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Effect of robot-assisted gait training on quality of life and depression in neurological impairment: A systematic review and meta-analysis

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Abstract

Objective: Robot-assisted gait training (RAGT) is often used as a rehabilitation tool for neurological impairments. The purpose of this study is to investigate the effects of rehabilitation with robotic devices on quality of life and depression.

Data sources: Two electronic databases (MEDLINE and Scopus) were searched for studies from inception up to December 2022.

Review methods: Randomized controlled trials (RCTs) and non-RCTs were pooled separately for analyses, studying each one's mental and physical health and depression. Random effect meta-analyses were run using standardized mean difference and 95% confidence interval (CI).

Results: A total of 853 studies were identified from the literature search. 31 studies (17 RCTs and 14 non-RCTs) including 1151 subjects met the inclusion criteria. 31 studies were selected for the systematic review and 27 studies for the meta-analysis. The outcome measure of mental health significantly improved in favor of the RAGT group in RCTs and non-RCTs (adjusted Hedges'g 0.72, 95% CI: 0.34–1.10, adjusted Hedges g = 0.80, 95% CI 0.21-1.39, respectively). We observed a significant effect of RAGT on physical health in RCTs and non-RCTs (adjusted Hedges'g 0.58, 95% CI 0.28, 0.88, adjusted Hedges g = 0.73, 95% CI 0.12, 1.33). After realizing a sensitivity analysis in RCTs, a positive impact on depression is observed (Hedges' g of −0.66, 95% CI −1.08 to −0.24).

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Conclusion: This study suggests that RAGT could improve the quality of life of patients with neurological impairments. A positive impact on depression is also observed in the short term. Further studies are needed to differentiate grounded and overgrounded exoskeletons as well as RCT comparing overground exoskeletons with a control group.

Keywords
Robot-assisted gait training, neuromuscular disorders, quality of life, depression, robotic devices

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Introduction

Approximately 60% of patients with neurological disorders are also affected with gait disorders which can be linked to motor and sensory deficits, proprioceptive disorders, spasticity, or bone and joint disorders.[1]

Rehabilitation with robotic devices began in 1994 with Lokomat® and the results of the first clinical tests with an overground exoskeleton (HAL®) were published in 2009.[2] Rehabilitation for improving walking ability remains a challenge for physicians although the use of robot-assisted gait training for rehabilitation has become more commonplace over the last few years.

There are a number of different types of robotic devices currently available for the lower limbs: end-effector devices, treadmill-based body weight-support exoskeletons, and wearable exoskeletons. The treadmill-based body weight support can be complemented with a supplementary assistance of the lower limb by a powered exoskeleton during gait training (e.g. Lokomat® (Switzerland), Walkbot® (Korea), and ReoAmbulator® (USA)). The treadmill speed, the amount of body weight support, and the guidance force can all be adapted to optimize training intensity in line with individual patient needs.

In recent years, a number of different types of overground exoskeletons have been developed. However, so far, only 6 have been awarded the CE mark and/or received Food and Drug Administration approval (Ekso®, HAL®, Indego®, REX®, ReWalk®, and SMA®).[2] Overground exoskeletons enable patients to explore their environment by walking overground on hard and flat surfaces. They are intended to be used in normal day-to-day activities.[2]

The use of robot-assisted gait training for rehabilitation has become relatively popular and, consequently, there is an increasing number of studies being published. A recent meta-analysis of randomized controlled trials (RCTs) and non-RCTs investigated the effects of robot-assisted gait training in patients with spinal cord injury.[3] Different aspects of walking ability were measured, and authors reported that robot-assisted gait training appeared to increase the endurance, muscle strength, and ambulatory ability of patients. A further meta-analysis, conducted on stroke patients, concluded that patients' balance was significantly improved following rehabilitation with robotic devices when compared to conventional therapy. Results were only significant for acute or subacute strokes. Moreover, the exoskeletons were found to be significantly superior when compared to end-effector devices.[4] An additional meta-analysis reviewed gait quality after stroke based on objective biomechanical measures.[5] This meta-analysis showed no effect of robot-assisted gait training on temporal, spatial, kinematic, or kinetic parameters. Finally, in patients with multiple sclerosis, robot-assisted gait training appeared to improve gait speed, walking ability, balance, and stride length compared to conventional walking training or sensory integration balance training.[6]

The majority of the above-mentioned studies focused their outcome measures on ambulation assessment rather than physical and psychological changes.[2] Nevertheless, because impaired walking,

pain, and spasticity can have a negative impact on health-related quality of life, is it possible to hypothesize that robot-assisted gait training could additionally have beneficial effects on the quality of a patient's life.

To obtain a global overview of the impact of robot-assisted gait training on quality of life and depression, we aim to develop a systematic review and meta-analysis. A systematic review attempted to collate all empirical evidence on one particular topic. Results of individual studies were combined to produce overall statistics, usually known as meta-analysis.[7]

Methods

The proposed systematic review and meta-analysis were conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). A protocol was developed and published in Open Science Framework prior to carrying out the systematic review. The research project can be summarized with the following PICO format: P (population): patients suffering from spinal cord injury, stroke, multiple sclerosis (MS), amyotrophic lateral sclerosis or myopathy; I (intervention): exoskeleton; C (comparator): usual care; O (outcome): quality of life.

A search, of English and French studies, was conducted on MEDLINE (via Ovid) and Scopus, to identify any studies that had assessed the effects of an exoskeleton on quality of life from the inception of databases up until December 2022. A combination of terms of Medical Subject Headings and keywords was used in the search strategy. The complete search strategies used in both databases are available in Supplementary Files (Figure S1). Additionally, bibliographies of all included studies were manually checked for other potentially relevant publications. Experts in the field were also contacted for additional resources.

The search results from electronic sources and manual searches were imported into Covidence software for data management. All identified articles were screened for eligibility by two reviewers. In the first instance, this was based on titles and abstracts, and secondly, based on full texts. Any discrepancy was resolved by the two reviewers. Any study that could not be included was recorded in the full-text paper screening stage and reasons for exclusion were duly noted. The inclusion of studies was based on a list of inclusion/exclusion criteria compiled by the two reviewers. Adults and children presenting a neuromuscular impairment such as spinal cord injury, stroke, multiple sclerosis, amyotrophic lateral sclerosis, or myopathy, between 2 and 80 years of age, were considered. All types of lower limb exoskeletons were included. For outcome measures, only validated instruments evaluating the quality of life, depression, well-being, and psychological status were chosen.

Interventional studies and longitudinal studies were included. However, qualitative studies, case reports, reviews, systematic reviews, letters to editors, and protocols were not accepted. Studies evaluating satisfaction with the use of the exoskeleton as well as non-English and non-French studies were considered inappropriate for the study.[8]

Data were extracted by two independent reviewers according to a standardized data extraction form pre-tested on a sample of 4 studies.

The following data were extracted:

- Article characteristics: first author, journal, year of publication, title, objectives, funding, conflict of interest.
- Study characteristics: study design, country, length of follow-up.
- Population: sample size, gender distribution, age range, description of the population, and pathology.
- Exoskeleton: type of exoskeleton and training proposed.
- Quality of life/depression instrument used for data collection.
- Study results: main results.

The quality of studies was assessed using the Cochrane Risk of Bias tool for interventional

studies and the National Institutes of Health scale for pre–post studies with no control group.[9] The Cochrane Risk of Bias tool allows for the detection of different types of bias: selection, performance, attrition, detection, and reporting bias by evaluating 7 different criteria. The National Institute of Health's scale for pre–post studies is based on 12 criteria for evaluating the internal validity of a study.[10]

Strategy for data synthesis

The findings were evaluated in a descriptive manner based on information provided by each of the studies that had been accepted on the study. For outcomes reported by three or more studies, a meta-analysis was performed. In total, 6 random effect meta-analyses were carried out, according to study designs and outcomes: (1) meta-analysis on mental health quality of life investigated through interventional studies with a control group; (2) meta-analysis on physical health quality of life investigated through interventional studies with a control group; (3) meta-analysis on depression investigated through interventional studies with a control group; (4) meta-analysis on mental health quality of life investigated through pre–post studies with no control group; (5) meta-analysis on physical health quality of life investigated through pre–post studies with no control group; (6) meta-analysis on depression investigated through pre–post studies with no control group. A random effect model was chosen due to the expected heterogeneity of protocols across individual studies. To provide a comparison between outcomes reported by the individual studies, effect size as a standardized mean difference with 95% CIs was measured for each outcome. Because of the small sample of studies, Hedges g was computed.

Original mean differences and standard derivations were extracted, when available, from each individual study. When only baseline and follow-up values were available, and the mean differences and standard derivations were missing, the authors of the individual study were contacted in an effort to obtain missing values. In case of non-response, the mean differences and standard derivations from these baseline and follow-up values for each individual group were estimated using the formula recommended in the Cochrane Handbook for Systematic Reviews. When only median and interquartile ranges were available, the formula suggested by Hozo et al.[11] to convert them into means and standard derivations was used.

When a study provided multiple follow-up measures, the follow-up time point as close as possible to the end of the intervention period was used. When different scales were used to measure the quality of life within one particular study, the total score of the scale was prioritized for extraction followed by, either the mental health/well-being scale (e.g. Mental Health Component for the SF-36 or positive affect and well-being scale of the NeuroQoL), the physical component scale (PCS; e.g. PCS for SF-36) or the physical health (e.g. PCS of the SF-36).

Results were examined for heterogeneity using Cochran's Q statistic and the I^2 statistic. Potential publication bias was explored by means of a funnel plot. Publication bias was measured in each meta-analysis including 10 studies or more using the Egger test.

One-way removed analysis was also used as a sensitivity test to assess the robustness of the results.

For all results, a two-sided p-value of 0.05 or less was said to be significant. All analyses were performed using R Software and appropriate packages.

Results

Studies included

A total of 853 references were identified from the search strategies applied on MEDLINE and Scopus in December 2022. After the removal of any duplicates ($n = 164$) from the two databases, 659 references remained. These were then assessed for eligibility based on their title/abstract and 46 of them were further assessed based on their full text. Of the 46 studies, 26 responded to the inclusion criteria and provided sufficient. All 31 references were included in the systematic review,[6,12,41] and

27 presented sufficient statistical data to be included in the quantitative meta-analysis (Figure 1).[6,12,18,21,29,32,41]

The characteristics of the included studies have been summarised in Table S1 (Supplementary material). Seventeen RCTs and 14 non-RCTs were included.

In the interventional studies with a control group, 10 RCTs evaluated stroke patients, 5 studied patients with MS, and 2 RCTs with a spinal cord injury. In pre–post studies, 8 studies focused on spinal cord injury, 3 on MS, 1 on stroke patients, 1 on hereditary spastic paraplegia, and 1 on different types of neuromuscular disease

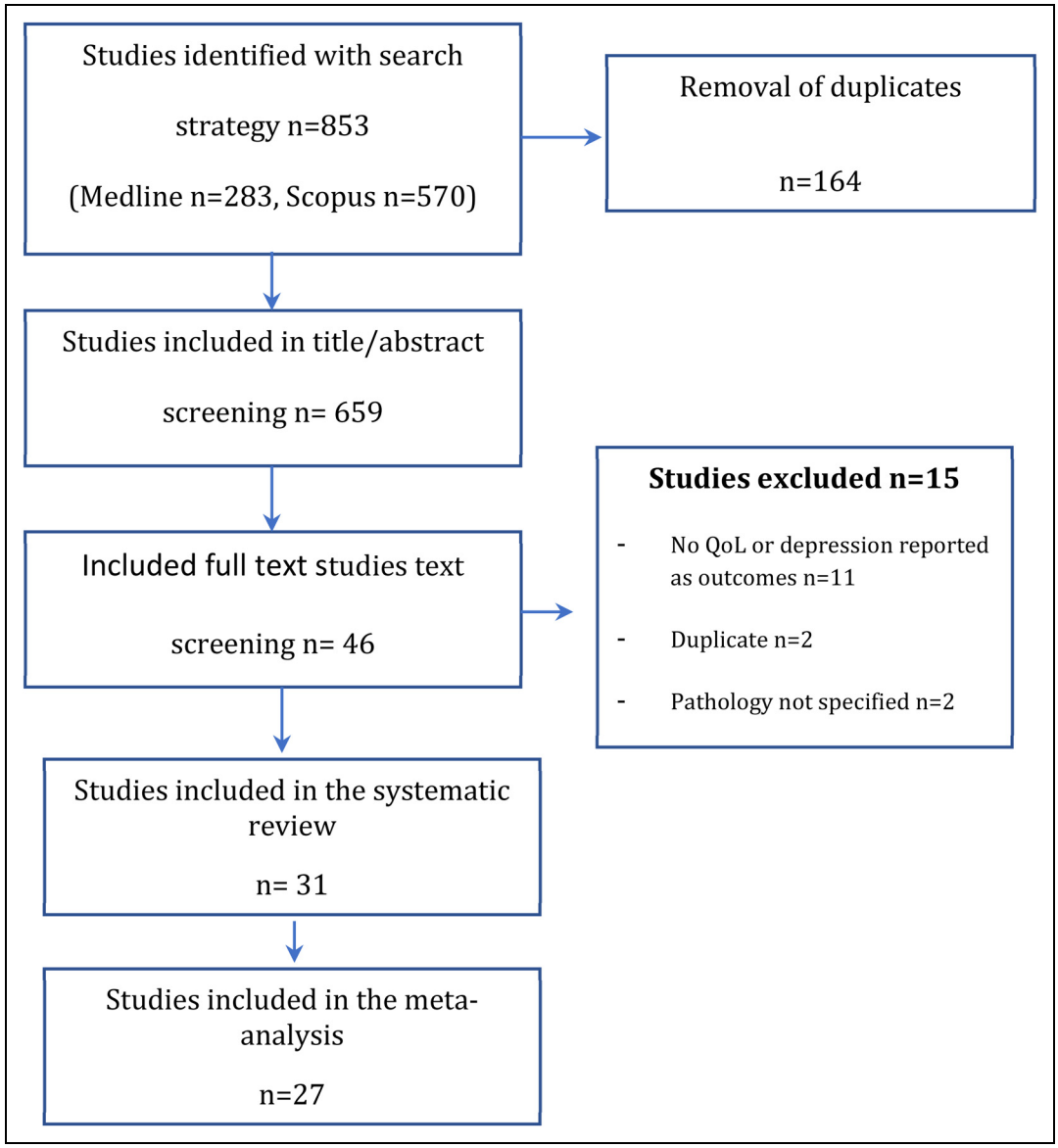

Figure 1. Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flowchart of study selection.

including amyotrophic lateral sclerosis and myopathy. A total of 1151 participants took part in these studies.

The robotic devices used in the interventional studies were Lokomat-Pro (4×), Lokomat (6×), Walkbot (2×), Ekso (4×), ReWalk (1×), and one robotic gait training system without a name specification.

In the pre–post studies, the devices were the Re-Walk (5×), H-MEX (1×), Lokomat (1×), Lokomat-Pro (1×), Ekso-GR (1×), Keogh (1×), Indego (1×), and three robotic gait training systems without a name specification.

The number of robot-assisted gait training interventions was 2 to 7 sessions per week, with sessions lasting between 30 min and 1 h for 2 to 24 weeks in RCTs. The training protocol of non-RCTs was 3 to 5 sessions with sessions lasting between 30 min and 6 h for 6 to 8 weeks.

Many different scales for quality of life and depression evaluation are available to assess the influence of robot-assisted gait training. For the quality of life, the evaluations were made using Euro-Quality of Life 5,[42] 12-Item Short Form Survey (SF-12),[43] 36-Item Short Form Survey (SF-36),[44] Stroke Specific Quality of Life,[45] Spinal Cord Injury-Quality of Life (SCI-QoL),[46] SCI-QoL Bowel Management,[47] NeuroQoL,[48] Satisfaction With Life Scale,[49] and a score evaluating life satisfaction and physical health and psychological health. The depression scores used were the Hamilton Depression Rating Scale (HRS-D),[50] Psychological General Well-Being Index,[51] Patient Health Questionnaire-9,[52] and Beck Depression Inventory-II.[53]

Risk of bias assessment

A high risk of bias was observed for all RCTs regarding the blinding participants. Indeed, patients were aware of their rehabilitation training group. The study of Dundar et al.[35] also reported a high risk of bias for these 3 other domains: random sequence generation, allocation concealment, and blinding outcome assessors. In 4 studies,[15,36,40,54] randomization was unclear. These 4 studies did not report the methodology of allocation concealment. Two studies[36,54] conducted a per-protocol analysis (Table S2).

In non-RCTs, the risk of bias was evaluated by 12 criteria (Table S3). Possible answers to each question were "yes," "no," "cannot determine," "not applicable," and "not reported." The quality of the studies was globally satisfactory: for 5 of the studies, 8 "yes" were attributed, to a further 6 studies 7 "yes" were given and 6 "yes" to the remaining 2 studies. Only the study by Poritz et al.[20] demonstrated a lower quality with 3 "yes."

Quantitative synthesis

Twenty-seven studies reported sufficient information to be included in the quantitative synthesis using meta-analysis.

Mental health quality of life

Interventional studies using a control group

A total of 12 interventional studies reported data on quality of life/mental health quality of life for both interventional and control groups.[12,15,17,35,41,54] On combining these studies, intervention using an exoskeleton appeared to significantly improve the quality of life/mental health quality of life of participants (adjusted Hedges'g 0.72, 95% CI: 0.34–1.10, Figure 2).

One study-removed sensitivity analysis confirmed a significant association between an exoskeleton and quality of life/mental health quality of life (lowest Hedges g was found when removing the study of Russo et al.[41] = 0.60, 95% CI 0.29–0.92; highest Hedges g was found when removing the study of Mustafaoglu et al.[39] = 0.79, 95% CI 0.41–1.17).

Nevertheless, a significant heterogeneity was found in the model ($I^2 = 77\%$, $p < 0.01$). Removing studies for which mean and standard derivation had been derived from median and interquartile range (i.e. Russo et al.[41] and de Luca et al.[40]) did not reduce the heterogeneity of the model ($I^2 = 74\%$, $p < 0.01$).

No publication bias was found in this meta-analysis ($t = 0.71$, df = 11, p-value = 0.49).

Pre–post studies with no control group

A total of 11 studies using a pre–post design with no control group reported data on quality of life/mental health quality of life.[13,14,18,22,29] Combining these studies revealed a significant effect of wearing an exoskeleton on quality of life/mental health quality of life (adjusted Hedges g = 0.80, 95% CI 0.21, 1.39, Figure 3)

One study-removed sensitivity analysis confirmed the significant association found between the exoskeleton and quality of life/mental health quality of life (lowest Hedges g was found when removing the study of Calabrò et al.[23] = 0.52, 95% CI 0.18, 0.87; highest Hedges g was found when removing the study of Sawada et al.[14] = 0.89, 95% CI 0.27, 1.51).

Nevertheless, a significant heterogeneity was found in the model ($I^2 = 87\%$, $p < 0.01$). When removing studies for which mean and standard derivations had been derived from median and interquartile range (i.e. Baunsgaard et al.,[25] Calabrò et al.,[23] and Van Nes et al.[13]) as well as one other study for which standard deviations were extracted from figures (i.e. Sawada et al.[14]),

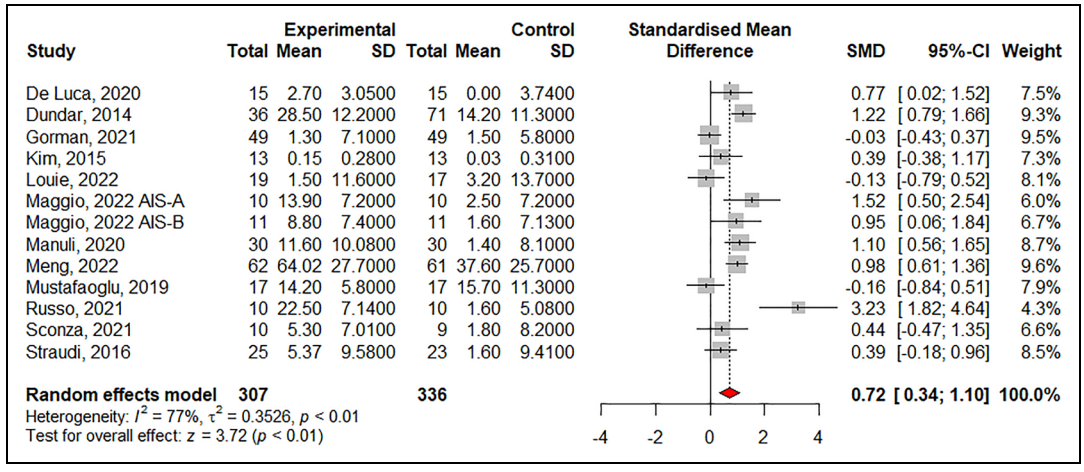

Figure 2. Effect of exoskeleton on mental health quality of life in interventional studies using a control group.

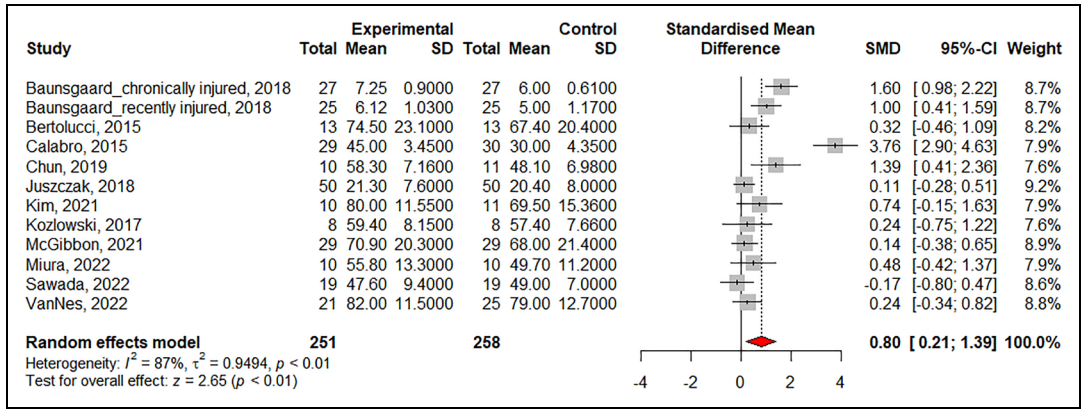

Figure 3. Effect of exoskeleton on mental health quality of life in pre–post studies with no control group.

heterogeneity was no more significant ($I^2 = 16\%$, $p = 0.31$).

No publication bias was found in this meta-analysis ($t = 1.55$, df = 10, p-value = 0.1524).

Physical health quality of life

Interventional studies using a control group

A total of 13 interventional studies reported data on quality of life/physical health quality of life for both interventional and control groups.[12,15,17,34,41,54] Pooling these studies, intervention using an exoskeleton appeared to improve the quality of life/physical health quality of life of participants (adjusted Hedges'g 0.58, 95% CI 0.28, 0.88; Figure 4).

One study-removed sensitivity analysis confirmed the significant association found between the exoskeleton and quality of life/physical health quality of life (lowest Hedges g was found when removing the study of Russo et al.[41] = 0.50, 95% CI 0.23, 0.77; highest Hedges g was found when removing the study of Mustafaoglu et al.[39] = 0.63, 95% CI: 0.33, 0.94).

Nevertheless, a significant heterogeneity was found in the model ($I^2 = 70\%$, $p < 0.01$). Removing studies for which mean and standard derivation had been derived from median and interquartile range (i.e. Russo et al.[41] and De Luca et al.[40]) did not reduce the heterogeneity of the model ($I^2 = 66\%$, $p < 0.01$).

No publication bias was found in this meta-analysis ($t = 0.28$, df = 12, p-value = 0.7871).

Pre–post studies with no control group

A total of 12 studies, using a pre–post design with no control group, reported data on quality of life/mental health quality of life.[13,14,18,21,29] A significant effect of wearing an exoskeleton on quality of life/physical health quality of life (adjusted Hedges g = 0.73, 95% CI 0.12, 1.33; Figure 5) was found.

One study-removed sensitivity analysis confirmed this significant association (lowest Hedges g was found when removing the study of Calabro et al.[23] = 0.46, 95% CI 0.08, 0.85; highest Hedges g was found when removing the study of Kim et al.[28] = 0.82, 95% CI 0.19, 1.44).

Nevertheless, a significant heterogeneity was found in the model ($I^2 = 87\%$, $p < 0.01$). Removing studies for which mean and standard derivations had been derived from median and interquartile range (i.e. Baunsgaard et al.[25] and Calabro et al.[23]) or one for which standard deviations were extracted from figure because not

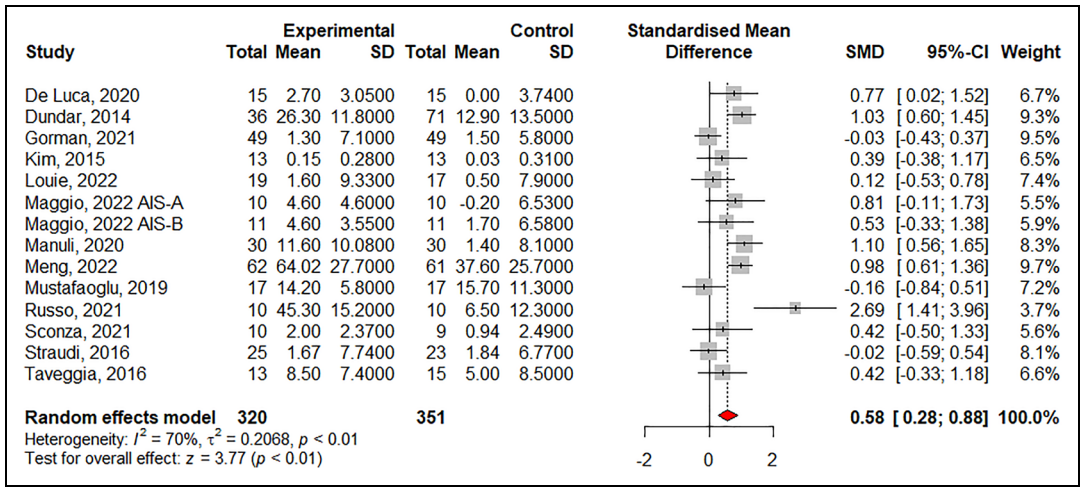

Figure 4. Effect of exoskeleton on physical health quality of life in interventional studies using a control group.

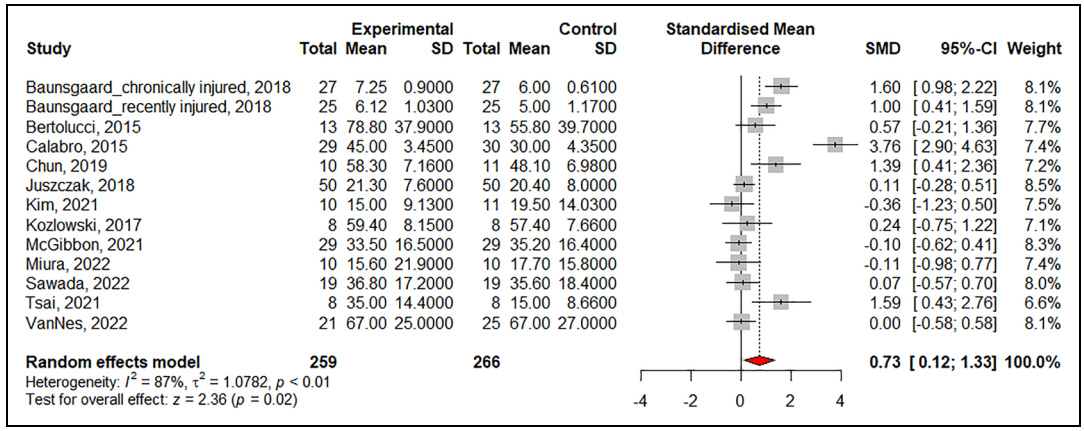

Figure 5. Effect of exoskeleton on physical health quality of life in pre–post studies with no control group.

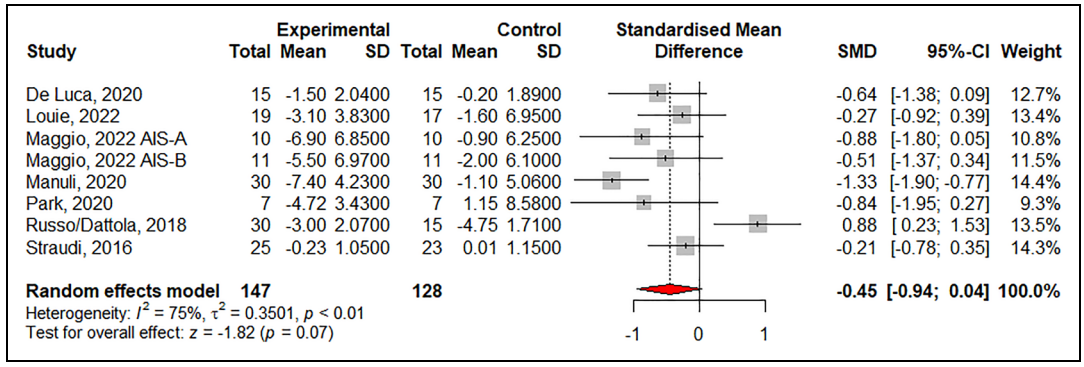

Figure 6. Effect of exoskeleton on depression in interventional studies with a control group.

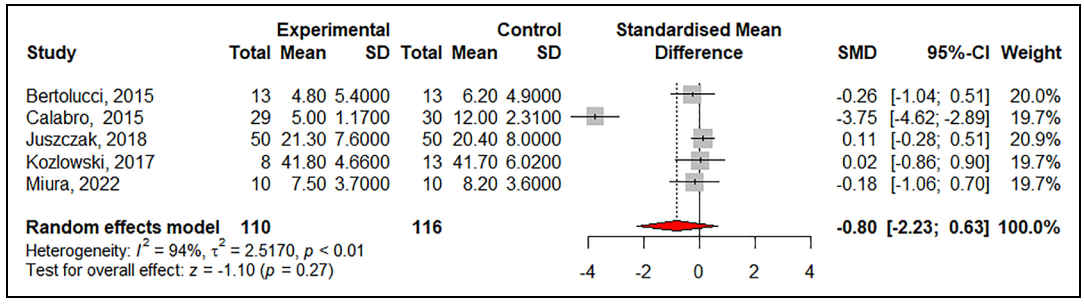

Figure 7. Effect of exoskeleton on depression in pre–post studies with no control group.

available in the manuscript (i.e. Sawada et al.[14]) did not affect heterogeneity ($I^2 = 50\%$, $p = 0.04$).

No publication bias was found in this meta-analysis ($t = 1.39$, df = 11, p-value = 0.1928).

Depression

Effect of exoskeleton on depression in interventional studies using a control group

A total of 7 interventional studies reported data on depression for both interventional and control groups.[15,16,32,33,37,38,40] When those studies were combined in a meta-analytical model, no significant decrease in depression for individuals wearing exoskeletons was found (adjusted Hedges'g −0.45, 95% CI −0.94, 0.04; Figure 6).

A significant heterogeneity was found in the model ($I^2 = 75\%$, $p < 0.01$). Removing studies for which mean and standard derivation had been derived from median and interquartile (i.e. De Luca et al.[40] and Russo et al.[32]) reduced this heterogeneity, but this heterogeneity remained significant ($I^2 = 48\%$, $p = 0.09$). This sensitivity analysis revealed a significant Hedges' g of −0.66 (95% CI −1.08, −0.24) highlighting that wearing an exoskeleton may have a beneficial effect on depression.

Due to the restricted number of studies included in this meta-analysis, publication bias was not assessed.

Effect of exoskeleton on depression in pre–post studies with no control group

A total of 5 studies using a pre–post design with no control group reported data on depression.[18,22,23,26,29] No significant decrease in levels of depression for individuals wearing an exoskeleton was found (adjusted Hedges'g −0.80, 95% CI −2.23, 0.63; Figure 7).

A significant heterogeneity was found in the model ($I^2 = 94\%$, $p < 0.01$). However, when removing studies for which calculations have to be done (i.e. Kozlowski et al.[29] and Calabro et al.[23]), the heterogeneity was no longer significant (i.e. $I^2 = 0\%$, $p = 0.63$).

Due to the restricted number of studies included in this meta-analysis, publication bias was not assessed.

Narrative synthesis

Among the 31 studies included in the systematic review, 4 could not be included in the quantitative meta-analytic synthesis, two RCTs (Wu et al.[30] and Calabro et al.[31]) and two pre–post studies (Poritz et al.[20] and Platz et al.[19])

In their RCT, Wu et al. [30] compared two types of robotic training (i.e. assistance versus resistance) and could therefore not be included in the intervention vs control meta-analysis. This study showed no beneficial impact of training on quality of life, assessed using the SF-36 questionnaire. In the second RCT, Calabro et al. [31] compared robotic training with virtual reality versus robotic training without virtual reality. Because no control group was included, this study could not be included in the meta-analysis. Calabro et al.[31] measured the effect of interventions on depression and showed that mood improved in both groups after intervention. However, no significant group interaction was observed.

In both pre–post studies, insufficient quantitative data were available to allow statistical combination. Platz et al. [19] reported a significant improvement from the pretest to the posttest of the SF-12 domain role physical in 7 patients with lumbar spinal cord injury. None of the other domains or summary measures indicated a significant change. In the last study, Poritz et al. [20] included 10 patients with MS and showed no beneficial impact of the training on HRQoL, measured with the MS Quality of Life-54 questionnaire.

Discussion

To the best of our knowledge, this was the first time that the impact of robot-assisted gait training on the

quality of life and depression had been assessed quantitatively by meta-analysis. As previously mentioned, the efficiency of robot-assisted gait training is often measured by an ambulation assessment, but a patient must also be considered from a holistic point of view.

The findings of this meta-analysis suggested that rehabilitation with an exoskeleton could indeed have a positive impact on the quality of life and mental and physical health. This improvement was observed in both RCTs and non-RCTs. The positive effect could be explained by the fact that improvement in walking is the most frequently demanded goal of rehabilitation after stroke and in patients with spinal cord injury.[34,55] Another explanation could be that the use of a robotic walking device decreases secondary health impairments such as spasticity and pain with a subsequent positive impact on quality of life. Additional beneficial effects of better standing and walking are improved blood circulation, bowel and bladder function, and reflex activity, as well as a decrease in respiratory and cardiovascular complications, obesity, osteoporosis, and pressure sores.[3,56,57]

In addition, this study has highlighted the fact that the use of robotic devices does not reduce depression in patients with neurological impairment. One explanation could be that the results are less representative considering that only 7 and 5 studies were included, respectively, for the RCTs and non-RCTs. Nevertheless, by performing a sensitivity analysis in RCTs excluding the study of Russo et al.[41] and De Luca et al.,[40] a positive impact on depression was observed. The remaining studies evaluated the depression score after 2 to 8 weeks. On the other hand, in the RCT of Russo et al.,[41] the evaluation by HRS-D was done after 18 weeks. This suggests that robot-assisted gait training may decrease depression in the short-term, but that the benefits do not persist long-term.

In the literature, many patients reported improved self-image, eye-to-eye-interpersonal contact, and life independence with robotic devices.[3] This observation mainly applied to overground exoskeletons which are intended to be used as assistive devices in day-to-day activities. Nevertheless, the use of overground exoskeletons at home is not yet common because most of the time patients require supervision and the cost is still high.[3,29] One meta-analysis which analyzed 14 exoskeleton studies, demonstrated that only 76% of patients could successfully use an overground exoskeleton without physical assistance.[58] However, at the current time, overground exoskeletons are the only rehabilitation devices used in hospitals, and the studies only assessed the quality of life and depression scores after the rehabilitation program. The question of whether the positive impact persists once robot-assisted gait training has finished or, whether its use has negative long-term effects on patients' well-being still needs to be answered.

In this meta-analysis, studies using grounded and wearable exoskeletons were included. A positive impact on quality of life was observed in robot-assisted gait training with both types of exoskeletons. It was observed that in RCTs, the use of grounded exoskeletons was clearly predominant and that in pre–post studies the robot-assisted gait training was mostly realized with overground exoskeletons. There is a lack of studies comparing grounded and overground exoskeletons and their impact on walking ability and quality of life. Moreover, there remains a need for differentiation of these devices and analysis to determine whether one of these has a greater impact on the quality of life. All these devices are interesting tools for gait rehabilitation, but do not replace a conventional rehabilitation program.

As demonstrated, robot-assisted gait training is an excellent rehabilitation device with a potential impact on the quality of life of patients displaying neurological impairment, especially following spinal cord injury or stroke. There are, however, fewer studies reporting on MS and myopathies. Despite this, the use of exoskeletons will probably become more and more frequent in the future with applications in different pathologies.

In much the same way as with every study, the present meta-analysis has some limitations that should be considered when interpreting the results. First, an important heterogeneity of the results can be observed. This heterogeneity could be explained by the fact that different pathologies presenting more than one mechanism of walking impairment were included in this work. Furthermore, the protocols of robot-assisted gait training in RCTs varied in duration, ranging between 2 and 24 weeks, and in frequency, from 2 to 7 times per week. Unfortunately, an insufficient number of studies were included to allow the realization of subgroup analyses to investigate the source of heterogeneity. A second limitation of this meta-analysis was a lack of evidence of the studies with no control group. In addition, in RCTs, patients were unblinded which could have reduced internal validity. Thirdly, these results make it impossible to determine whether the improvement of parameters was due to the robot-assisted gait training or only to a rehabilitation intervention. Indeed, in 5 RCTs, an improvement in quality of life and depression was observed, but without a significant difference between the experimental and control group. Also, the majority of studies proposed a short-term follow-up. The evaluations were performed on average after 7.6 weeks of training with only three studies proposing a longer duration of treatment (i.e. between 18 and 24 weeks[32,36,41]). No study offered a follow-up after stopping rehabilitation treatment and it was, therefore, impossible to predict whether the positive effect persists. Finally, none of the articles mentioned whether the patients benefitted, simultaneously, from another rehabilitation or drug treatment (anti-spastic, pain-relieving medication, antidepressants, etc.)

Conclusions

Findings from this study suggest that robot-assisted gait training, including grounded and wearable exoskeletons, could improve the quality of life of patients with neurological impairment. The impact was observed immediately following robotic training although no long-term follow-up was carried out in the different studies. A positive impact on depression was also observed in the short term (after 7–8 weeks of training).

Clinical messages

- Based on the results of 26 interventional studies including patients with neurological impairments, a significant improvement of both the mental component and the physical component of health-related quality of life was observed following robot-assisted gait training.
- The question of whether the positive impacts of robot-assisted gait training on health-related quality of life persist once robot-assisted gait training has finished or, whether its use has negative long-term effects on patients' well-being still needs to be answered.
- Based on the results of 12 interventional studies including patients with neurological impairments, no improvement in depression was observed following robot-assisted gait training.

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Supplemental material

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