Journal of Health and Social Sciences (JHSS)
The Italian Journal for Interdisciplinary Health and Social Development *EDIZIONI FS Publishers*
Original Article in Neurology and Pediatric

Clinical study and Health Technology Assessment (HTA) of a Robot-Assisted Gait Training on children with neurological disorders: A quasi-experimental study

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Abstract

Background: Even if clinical evidence on effectiveness is still lacking, innovative technological solutions like robotic gait training technologies are gaining increasing attention in pediatric neuromotor rehabilitation.

Aim: This study aims to provide clinical-technological analysis for pediatric rehabilitation centers, build a rationale for driving future ideal rehabilitative pathways, and identify the most relevant criteria to evaluate robotic rehabilitation of the gait.

Design: Pre-post test design.

Setting: The robotic device comprises a bilaterally driven gait orthosis, computer-controlled guidance, and a non-immersive virtual reality system. Robotic-assisted locomotor treadmill therapy (RAGT) training was customized regarding training onset, duration, and specific gait parameters.

Population: We assessed 47 patients (mean age: 9.6 years, SD: 3.8 years; 23 females) with several neurologic diseases subjected to RAGT and patient-centered therapy (i.e., traditional therapy).

Methods: Inpatients were assessed in motor control, gait, cognition, and autonomies. The clinical investigation was integrated with a Health Technology Assessment (HTA) study, to investigate the introduction and impact of RAGT compared to patient-centered rehabilitation techniques and identify the most relevant criteria to assess the use of robotic rehabilitation technologies.

Results: The Patient-centered vs. Hybrid (RAGT+patient-centered) group showed a statistically significant difference between pre-treatment and post-treatment in Gross Motor Function Classification System (GMFM) total mean score (p=0.02). A significant increase in the distance walked

in 6 minutes was found in the comparison between pre and post-treatment evaluation in the hybrid group: average pre-post 126 vs. 156 meters ($t(13) = 2.78$: $p<0.01$).
Conclusions: The HTA process provided the weights of each evaluation element described in the decision tree. Safety is considered the most important domain, followed by Ethical Aspects and Clinical Effectiveness, which reached about the same weight as the technical characteristics. Less importance was given to organizational aspects and costs.

Take-home message: This study provides a detailed analysis of all the possible implications and aspects that should be considered in decision-making about introducing a robotic rehabilitation system in clinical units.
Keywords: Neurological disease, cerebral lesion, paediatric, robotic rehabilitation, HTA.

Cite this paper as: Gazzellini S, Andellini M, De Falco F, Casasanta D, Cordone G, Colazza A, Lettori D, Raponi M, Castelli E, Di Prinzio RR, Petrarca M, Ritrovato M, Zaffina S. A Clinical study and Health Technology Assessment (HTA) of a Robot-Assisted Gait Training on children with neurological disorders: A quasi-experimental study. J Health Soc Sci. 2023;8(1):76-92. Doi:10.19204/2023/clnc6

Received: 10 January 2023; Accepted: 10 March 2023; Published: 15 March 2023

INTRODUCTION

During the early years of development, neurological pathologies represent one of the most important clinical challenges for a national health service. Many neurological disorders originate during the perinatal period (congenital), whereas others develop after birth (acquired). World Health Organization's data suggest that neurological disorders are an important and growing cause of morbidity. According to the Global Burden of neurological disorders in children [1], the number of years children live with a disability has slightly increased, highlighting the need for early diagnosis improvement and neurological disorder management.

During the last 50 years, numerous rehabilitation strategies have been employed to increase children's functional recovery, everyday autonomy, and quality of life. Recovery function after brain injury is achieved through the plasticity of the human organism: the post-injury available neuronal and peripheral resources [2]. Neuronal plasticity is centered on the brain's ability to modify its functional and anatomical organisation as a result of experience. Brain plasticity is activated through the intensity of specific training valuable to stabilize neural coordinative dynamics and is triggered by specific properties of behaviors such as motivation, acquisition of new motor skills, and generalisation to different fields3. Peripheral plasticity involves changes in muscles, tendons, soft tissues, and bones over time. Remarkable improvements have been achieved thanks to a multidisciplinary clinical and rehabilitative approach to children's needs. The study and development of new materials and orthosis structures, the application of drugs for spasticity, and functional surgery proved helpful in rehabilitation.

However, analyzing the young patients' motor clinical outcomes in the last decades, no significant functional or structural brain modifications have been recorded. It was principally due to the shortage of objective measure parameters for assessing deficit level, active recovery, and evaluating precise aspects of the rehabilitative treatment provided [3,4].

Innovative technological solutions like robotic gait training technologies are gaining increasing attention from the scientific community. Their availability on the market is growing, aimed at assessing and rehabilitating motor functions, or replacing definitively lost functions [5]. One of the essential rehabilitative characteristics of robotic devices is to generate and control several force fields with high precision (e.g., viscous, elastic, gravitational), which allows customizing the sensory stimulation and the training. Furthermore, robotic devices provide sensory-motor feedback that adapts to the actual participant's performance at any given time and promises to achieve

progressively more and more efficient modalities of motor control. Therefore, by steadily measuring the characteristics of residual motor skills, robotic devices allow an objective assessment of patient's improvements following the criteria of evidence-based medicine, but only when the appropriate indicators are collected. Robotic rehabilitation hence promises to: i) represent a new opportunity to refund and increase children's motivation, ii) re-open the research process of adaptive solutions, iii) and create new possibilities to interact with otherwise inaccessible functions characteristics like locomotor coordination.

Notwithstanding robotic devices are considered promising for gait rehabilitation, but limited evidence demonstrated their real-world benefits in diplegic children affected by neurological disorders. Analysing the recent literature on Robotic-assisted locomotor treadmill therapy (RAGT) effectiveness in children with cerebral palsy (CP), controversial conclusions emerge. They can be ascribed to: i) the lack of specific analysis on the gait pattern; ii) the lack of a standard analysis method; iii) the limited selected samples: iv) the limited number of parameters analyzed; v) and to the confidence with which the results were discussed [6,7]. A meta-analysis study showed that the evidence is poor and restricted to limited effects on mobility, with no link to the recovery of the function [8]. The studies mainly analysed mobility's effect using the Gross Motor Function Classification System (GMFM, see below for description) applied to CP6-12. Among the GMFM sub-scales, the dimensions D and E that assess the standing skill (D) and the walking, jumping, and running ability (E) have been generally considered. Even in that case, the conclusions were controversial, since CP is not a homogeneous clinical condition, and the participants' age in the clinical sample was not homogeneous. However, these studies raised a tendency to increase standing (D) mobility and occasional mobility improvement in the E dimension. Meanwhile, a recent gait analysis study evidenced the absence of gait pattern modification using RAGT [13].

Even if clinical evidence on effectiveness is still lacking, technological innovations have been spreading over the last decades.The significant diffusion of technological solutions seems driven mainly by secondary factors, like the confidence of the single clinician with the device, rather than by a scientific rationale on the principles of recovery [14]. Because of the lack of clinical evidence, it is pivotal to conduct a comprehensive evaluation of the gait training rehabilitation devices, which integrates the clinical analysis with a detailed investigation of the safety, organizational, ethical, economic, and legal aspects. For these reasons, a Health Technology Assessment process (HTA) was carried out focusing on the Lokomat® system (Hocoma Inc., Volketswil, Switzerland - CE mark) and investigating all the aspects related to everyday Lokomat® use in a pediatric hospital context.

This study aimed to build a rationale for driving future ideal rehabilitative pathways, to provide a clinical-technological valuable analysis for the pediatric rehabilitation centers' strategical evaluations, to identify the most relevant criteria to assess the introduction and the use of robotic rehabilitation technologies in a hospital context. In the following section, the full HTA process will be described.

However, we underline that this study is not designed to respond to the question of training efficacy, due to the number and heterogeneity of participants recruited and clinical measures and to the endpoints selected. Nevertheless, the data from the clinical scales administered to provide a clinical description of the recruited.

METHODS

Search strategy

This quasi-experimental research with a pre-post study design conforms to the ethical principles of the Good Clinical Practice, and the Helsinki Declaration and follows the current regulations. The Independent Ethics Committee of "Bambino Gesù" Children's Hospital (Protocol n. 1787/2019) approved it. Informed consent from participants' parents was obtained when the patients were enrolled in the study, and confidentiality was ensured.

Technology

The RAGT (Lokomat®, Hocoma Inc., Volketswil, Switzerland) system consists of: i) a bilaterally driven gait orthosis which is adjustable to the anatomy of each patient; ii) a bodyweight support

system gait pattern, while computer-controlled guidance allows individual adjustments of different gait parameters; iii) a non-immersive virtual reality system comprehensive of an avatar. An adult device (femur length between 35 and 47 cm) and a pediatric device (femur length between 21 and 35 cm: Figure 1) are available. The dorsiflexion of the ankle joint is provided by a passive elastic foot strap, while hip and knee joints are actuated by linear back-drivable actuators integrated into the exoskeletal structure. All movements can be performed on the sagittal plane only.

Figure 1. Pediatric Lokomat® system (Hocoma Inc., Volketswil, Switzerland, 2013).

Nowadays, the RAGT training is variable in terms of training onset, duration, specific training parameters (e.g., walking speed, level of body-weight support, and guidance force), and the amount and type of conventional physiotherapy the patients receive in parallel with Lokomat therapy. Nevertheless, it is commonly accepted that the Lokomat training can be integrated for ethical considerations with the standard therapy program and used to treat different developmental pathologies such as spinal cord injury, stroke, multiple sclerosis, and CP.

Participants

A total amount of 47 inpatients, with written consent, participated in the study. The patients were 24 males and 23 females, with a mean age of 9.6 years, SD=3.8 years, ranging from 5 to 17 years. Participants ' recruitment was carried out in the pediatric neuro-rehabilitation unit at the "Bambino Gesù" Children's Hospital (Rome, Italy) among the inpatients. We included patients with gait impairments due to neurological diseases. The exclusion criteria were: the presence of articular limitation at the lower limb, arteriovenous disorders, cutaneous lesions, visual and cognitive severe impairments, and severe spasticity. Patients with age inferior to 5 years were excluded due to the

limits of the Lokomat exoskeleton structure. The patients were randomly selected and assigned to the treatments according to their motor performance and cognitive levels. All the participants were screened by specially trained therapists to determine the subject's suitability to robot-assisted gait training (RAGT). 16 were subjected to a "patient-centered" therapy (i.e., traditional therapy) of gait skills, and 31 were treated with a "hybrid" approach (patient-centered and RAGT). Among the patients subjected to RAGT, 8 were at the first Lokomat cycle, 5 at the second one, 6 at the third and 12 at the fourth cycle (Figure 2).

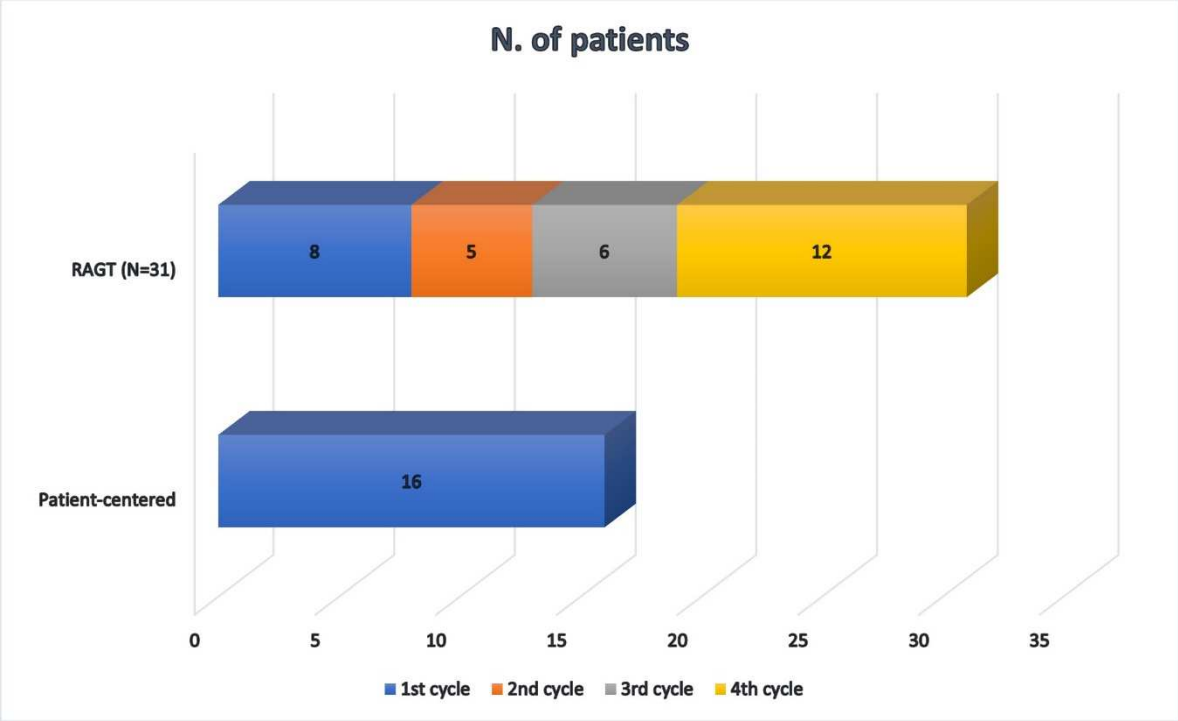

Figure 2. Amount of patients in each treatment type.

As far as the etiology is concerned, forty-three patients had major neurological damage, one patient had a diagnosis of Guillain-Barré syndrome, one patient presented polytrauma, and two children suffered from rare genetic pathologies. Among the four non-neurological patients, three of them were included in the control Patient-centered group (in particular, the patients with Guillain-Barré syndrome, polytrauma, and one with rare genetic pathology). The other patients with genetic etiology were subjected to hybrid treatment: all had a cognitive level in the normal range. According to the patients' clinical features, measures of cognitive level were obtained by the following scales:

- Wechsler Intelligence Scale for Children-Fourth Edition [15] (WISC-IV), evaluating verbal and visuo-spatial cognitive level (IQ) of children aged from 6 years to 16 years and 11 months.
- Wechsler Primary Preschool Scale for Children-Third Edition [16] (WPPSI-III), evaluating verbal and visuo-spatial IQ of children aged from 2.6 years to 7. 7 months.
- Leiter-III [17] is a non-verbal battery, measuring QI of children, adolescents, and adults (from 3 to 75 years old). Contrary to the other Wechsler scale, it can be used with non-verbal children and underlines the visuospatial modality of fluid reasoning.
- Coloured Progressive Matrices [18] (CPM) and Standard Progressive Matrices provide a rapid and culture-independent measure of visuo-spatial reasoning of patients aged 3-11 years (CPM) and 6-18 years (SPM).

The clinical sample described was administered with 17+6 mean RAGT and/or Patient-centered sessions. The therapy time for each participant was 90 min, including patient screening, setup time, explanation of the study procedure, patient-centered therapy, and hybrid training.

Motor Function Assessment

Inpatients were assessed in motor control, gait, cognition, and autonomies. In addition, the child's everyday life autonomies were assessed by administrating the Functional Independence Measure (Wee-FIM). Wee-FIM is a standardized questionnaire for children aged 6 months to 7 years, divided into three areas: self-care, mobility, and cognition.

The following standardized test and questionnaire were administrated before and after the treatments, if compatible with the patient's clinical conditions:

1) The Gross Motor Function Classification System (GMFCS)[1] is a widely shared classification system of patients aged between 2 and 18 years with CP. Patients with enough gait autonomy are included in the first level. Patients with no possibility of autonomous movement, neither chair moving, are at Level 5.
2) The Six-minutes Walking Test (6MWT) measures the patient's gait skill: the meters walked in 6 minutes at a self-paced speed and rest number and duration.
3) The Ten-meters walking test (10MWT) requires three walking repetitions at the highest speed: the mean time duration is calculated on the 10 meters central part of the pathway.
4) Gillette Functional Assessment Questionnaire is made up of 10 definitions of the child's mobility skills. The parents are required to rate the skills presented from 0 to 10.

Statistical analyses were performed using MatLab and SPSS. Pre-treatment scores were compared with post-treatment scores using the paired t-test after the normality test, $p < 0.05$.

Health Technology Assessment

The clinical investigation of the effect of rehabilitation treatment (pre-post treatment analysis) was integrated with a Health Technology Assessment study. It aimed to investigate the impact of RAGT compared to the patient-centered rehabilitation technique and identify the most relevant criteria to assess the introduction and the use of robotic rehabilitation technologies in a hospital context. More specifically, clinical and non-clinical aspects related to introducing and using the robotic technology in the hospital setting compared to the patient-centered gait rehabilitation process have been investigated. In addition, a working group with different professional skills was involved in identifying all the pertinent aspects to be analysed in assessing the RAGT. The working group comprised 15 professionals: 4 Medical Doctors, 3 Engineers, one Health Economist, 2 Psychologists, 4 Therapists, 1 Nurse.

The HTA process was carried out following the Decision Oriented HTA (DoHTA) method [19]. An accurate literature review was conducted to identify all the evaluation criteria and key performance indicators (KPIs) representing the discriminant assessment factors between the technologies under evaluation (details of the literature review are reported in the supplementary materials). The working group defined the main areas (Domains) that should be evaluated within the current HTA process, selecting only those that represent discriminant factors between the technologies compared, considering the evidence from the literature review together with the professionals' expertise. Furthermore, the method intends to explicit each domain, coordinating the collected evidence of the technology chosen in different "assessment elements" of the domains. The working group was able to identify the KPIs and associate to each domain one or more KPIs that are representative of the assessment area, through a critical review and assessment of scientific evidence gathered from the literature. A decisional hierarchy structure (decision tree) was created to stratify all the KPIs concerning each evaluation area. Following the DoHTA method, the relevance of each evaluation criterium within the overall evaluation was measured, through pairwise comparison. More specifically, each professional in the working group was asked to answer a list of pairwise comparisons between all the elements of the decision tree. In this way, it was possible to assign a

[1] The Gross Motor Function Measure is a 88 items scale evaluating overall motor skills, divided into 5 dimensions: (A) lying and rolling, (B) sitting, (C) crawling and kneeling, (D) standing, and (E) walking, running and jumping. Each item is evaluated by a 0 (skill absence) to 4 (appropriate skill) Likert-scale.

relative weight to each assessment element, representing the relative importance of each evaluation element within the overall assessment [19].

Moreover, the cost analysis was carried out by calculating the break-even point to assess the sustainability of the investment in robotic technology. More specifically, costs were collected from hospital databases. We included fixed and variable costs, with a discount rate of 1,88%. The former includes fees for inpatient/day service (502.90 €), investment costs (350,000 €), preventive maintenance costs every two years (12,151.20 €), and corrective maintenance costs (estimated as the 5% of the initial investment costs); the latter consist of healthcare professionals' cost.

Data availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

RESULTS

The cognitive level of the patients recruited is represented in the sample as follows: n. 30 (63.8%) participants had a cognitive level in the normality range (IQ from ≥ 71 up), n. 10 (21.3%) children had mild cognitive retardation (55≤IQ<70), n. 5 (10.6%) with middle cognitive retardation (40≤IQ≤54) and n. 2 (4.3%) participants had mild-severe cognitive retardation (IQ<40). The participants in the Patient-centered therapy group showed a mean IQ of 93.7, and the participants in the Hybrid therapy group presented a mean IQ of 79.4.

The whole sample recruited in the study shows difficulties in standing and in the more complex moving functions, such as walking, running, and jumping at the GMFM. According to the evaluation by the WeeFIM scale, the sample presented significant limitations of all the three standard dimensions investigated: self-care, mobility, and cognition. Table 1 shows the average values and the standard deviations of clinical parameters of all the indexes of the GMFM and WeeFIM scales concerning the whole sample (Patient-centered therapy group + Hybrid therapy group).

Table 1. Average values and standard deviation (SD) of the relevant clinical parameters in the whole group.

Whole group	Mean ± Standard Deviation
Age (training)	9.6±3.8
Sex: F/M	23/24
N°of training sessions	17.3±6.2
GMFM TOT	58.5+ 21.7
GMFM A	92.2+ 8.6
GMFM B	75.9+ 22,9
GMFM C	60.8±29.4
GMFM D	32.1+ 30.2
GMFM E	30.1+ 24.9
WeeFIM Tot	62.9±18.5
WeeFIM self-care	60.2±19.3
WeeFIM mobility	54±27
WeeFIM cognition	77.1±16.4
6MWT (m)	178.7±106.8
10MWT (sec)	21±14
Gillette	5.1±2.3

Pre-treatment and post-treatment measures have been carried out for GMFM, 6MWT, and 10MWT, but not for all the participants: see df on Table 2 for the numerosity (df=n-1). Pre-treatment and post-treatment measures of the WeeFIM and Gillette scales were not applicable for a time frame of one treatment cycle.

As shown in Table 2, the overall clinical sample (Patient-centered group + Hybrid group) showed a statistically significant difference between pre-treatment and post-treatment in GMFM total mean

score (p=0.02). This difference seems to be due to the hybrid group performance since only the GMFM total mean score revealed a statistically significant difference between pre vs. post-treatment comparison (t-test repeated measure: $t(8) = 2.6$; $p<0.05$, mean "pre" 48.1 – "post" 49.5). Comparing the single GMFM sub-dimensions (A, B, C, D, and E) pre- and post-treatment, they did not reach the significance at the t-test. Finally, a significant increase in the distance walked in 6 minutes was found in the comparison between pre and post-treatment cycle evaluation on the hybrid group: average pre-post 126 vs. 156 meters ($t(13) = 2.78$: $p<0.01$). Consistently, the time required to walk 10 meters decreased from 32.2 sec to 24.7 sec in the pre-post comparison. However, this difference was not statistically significant.

Table 2. Average values, standard deviation (SD) and statistics of the pre- vs post- comparisons. Group numerosity (n) for each measure can be calculated by the formula: df=n-1.

	Pre-treatment (average, SD)	**Post-treatment (average, SD)**	**t-Student**	**Df**	**p level**
GMFM TOT	51.1±23.3	52.1±23.4	2.6	14	0.02
GMFM A	89±10.7	90.3±9.6	1.72	14	0.11
GMFM B	66.9±27.6	69.1±26.5	1.8	14	0.09
GMFM C	50.4±32.4	52.4±32	1.8	13	0.09
GMFM D	37.9±34.4	38.6±33.5	0.89	8	0.38
GMFM E	27.1±23.8	25±23.9	1.85	12	0.09
6MWT (m)	125.6±68.5	155.7±94	2.78	13	0.01
10MWT (sec)	32.2±26.2	24.7±15.2	1.13	13	0.21

The health technology assessment process results include a hierarchy decision tree incorporating the assessment criteria (Figure 3).

As Figure 3 shows, the assessment criteria (KPIs) able to compare the robotic gait train rehabilitation system and the traditional therapy are incorporated in six evaluation areas: safety, clinical aspects, costs, economic evaluation, technical characteristics, organizational aspects, and social and legal aspects (Domains).

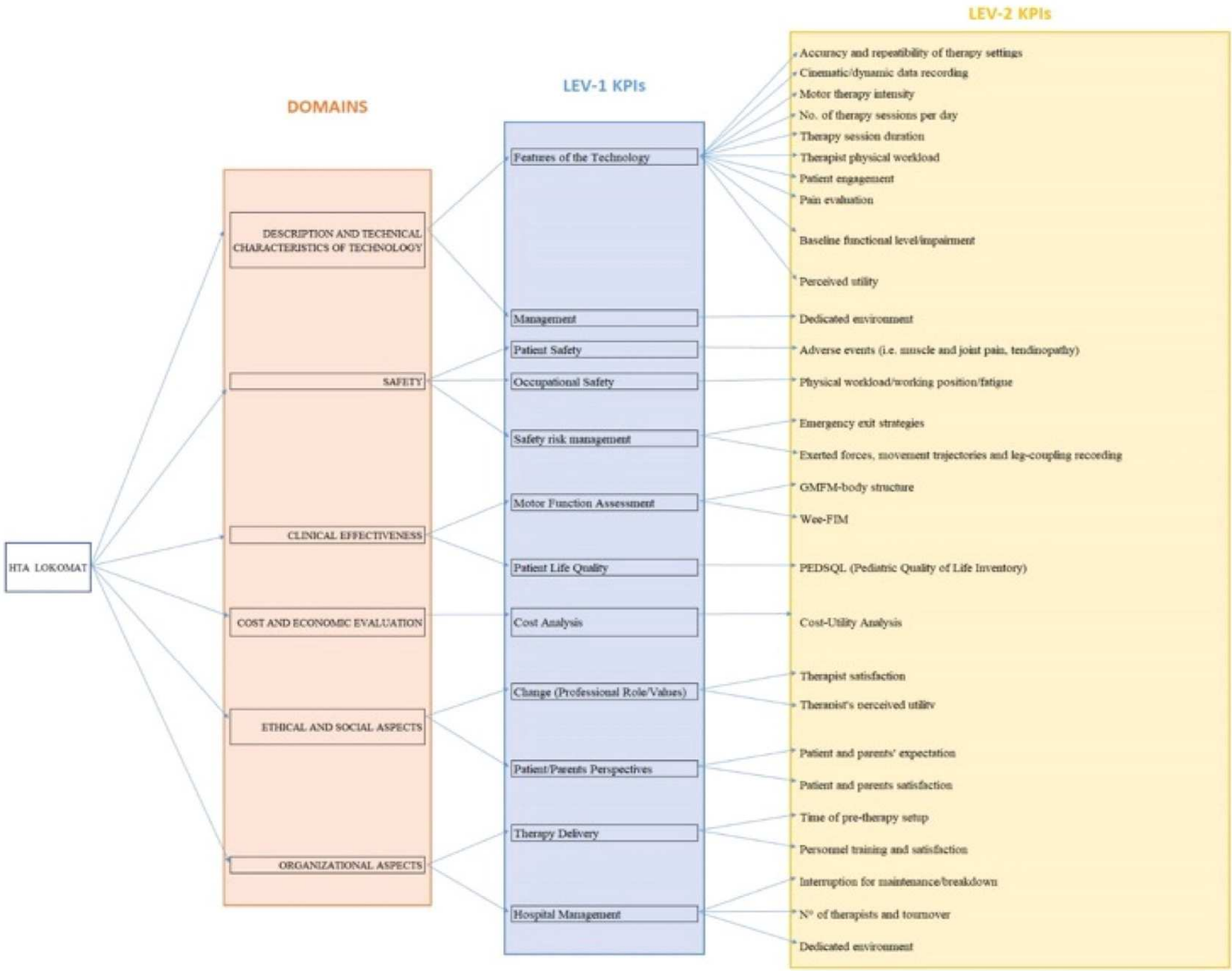

Figure 3. Health technology assessment: Hierarchy decision tree made up of the Domains, each one is then described by several detailed KPIs.

Table 3. The six HTA evaluation domains that have been selected: Safety, clinical aspects, costs and economic evaluation, technical characteristics, organizational factors, and ethical and social aspects. Each domain is then described by several KPIs (Lev1-KPIs and Lev2-KPIs). The fourth column shows the relative weight of each assessment element.

DOMAINS	LEV-1 KPIs	LEV-2 KPIs	Weights
Technical Characteristics of Technology			**15,9%**
	Features of the Technology		**11,0%**
		Accuracy and repeatability of therapy settings	1,9%
		Cinematic/dynamic data recording	1,0%
		Motor therapy intensity	1,4%
		No. of therapy sessions per day	0,5%
		Therapy session duration	0,6%
		Therapist physical workload	0,8%
		Patient engagement	2,0%
		Pain evaluation	1,0%
		Baseline functional level/impairment	1,0%
		Perceived utility	0,8%
	Management		**5,0%**
		Dedicated environment	5,0%
Safety			**28,1%**
	Patient Safety		**14,7%**
		Adverse events (i.e., muscle and joint pain, tendinopathy)	14,7%
	Occupational Safety		**8,9%**
		Physical workload/working position/fatigue	8,9%
	Safety risk management		**4,5%**
		Emergency exit strategies	2,1%
		Exerted forces, movement trajectories, and leg-coupling recording	2,4%
Clinical Effectiveness			**17,2%**
	Motor Function Assessment		**6,4%**
		Wee-FIM	6,4%
	Patient Life Quality		**11,0%**
		PEDSQL (Pediatric Quality of Life Inventory)	10,8%
Cost and Economic Evaluation			9,1%
	Cost Analysis		9,1%

		Break-even point	9,1%
Ethical and Social Aspects			**20,9%**
	Change (Professional Role/Values)		**8,9%**
		Therapist satisfaction	3,4%
		Therapist's perceived utility	5,5%
	Patient/Parents Perspectives		**12,0%**
		Patient and parents' expectation	3,7%
		Patient and parents' satisfaction	8,3%
Organisational Aspects			**8,8%**
	Therapy Delivery		**6,5%**
		Time of pre-therapy setup	2,2%
		Personnel training and satisfaction	4,4%
	Hospital Management		**2,3%**
		Interruption for maintenance/breakdown	0,3%
		N° of therapists and turnover	1,1%
		Dedicated environment	0,9%
Total			**100%**

Following the DoHTA method19, the Health Technology Assessment process provided each evaluation element's weights (relative importance) described in the decision tree. More specifically, Table 3 and the pie chart depicted in Figure 5 show in detail the results.

Results from pairwise comparisons showed that safety is considered the most crucial domain, followed by Ethical Aspects and Clinical Effectiveness, which reached about the same weight as the technical characteristics. Less importance was given to organizational aspects and costs.

Regarding the safety aspects, patient safety was the most important criterion including the generation of adverse events like muscular and joint pain, tendinopathies, skin lesions and erythema, and fatigue. A lower level of importance was assigned to the occupational safety indicator, which included aspects such as physical workload, working position, and fatigue, and the risk management indicator concerning strategies for emergency exits and extended forces.

Professional and patient-related ethical aspects were investigated. Patient and family's expectations before the therapy and satisfaction after the treatment were slightly more important than the professional-related ethical aspects (perceived utility and therapist satisfaction).

Regarding clinical effectiveness, the quality-of-life key performance indicator was paid particular attention. Each patient was subjected to a pediatric quality of life questionnaire (PedSqL) before and after the rehabilitation protocol. Results revealed that both RAGT and Patient-centered training seemed to improve the patients' quality of life after rehabilitation protocol. However, the former slightly overcame the latter (Table 4; see also [20] Gilardi et al., 2020).

Table 4. Results of pediatric quality of life questionnaire (PedSqL) before and after the entire rehabilitation protocol for RAGT and patient-centered therapy.

Quality of life		RAGT	Patient-centered therapy
Before therapy			
	Mean	63,76302083	64,13411458
	Standard Deviation	12,95527292	11,16299363
After therapy			
	Mean	70,25173611	69,4140625
	Standard Deviation	14,03295215	11,36650671
Increment of quality of life	Mean	6,488715278	5,279947917
	Standard Deviation	6,223961635	4,415464226

Indeed, from a technical point of view, Robotic systems are remarkably innovative compared with traditional therapy. The robotic system intrinsically offers many advantages, such as the accuracy and repeatability of the therapy setting, the possibility to record cinematic and/or dynamic data, and the possibility to monitor and manage the therapy intensity.

Regarding the organizational aspects, the therapy delivery (time of pre-therapy setup, personnel training, and satisfaction) reached more importance than the hospital management as the latter does not differ between the two rehabilitation techniques except for the management of the robotic system that requires preventive and eventually corrective maintenance.

Regarding the cost and economic evaluation, the traditional therapy, requiring no investments or maintenance, resulted in the favorite. However, the result of the break-even point (BEP) analysis shows that the investment in robotic technology can be easily balanced if several patients, ranging from 54 to 63, were treated with robotic gait rehabilitation in a period (payback period) ranging from 2.5 and 3 years (Figure 4).

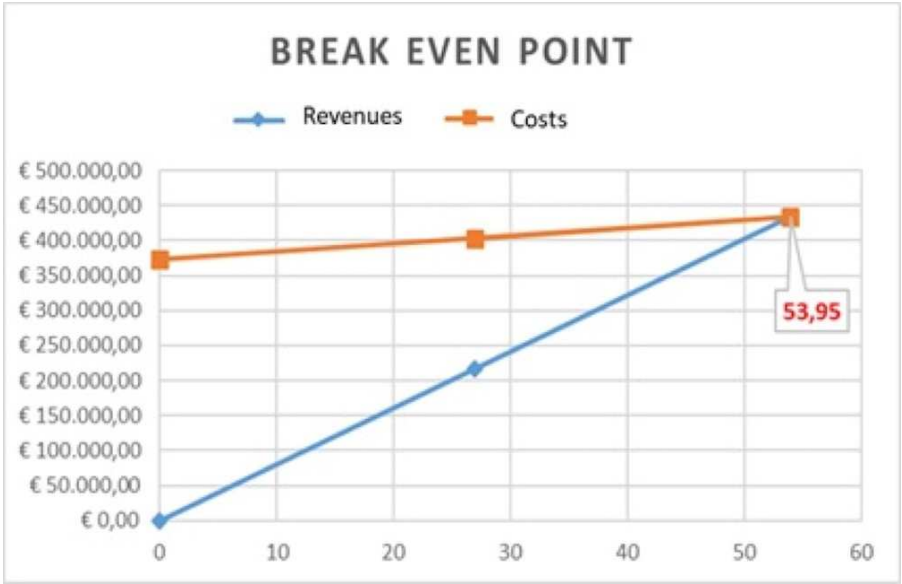

Figure 4. Break-even point.

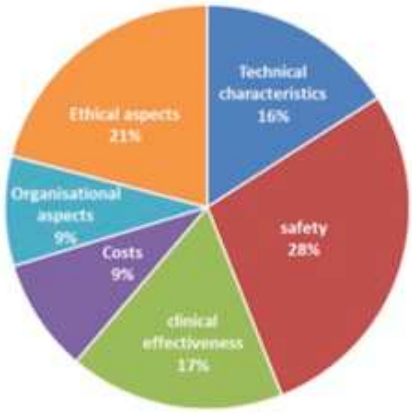

Figure 5. HTA results in terms of the weight system.

DISCUSSION

This study aimed to build a rationale for driving future ideal rehabilitative pathways and to provide a clinical-technological valuable analysis for the pediatric rehabilitation centers' strategical evaluations. Our study identified the most relevant criteria to assess the introduction and the use of robotic rehabilitation technologies in a hospital context. The study was not designed to respond to the question of RAGT or patient-centered training efficacy.

In this paper, we analyzed the impact of RAGT on rehabilitating children with neurological disorders as an inpatient. We carried out a detailed clinical analysis to build a rationale for driving future ideal rehabilitative pathways. In addition, we performed an HTA analysis to identify the most relevant criteria to assess the introduction and use of robotic rehabilitation technologies in a hospital context.

Following the DoHTA method, and with the working group's consensus, six domains were defined as the most relevant assessment criteria to evaluate when a hospital decides to implement a robotic technology.

More specifically, concerning the safety aspects, patient safety was considered crucial for comparing the robotic and conventional rehabilitative treatments in terms of adverse events generation like muscular and joint pain, tendinopathies, skin lesions, erythema, and fatigue. A lower level of importance was assigned to the occupational safety indicator, which included aspects such as physical workload, working position, and fatigue, and the risk management indicator, concerning strategies for emergency exits and extended forces. Patients' safety aspects were investigated, and the RAGT system was more likely to generate adverse events, whereas, regarding occupational safety, robotic rehabilitation reduced physical workload, working position, and fatigue [20]. Final considerations lead to the claim that patient-centered therapy appears slightly safer than robotic one, principally since robotic therapy is more likely to generate adverse events.

Ethical issues are also considered pivotal for this evaluation. More specifically, both professional and patient-related ethical aspects were considered. Whereas patient-centered therapy favored therapists' related ethical aspects, the patients' and families' expectations and satisfaction with robotic therapy doubled compared to the patient-centered one [20]. Providing medical practitioners with training in artificial intelligence management can help them adhere to rules more closely and reduce their exposure to legal danger [21].

Clinical analysis results, evaluating patients changes before and after the treatment cycle with RAGT, highlighted a significant increase in the distance walked in 6 min (126 vs 156 mt: t-test: $p<0.01$) and no significant time decrease in walking 10 mt. In addition, the Quality-of-life questionnaire results showed a slight increase of the quality of life of patients who underwent RAGT therapy compared to those with traditional therapy. In any case, in this study RAGT therapy does not decrease the life quality of our young patients.

However, the rational framework of technologies in rehabilitation has been placed side by side by other cultural and commercial factors. The end of the previous century was characterized by the computerization of research activities and the beginning of the current century by an acceleration of robotisation. The next step is characterised by the increasing use of techniques for exploiting Artificial Intelligence. The "availability" of these technologies is at the basis of their application in the rehabilitation field before every evidence of their effectiveness. Visionary people see mainly the opportunity to create a market introducing something new in a rehabilitative context in which the change and the improvement are naturally limited by the chronic or progressive evolution of the diseases. Among the other proposals, the emerging Lokomat represents a device that reached great commercial success. Even if technologies can accomplish and enhance some aspects of the rehabilitative process, the selected path has not been driven by selecting the more appropriate rehabilitative solution but has been characterised by market competition. Consequently, many devices were sold without evidence of rehabilitative effectiveness, but only by providing proof of human safety. Safety needs furthermore limited robotic operability. Providing rehabilitative evidence was delegated to users. Notoriously, users have generally restricted the availability of resources for conducting research protocols that need large population samples and rigorous methodology, especially for children with cerebral palsy, as described in the literature with great accuracy [6,22]. A similar study was never conducted due to the required resources, and only studies with limited or low evidence levels were performed.

In introducing new solutions, the regulation is currently oriented toward requiring evidence of effectiveness. Moreover, this latter aspect represents an additional risk for freezing the market and prolonging the success of the current solution. Indeed, while the process of validation proceeds slowly, as mentioned above, the technological solutions go on with exponential speed, and new device versions are provided even before any evidence of effectiveness is achieved. That is the case of introducing a new dynamic control on foot trajectory [23]. An event that re-opens or changes de facto any ongoing validation path and prolongs the life of the never assessed technologies. That is, technologies sustain themselves, by transforming themselves from tools for an aim, to the goal itself. This is happening, although the literature underlined the usefulness of technology for assessing specific principles of motor learning before defining a rehabilitative solution [24–26].

The need for a recovery rationale opens another issue: the link between motor learning principles and the selected technological solutions. A crucial aspect of the rehabilitative process, mainly neglected or simplified by the market introducing a gaming approach based its rationale on repetition and motivation. From a rehabilitative perspective, it is notorious that motivation can lead to bad learning and that pathology expresses itself with stereotyped (repetitive) behaviour. Rehabilitation concerns the process of "re-opening the research of adaptive solutions" each specific for optimizing biological functional goals in different tasks and contexts. Locomotion is a family of behaviors specific to different terrains and goals that "affords" navigation on all landscapes. Each behavior shares some common elements and specific characteristics for better matching body-environment coupling, exploiting internal dynamic coordination for pairing external dynamics [27,28]. This active control during locomotion is triggered and needs to anticipate the settings of the stretch reflex threshold, allowing the dynamic muscle response [29]. These concepts are far from the idea of locomotion implied in the RAGT vision: a mere repetitive pattern of reciprocal flexion/extension movements of the lower limbs. A perspective that seems more addressed to the maintenance of spinal cord servo mechanism in spinal cord adults injured rather than in children with CP. Furthermore, Lokomat presents an embedded, non-immersive virtual system, including an avatar. Not all children with cerebral palsy can take advantage of this support [23]. New solutions are under study from the perspective of developing adaptive and versatile solutions aimed at early training in children with CP [30,31].

Of course, several limitations to the study must be considered. In particular: the sample size varies according to the parameters, depending on the possibility of completing the measure, and is sometimes small. For some measures, a pre-post comparison is meaningless. All the participants

received patient-centered gait rehabilitation, and only a subgroup received a robotic training as well. Hence the two samples were not entirely different.

CONCLUSION

According to the One Health approach, the multidisciplinary management of public health issues in healthcare settings is becoming increasingly important [32,33]. Public authorities must address the complex issue of human-machine interaction, as was the case during the COVID-19 pandemics, when much of the working population was equipped with remote/agile/smart work [34]. This study was conducted to guide robotic gait training introduction in rehabilitation structures. It provides a detailed analysis of all the possible implications and aspects that should be considered in decision-making about introducing a robotic rehabilitation system in clinical units. The research conducted in our pediatric hospital leads to the preliminary conclusion that the robotic system might be considered an option for a rehabilitation service thanks to its applicability to a wide range of patients and its significant ethical and social impact. Moreover, revealing no significant differences in KPIs analyzed between the two alternatives, i.d., robotic and traditional rehabilitation techniques, the results showed the complementarity of the two systems. Indeed, we can conclude that robotics solutions are just at the initial study stage. Lokomat represents one possible path for exploiting gait recovery, while the recovery rationale can promote other solutions. Therefore, further research on alternative robotic configurations is required.

Author Contributions: Conceptualization, S.G., M.A., F.D.F., M.P., E.C., D.L., M.R., and e S.Z.; Data curation, D.C., F.D.F., G.C., A.C.; Formal analysis, S.G., M.A., and M.P.; Investigation, F.D.F., D.C., M.A., S.G., M.P., G.C., and A.C.; Methodology, S.G., M.A., F.D.F., M.P., M.R., G.C., S.Z.; Supervision, E.C., M.R., and S.Z.; Writing original draft, S.G., M.A., M.P.; Writing review and editing, S.G., M.A., M.R.V., R.R.D.P., M.P. All authors read and approved the final version of the manuscript.

Funding: None.

Acknowledgments: None.

Conflicts of Interest: None.

Data Availability Statement: All data that support the findings of this study is presented in Table 1.

Publisher's Note: Edizioni FS stays neutral with regard to jurisdictional claims in published maps and institutional affiliation.

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