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Comparative Effect of Weight-Bearing and Non-Weight-Bearing Exercises on Psychological Well-Being, Neurobiological, and Cellular Oxygenation Outcomes: A Pathway to Recovery

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Abstract

Background: Knee osteoarthritis (OA) is a degenerative and complex disease influenced by mechanical, neurological, and psychological factors. Due to its increasing prevalence associated with aging and obesity, it is essential to understand how different types of exercise affect psychological well-being, neurobiological indicators, and cellular oxygenation is essential for optimizing recovery.
Objective: To compare the effectiveness of weight-bearing and non-weight-bearing exercises on psychological well-being, neurobiological markers, and cellular oxygenation.
Methods: Eighty volunteers with persistent knee pain (≥3 months) were enrolled in a single-blind randomized controlled trial conducted at the Riphah Rehabilitation Center in Lahore, Pakistan. Participants aged 40 years and older were randomly allocated to two intervention groups. Both groups received baseline treatment, Group A additionally performed non-weight-bearing exercises, whereas Group B performed weight-bearing exercises, including quadriceps strengthening, for a duration of six weeks. Outcomes were assessed using the Depression Anxiety and Stress Scale (DASS 2.1), ELISA, and arterial blood gas analysis to evaluate oxygenation. Data were analyzed using SPSS version 25, with a $p < 0.05$ considered statistically significant.
Results: Following the intervention, significant improvements were observed in stress, anxiety, depression, BDNF level, and oxygenation in both the weight-bearing and non-weight-bearing exercise groups ($p < 0.05$). Comparative analysis revealed no significant difference in anxiety between the groups; however, the weight-bearing group demonstrated significantly greater improvements in stress, depression, BDNF levels, and oxygenation ($p < 0.05$).
Conclusion: Both interventions resulted in improvements in psychological and physiological outcomes among patients with knee osteoarthritis. However, weight-bearing exercises demonstrated greater benefits in terms of neurobiological markers and psychological well-being.
Keywords: knee osteoarthritis, brain-derived neurotrophic factor, anterior knee pain syndrome, weight-bearing exercise, anxiety
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Сравнительный эффект упражнений с осевой нагрузкой и без на психологическое благополучие, нейробиологические показатели и параметры клеточной оксигенации: путь к восстановлению

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Резюме

Остеоартрит коленного сустава – это дегенеративное и комплексное заболевание, на которое влияют механические, неврологические и психологические факторы. В связи с увеличением его распространённости, обусловленной старением и ожирением, важно понимать, как различные типы упражнений влияют на психологическое состояние, нейробиологические показатели и клеточную оксигенацию, чтобы оптимизировать процесс восстановления.

Цель: Сравнить эффективность упражнений с осевой нагрузкой и без неё с точки зрения психологического состояния, нейробиологических показателей и клеточной оксигенации.

Методы: В исследование включено 80 добровольцев с персистирующей болью в коленном суставе (>3 мес.) в рамках одностороннего слепого рандомизированного контролируемого исследования, проведённого в Центре реабилитации Riphah в Лахоре, Пакистан. Участники в возрасте 40 лет и старше были случайным образом разделены на две группы. Обе группы получили базовое лечение; группа А дополнительно выполняла упражнения без осевой нагрузки, а группа Б – упражнения с осевой нагрузкой, включая укрепление квадрицепсов, в течение 6 недель. Оценка результатов проводилась с использование шкалы депрессии, тревожности и стресса (DASS 2.1), анализа ELISA и анализа газов артериальной крови для оценки оксигенации. Данные анализировались с помощью SPSS версия 25 (p<0,05).

Результаты: После вмешательства обе группы продемонстрировали значительное улучшение показателей стресса, тревожности, депрессии, уровня BDNF и оксигенации (p<0.05). Сравнительный анализ показал отсутствие значимых различий в уровне тревожности; однако группа, которая выполняла упражнения с осевой нагрузкой, продемонстрировала значительно более выраженные улучшения в показателях стресса и депрессии, уровня BDNF и клеточной оксигенации.

Заключение: Оба подхода привели к улучшению психологических и физиологических показателей у пациентов с остеоартрозом коленного сустава. При этом упражнения с осевой нагрузкой характеризовались более выраженным положительным влиянием на нейробиологические маркеры и психологическое благополучие.

Ключевые слова: остеоартроз коленного сустава, нейротрофический фактор мозга (BDNF), синдром передней боли в колене, упражнения с осевой нагрузкой, тревожность

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Introduction

With aging, joint stiffness and discomfort are common complaints, but they may be signs of the osteoarthritis (OA), a chronic degenerative joint condition rather than merely normal aging. The knee is the most frequently affected joint worldwide and a major contributor to disability. OA involves the entire joint – including cartilage, subchondral bone, ligaments, and synovium – and often causes pain, stiffness, and functional loss that can substantially reduce quality of life over many years. Although OA has historically been viewed as an inevitable consequence of aging, it is now understood as a disorder with modifiable risk factors and potential for prevention and treatment through early intervention. With an aging population and rising obesity rates, the prevalence of knee OA is increasing worldwide.

In the United States, around 12 million people have been affected by knee osteoarthritis, predominantly adults aged 65 years or older. The condition affects females more frequently than males.[1] According to the Global Burden of Disease (GBD) study, the number of diagnosed cases of knee osteoarthritis has increased at an annual rate of approximately 8%.[2] Approximately 20 years prior to 2017, the incidence of clinically diagnosed knee OA was reported to be 7 per 1,000 person-years.[3] A systematic review has shown that the lifetime risk of developing knee OA ranges from approximately 14% to 45%.[4]

OA, as a progressive disease, is associated with multiple factors, including but not limited to mechanical loading, inflammatory mechanisms, metabolic and biochemical processes, genetic variations, and overall joint integrity.[5] Malalignment leads to uneven load distribution across the joint, thereby accelerating mechanical wear over time and constituting a major risk factor for joint injury.[6] This process may initiate a cycle of progressive deterioration that ultimately results in joint failure. Inflammation of the cartilage and synovial lining also contributes to joint degeneration and pain.[7] Identified risk factors include advanced age, higher body mass index, poor joint alignment, osteoarthritis in the contralateral knee, early structural joint changes, and low fasting glucose levels during the two to four years preceding the radiographic onset of accelerated knee osteoarthritis (AKOA).[8] Individuals commonly exhibit signs of meniscal injury, increased bone marrow lesions, joint effusion and inflammation, rapid cartilage loss, reduced mobility, and greater arthritis-related impact within 1–2 years prior to disease onset. As joint pathology progresses, traumatic events may occur, most commonly in the form of severe meniscal tears that compromise joint stability.[9]

The development and progression of knee osteoarthritis (OA) are strongly influenced by psychological distress, which also has a substantial impact on pain perception and overall disease burden.[10] Elevated levels of knee pain, greater disability, and reduced quality of life have been associated with stress and related psychosocial factors, such as anxiety and depression; these associations appear to be particularly pronounced in women. In addition to exacerbating pain, these psychological conditions influence how individuals respond to and cope with chronic pain.[11]

Maladaptive cognitive and behavioral responses, including catastrophizing, fear-avoidance, and negative thinking, may accelerate the transition from acute to chronic pain.[12] Chronic psychological stress also adversely affects physical health by contributing to sleep disturbances, elevated cortisol levels, obesity, and metabolic syndrome, all of which are recognized risk factors for OA.[13] Persistent pain, stiffness, and functional limitation associated with knee OA may give rise to a cycle of psychological distress and physical deterioration.[14] This cycle often results in social isolation, reduced mobility, and, in some cases, substance misuse. Consequently, effective management of OA requires the identification and treatment of psychological distress, underscoring the importance of a biopsychosocial approach in both clinical practice and research.[15]

Another key factor involved in the development of pain in knee osteoarthritis is elevated levels of brain-derived neurotrophic factor (BDNF).[16] Peripheral sensitization is a process that is enhanced by increased BDNF levels, as BDNF amplifies the responsiveness of nociceptive receptors within the knee joint.[17] Fusion proteins known as TrkB–Fc chimeras are generated by linking the extracellular domain of the TrkB receptor to the Fc portion of an antibody.[18] These chimeras are commonly used in research settings to investigate the role of TrkB and its ligands, including BDNF, by inhibiting TrkB-mediated signaling and thereby reducing pain in OA.[19]

Furthermore, BDNF contributes to the progression of joint degeneration by enhancing inflammatory processes within the synovial fluid of the knee joint.[20] This inflammatory activity further exacerbates pain and discomfort in patients with OA. By influencing neuronal survival and growth, BDNF promotes neuroplastic changes that contribute to the development of chronic and persistent pain in OA.[21] Collectively, these findings suggest that modulation of BDNF and its receptor represents a potential therapeutic strategy for the management of osteoarthritis.

The pathophysiology of knee osteoarthritis (OA), a condition increasingly recognized as a whole-joint disease affecting not only cartilage but also subchondral bone, synovium, and periarticular tissues, is strongly influenced by oxygen availability within joint tissues, particularly articular cartilage.[22] Because articular cartilage is avascular, chondrocytes reside in a hypoxic environment and require tightly regulated oxygen homeostasis to maintain normal cellular function and extracellular matrix integrity.[23] Evidence suggests that disturbances in local oxygen tension may contribute to the imbalance between anabolic and catabolic processes in OA by promoting the expression of matrix-degrading enzymes and the generation of reactive oxygen species (ROS), which damage cellular structures and the extracellular matrix.[24]

Although knee OA has been associated with systemic oxidative stress, the role of tissue oxygenation in the development of the disease remains poorly understood. To determine whether altered oxygen transport or cellular oxygen utilization contributes to cartilage degradation and joint dysfunction, measurement of arterial blood gas (ABG) levels represents a novel and potentially informative approach for assessing systemic oxygen status in patients with OA.[25]

Methods

This single-blind, randomized controlled trial (RCT) was conducted at the Riphah Rehabilitation Center in Lahore, Pakistan, between September 2022 and February 2023. The trial was performed in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines and registered with ClinicalTrials.gov (IRCT20230427058007N1) following approval by the Ethics Review Committee of Riphah International University, Lahore. G*Power 3 software was used to estimate the sample size based on previous literature, with a 95% confidence interval (CI) and 80% statistical power. To account for an anticipated 20% dropout rate, the calculated sample size was increased accordingly.

Participants were recruited from the outpatient department (OPD) using a non-probability purposive sampling technique. Eligible participants were men and women aged 40 years or older who had experienced knee pain for at least three months. All participants demonstrated tibiofemoral osteophytes on radiographic examination and reported an average overall pain intensity of at least 4 on an 11-point numeric rating scale (NRS) during the preceding week. Participants were willing to receive text message reminders during the study, if required, and possessed a mobile phone with text-messaging capability.

Participants were excluded if they had open wounds or ulcers on the ankles or feet, or systemic diseases such as severe cardiovascular, renal, or hepatic conditions. Additional exclusion criteria included lateral joint space narrowing greater than or equal to medial joint space narrowing on radiographs (as assessed using a radiographic atlas), knee surgery or intra-articular injection within the past six months, planned knee surgery within the next nine months, recent (current) or remote (within four weeks) use of oral corticosteroids, any systemic arthritic conditions, a history of knee fracture or cancer, prior hip or knee joint replacement, tibial osteotomy, or any other condition currently affecting lower limb function. Participants who had engaged in knee strengthening or neuromuscular/functional exercises within the previous six months, or who planned to initiate such exercise within the following nine months, were also excluded.

After obtaining written informed consent, participants were randomly assigned to two equal groups using computer-generated numbers by an independent researcher who was not involved in data collection or analysis. To ensure allocation concealment, the independent

researcher prepared opaque, sealed envelopes, which were opened sequentially to assign participants to their respective groups. Group A received standard non-weight-bearing exercises, while Group B underwent weight-bearing quadriceps strengthening exercises, combined with a baseline protocol of breathing exercises and grade I–II oscillatory therapy. Both groups also received gentle stretching and breathing techniques. Pre- and post-intervention assessments of cellular hypoxia, BDNF levels, and psychological profiles were conducted after six weeks. Participants in the intervention group attended five individual physiotherapy sessions over the six-week period, with each session lasting 30–40 minutes.

The exercise program lasted six weeks. The prescribed number of repetitions progressed from two sets of 20 repetitions to two sets of 10 repetitions per exercise, and subsequently to three sets per week. Participants were encouraged to follow the same routine for daily at-home exercises.[26] Exercise progression, based on the modified Borg Rating of Perceived Exertion CR-10 scale, proceeded from passive range of motion (ROM) to active ROM and finally to resisted activities using 0.5 kg ankle weights. The program was adjusted for any participant experiencing joint swelling or pain lasting more than one day by reducing repetitions, intensity, or frequency by half. All exercises were performed under the supervision of a physiotherapist. Weight-bearing activities, including toe standing, squats, single-leg standing, side leg lifts, and assisted leg extensions, were gradually advanced to independent performance without support.[27]

Non-weight-bearing exercises included knee flexion and extension in the supine position, hip abduction and adduction, side-lying leg lifts, and knee extensions (short-arc quadriceps exercises in sitting and supine, progressing from 0–45° and subsequently returning to 0°).[28] Assessments included ELISA, DASS 2.1, and arterial blood gases (ABGs), with measurements recorded both before and after the intervention. The examiner was blinded to group allocation.

Data analysis was performed using SPSS version 25. Qualitative data were presented as frequencies and percentages, while quantitative data were expressed as mean ± standard deviation. The Shapiro-Wilk test was used to assess data normality. For non-normally distributed data, non-parametric tests were applied, with results reported as median and interquartile range (IQR). Intragroup differences were analyzed using the Friedman test, and intergroup differences were assessed using the Mann–Whitney U test. A p-value of less than 0.05 was considered statistically significant.

Table 1
Shapiro-Wilk Test for Normality of Outcome Variables
Таблица 1
Тест Шапиро-Уилка на нормальность распределения исходных переменных

Variable	Shapiro Wilk-Statistic	p-Value
Stress Pre	0.9785	0.7835
Stress Post	0.9392	0.0864
Anxiety Pre	0.9871	0.9668
Anxiety Post	0.9685	0.4997
Depression Pre	0.9608	0.3237
Depression Post	0.9499	0.1679
BDNF Pre	0.971	0.5662
BDNF Post	0.98	0.8258
Oxygen Levels Pre	0.9733	0.6328
Oxygen Levels Post	0.9646	0.4033

Note: BDNF, brain derived neurotropic factor

Прим.: BDNF, нейротрофический фактор мозга

Table 2
Comparison of Continuous Baseline Characteristics Between Groups
Таблица 2
Сравнение непрерывных исходных характеристик между группами

Variable	Mean ± SD	Mean ± SD	*p*-Value
Age	56.20 ± 6.78	58.00 ± 7.75	0.504
Height	170.51 ± 11.12	169.82 ± 8.98	0.8538
Weight	69.17 ± 6.24	67.33 ± 4.79	0.3749
BMI	23.67 ± 1.72	23.40 ± 1.55	0.6588

Note: BMI, Body Mass Index; SD, Standard Deviation

Прим.: BMI – индекс массы тела, SD – стандартное отклонение

Results

The statistical analysis provides insights into the efficacy of the interventions by comparing the Weight-Bearing Exercise (WBE) and Non-Weight-Bearing Exercise (NWBE) groups across demographic characteristics, adherence, and outcome measures. Baseline characteristics of the two groups were comparable. There were no significant differences in gender distribution (60% female, 40% male) or adherence levels (66.7% high, 16.7% moderate, 16.7% poor) between groups ($p > 0.05$). Table 1 presents the results of the Shapiro-Wilk test, which assessed the normality of each outcome variable. Both pre- and post-intervention measures satisfied the assumption of normality, with all p-values greater than 0.05, thereby supporting the use of parametric tests, such as the t-test, for subsequent within-group and between-group analyses.

Baseline continuous demographic characteristics for the WBE and NWBE groups are summarized in Table 2. Age, height, weight, and BMI did not differ significantly between groups ($p > 0.05$ for all), indicating that the two groups were comparable prior to the intervention.

Table 3 shows the distribution of categorical variables, including gender and exercise adherence, for both intervention groups. Chi-square tests confirmed baseline comparability between groups for these categorical characteristics, with no significant association observed between group assignment and gender (p = 0.456) or adherence (p = 0.333).

Table 4 summarizes psychological outcomes, including stress, anxiety, and depression, for both groups. Post-intervention, depression and stress scores were significantly lower in the Weight-Bearing Exercise group (p = 0.0137 and p = 0.0155, respectively), whereas anxiety scores did not differ significantly between groups. These findings suggest that weight-bearing exercise regimens may confer mental health benefits.

Table 5 compares Brain-Derived Neurotrophic Factor (BDNF) levels before and after the intervention between the two groups. Pre-intervention BDNF levels did not differ significantly between groups (p = 0.5689). Post-intervention, BDNF levels were significantly higher in the Weight-Bearing Exercise group, with a mean difference of 1.54 ng/mL (95% CI: 0.44–2.66; p = 0.0084). These results indicate that the intervention led to a significant increase in BDNF levels.

Table 6 presents oxygen level measurements before and after the intervention. Pre-intervention oxygen levels did not differ significantly between groups (p = 0.4853). Post-intervention, oxygen levels were significantly higher in the Weight-Bearing Exercise group, with a mean difference of 4.10% (95% CI: 1.79–6.41; p = 0.0011), indicating a significant improvement in oxygen saturation following the intervention.

Table 7 presents a within-group pre- and post-intervention analysis of psychological and physiological outcomes for the Weight-Bearing Exercise group. Post-intervention, all measured outcomes showed notable improvements.

Table 3

Distribution of Categorical Variables and χ^2 Test Comparison

Таблица 3

Распределение категориальных переменных и проверка с помощью критерия χ^2

Variable	Category	Weight-Bearing (n=15)	Non-Weight-Bearing (n=15)	*p*-Value
Gender	Male	5	7	
	Female	10	8	0.456
Adherence to Exercises	High	9	11	
	Moderate	2	3	
	Low	4	1	
	Chi-Square p-value			0.333

Table 4

Comparison of psychological parameters across groups

Таблица 4

Сравнение психологических параметров между группами

Variable	Mean ± SD	Mean ± SD	t-Statistic	df	*p*-Value	95% CI (Diff)
Stress Pre	28.67 ± 4.35	31.33 ± 4.12	-1.724	27.9	0.0958	[-5.84, 0.50]
Stress Post	2.86 ± 0.18	3.02 ± 0.14	-2.587	26.4	0.0155	[-0.28, -0.03]
Anxiety Pre	25.33 ± 5.54	28.20 ± 6.00	-1.359	27.8	0.1849	[-7.19, 1.45]
Anxiety Post	12.93 ± 2.22	14.20 ± 3.23	-1.251	24.8	0.2227	[-3.35, 0.82]
Depression Pre	26.00 ± 4.47	24.93 ± 3.71	0.711	27.1	0.4833	[-2.01, 4.15]
Depression Post	15.47 ± 4.10	19.07 ± 3.33	-2.639	26.9	0.0137	[-6.40, -0.80]

Table 5

Comparison of biochemical outcomes across groups

Таблица 5

Сравнение биохимических показателей между группами

Variable	Mean ± SD	Mean ± SD	t-Statistic	df	*p*-Value	95% CI (Diff)
BDNF Pre	22.13 ± 1.44	22.48 ± 1.85	-0.577	26.4	0.5689	[-1.60, 0.90]
BDNF Post	26.09 ± 1.09	24.55 ± 1.78	2.879	23.2	0.0084	[0.44, 2.66]

Table 6

Comparison of cellular oxygenation outcomes across groups

Таблица 6

Сравнение показателей клеточной оксигенации между группами

Variable	Mean ± SD	Mean ± SD	t-Statistic	df	*p*-Value	95% CI (Diff)
Oxygen Levels Pre	90.03 ± 2.98	89.34 ± 2.33	0.708	26.5	0.4853	[-1.32, 2.70]
Oxygen Levels Post	96.49 ± 3.17	92.39 ± 3.01	3.635	27.9	0.0011	[1.79, 6.41]

Table 7
Pre- and Post-comparison in the Weight-Bearing Exercise Group
Таблица 7
Сравнение показателей до и после упражнений с нагрузкой на вес тела

Variable	Pre Mean ± SD	Post Mean ± SD	t-Statistic	df	*p*-Value	95% CI (Diff)
Stress	28.67 ± 4.35	2.86 ± 0.18	23.064	14	0.000	[23.40, 28.20]
Anxiety	25.33 ± 5.54	12.93 ± 2.22	7.542	14	0.000	[8.87, 15.93]
Depression	26.00 ± 4.47	15.47 ± 4.10	6.657	14	0.000	[7.14, 13.93]
BDNF	22.13 ± 1.44	26.09 ± 1.09	-9.479	14	0.000	[-4.87, -3.07]
Oxygen Levels	90.03 ± 2.98	96.49 ± 3.17	-16.124	14	0.000	[-7.31, -5.60]

Table 8
Pre- and Post- Comparison in the Non-Weight-Bearing Exercise Group
Таблица 8
Сравнение показателей до и после упражнений без осевой нагрузки

Variable	Pre Mean ± SD	Post Mean ± SD	t-Statistic	df	*p*-Value	95% CI (Diff)
Stress	31.33 ± 4.12	3.02 ± 0.14	26.829	14	0.000	[26.05, 30.58]
Anxiety	28.20 ± 6.00	14.20 ± 3.23	8.635	14	0.000	[10.52, 17.48]
Depression	24.93 ± 3.71	19.07 ± 3.33	5.358	14	0.0001	[3.52, 8.21]
BDNF	22.48 ± 1.85	24.55 ± 1.78	-2.873	14	0.0123	[-3.62, -0.52]
Stress	31.33 ± 4.12	3.02 ± 0.14	26.829	14	0.000	[26.05, 30.58]
Oxygen Levels	89.34 ± 2.33	92.39 ± 3.01	-9.332	14	0.000	[-3.75, -2.35]

Stress, anxiety, and depression scores decreased significantly ($p < 0.001$ for all), indicating clear psychological benefits. Physiologically, both BDNF and oxygen saturation levels increased significantly ($p < 0.001$), reflecting enhanced neuronal and respiratory function. Overall, these results demonstrate that the weight-bearing intervention improved both mental and physical well-being.

Table 8 presents a within-group pre- and post-intervention analysis of psychological and physiological outcomes for the Non-Weight-Bearing Exercise group. Post-intervention, stress, anxiety, and depression scores decreased significantly (all $p < 0.0001$), indicating notable improvements in mental health. BDNF levels also increased significantly ($p = 0.0123$), although the magnitude of change was smaller than that observed in the Weight-Bearing Exercise group. Additionally, oxygen saturation levels increased significantly after the intervention ($p < 0.001$), reflecting improved respiratory function. Overall, the non-weight-bearing intervention led to improvements in both physiological measures and psychological well-being.

Discussion

This study aimed to evaluate the effects of weight-bearing and non-weight-bearing exercises on psychological outcomes, biochemical markers, and cellular oxygenation in patients with knee osteoarthritis (OA). The findings indicate that while both intervention groups demonstrated improvements in BDNF levels, cellular oxygenation, and reductions in stress, anxiety, and depression over the six-week intervention period, the Weight-Bearing Exercise group exhibited significantly greater improvements compared with the Non-Weight-Bearing Exercise group.

The results demonstrated that stress levels decreased in both the Weight-Bearing and Non-Weight-Bearing Exercise groups, with post-intervention mean scores significantly lower than baseline. Interestingly, the reduction in stress was slightly greater in the Non-Weight-Bearing group. These findings align with previous research showing that low-impact, non-weight-bearing interventions, such as aquatic therapy, can substantially reduce stress in individuals with osteoarthritis by promoting relaxation and minimizing joint loading.[29]

Conversely, a study investigating challenges associated with strengthening exercises reported that exercise can present several psychological and physical obstacles for patients and therapists, including pain-related fear, misconceptions about exercise, difficulty performing exercises, use of cuff weights, and negative effects of comorbid medical conditions.[30] The present findings, however, contradict this notion, demonstrating that even weight-bearing exercises, when properly tailored, can substantially reduce stress. These results suggest that individualized exercise programs and professional supervision may help alleviate such concerns.

Both intervention groups exhibited a substantial decrease in depression scores following the intervention, with the Weight-Bearing Exercise group showing a greater mean reduction than the Non-Weight-Bearing Exercise group. Similarly, Hall (2021) reported that strengthening

exercises were more effective for overall mental health compared with aerobic and mind-body exercises (mean difference 12.51, 95% CI: 4.25–20.77) and also demonstrated superior effectiveness for reducing depressive symptoms compared with stretching exercises.[32]

Anxiety levels were also significantly reduced in both intervention groups, with the Non-Weight-Bearing Exercise group showing a slightly larger effect. A study by Xiao Ma et al. (2024) investigating the relationship between anxiety and weight-bearing joints in osteoarthritis found no evidence that anxiety was induced by weight-bearing joint OA (knee or hip). Nevertheless, clinical research supports a substantial association between generalized anxiety disorder (GAD) and weight-bearing joint OA. Further studies are needed to clarify whether weight-bearing joint OA and GAD are causally related.[32]

Both Weight-Bearing and Non-Weight-Bearing Exercise regimens led to a significant increase in blood BDNF levels, with post-intervention levels significantly higher in the Weight-Bearing Exercise group. This finding is consistent with previous research demonstrating the effect of exercise on neurotrophic factors. For example, S. Puts et al. (2023) reported that acute exercise increased BDNF and induced a myokine response compared with other inflammatory markers. Exercise training may provide intra-articular and systemic anti-inflammatory benefits for patients with knee osteoarthritis, highlighting the importance of educating patients and clinicians about the anti-inflammatory properties of exercise.[33]

Baseline oxygen saturation levels did not differ between the Weight-Bearing and Non-Weight-Bearing Exercise groups ($p = 0.4853$). Post-intervention, however, the Weight-Bearing Exercise group showed a significantly greater increase in oxygen saturation ($p = 0.0011$), suggesting that weight-bearing exercise may more effectively improve cardiopulmonary efficiency. Previous research examining oxidative stress in patients with knee osteoarthritis indicated that antioxidant levels or markers of oxidative stress are linked to disease development. These findings emphasize the importance of individualized therapeutic approaches that support antioxidant effects and redox balance for joint health and overall systemic well-being.[34]

Controlled weight-bearing exercise may improve oxygenation in the affected joint by enhancing blood flow and cartilage health, making it a valuable intervention for managing knee osteoarthritis. Excessive exercise, however, should be avoided, as it can reduce oxygen levels and potentially damage cartilage. Optimizing the benefits of exercise while minimizing risks requires an individualized approach that considers each patient's tolerance and the severity of their OA.

The safety and feasibility of both interventions are further supported by high adherence rates and the absence of significant adverse events in either group. Individualization enhances the clinical relevance of the findings and improves the generalizability of outcomes; for example, exercise intensity can be adjusted according to pain and swelling. Overall, when properly tailored and supervised, weight-bearing functional exercises are supported by evidence as an effective component of physiotherapy programs for patients with knee OA.

Conclusion

This randomized controlled trial demonstrates that both Weight-Bearing and Non-Weight-Bearing exercise protocols effectively reduce psychological stress and improve biochemical and oxygenation parameters in patients with knee osteoarthritis. Compared with Non-Weight-Bearing exercises, Weight-Bearing exercises produced significantly greater improvements in BDNF levels and cellular oxygenation. Regarding psychological outcomes, Non-Weight-Bearing exercises showed slightly greater reductions in stress and anxiety, whereas depression levels decreased more substantially in the Weight-Bearing group. These findings highlight the importance of addressing mental well-being alongside biochemical and functional factors in OA rehabilitation and support the incorporation of progressive, weight-bearing resistance exercises into standard physiotherapy programs. Large-scale, multi-center studies with longer follow-up periods are recommended to further validate and extend these results.

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