 1. The Core Set of ICF Categories for Knee Osteoarthritis, abbreviated form.

In clinical studies, a condensed version of the ICF Core Set has been developed to facilitate functional assessment (Figure 1).

The Short ICF Core Set comprises 13 second-level categories, accounting for 23% of the categories found in the Comprehensive ICF Core Set. These categories encompass 3 from the body functions component, 3 from the body structures component, 3 from the activities and participation component, and 4 from the environmental factors component [8].

In addition to the category codes, the ICF employs qualifiers-numeric descriptors that follow the code with a period. The first qualifier serves as a general indicator of the problem's extent, typically indicating severity. For body structures, the second and third qualifiers specify the nature (e.g. partial absence) and location (e.g. left side) of the impairment, respectively (Figure 2).

In the context of Activity Limitation and Participation Restriction, two qualifiers are utilized to describe the environments where measurements are taken. The first qualifier assesses performance, reflecting what an individual accomplishes in their current or usual environment, including any aids or personal assistance used. The second qualifier, capacity, characterizes the individual's unassisted ability.

Environmental Factors also utilize the same set of generic qualifiers to denote the extent of barriers, while facilitators are indicated with the same codes prefixed by a plus sign (+) [6].

Qualifiers for ICF codes			
First qualifier (generic)		Second qualifier (nature) for body structure	Third qualifier (location) for body structure
Code	Percentage		
0 – no problems	0-4	0 – no change	0 – more than one region
1 – mild problem	5-24	1 – total absence	1 – right
2 – moderate problem	25-49	2 – partial absence	2 – left
3 – severe problem	50-95	3 – additional part	3 – both sides
5 – complete problem	96-100	4 – aberrant dimensions	4 – front
		5 – discontinuity	5 – back
8 – not specified		6 – deviating problem	6 – proximal
9 – not applicable		7 – qualitative changes in structure, including accumulation of fluid	7 – distal
			8 - not specified
		8 - not specified	9 - not applicable
		9 - not applicable	

Figure 2. The qualifiers for components of the Core Set of ICF, abbreviated form for Osteoarthritis of the Knee.

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Through comprehensive evaluation, patients with knee osteoarthritis (KOA) can be phenotypically classified. KOA is a multifactorial syndrome composed of several phenotypes with different pathophysiological pathways [9], providing an explanation for the inconsistencies among various clinical, laboratory, and imaging studies in OA, as well as the lack of translational results to date. In 2016, six distinct primary phenotypes were proposed for KOA: 1) chronic pain; 2) mechanical overload; 3) minimal joint disease; 4) inflammatory mechanisms; 5) metabolic syndrome; 6) metabolic mechanisms of bone and cartilage localized to the joint. It is acknowledged that there is a possibility that these phenotypes may exhibit overlapping characteristics among them. [10].

In the present study, we considered this classification, which is also found in the classification proposed by Lv et al., in 2021 [11].

In 2020, a consensus was considered for OA phenotypes based not only on distinct biological mechanisms but also on pain patterns and structural and functional consequences [12].

The aim of the study was the phenotypic classification of patients with KOA and the dynamic assessment of functional status, monitored both numerically and according to the ICF classification (basic set, shortened form).

Materials and Methods

Ethical Approval

Before being included in the study, the details of the current research were explained to patients with knee osteoarthritis (KOA). Written informed consent was obtained from each patient. The protocol adhered to the Declaration of Helsinki and Good Clinical Practice guidelines and received approval from the local independent ethics committee (approval no. 138/07.12.2020).

Study Design

We conducted a prospective study in the Department of Physical Medicine and Rehabilitation, Filantropia Hospital, Craiova, from June of 2022 to November of 2023 (Figure 3).

A number of 100 patients with KOA were included in our research. The diagnosis of KOA was established in accordance with the recommendations from the specialized literature [13].

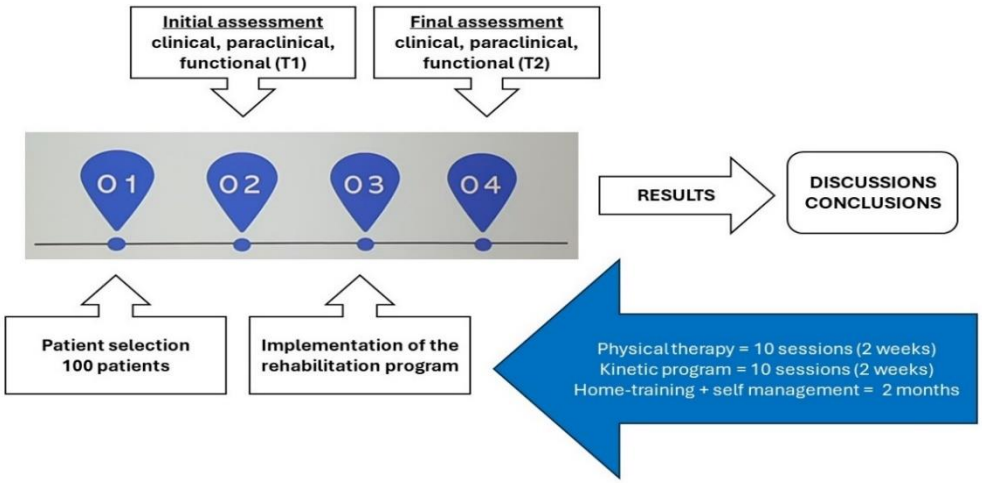

Figure 3. The stages of the study.

Before designing and implementing the medical rehabilitation program, an initial assessment of each patient was conducted from the perspective of the physiotherapy specialist. It should be noted that the clinical diagnosis of the disease was established by the attending physician. This assessment involved the following aspects:

1. Evaluation of symptoms and signs associated with knee impairment.
2. Documentation of comorbidities-cardiovascular (coronary artery disease, hypertension, varicose disease), metabolic (diabetes mellitus, dyslipidemia, overweight/obesity), gastrointestinal (history of hepatitis, peptic ulcer, irritable bowel syndrome).
3. Examination of the musculoskeletal system-range of motion (passive and active, for flexion and extension, using a standard goniometer) and manual muscle testing (especially for the muscle groups included in the kinetic program-gluteus medius, quadriceps, hamstrings, triceps surae), gait, and physical performance.
4. Functional evaluation in accordance with the ICF classification, using the minimum assessment set for KOA.

Three scales were also used for the global functional evaluation of the patient:

- VAS-Visual Analog Scale (from 0 to 10, 0=no pain and 10=maximum pain score, other values between 0 and 10 are directly proportional to pain intensity, the characterization may vary depending on the individual's pain threshold).
- Lequesne Functional Index (a 10-step questionnaire)-the scale ranges from 0, representing minimal functional impairment or maximum functional status (pain, maximum walking distance, and daily activities), to 24, indicating the most unfavorable outcomes. Lower limb dysfunction is graded as follows: 0 (none), 4 (mild), 5-7 (moderate), 8-10 (severe), 11-13 (very severe), and above 14 denotes extremely severe limitations and dysfunctions [14].
- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-contains 24 specific questions divided into three domains: physical function (PF-WOMAC; 17 items), stiffness (S-WOMAC; 2 items), and pain (P-WOMAC; 5 items). The score ranges from 0 to 4. A score of 0 is equivalent to maximum functional status, while high scores up to 96 indicate minimal status, with significant disruptions in daily activities [15].

According to the literature, these three scales (WOMAC, Lequesne index and VAS) allow the assessment of both the structures and functions of patients with KOA, as well as the activities they undertake [7].

The objectives of the physical-kinetic program were established in terms of the ICF, with a focus on activity limitations and participation restrictions:

- Control of pain,
- Control of the inflammatory process,
- Restoration of knee stability and mobility, rebalance among the muscle groups that support the entire knee complex.,
- Correction of anomalous gait patterns,
- Recovery of motor control and optimal knee function.
- To achieve these objectives, the following methods were used:
- Educational measures, promoting self-management, providing general knowledge about the disease and the importance of the kinetic program, adopting a rational lifestyle and diet, and fostering a positive attitude towards the continuity of the program;
- Physical therapy-including magnetotherapy, transcutaneous electrical nerve stimulation (TENS), low-intensity laser therapy and ultrasound;
- Kinetic training-adapted to the functional status of each patient. Upon discharge, all patients were prescribed a series of home exercises (home-training program). The physical-kinetic program was differentiated according to the corresponding phenotype.

Statistical methods

Observational studies are frequently constrained by disparities that may emerge among both recognized and unrecognized confounding factors. To mitigate these potential confounding effects in the assessment of variables pre- and post-treatment, we used SPSS software, version 26.0, IBM Corporation, Armonk, NY, USA, for all statistical analyses. Additionally, Python version 3.10 was used for data preprocessing and supplementary visualizations.

Data were loaded and prepared for analysis, and variables were assessed for normal distribution using histograms and the Shapiro-Wilk test. Quantitative variables are expressed as means±standard deviation and were analyzed using the independent samples t-test and the paired samples t-test.

To compare the initial and final means within each group, we employed the paired samples t-test. A p-value <0.05 was considered statistically significant.

Results

Using data from the literature, physiotherapeutic examination, and results from paraclinical examinations, we classified patients in Study Group 2 into the following phenotypic categories (Figure 4):

- Chronic pain (F1)-VAS scale values above 7 and WOMAC pain subscale scores above 15.
- Local pathology with predominance of inflammatory mechanisms (F2)-C-reactive protein (CRP) levels above normal limits (above 0.5 mg/l) and fibrinogen levels above 400 mg/dl, as well as a neutrophil-to-lymphocyte ratio (NLR) above 2.1.
- Local pathology with predominance of metabolic mechanisms of bone and cartilage structures (F3)-Beta-crosslaps levels above normal (above 1 ng/ml in postmenopausal women, above 0.7 ng/ml in men under 70 years, and above 0.85 ng/ml in men over 70 years).

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- Metabolic disorders (F4)-Obese patients with BMI above 30, diabetes mellitus, mixed dyslipidemia.
- Comorbidities (F5)-Primarily chronic venous insufficiency of the lower limbs.

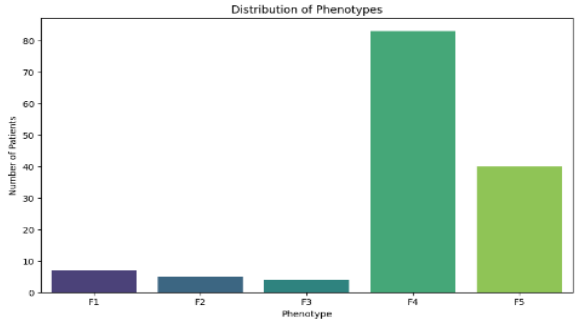

Figure 4. The distribution of phenotypes in Batch 2.

Phenotype 1 (F1-Chronic Pain)

Phenotype 1, characterized by intense chronic knee pain without other clinical elements but with specific radiological changes, was identified in 7 patients. Intense chronic pain was defined by VAS scale values above 7 (out of 10) and WOMACP pain subscale scores above 15 (out of 20), indicating over 75% of the maximum scores on both scales. This suggests a significant portion of patients experiencing intense chronic pain, necessitating appropriate interventions for pain management.

Phenotype 2 (F2-Inflammatory Mechanism)

Phenotype 2, characterized by local pathology predominantly driven by inflammatory mechanisms, was defined by C-reactive protein (CRP) levels above normal limits (above 0.5mg/l), fibrinogen levels above 400 mg/dl, and a neutrophil-to-lymphocyte ratio (NLR) above 2.1. This phenotype was observed in 5 patients. This result indicates that inflammation plays a significant role but not exclusively, as it may precede other pathogenic changes that complicate the clinical-functional status in knee osteoarthritis (OA).

Phenotype 3 (F3-Metabolic Mechanisms of Bone and Cartilage)

Phenotype 3, characterized by local pathology predominantly driven by metabolic mechanisms of bone and cartilage structures, identified by serum βCTx levels above normal (above 1ng/ml in postmenopausal women, above 0.7ng/ml in men under 70 years, and above 0.85ng/ml in men over 70 years), was identified in 4 patients. This suggests significant metabolic imbalances in a limited number of patients, indicating the need for specialized interventions.

These phenotypic classifications were based on established criteria and thresholds from literature and clinical assessments, highlighting distinct subgroups within the study population experiencing knee osteoarthritis. Each phenotype underscores the complexity of OA presentations and the importance of tailored treatment approaches.

Phenotype 4 (F4-Metabolic Disorders)

Metabolic disorders, including obesity with BMI over 30, diabetes mellitus, and mixed dyslipidemia, were the most frequent clinical conditions associated with the studied patients, affecting 83 individuals. This highlights osteoarthritis of the knee (OA) as a major public health concern in the study group, necessitating physiotherapeutic interventions targeting weight loss, glycemic control, and management of dyslipidemia.

Phenotype 5 (F5-Chronic Venous Insufficiency of Lower Limbs)

Chronic venous insufficiency of the lower limbs was present in 40 patients with knee OA. This significant number underscores the need for an integrated and personalized approach for optimal therapeutic and rehabilitative outcomes, aiming to restore and maintain optimal quality of life for the patient.

Comparative analysis of initial and final parameters for each phenotype (Table 1) highlights the differences/similarities in patient responses. Following the application of the adapted physiotherapeutic algorithm tailored to each phenotype, improvements in functional parameters (Figure 5) and pain were achieved for all patients, regardless of their initial phenotype.

This underscores the effectiveness of the interventions applied for pain, inflammation, and associated comorbidities.

It should be noted that patients in phenotypes 4 and 5 showed statistically significant improvements in average values, demonstrating that meticulous selection and correct implementation of physiotherapeutic procedures lead to optimal outcomes. For phenotype 1, where the primary goal of the program was pain control, significant differences were observed between initial and final mean values for VAS and WOMAC-P subscale, with statistically significant positive impacts on 6-minute walking distance and functionality scales. Undoubtedly, the direct conditioning of pain to functionality explains these results.

For the other two phenotypes, involving inflammatory processes and chondrocyte-bone metabolism, the lack of statistical significance can be attributed to the complex pathogenesis which physiotherapeutic programs do not address as a first-line therapy.

Table 1. Functional parameters for the established phenotypes.

Parameter	F1	F2	F3	F4	F5
	Mean±DS	**Mean±DS**	**Mean ±DS**	**Mean ±DS**	**Mean ±DS**
VAS 1	8.14±0.38	6.60±0.89	6.75±0.96	6.72±0.97	7.12±0.85
VAS 2	5.86±0.69	4.80±0.84	5.25±0.96	5.28±1.02	5.58±0.87
p-value	**0.0000***	**0.0112***	0.0686	**0.0000***	**0.0000***
WOMAC1	71.57±3.99	56.20±8.53	59.25±8.14	63.78±7.92	66.70±8.05
WOMAC2	63.00±6.38	49.20±4.76	51.75±3.77	56.46±6.44	59.00±6.84
p-value	**0.0129***	0.1580	0.1659	**0.0000***	**0.0000***
WOMACP1	16.29±0.49	13.80±1.79	14.25±1.71	13.94±1.44	14.45±1.15
WOMACP2	11.86±0.38	10.00±1.58	10.25±1.50	10.12±1.27	10.45±1.20
p-value	**0.0000***	**0.0076***	**0.0129***	**0.0000***	**0.0000***
WOMACF1	49.43±4.20	36.80±7.33	39.75±7.27	44.29±7.43	46.53±7.89
WOMACF2	46.57±6.21	35.20±3.77	37.75±3.40	42.02±6.19	44.18±6.86
p-value	0.3360	0.6794	0.6431	**0.0343***	0.1591
Lequesne Index 1	11.21±1.19	7.60±1.82	8.25±2.36	8.65±2.50	9.70±2.30
Lequesne Index 2	8.57±1.13	6.60±1.14	7.00±1.41	7.11±1.89	7.79±1.76
p-value	**0.0011***	0.3332	0.4064	**0.0000***	**0.0001***

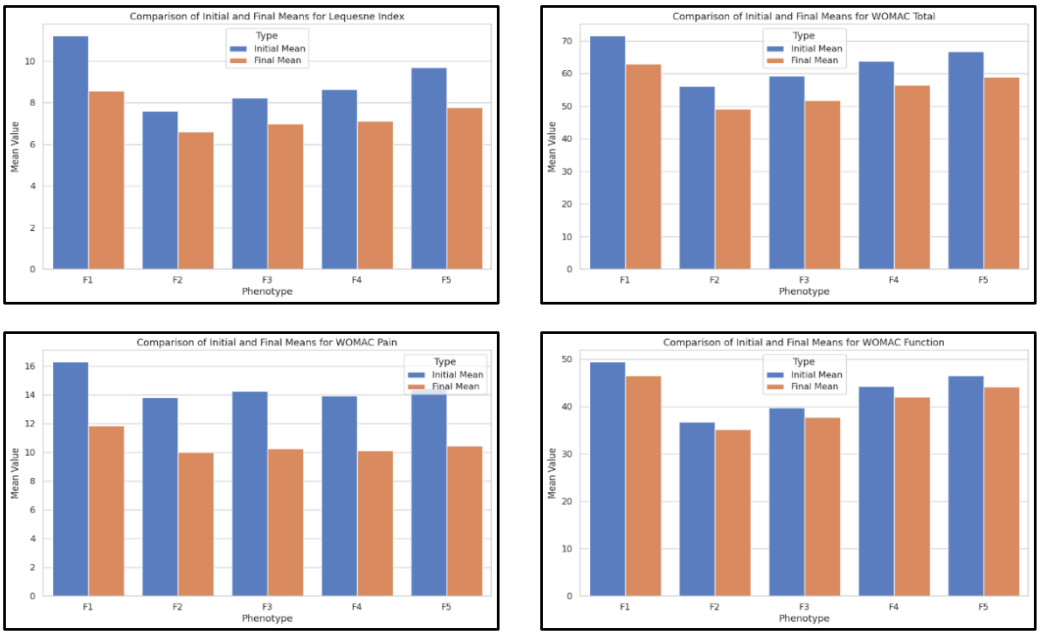

Figure 5. Mean values (initial/final) of functional parameters.

The evolution of ICF phenotypes for OAG.

We analyzed the values of generic qualifiers (at two evaluation time points) for the most significant elements of the core ICF set, abbreviated form, used in OAG, across each of the five phenotypes. Specifically:

- The three functions-pain sensation (b280), joint mobility (b710), and muscle functions (b730)-Figure 6;
- Two structures (from the three classifications)-lower extremity (s750) and additional musculoskeletal structures related to movement (s770)-Figure 7;
- The three elements for activities and participation-walking and moving (d450), dressing (d540), using the upper limb (d445)-Figure 8;
- Two environmental factors (from the four classifications)-family (e310), personal-use products and technologies (e115)-Figure 9.

It should be noted that improved functioning corresponds to a reduction in the qualifier value.

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Para-meter	F1 Initial	F1 Final	F2 Initial	F2 Final	F3 Initial	F3 Final	F4 Initial	F4 Final	F5 Initial	F5 Final
b280	3.29 ± 0.49	1.86 ± 0.69	2.40 ± 0.55	1.80 ± 0.45	2.50 ± 0.58	1.75 ± 0.50	2.61 ± 0.64	1.49 ± 0.53	2.80 ± 0.56	1.57 ± 0.50
b710	2.43 ± 0.53	2.00 ± 0.00	2.60 ± 0.55	2.00 ± 0.00	2.50 ± 0.58	2.00 ± 0.00	2.37 ± 0.53	2.02 ± 0.38	2.40 ± 0.55	2.05 ± 0.32
b730	2.29 ± 0.49	2.00 ± 0.58	2.20 ± 0.45	1.80 ± 0.45	2.00 ± 0.00	1.50 ± 0.58	2.19 ± 0.40	1.87 ± 0.54	2.20 ± 0.41	1.95 ± 0.50

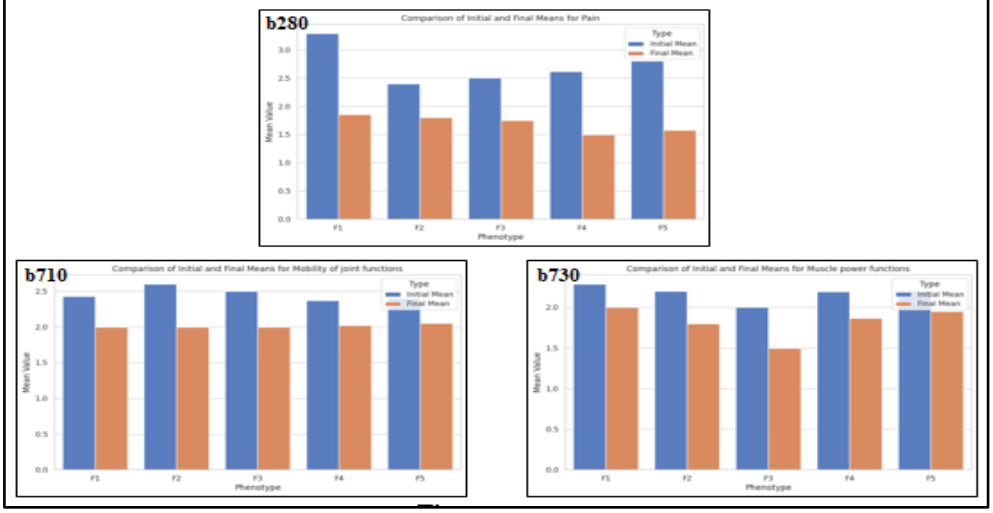

Figure 6. Mean values (initial/final)-ICF function qualifiers for phenotypes.

Para-meter	F1 Initial	F1 Final	F2 Initial	F2 Final	F3 Initial	F3 Final	F4 Initial	F4 Final	F5 Initial	F5 Final
s750	3.71 ± 0.49	2.71 ± 0.49	4.00 ± 0.00	2.80 ± 0.45	4.00 ± 0.00	2.75 ± 0.50	3.65 ± 0.50	2.64 ± 0.60	3.67 ± 0.47	2.65 ± 0.58
s770	2.14 ± 0.69	1.71 ± 0.49	2.60 ± 0.89	1.80 ± 0.45	3.00 ± 0.00	2.00 ± 0.00	1.81 ± 0.77	1.46 ± 0.55	1.85 ± 0.70	1.45 ± 0.55

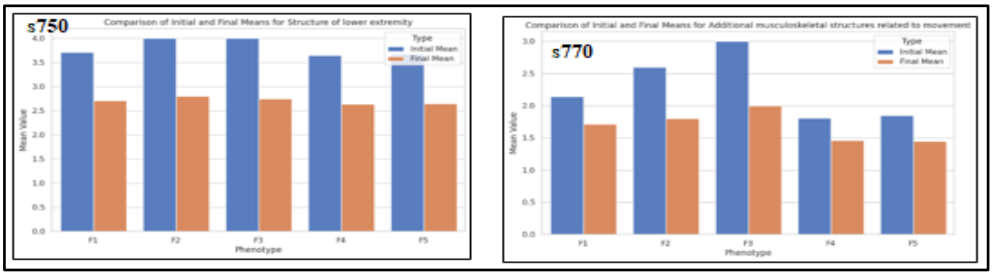

Figure 7. Mean values (initial/final)-ICF structure qualifiers for phenotypes.

Para-meter	F1 Initial	F1 Final	F2 Initial	F2 Final	F3 Initial	F3 Final	F4 Initial	F4 Final	F5 Initial	F5 Final
d450	3.14 ± 0.38	2.14 ± 0.38	2.80 ± 0.45	2.20 ± 0.45	2.75 ± 0.50	1.75 ± 0.50	2.67 ± 0.66	2.01 ± 0.67	2.98 ± 0.58	2.25 ± 0.59
d540	2.00 ± 0.00	1.29 ± 0.49	1.40 ± 0.55	1.20 ± 0.45	1.50 ± 0.58	1.00 ± 0.00	1.82 ± 0.39	1.45 ± 0.50	1.90 ± 0.30	1.48 ± 0.51
d445	1.57 ± 0.53	1.29 ± 0.49	1.40 ± 0.55	1.20 ± 0.45	1.75 ± 0.50	1.50 ± 0.58	1.46 ± 0.50	1.28 ± 0.45	1.48 ± 0.51	1.23 ± 0.42

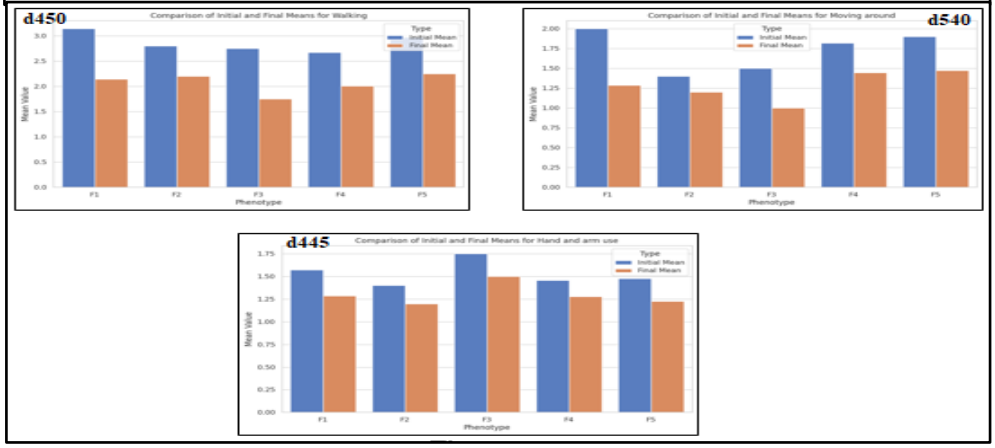

Figure 8. Mean values (initial/final)-ICF activity and participation qualifiers for phenotypes.

Para-meter	F1 Initial	F1 Final	F2 Initial	F2 Final	F3 Initial	F3 Final	F4 Initial	F4 Final	F5 Initial	F5 Final
e310	1.43 ± 0.53	1.14 ± 0.38	1.20 ± 0.45	1.00 ± 0.00	1.50 ± 0.58	1.00 ± 0.00	1.52 ± 0.50	1.24 ± 0.43	1.45 ± 0.50	1.23 ± 0.42
e115	2.43 ± 0.53	1.29 ± 0.49	2.80 ± 0.45	1.80 ± 0.45	2.50 ± 0.58	1.75 ± 0.50	2.48 ± 0.50	1.58 ± 0.57	2.55 ± 0.50	1.48 ± 0.51

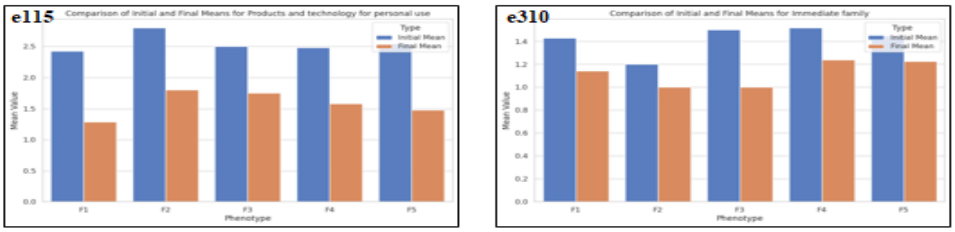

Figure 9. Mean values (initial/final)-ICF environmental factor qualifiers for phenotypes.

Phenotypes F4 and F5 showed significant improvements across all evaluated functions, indicating increased efficacy in patients with comorbidities and metabolic diseases (Figure 10).

Reduction in pain sensation, improvement in joint and muscle mobility, as well as enhancements in functions related to walking, dressing, and hand use, reflect an overall improvement in the quality of life for these patients.

Parametru	1 Mean ± SD	F1 p-value	F2 Mean ± SD	F2 p-value	F3 Mean ± SD	F3 p-value	F4 Mean ± SD	F4 p-value	F5 Mean ± SD	F5 p-value
b280_1	3.29 ± 0.49	0.0010*	2.40 ± 0.55	0.0958	2.50 ± 0.58	0.0981	2.61 ± 0.64	0.0000*	2.80 ± 0.56	0.0000*
b280_2	1.86 ± 0.69		1.80 ± 0.45		1.75 ± 0.50		1.49 ± 0.53		1.57 ± 0.50	
b710_1	2.43 ± 0.53	0.0781	2.60 ± 0.55	0.0705	2.50 ± 0.58	0.1817	2.37 ± 0.53	0.0000*	2.40 ± 0.55	0.0008*
b710_2	2.00 ± 0.00		2.00 ± 0.00		2.00 ± 0.00		2.02 ± 0.38		2.05 ± 0.32	
b730_1	2.29 ± 0.49	0.3376	2.20 ± 0.45	0.1950	2.00 ± 0.00	0.1817	2.19 ± 0.40	0.0000*	2.20 ± 0.41	0.0168*
b730_2	2.00 ± 0.58		1.80 ± 0.45		1.50 ± 0.58		1.87 ± 0.54		1.95 ± 0.50	
s750_1	3.71 ± 0.49	0.0024*	4.00 ± 0.00	0.0039*	4.00 ± 0.00	0.0154*	3.65 ± 0.50	0.0000*	3.67 ± 0.47	0.0000*
s750_2	2.71 ± 0.49		2.80 ± 0.45		2.75 ± 0.50		2.64 ± 0.60		2.65 ± 0.58	
s770_1	2.14 ± 0.69	0.2072	2.60 ± 0.89	0.1248	3.00 ± 0.00	0.0000*	1.81 ± 0.77	0.0010*	1.85 ± 0.70	0.0059*
s770_2	1.71 ± 0.49		1.80 ± 0.45		2.00 ± 0.00		1.46 ± 0.55		1.45 ± 0.55	
d450_1	3.14 ± 0.38	0.0003*	2.80 ± 0.45	0.0667	2.75 ± 0.50	0.0300*	2.67 ± 0.66	0.0000*	2.98 ± 0.58	0.0000*
d450_2	2.14 ± 0.38		2.20 ± 0.45		1.75 ± 0.50		2.01 ± 0.67		2.25 ± 0.59	
d540_1	2.00 ± 0.00	0.0082*	1.40 ± 0.55	0.5454	1.50 ± 0.58	0.1817	1.82 ± 0.39	0.0000*	1.90 ± 0.30	0.0000*
d540_2	1.29 ± 0.49		1.20 ± 0.45		1.00 ± 0.00		1.45 ± 0.50		1.48 ± 0.51	
d445_1	1.57 ± 0.53	0.3170	1.40 ± 0.55	0.5454	1.75 ± 0.50	0.5374	1.46 ± 0.50	0.0156*	1.48 ± 0.51	0.0189*
d445_2	1.29 ± 0.49		1.20 ± 0.45		1.50 ± 0.58		1.28 ± 0.45		1.23 ± 0.42	
e310_1	1.43 ± 0.53	0.2731	1.20 ± 0.45	0.3739	1.50 ± 0.58	0.1817	1.52 ± 0.50	0.0002*	1.45 ± 0.50	0.0337*
e310_2	1.14 ± 0.38		1.00 ± 0.00		1.00 ± 0.00		1.24 ± 0.43		1.23 ± 0.42	
e115_1	2.43 ± 0.53	0.0013*	2.80 ± 0.45	0.0077*	2.50 ± 0.58	0.0981	2.48 ± 0.50	0.0000*	2.55 ± 0.50	0.0000*
e115_2	1.29 ± 0.49		1.80 ± 0.45		1.75 ± 0.50		1.58 ± 0.57		1.48 ± 0.51	

Figure 10. Mean values and standard deviation compared at the two evaluation time points for ICF ratings across the five phenotypes.

Discussions

The original dimension of the study is supported by:

- Assessing OAG phenotypes in patients from the Oltenia region, defining and applying an adapted physical-kinetic program.
- Utilizing qualifiers for functional aspects in patients with OAG.

Due to these considerations, we could not refer to similar data from the literature. OAG is recognized as the tenth leading cause of years lived with disability globally [16].

Therefore, research focuses on improving patients' quality of life by managing disability and addressing deficiencies caused by structural and functional changes, as well as limitations in activities and participation.

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In addition to mortality and morbidity, functional status is a crucial health indicator, with walking being essential for daily life. The knee joint, the body's most complex joint and bearing the greatest load, makes knee osteoarthritis (KOA) a prevalent chronic joint disease worldwide, characterized by high rates of morbidity and disability [17].

Functional assessment scales:

Patient-reported measures in this study included three widely used scales in rehabilitation research-VAS, WOMAC, and Lequesne Index. These scales assess their psychometric properties in KOA research.

The VAS is primarily used to measure pain. A reduction of 1.75cm on the scale is considered the minimal clinically important difference (MCID) in OA research. In our study, we achieved a reduction of 1.8cm [18].

The WOMAC scale is a standardized instrument, widely employed in osteoarthritis clinical trials [19], assesses subjects' mobility and their ability to perform various activities. An improvement of 12% or more from baseline is considered the minimal clinically important difference (MCID) in OA research [20].

In 2022, Rynne et al. showed statistically significant improvements in total WOMAC scores favoring gait retraining over a control intervention in patients with hip or knee osteoarthritis [21].

In our study, the improvement in WOMAC scores was 7%, which falls below the recommended MCID. A possible explanation could be the relatively short duration during which significant functional improvements can be achieved. Many studies suggest a timeframe of 6 to 12 months, during which the benefits of the program become more apparent in enhancing patient function.

It is noteworthy that the obtained values were statistically significant, and the WOMAC functional subscale showed favorable progression, which is a significant argument for the effectiveness of gait training in improving the functional status of patients.

The MCID for the Lequesne Index has not yet been established in knee OA research [22].

However, in our study, the index significantly decreased from 8.1±2.4 to 6.6±1.8 (p=0.0079), indicating a 22% improvement. The scores of functional scales correlated statistically with physical performance and gait parameters, supporting the functional conditioning of OAG patients by these variables.

Regardless of the phenotype classification, patients showed improvement in functional scale scores, a crucial aspect for enhancing the quality of life in OAG patients.

ICF Evaluation

In knee osteoarthritis (KOA), gait dysfunction and symptoms such as pain adversely affect an individual's activity and participation levels, as outlined by the International Classification of Functioning, Disability and Health Framework (ICF). According to the ICF model, an individual's functioning results from the interactive influence of their health condition, environmental factors, and personal factors [23], which were not extensively measured in the present study.

Ideally, any study in rehabilitation research should assessed the main aspects of functioning according to ICF categories. This included ICF body function domains (*e.g.* b2 sensory functions and pain), activities domains (*e.g.* d4 mobility) and participation domains (*e.g.* d9 community, social and civil life). Walking (d450) and moving around (d455) are among the functional aspects that should be incorporated into studies investigating health interventions aimed at improving specific outcomes like mobility and self-care [24].

The function and participation domains have correspondence in used scale`s items for our patients (e.g. d4105 bending-can be operationalized with the item 'Bend down to pick up clothing from the floor' from the Lequesne Index). In 2018, Madden et.al. mentioned that future research would provide empirical evidence for employing the ICF Standardized Assessment and Reporting System (ICF-StARS) methodology in meta-analysis in Cochrane Reviews [25]. One year later, participants in 16 studies reported experiencing functional limitations in movements due to their knee osteoarthritis (KOA), particularly restrictions in mobility, difficulties in self-care activities, and limitations in leisure pursuits such as walking, gardening, sports, and other forms of exercise, along with a fear of falling. Subjects attributed these impacts to the severity of their KOA, affecting their physical activities significantly [26]. To control these functional aspects, people with KOA should be emboldened to participate in achievable amounts of physical activity, of even modest intensities.

Although the literature provides recommendations for using elements from the ICF classification, to date, there is no study that objectively justifies the benefit of a physical-

kinetic program for patients with OAG. Through evaluation using qualifiers for ICF classification elements, both pre-and post-program, an objective assessment of subjective complexity can be made regarding the patient's functional status.

Pain sensation (b280) improved significantly, especially for patients in phenotypes F1, F4, and F5, joint mobility (b710) for phenotypes F1, F2, and F3, and muscle functions (b730) for F2 and F3. It is noteworthy that favorable progress was observed for all patients.

Lower extremity structures (s750) showed significant improvement across all phenotypes except F5, while additional musculoskeletal structures related to movement (s770) exhibited significant correction for the first three phenotypes. Patients with comorbidities had less pronounced improvement, possibly due to the complex impact of different conditions on striated muscle groups.

Significant favorable progress in activities and participation was achieved for phenotypes F1 and F3-specifically in walking and moving (d450) and dressing (d540), and in the use of the upper limb (d445) for F1 only. Other phenotypes showed improvement in these areas but to a lesser extent. This functional aspect underscores that inflammatory processes and various comorbidities significantly affect the overall status of the patient, impacting not only somatic but also overall body functioning complexity.

Environmental factors (from the four in the classification)-personal-use products and technologies (e115) and family support (e310)-evolved similarly to the previously mentioned factors, highlighting the essential role of family in comprehensive OAG management.

Conclusions

Phenotypic classification of patients with knee osteoarthritis (KOA) enables the application of a personalized, adapted physical-kinetic program.

In conclusion we can point out that the assessment of functioning in patients with OAG should be conducted with careful attention and patience to highlight functional and biomechanical limitations.

The use of the minimal ICF set in the functional assessment of patients with OAG is essential, serving as a practical tool for monitoring the effectiveness of the applied physical-kinetic program and phenotypic classification of patients with OAG is crucial for personalizing the physical-kinetic program, aimed at restoring and maintaining quality of life.

Conflict of interests

None to declare

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Corresponding Author: Rădulescu Dumitru, Department of Surgery, The Military Emergency Clinical Hospital „Dr. Stefan Odobleja", Strada Caracal 150, 200749 Craiova, Romania, e-mail: dr_radulescu_dumitru@yahoo.com