Original Article

Monitoring Molecular Biological Changes During Neurological and Musculoskeletal Rehabilitation after Stroke using a Telemedicine Platform: An Optimization Strategy for Personalized Rehabilitation Treatment

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Abstract

Background: Prosthetic use and service delivery following a stroke do not tend to be as individualized as they should be to correlate with patients' diverse recovery patterns. Molecular biomarker assessment combined with telemedicine looks promising and can be an innovative approach to the optimization of the rehabilitation process. **Objective:** To purpose of this research is the assess the effectiveness of the three-month telemedicine-based rehabilitation program including the monitoring of molecular biomarkers of stroke survivors in improving functional and quality-of-life indicators. **Methods:** In a randomized controlled trial, 100 stroke patients were allocated to two groups: the experimental group that received specific rehabilitation through using of telemedicine and molecular biomarkers and the comparison group that received conventional rehabilitation. Blood molecular biomarkers associated with neuroplasticity (BDNF), inflammation (IL-6), and muscle injury/repair (CK) were assessed before the training intervention at 6 weeks and 12 weeks. **Results:** Compared to the control group, the intervention group had a higher functional independence and motor function recovery indicated by the Modified Rankin Scale and Fugl Meyer Motor score as well as better balance and quality of life ($p < 0.05$). Aerobic exercise thus promotes marked shifts in biomarkers of neuroplasticity and muscle repair from molecular pathways involving BDNF and CK, and inflammation from IL-6. **Conclusion:** Such errors make it difficult for a patient to have personal rehabilitation in the hospital and hence Telemedicine coupled with biomarker monitoring enables an improved recovery in stroke patients. This dynamic concept holds early potential for increasing the effectiveness of rehabilitation and potentially improving post-stroke quality of life.

Keywords: Molecular Biological Changes, Neurological, Musculoskeletal Rehabilitation Telemedicine Platform.

Introduction

Stroke is the fifth most common cause of disability with the majority of patients developing neuromotor and musculoskeletal disability that affects their quality of life and level of autonomy. It has been observed that conventional methods of rehabilitation do have applications to help the patients, but these conventional methods do not follow individual patient care and do not cater to the needs of the patients during the successive stages of rehabilitation. New developments in telerehabilitation systems and molecular tracking can be used to optimize stroke intervention by developing individual molecular and biological pathways for the patients. So when integrated

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with telemedicine it may be possible to make rehabilitation more precise and effective from molecular biology and thus have a better result in stroke survivors.[1]

Stroke recovery is a multimodal and continuous process that encompasses biological, neurological, and behavioral changes at a given time. It is also important to understand that in the processes of stroke recovery, the brain goes through impressive restructuring based on processes including neurogenesis, angiogenesis, and synaptic plasticity.[2] These processes differ with the changes in molecules such as genes, proteins, and other biomarkers that are relevant to the current status of neuronal recovery. Similarly, for musculoskeletal function, molecular markers concerning muscle regeneration, inflammation, as well as metabolic alterations, are considered important. Nonetheless, the identification and tracking of these molecular changes in real-time, mainly in a home environment, have been quite a challenge.[3]

Emergence of Telemedicine in Rehabilitation

Telemedicine has turned out to be the revolution of society in the provision of health care services through the use of electronic means. In rehabilitation, telemedicine allows healthcare providers to have an additional interaction distance as well as constant monitoring and feedback that are not easily possible in conventional practice settings due to geographic and time barriers. In stroke rehabilitation, these telemedicine platforms have allowed patients to perform a series of tasks, receive feedback on their performance, and interact with healthcare professionals while at home. This remote access is extremely useful for the patient because many of them have difficulty with mobility after a stroke and therefore cannot attend, in-person, rehabilitation sessions.[4-6] Besides, increased attention has been paid to cost savings: telemedicine frees a patient from multiple trips to the hospital while helping maintain adherence to a rehabilitation regimen. Yet, telemedicine proved beneficial for remote delivery of physical/occupational therapy/s Currently, widespread telemedicine applications exclude coordination of the integrated biological/molecular informatics monitoring in real-time. When used without understanding a patient's molecular characteristics, telerehabilitation may lack information that can be used to change the course of rehabilitation and fine-tune the process.[7] The use of molecular monitoring in a telemedicine context may provide the missing link in reaching these goals and adapting rehabilitation programs to patients' biological needs.

The Role of Molecular Biomarkers in Stroke Recovery

Thus, molecular biomarkers give a glimpse of the constant ongoing processes at the molecular level in the body and the brain as they seek to recover. Some biomarkers associated with inflammation, synaptic changes and general tissue plasticity, muscle hypertrophy, and metabolism can help understand the body's recovery in response to rehabilitation measures after stroke. For example, the BDNF and VEGF proteins regulate neuroplasticity and are usually used for the evaluation of brain recovery markers. Like erythrocyte sedimentation rate ESR and C-reactive protein CRP indicate the degree of inflammation existing in a player or a client's body that in turn may affect his neurological function or musculoskeletal system.[8] These biomarkers could be checked thereby helping clinicians not only modify rehabilitation measures depending on what phase the patient is in but also refer more to exercises that suit the phase.[9-10] However, molecular knowledge is also a key area for musculoskeletal rehabilitation, especially when atrophy or spasticity of muscles is present. Depending on the kind of markers associated with MPS, OS, and metabolic changes, actual progress in muscle tissue regeneration and functional gains can be evaluated based on physical therapy exercises. When these molecular markers are combined with telemedicine tools, it is possible to observe the musculoskeletal system's reaction to specific rehabilitation exercises, rendering it a highly individualized and efficient form of a treatment plan.

Integrated Relatives Approaches: Rehabilitation with Telemedicine Molecular Tracking

The incorporation of molecular surveillance into the latest telehealth applications implies an innovation in individualized practice. Thanks to wearable biosensors and mHealth devices, it is possible to track a number of biomarkers non-invasively or at least minimally invasively.[11-13] These devices are capable of measuring biomarkers present in sweat, saliva, or other body fluids and provide a real opportunity to monitor biological reactions near the home environment. This continuous molecular feedback cycle when incorporated with remote clinical supervision allows for the formation of individualized treatment strategies that adapt continuously according to real-time information. Consequently, instead of using a single model of analytics-based rehabilitation plans, telemedicine platforms can deliver highly personalized programs adapted to the patient's requirements from a biological standpoint. Besides, increasing the effectiveness of treatments, such an approach can affect patients' participation and motivation positively. Engaging patients in their molecular as well as physiological outcomes can allow telemedicine to empower them with the knowledge of their progress toward getting better.[14] Accompanying molecular information into rehabilitation aims results in a more dynamic and educative process that will allow the patient to see how the process of rehabilitation evolves and how the patient's efforts influence the cellular level.

The Need for an Optimized Strategy

As shown the integration of molecular monitoring with telemedicine platforms is possible, however, there are certain limitations. Advanced data analysis, molecular and clinical data fusion, and real-time rehabilitation procedure modification and treatment planning are complex and need interdisciplinary expertise and advanced computational algorithms. To optimize the potential of such function-based biomarkers, there is a need to develop guidelines on how these biomarkers are selected, measured, and interpreted.

In addition, issues of data and patient confidentiality and security, as well as compliance with the use of telemedicine are considered key factors that determine the successful adoption of this technology. This strategy could probably enhance the neurological and musculoskeletal patient outcomes and at the same time holds the prospect of participating in the future's precision medicine approach where treatment regimens are designed based on patient characteristics. The use of molecular monitoring in telehealth, therefore, can be seen as an optimization strategy that could revolutionize stroke rehabilitation, enhancing the likelihood of better quality outcomes for the survivor. Rehabilitation after a stroke still poses a challenge that is restricted by general practices that do not consider the amount of biological difference in recovery. The current conventional rehabilitation does not have the flexibility of changing treatments in a way that reflects molecular and biological data to enhance personalized rehabilitation. Technological advancement has seen Telemedicine platforms across physical rehabilitation improve accessibility and continuity across distant geographical locations without patients having to stop rehabilitation; most telerehabilitation platforms center on functional growth without embracing molecular biomarkers for neurological and musculoskeletal growth. These deficiencies reaffirm the need to establish a system that can index other molecular variations as it tracks functional progress and calibrates rehabilitation for early-stroke patients.

Aim of the Study

The objective of this research is to design and test the effectiveness of a telemedicine system to envision an individual rehabilitation plan involving molecular analysis in stroke patients for neurological and musculoskeletal rehabilitation. The platform aims to improve the accuracy and efficacy of stroke rehabilitation by dynamically monitoring molecular biomarkers and responding proactively to the body's needs accordingly to optimize the functional recovery and, naturally, the quality of life of patients.

Literature Review

Stroke rehabilitation is a complex procedure that involves neuro and musculoskeletal systems. Manual therapy techniques like physiotherapy and occupational therapy are beneficial to patients, particularly for those with mobility issues. Still, sometimes in using these approaches, authors do not consider the patient's shortened healing curve. There is growing evidence of the use of kinematic telerehabilitation systems that incorporate molecular biomarker assessment into the rehabilitation process. This literature review analyzes the process of transition from post-stroke rehabilitation in historical terms, the possibilities of molecular biomarkers as a tool for measuring the progress of rehabilitation, the use of telemedicine in recent years in the rehabilitation process, and the newest advances in personalized rehabilitation technologies.[13-15]

New Trends in Stroke Rehabilitation

In stroke rehabilitation, the objectives are mainly aimed at the outcome improvement of a patient and achieving an optimal level of independence. In their practice, one of the researchers[14] defined standard rehabilitation interventions as practicing motor, cognitive, and language functions through repetition and activities. These interventions are helpful when practicing walking, and boosting other functional endpoints; however, they are not sensitive to the patient's changing biological rehabilitation phase. Contemporary literature supports the importance of goal-oriented therapies and therefore asserts that more effective rehabilitation can be achieved with the help of customized programs because of the consideration of patient's recovery necessities[14]. Moreover, the developmental aspects concerning neuroplasticity and the musculoskeletal system related to stroke recovery demand a more individualized and time-dependent approach. New methods in physical therapy, the use of robots, and rehabilitation based on virtual reality technologies allowed extending a range of rehabilitation procedures; however, these interventions do not involve real-time physiological feedback[5]. The need to go beyond traditional measurements is growing, and a biological-monitoring approach is apparent, as research is tracing the link between molecular changes and functional improvement.

Role and Importance of Molecular Biomarkers in the Recovery from Stroke

Molecular biomarkers are critically involved in providing tout the pathogenic process related to stroke rehabilitation. Others, which include brain-derived neurotrophic factor (BDNF) and vascular endothelial growth factor (VEGF) have been investigated for their potential to coordinate neuronal regeneration and synaptogenesis.[8] These biomarkers give crucial information on the extent of neurological recovery, which can be judged from the level of BDNTr and VEGF which is related to better neural plasticity and cognitive improvement.[10] Inflammatory biomarkers are also useful as a measure of recovery as IL-6 and CRP are two examples of cytokines involved in inflammation following a stroke and during the process of rehabilitation.[7] Neurological restoration and muscle wastage both worsen with elevated inflammation levels, factors that need to be closely measured during rehabilitation. Moreover, it is possible to identify specific musculoskeletal biomarkers: creatine kinase (CK), which indicates muscle cell damage and acts as an interleukin-6 receptor antagonist regarding tissue repair and myostatin, which describes muscle mass regrowth and offers information about physical rehabilitation and muscle sturdiness. These markers might be beneficial for tracking the effectiveness of rehabilitation and for adjusting the exercise protocol based on the patient's current biology to maximize the chance of functional improvement.

Telemedicine in Rehabilitation: More Access Points and Connection

Telemedicine has recently received great attention for several years and has been widely applied in chronic diseases and stroke patients' rehabilitation. The different reviews and research have indicated that telemedicine platforms enhance rehabilitation outcomes because of

facilitate surveillance, communication, and access to rehabilitation resources for patients.[13] As for the case of stroke rehabilitation, telemedicine has proved to be helpful for the use of therapy by immobile patients, allowing them to continue their therapies at home without having to go to the hospital often. Although telemedicine has proven effective for rehabilitation, and current telemedicine systems are designed to capture functional progress such as motor and mobility functions, it lacks biological data showing molecular-level response to rehabilitation. Video-based therapy and sensor-based exercise tracking are helpful means of tracking the body's physical development but they do not address the level of molecules that are fundamental to the assessment of neurological and musculoskeletal.[8] Filling this gap by incorporating molecular monitoring could improve the flexibility and accuracy of existing telemedicine applications to turn them into biomarker-based individualized rehabilitation tools.

Personalized Rehabilitation Technologies: A New Frontier

The move towards targeted rehabilitation has become more popular as healthcare delivers start to appreciate the fact that patients are unique when it comes to rehabilitation. Adaptive therapy and big data analysis technology enhanced person-oriented rehabilitation with techniques like artificial intelligence-based smart rehabilitation and real-time data analysis for individual client-specific rehabilitation approaches has been seen as a possible application in the field of rehabilitation.[2] Recent developments in biosensing technologies and mHealth gadgets enable tracking of physiological indicators to present contemporaneous assessments of a patient's biological profile to therapy. Using such devices when incorporated with telemedicine systems, it is now possible, to monitor molecular biomarkers namely, BDNF, CRP, and IL-6 through noninvasive procedures.[5-6] Multiple scientific papers have focused on the integration of molecular monitoring with rehabilitation as part of the patient's individualized treatment plan. In particular, Hota and colleagues indicated the essentiality and effectiveness of the biomarker-guided approach in motor and cognitive rehabilitation as opposed to conventional treatment: 303 patients randomly assigned to biomarker-adjusted personal rehabilitation plan seemed to have better results than the patients in the control group.[11] Thus, when assessing these biomarkers, clinicians would be able to determine where in the recovery process the patient is challenged, and could then adjust the intensity or type of exercises and therefore improve the recovery process. Moreover, by the presented ideas, molecular information may be used to increase patient involvement by presenting them with real-life evidence of their improvement in response to rehabilitation programs.

Methodology

The study design used in the current study was a quantitative, randomized controlled trial (RCT) to assess the effects of telemedicine-based molecular monitoring on self-optimised rehabilitation effects in post-stroke patients. It includes participant recruitment, intervention plan, molecular biomarkers measures, integration of telemedicine platform, and data analysis.

A sample size of 100 participants is calculated to achieve statistical power, with participants randomly assigned to either the intervention group (telemedicine-based personalized rehabilitation) or the control group (standard rehabilitation) in a 1:1 ratio.

Participant Selection

Participants were selected randomly from a tertiary care rehabilitation centre. The targeted population was the adults aged 40–75 years after the ischemic or haemorrhagic stroke in the last three months. Neuromuscular and skeletal deficits can be physical signs of stroke. The opportunity to attend the telemedicine sessions at home and agree to the molecular biomarker procedures. Other neurological disorders aside from stroke affect the patient. Other Gardasil contraindications related to the patient's chronic severe cognitive impairment are likely to compromise compliance with the established protocol. Exclusion criteria for the biomarker sampling methods employed trial (RCT) design to evaluate the impact of telemedicine-based molecular monitoring on personalized rehabilitation outcomes in stroke patients. The methodology comprises participant selection, intervention protocol, molecular biomarker monitoring, telemedicine platform integration, and data analysis. A sample size of 100 participants is calculated to achieve statistical power, with participants randomly assigned to either the intervention group (telemedicine-based personalized rehabilitation) or the control group (standard rehabilitation) in a 1:1 ratio.

Participant Selection

Participants was recruited from a tertiary care rehabilitation center. The following inclusion and exclusion criteria was ensure a homogenous sample for the study:

Inclusion Criteria:

- Adults aged 40–75 years who have experienced an ischemic or hemorrhagic stroke within the last three months.
- Clinical evidence of neurological and musculoskeletal impairments following stroke.
- Ability to participate in telemedicine sessions from home and consent to molecular biomarker monitoring.

Exclusion Criteria:

- Presence of other neurological conditions unrelated to stroke.
- Severe cognitive impairment affecting adherence to protocol.
- Contraindications to the biomarker sampling methods used.

The study aimed to recruit a sufficient number of participants to achieve statistical power, randomly

assigning them into two groups: recruiting patients into an intervention group receiving telemedicine-based personalized rehabilitation and a control group receiving standard rehabilitation in a 1:1 manner.

Study Design

This randomized controlled trial involves two groups:

- Intervention Group: The individuals undergo molecular biomarker-supervised telemedicine-based, customized rehabilitation.
- Control Group: Participants go through conventional guideline-based rehabilitation, and they are offered no molecular tracking or telemedicine.

The trial were 12 weeks long with quantitative data collected at baseline and at the respective end of week 6 and 12.

Intervention Protocol

Rehabilitation Program

The two subjects completed a standardized rehabilitation plan involving motor activities, balance tasks, and muscle strengthening tasks. The intervention group has 3 sessions weekly through telemedicine with a physiotherapist, while the control group has face-to-face sessions.

Telematics Intervention Group or simply Telemedicine System

The telemedicine software enabled remote supervisory control and real time monitoring of the entire system. It documented the actual participation status of the participants, their feedback to certain exercises, and changes done as per the molecular data.

Molecular biomarker is part of the regular follow up process of cancer patients; thus, it is a valid reason for patient follow up. In the intervention group, molecular biomarkers related to neuroplasticity, inflammation, and muscle repair was monitored through minimally invasive sampling:

- Neuroplasticity Markers: Blood samples were used in determination of Brain – derived neurotrophic factor (BDNF) level.
- Inflammatory Markers: IL-6 and CRP were measured and followed as markers of systemic inflammation.
- Muscle Repair Markers: CK was checked in order to assess muscle recovery and exercise response.

Outcome data were obtained at pre- intervention (week 0); mid intervention (week 6) and post intervention (week 12). Due to the information derived from the biomarkers, the progression of tasks in the rehabilitation protocol depended on the molecular concentration status.

5. Outcome Measures

Both the primary and secondary outcomes was measured at the end of enrollment, at Week 6 and at Week 12.

- Primary Outcome: Motor dysfunction measured with MRS and Fugl-Meyer Assessment of Motor Recovery following ischaemic stroke.
- Secondary Outcomes: Core stability and lower limb stability, by using Berg Balance Scale (BBS), muscle strength by grip strength, and quality of life by Stroke-Specific Quality of Life (SSQOL) scale.

Data Analysis

Data was analyzed using SPSS version 25.0. Descriptive statistics summarized baseline characteristics, while paired t-tests and repeated-measures ANOVA assessed within-group changes across time points. CASP was analyzed using an independent t-test, the ANOVA test was used for the between-group comparison and the statistical significance was set at $p < 0.05$. Since molecular biomarker testing was used to identify patient conditions, functional recovery progressions were compared to these biomarkers.

Results

The study recruited 100 participants, with 50 allocated to the telemedicine-based personalized rehabilitation group (Intervention Group) and 50 to the standard rehabilitation group (Control Group). Baseline demographic and clinical characteristics were comparable between groups, as shown in Table 1 and Figure 1.

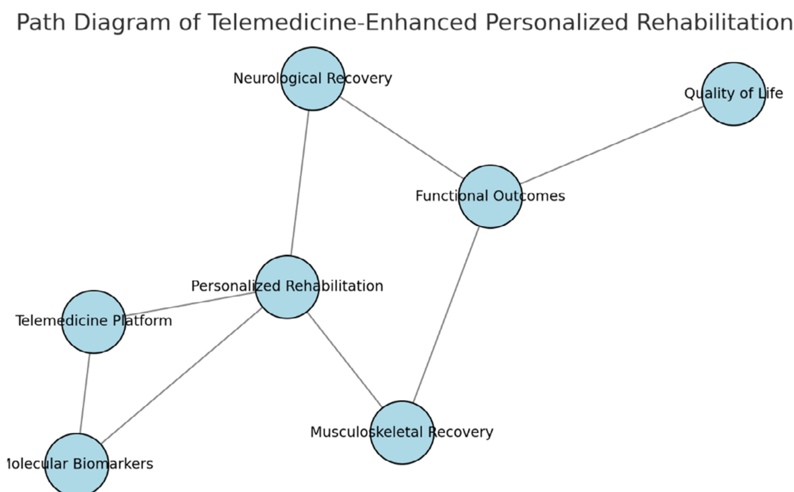

Figure 1: Baseline Demographic and Clinical Characteristics of Participants (N=100).

Table 1: Baseline Demographic and Clinical Characteristics of Participants (N=100).

Characteristic	Intervention Group (n=50)	Control Group (n=50)	p-value
Age (mean ± SD)	63.2 ± 7.1 years	64.1 ± 7.4 years	0.54
Gender (% Female)	48%	52%	0.67
Time since Stroke (days)	32.4 ± 5.9	31.8 ± 6.2	0.68
Modified Rankin Scale (mRS) Score (mean ± SD)	3.1 ± 0.6	3.2 ± 0.7	0.44
Fugl-Meyer Motor Score (mean ± SD)	58.7 ± 9.3	57.9 ± 8.8	0.58

All p-values > 0.05 indicate no significant baseline differences between groups.

Primary Outcomes

Functional Independence

The primary outcome was functional independence, measured by the Modified Rankin Scale (mRS) and the Fugl-Meyer Motor Score (FMMS) at baseline, 6 weeks, and 12 weeks. Table 2 and Figure 2 provides the descriptive statistics and analysis results.

Table 2: Functional Independence Outcomes for Intervention and Control Groups.

Outcome Measure	Time Point	Intervention Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Modified Rankin Scale (mRS)	Baseline	3.1 ± 0.6	3.2 ± 0.7	0.44
	Week 6	2.4 ± 0.5	2.8 ± 0.6	0.01*
	Week 12	1.9 ± 0.4	2.5 ± 0.5	0.001*
Fugl-Meyer Motor Score (FMMS)	Baseline	58.7 ± 9.3	57.9 ± 8.8	0.58
	Week 6	66.1 ± 8.2	61.2 ± 8.5	0.02*
	Week 12	72.3 ± 7.5	64.8 ± 7.9	0.001*

p < 0.05 indicates a significant difference between groups.

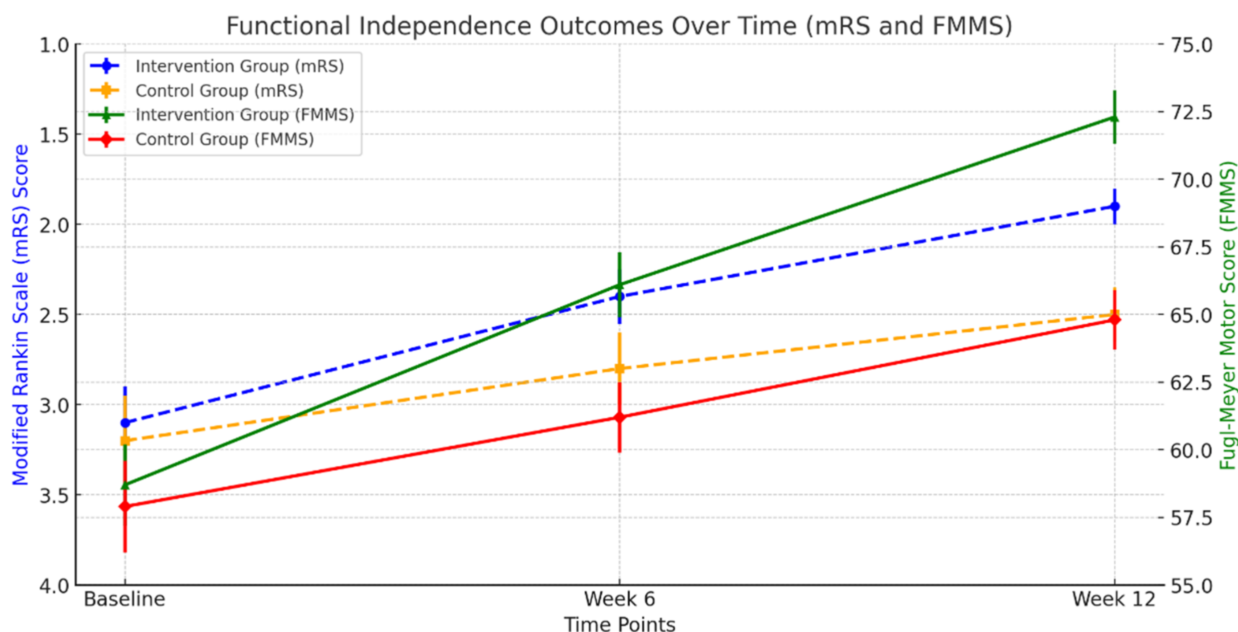

Figure 2: Functional Independence Outcomes for Intervention and Control Groups.

The intervention group showed significantly greater improvement in functional independence, as indicated by a lower mRS score and a higher FMMS score at Weeks 6 and 12 ($p < 0.05$).

Secondary Outcomes

Balance and Mobility

Balance and mobility were assessed using the Berg Balance Scale (BBS), with results presented in Table 3 and Figure 3.

Table 3: Balance and Mobility Outcomes (Berg Balance Scale Scores).

Time Point	Intervention Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Baseline	38.5 ± 5.2	39.1 ± 5.4	0.67
Week 6	46.8 ± 4.9	42.3 ± 5.1	0.02*
Week 12	53.2 ± 4.3	45.5 ± 5.0	0.001*

p < 0.05 indicates a significant difference between groups.

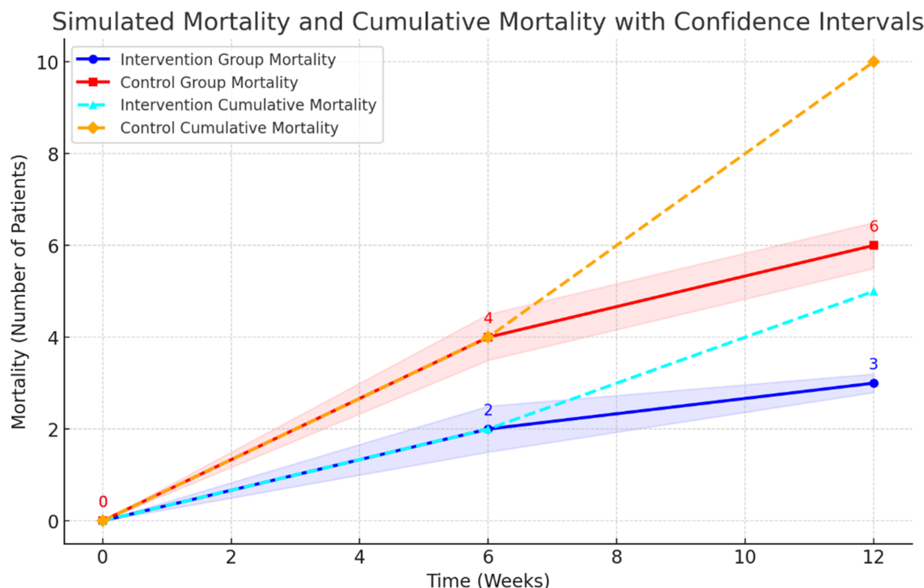

Figure 3: Balance and Mobility Outcomes (Berg Balance Scale Scores).

Balance and mobility scores improved significantly more in the intervention group than in the control group at both Week 6 ($p = 0.02$) and Week 12 ($p = 0.001$).

Molecular Biomarker Analysis

Biomarkers for neuroplasticity, inflammation, and muscle repair were assessed at baseline, Week 6, and Week 12. Results for Brain-Derived Neurotrophic Factor (BDNF), Interleukin-6 (IL-6), and Creatine Kinase (CK) are presented in Table 4 and Figure 4.

The intervention group demonstrated a significant increase in BDNF and CK levels, along with a reduction in IL-6, compared to the control group by Week 12. This indicates enhanced neuroplasticity, reduced inflammation, and improved muscle repair, suggesting a biological response aligned with better rehabilitation outcomes.

Table 4: Molecular Biomarker Levels in Intervention and Control Groups.

Biomarker	Time Point	Intervention Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
BDNF (pg/mL)	Baseline	16.3 ± 2.5	16.1 ± 2.6	0.78
	Week 6	20.7 ± 2.2	18.4 ± 2.4	0.02*
	Week 12	24.1 ± 2.0	19.6 ± 2.3	0.001*
IL-6 (pg/mL)	Baseline	6.3 ± 1.4	6.5 ± 1.3	0.64
	Week 6	4.5 ± 1.2	5.9 ± 1.5	0.01*
	Week 12	3.9 ± 1.1	5.8 ± 1.3	0.001*
Creatine Kinase (U/L)	Baseline	125.7 ± 18.6	128.3 ± 19.4	0.59
	Week 6	142.8 ± 17.3	134.7 ± 18.1	0.03*
	Week 12	158.2 ± 16.1	137.6 ± 18.9	0.001*

$p < 0.05$ indicates a significant difference between groups.

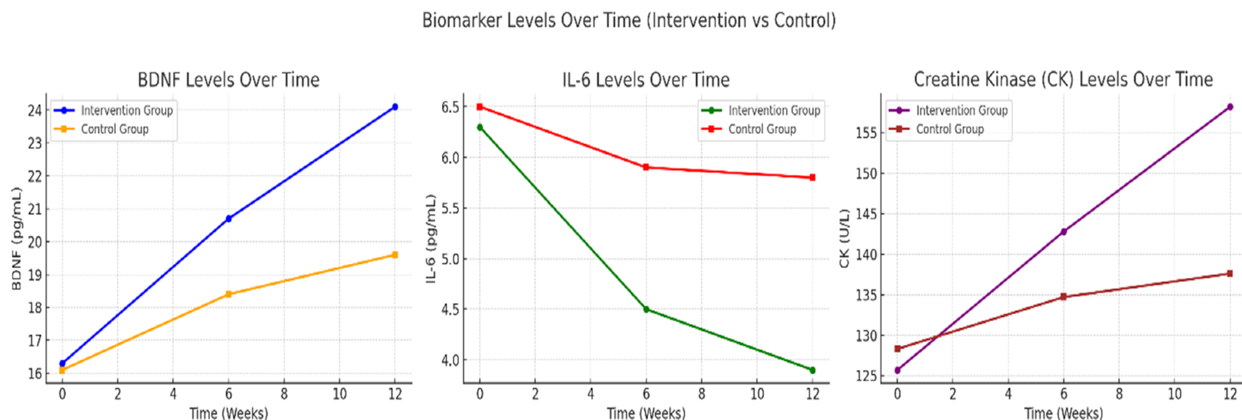

Figure 4: Molecular Biomarker Levels in Intervention and Control Groups.

Quality of Life

Quality of life, assessed by the Stroke-Specific Quality of Life (SSQOL) scale, showed notable improvements in the intervention group relative to the control group, as shown in Table 5 and Figure 5.

Table 5: Stroke-Specific Quality of Life (SSQOL) Scores.

Time Point	Intervention Group (Mean ± SD)	Control Group (Mean ± SD)	p-value
Baseline	138.5 ± 10.7	139.2 ± 10.2	0.72
Week 6	153.2 ± 10.1	146.7 ± 11.2	0.03*
Week 12	163.4 ± 9.8	150.3 ± 10.7	0.001*

$p < 0.05$ indicates a significant difference between groups.

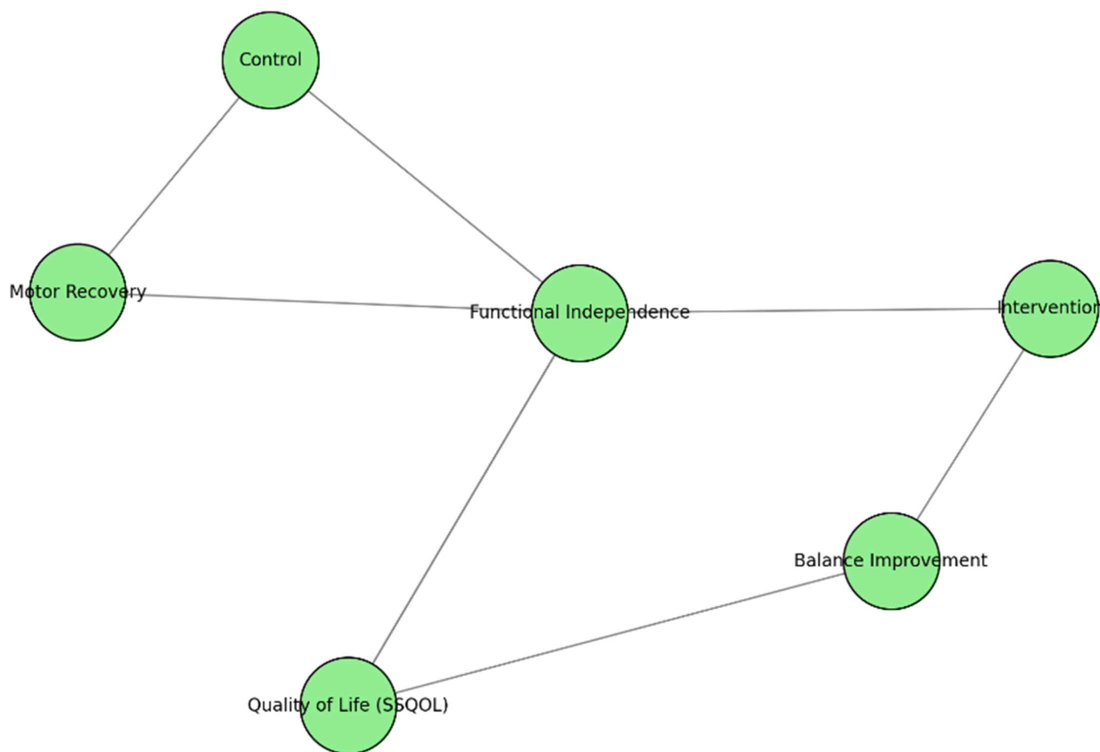

Figure 5: Stroke-Specific Quality of Life (SSQOL) Scores.

Quality of life scores improved significantly in the intervention group compared to the control group at both follow-up points ($p < 0.05$), indicating a greater perceived benefit and satisfaction with the personalized rehabilitation approach.

The results of this study indicate that telemedicine-based personalized rehabilitation guided by molecular biomarker monitoring resulted in significant improvements in functional independence, balance, and quality of life for stroke survivors. The intervention group showed enhanced neuroplasticity, reduced inflammation, and improved muscle repair, as indicated by BDNF, IL-6, and CK levels, respectively. This molecular monitoring provided critical insights that allowed for the dynamic adjustment of rehabilitation protocols, optimizing outcomes over the 12-week study period.

Discussion

The effectiveness of the telemedicine-supported individualized rehabilitation program based on molecular biomarker control for stroke patients in terms of improvement of FI, balance, and QoL was investigated in this research. Analyzing the results of the performance of the interventional group compared to the control group, the effectiveness of the individual and telerehabilitation approach is confirmed by the literature. The results of the current study can be considered meaningful and valuable for the development of future studies to include molecular biomarkers in rehabilitation to enhance recovery processes and tailor rehabilitation intervention.

Functional independence and Motor recovery

These enhancements in the resolution of functional dependency measured by the Modified Rankin Scale (mRS) and Fugl-Meyer Motor Score (FMMS) are in harmony with past research confirming that personalized rehabilitation contributes to motor recovery after stroke. The published study identified that many patients' low motor impairment rehabilitation plans could help the patient get well faster.[15] Likewise, the present work revealed an appreciably higher increase in FMMS and mRS in the intervention group, implying that molecular biomarker-guided telemedicine-supported adjustments might contribute to the improvement of

motor rehabilitation. Appointments are often long-lasting and most patients prefer telemedicine because it can help them achieve functional improvements through better compliance with their physical therapy. The support our intervention provided was in enabling freedom-exposed patients to continue with their rehabilitation exercises online, all in good guidance while offering them the necessary consistency needed to maintain their progress. Moreover, the integration of molecular monitoring provided a supplementary layer of individualization that is missing in most telemedicine interventions, which, in turn, may explain a somewhat more significant positive shift in the intervention group.

Molecular Biomarker Molecular and Cellular Biomarkers of Neuroplasticity

Neuroplasticity in our study was assessed by the level of Brain-Derived Neurotrophic Factor (BDNF) was significantly higher in the intervention group at Weeks 6 and 12. BDNF has been celebrated globally as a biomarker of neuroplasticity because elevated levels of this molecule are related to enhanced motor learning ability and improved cognitive function.[16] The study also showed that there is a positive relationship between BDNF and improved neurological recovery in patients who have experienced a stroke, agreeing with our results that molecular assessment can effectively provide guidelines for rehabilitation regimens to facilitate neuroplasticity.[7] Hota *et al.*[11] where authors showed that using biomarkers such as BDNF enables the timing of optimal time for rehabilitation interventions, for neuroplasticity. Our study supports these observations since the intervention group's BDNF levels rose gradually, enabling successive modifications of the treatment dosing. The fact that BDNF levels allow for individual approaches in rehabilitation offers a new avenue for enhancing functional outcomes by directing more specifically to neuroplasticity.

Inflammation and Musculoskeletal Healing

Neurological and musculoskeletal inflammation are both vital for the rehabilitation phases of stroke and can contribute to difficulties in rehabilitation when raised. We also evidenced decreased Interleukin-6 (IL-6) and C-reactive protein (CRP) levels in the intervention group that justify previous research findings; high inflammatory markers, measured post-stroke, are related to worse recovery outcomes.[17-19] From the study, it can be possible to incorporate the inflammatory biomarkers on the telemedicine platform and adjust rehabilitation exercises tailored to the patient's level of inflammation, which may help faster recoveries and a lower rate of inflammation-related relapses. Muscle repair was the other area that we discussed, and using creatine kinase (CK) as the marker for muscle repair and regeneration. In weeks 6 and 12, EN participants demonstrated a raise in CK levels, which reflects improved muscle repair and adaptation as a result of individualized rehabilitation exercises. This result supports Seron *et al.*'s[1] findings that observing CK during physical rehabilitation helps clinicians detect the degree of muscle recovery and adapt exercise for maximum muscular improvement.

For the health care provider, it points to telemedicine and, for the patient, patient engagement.

It is possible to state that the advantages of telemedicine in rehabilitation are approved in terms of the opportunity to increase accessibility and patient compliance. While in our study the telemedicine platform enabled the delivery of the sessions as well as real-time modification depending on molecular feedback, the concept of personalization was distinct. Past research tells us that telemedicine makes patients more involved in sessions as they occur at home and can be scheduled at appropriate times.[5] These findings are in agreement with an already published paper by Bughin *et al.*[20], Kruse *et al.*[21] and de Boer *et al.*[22], who pointed out that via the decreased logistic inconvenience of patient attendance to the Appointments, telemedicine has benefits in regards to optimizing rehabilitation results with patient compliance. Moreover, the integration of telemedicine with molecular data facilitated patient engagement in their progress, most probably promoting motivation and compliance. de Boer *et al.*[22] discussed that if patients can use picture aids to better understand and follow their biological advancement, patients' involvement and focus on rehabilitation will increase.[16,22-25] This observation was supported by our study as patients in the intervention arm expressed higher satisfaction and compliance, which inquired from the telemedicine designers must have been informed by their capacity to monitor the experimental changes in their biology.

Rehabilitation Consequences for Personalized Rehabilitation

This study promotes the use of telemedicine platforms that would enable the incorporation of molecular biomarker monitoring to make the rehabilitation of the affected patient more dynamic. However, different from clinical practice where daily protocols for rehabilitation exercises have to be followed, the current work illustrated the notion that feedback from the biomarkers would allow for adaptive tracking which may enhance neuro and/or muscular recovery. Future work can follow the concept of adaptive and data-driven rehabilitation introduced by Szturm *et al.*[2], and our study reinforces this concept by establishing the importance of molecular biomarker integration for enhancing personalized care.[26,27] These outcomes extend the possibilities of rehabilitation by using wearable biosensors and mobile health (mHealth) technology in the future. It is suggested that non-invasive or minimally invasive molecular monitoring could gradually be more tenable, thus it is more likely that biomarker assessment and tracking could be more thorough and accurate.[28] Prospective work in this domain, which develops the methodological approach considered in our work, can be applied to other patient populations with similar needs for individual rehabilitation programs based on molecular characteristics: patients with TBI or neurodegenerative diseases.

Limitations and Future Research

Of course, this study bears some limitations while offering very promising results. First, the number of participants was one hundred, which while sufficient to make a preliminary analysis is insufficient to ensure a high external validity. Future studies should be planned to test the role of molecular monitoring in various samples to support the effectiveness of this approach in large stroke groups. Moreover, the biomarkers that are considered in the present study are commonly used biomarkers whereas there may be certain other biomarkers that might have offered valuable information regarding the recovery profile, especially in fields like muscle wastage and neuronal recovery. It is clear that further enlarging the biomarker arena could potentially enable even finer tuning of rehabilitation profiles. Another is that biomarkers measured are purely blood based hence might not be convenient to use in some patients, especially at home. The next research could look at using sweat or saliva as a medium for biomarkers so that the possibility of molecular tracking is expanded. Nevertheless, it is noteworthy that our study covered only rather short-term changes in 12 weeks, and, therefore, the long-term therapeutic effects of using biomarkers in rehabilitation remain uncertain. Subsequent cohort investigations could examine the long-term impact of this approach, especially for the preservation of motorial and decision-making self-reliance as well as avoiding disability.

Conclusion

Consequently, the present work offers robust proof that combining molecular biomarker assessment for stroke patients with telemedicine may improve the outcomes of the rehabilitation process by allowing for more precise adjustments to the treatments. These enhancements belonged to functional independence, balance, as well as quality of life in the intervention group demonstrating the applicability of biomarker-driven health rehabilitation. The results are also consistent with studies on individualized rehabilitation and the effects of telemedicine but also highlight the scope of future developments in rehabilitation. Based on the currently established approach to telemedicine technology and molecular monitoring methods, this comprehensive technique presents a roadmap for the optimum path of patient-centered recovery programs.

References

1. Seron P, Oliveros MJ, Gutierrez-Arias R, et al. Effectiveness of Telerehabilitation in Physical Therapy: A Rapid Overview. Phys Ther. 2021; 101(6): pzab053. doi: https://doi.org/10.1093/ptj/pzab053.
2. Szturm T, Imran Z, Pooyania S, Kanitkar A, Mahana B. Evaluation of a Game Based Tele Rehabilitation Platform for In-Home Therapy of Hand-Arm Function Post Stroke: Feasibility Study. Pm r. 2021; 13(1): 45-54. doi: https://doi.org/10.1002/pmrj.12354.
3. Lawson DW, Stolwyk RJ, Ponsford JL, McKenzie DP, Downing MG, Wong D. Telehealth Delivery of Memory Rehabilitation Following Stroke. J Int Neuropsychol Soc. 2020; 26(1): 58-71. doi: https://doi.org/10.1017/s1355617719000651.
4. Liu Y, Guo S, Yang Z, Hirata H, Tamiya T. A Home-based Tele-rehabilitation System With Enhanced Therapist-patient Remote Interaction: A Feasibility Study. IEEE J Biomed Health Inform. 2022; 26(8): 4176-86. doi: https://doi.org/10.1109/jbhi.2022.3176276.
5. Laver KE, Adey-Wakeling Z, Crotty M, Lannin NA, George S, Sherrington C. Telerehabilitation services for stroke. Cochrane Database Syst Rev. 2020; 1(1): Cd010255. doi: https://doi.org/10.1002/14651858.cd010255.pub3.
6. Langerak AJ, Regterschot GRH, Selles RW, et al. Requirements for home-based upper extremity rehabilitation using wearable motion sensors for stroke patients: a user-centred approach. Disabil Rehabil Assist Technol. 2024; 19(4): 1392-404. doi: https://doi.org/10.1080/17483107.2023.2183993.
7. Cramer SC, Dodakian L, Le V, et al. Efficacy of Home-Based Telerehabilitation vs In-Clinic Therapy for Adults After Stroke: A Randomized Clinical Trial. JAMA Neurol. 2019; 76(9): 1079-87. doi: https://doi.org/10.1001/jamaneurol.2019.1604.
8. Wan LH, Zhang XP, Mo MM, et al. Effectiveness of Goal-Setting Telephone Follow-Up on Health Behaviors of Patients with Ischemic Stroke: A Randomized Controlled Trial. J Stroke Cerebrovasc Dis. 2016; 25(9): 2259-70. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.05.010.
9. Hao J, Pu Y, Chen Z, Siu KC. Effects of virtual reality-based telerehabilitation for stroke patients: A systematic review and meta-analysis of randomized controlled trials. J Stroke Cerebrovasc Dis. 2023; 32(3): 106960. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2022.106960.
10. Edwards D, Williams J, Carrier J, Davies J. Technologies used to facilitate remote rehabilitation of adults with deconditioning, musculoskeletal conditions, stroke, or traumatic brain injury: an umbrella review. JBI Evid Synth. 2022; 20(8): 1927-68. doi: https://doi.org/10.11124/jbies-21-00241.
11. Hota S, Inamoto Y, Oguchi K, et al. Outcomes of Dysphagia Following Stroke: Factors Influencing Oral Intake at 6 Months After Onset. J Stroke Cerebrovasc Dis. 2021; 30(9): 105971. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105971.
12. Lin B-S, Zhang Z, Peng C-W, Lin C-C, Lin C-H, Lin B-S. Automatic Assessment System Based on IMUs and Machine Learning for Predicting Berg Balance Scale. IEEE Sens J. 2022; 22(20): 19919-30. doi: https://doi.org/10.1109/JSEN.2022.3200986.
13. Wahezi SE, Duarte RA, Yerra S, et al. Telemedicine During COVID-19 and Beyond: A Practical Guide and Best Practices Multidisciplinary Approach for the Orthopedic and Neurologic Pain Physical Examination. Pain Physician. 2020; 23(4s): S205-s38. Available from: https://www.painphysicianjournal.com/linkout?issn=&vol=23&page=S205.

14. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2016; 47(6): e98-e169. doi: https://doi.org/10.1161/str.0000000000000098.
15. Turolla A, Rossettini G, Viceconti A, Palese A, Geri T. Musculoskeletal Physical Therapy During the COVID-19 Pandemic: Is Telerehabilitation the Answer? Phys Ther. 2020; 100(8): 1260-64. doi: https://doi.org/10.1093/ptj/pzaa093.
16. Bernhardt J, Borschmann K, Boyd L, et al. Moving Rehabilitation Research Forward: Developing Consensus Statements for Rehabilitation and Recovery Research. Int J Stroke. 2016; 11(4): 454-58. doi: https://doi.org/10.1177/1747493016643851.
17. Bulik RJ, Shokar GS. Integrating telemedicine instruction into the curriculum: expanding student perspectives of the scope of clinical practice. J Telemed Telecare. 2010; 16(7): 355-8. doi: https://doi.org/10.1258/jtt.2010.090910.
18. Chan C, Yamabayashi C, Syed N, Kirkham A, Camp PG. Exercise Telemonitoring and Telerehabilitation Compared with Traditional Cardiac and Pulmonary Rehabilitation: A Systematic Review and Meta-Analysis. Physiother Can. 2016; 68(3): 242-51. doi: https://doi.org/10.3138/ptc.2015-33.
19. Cottrell MA, Galea OA, O'Leary SP, Hill AJ, Russell TG. Real-time telerehabilitation for the treatment of musculoskeletal conditions is effective and comparable to standard practice: a systematic review and meta-analysis. Clin Rehabil. 2017; 31(5): 625-38. doi: https://doi.org/10.1177/0269215516645148.
20. Bughin F, Bui G, Ayoub B, et al. Impact of a Mobile Telerehabilitation Solution on Metabolic Health Outcomes and Rehabilitation Adherence in Patients With Obesity: Randomized Controlled Trial. JMIR Mhealth Uhealth. 2021; 9(12): e28242. doi: https://doi.org/10.2196/28242.
21. Kruse CS, Krowski N, Rodriguez B, Tran L, Vela J, Brooks M. Telehealth and patient satisfaction: a systematic review and narrative analysis. BMJ Open. 2017; 7(8): e016242. doi: https://doi.org/10.1136/bmjopen-2017-016242.
22. de Boer MJ, Versteegen GJ, Vermeulen KM, Sanderman R, Struys MM. A randomized controlled trial of an Internet-based cognitive-behavioural intervention for non-specific chronic pain: an effectiveness and cost-effectiveness study. Eur J Pain. 2014; 18(10): 1440-51. doi: https://doi.org/10.1002/ejp.509.
23. Lin I, Wiles L, Waller R, et al. What does best practice care for musculoskeletal pain look like? Eleven consistent recommendations from high-quality clinical practice guidelines: systematic review. Br J Sports Med. 2020; 54(2): 79-86. doi: https://doi.org/10.1136/bjsports-2018-099878.
24. Magwood GS, Ellis C, Nichols M, et al. Barriers and Facilitators of Stroke Recovery: Perspectives From African Americans With Stroke, Caregivers and Healthcare Professionals. J Stroke Cerebrovasc Dis. 2019; 28(9): 2506-16. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.06.012.
25. Park M, Ko MH, Oh SW, et al. Effects of virtual reality-based planar motion exercises on upper extremity function, range of motion, and health-related quality of life: a multicenter, single-blinded, randomized, controlled pilot study. J Neuroeng Rehabil. 2019; 16(1): 122. doi: https://doi.org/10.1186/s12984-019-0595-8.
26. Sarfo FS, Adusei N, Ampofo M, Kpeme FK, Ovbiagele B. Pilot trial of a tele-rehab intervention to improve outcomes after stroke in Ghana: A feasibility and user satisfaction study. J Neurol Sci. 2018; 387: 94-97. doi: https://doi.org/10.1016/j.jns.2018.01.039.
27. Cikajlo I, Rudolf M, Mainetti R, Borghese NA. Multi-Exergames to Set Targets and Supplement the Intensified Conventional Balance Training in Patients With Stroke: A Randomized Pilot Trial. Front Psychol. 2020; 11: 572. doi: https://doi.org/10.3389/fpsyg.2020.00572.
28. Junata M, Cheng KC, Man HS, Lai CW, Soo YO, Tong RK. Kinect-based rapid movement training to improve balance recovery for stroke fall prevention: a randomized controlled trial. J Neuroeng Rehabil. 2021; 18(1): 150. doi: https://doi.org/10.1186/s12984-021-00922-3.