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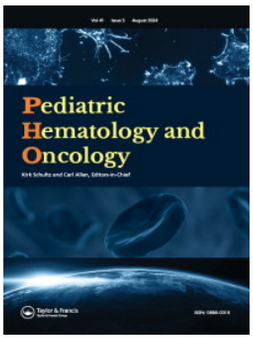

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The Italian Consensus Conference on the role of rehabilitation for children and adolescents with leukemia, central nervous system tumors, and bone cancer, part 2: general principles for the rehabilitation treatment of motor function impairments

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ABSTRACT

In Italy, 1400 children and 800 adolescents are diagnosed with cancer every year. About 80% of them can be cured but are at high risk of experiencing severe side effects, many of which respond to rehabilitation treatment. Due to the paucity of literature on this

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topic, the Italian Association of Pediatric Hematology and Oncology organized a Consensus Conference on the role of rehabilitation of motor impairments in children/adolescents affected by leukemia, central nervous system tumors, and bone cancer to state recommendations to improve clinical practice. This paper includes the consensus on the rehabilitation of children and adolescents with these cancers.

KEYWORDS
Rehabilitation; rehabilitative intervention; physical therapy; pediatric oncology

Introduction

Based on the data collected by the International Agency for Research on Cancer (IARC), each year approximately 215,000 cancers are diagnosed in children under the age of 15 and approximately 85,000 in children between the ages of 15 and 19.[1] In Italy around 1400 children and 800 adolescents are diagnosed with cancer every year.[2] In high-income countries 80% of pediatric patients can be cured, while in low-resource settings survival rates are only about a quarter of those in high-resource settings.[1] Cancer and cancer treatments can negatively impact major body systems, including the musculoskeletal, cardiorespiratory, and neurological systems.[3] The side effects of treatments can negatively impact the child's quality of life (QoL) and participation in daily activities (e.g. playing and attending school).[4] Exercise programs for children and adolescents affected by cancer have shown benefits on body composition, flexibility, cardiorespiratory fitness, muscle strength and QoL.[5] The European Society of Oncological Pediatrics (SIOP Europe) promoted the implementation of health care professional (HCPs) networks to support care activities, research, and training to create innovative, high-quality models of care.[6] The high variability in rehabilitation approaches to pediatric cancer patients resulting from the lack of high-quality evidence[5] led the Italian Association of Pediatric Hematology and Oncology (AIEOP) to promote the Italian Consensus Conference (CC) on the role of rehabilitation for children and adolescents with cancer, focusing on motor function. The main goal of the CC was to define the role of the rehabilitation team in the assessment (part 1)[7] and the general principles for the rehabilitation treatment (part 2) of motor impairments (sensorimotor, neuro and psychomotor). This paper includes the results of the CC on the rehabilitation treatment of these patients.

Materials and methods

A systematic approach based on the Italian National System for Guidelines was followed for the CC.[8] The Patient Intervention Comparison Outcome (PICO) method was used to generate clinical questions for three major subgroups of pediatric cancers: leukemia, central nervous system (CNS) tumors and bone cancer. Relevant outcomes were selected and approached accordingly to the grading of recommendation assessment, developing and evaluation (GRADE) method.[9]

Literature review strategies are reported in Supplemental Table S1. In both papers, the term "physiotherapist" refers to the physiotherapist and to the Neuro and Psychomotricity Therapist of Developmental Age (TNPEE),[10] who in Italy works with

other specialists (occupational therapist, speech therapist, orthoptist) for the rehabilitation of patients in the developmental age ranges.

The Consensus Conference

The promoter (AIEOP) established a lead committee who selected two panels of experts: a Technical Scientific Committee (TSC) and a Multidisciplinary Jury (MJ), composed of 10 and 19 professionals respectively, including experts from oncology (pediatricians, oncologists, psycho-oncologists, nurses, pediatric nurses) and rehabilitative medicine (child neuropsychiatrist, physiatrist, physiotherapist, speech therapist, orthoptist), social workers, and patient representatives. A panel of 31 experts (PoE) in pediatric cancer rehabilitation was selected by TSC. The PoE was then divided into three subgroups: leukemia, CNS tumors, and bone cancers.

Topics, research questions building and literature search

The promoter opted to focus the CC on leukemia, CNS tumors, and bone cancer, which represent the most frequent oncological diseases affecting pediatric patients as well as the major illnesses requiringre habilitation.[11] Initially, the TSC formed background questions that were divided into three parts: (a) the role of rehabilitation HCPs, (b) assessment, and (c) treatment of sensorimotor, neuro-, and psychomotor function impairments. The PICO method was then used to establish suitable clinical questions for each subgroup. The resulting outcomes were divided into those that were considered "critical," "relevant but not critical," or "not relevant" according to the GRADE method[9] and, following that, a final list of questions was chosen by the PoE.

PubMed, CINHAL, PsycINFO, and Scopus databases had used for literature searching (in Supplemental Table S1 the detailed searching strategy is reported), The PoE subgroups summarized the retrieved papers for relevance, population, design, intervention, comparison, outcomes, methodological issues, and results by categorizing the reviews, clinical trials, observational studies, and gray literature.

Evidence appraisal and recommendation building

GRADE method considers four levels of evidence: very low (the true effect is probably markedly different from the estimated effect), low (the true effect might be markedly different from the estimated effect), moderate (the authors believe that the true effect is probably close to the estimated effect), and high (the authors have a lot of confidence that the true effect is similar to the estimated effect). Accordingly to the method, the level of evidence can be increased or decreased for several reasons due to the quality of the studies.[9] A member of the lead committee assessed quality of evidence, and the GRADE method was used to up- down-grade the evidence. The findings were presented at PoE subgroups, with any disagreements being resolved through discussion into them. Where no comprehensive data were found in the pediatric literature, the

PoE used evidence from systematic reviews and randomized clinical trials in adults. However, in the case where recommendations were based on evidence obtained from adult literature only, the piece was downgraded due to its indirectness in agreement with other authors.[12]

A 3-day PoE meeting was organized, where each subgroup produced the first draft of 15 recommendations and 51 statements. Agreement had obtained by voting on a 1–9 scale for recommendations and statements, with the results analyzed for central tendency values (average, median) and ranges. The consensus report was submitted to MJ for peer review, and following the jury's recommendations the PoE performed a second review, voting on the quality, equity, feasibility, acceptability, relevance, risks-benefits balance, and costs for each recommendation. This determined the definitive strength of recommendations. The final set of recommendations had shared at the CC celebration taken place in November 2018 in Turin. Experts in the field of cancer rehabilitation, pediatrics, oncologists, members of scientific societies, and patients' representatives were invited. Further detailed information on the composition of CC working groups, on the identification of questions, critical appraisal of the evidence, and recommendations development are available in the previous paper (Table 1).[7]

Results

The CC produced seven general recommendations (Table 2) and sixteen statements (Table 3), thirteen of which were specific for the three subpopulations.

Question 1: "What are the rehabilitation goals for subjects in developmental age affected by cancer and when should rehabilitation be done?"

Recommendations

- "Rehabilitation should aim at preventing and/or improving alterations in sensorimotor, cognitive, and psychosocial functions during and after anticancer treatments."
- "When indicated, rehabilitation should start as early as possible."
- Statements are reported in Table 3.

Table 1. The council for physical education in children (COPEC) of the national association for sport and physical education (NASPE) recommendations.

The Council for Physical Education in Children (COPEC) of the National Association for Sport and Physical Education (NASPE) recommends children to:
• perform at least from 60 minutes to several hours of age-appropriate physical activity, all or most days of the week.
• make bouts of intense physical activity lasting 15 minutes or more every day.
• In children, long periods (2 hours or more) of inactivity (videogames, TV) are not recommended, especially during daylight hours.

Adapted from: Corbin CB, Pangrazi RP. Guidelines for Appropriate Physical Activity for Elementary School Children 2003 Update. A Position Statement. Council for Physical Education for Children (COPEC) of the National Association for Sport and Physical Education an association of the American Alliance for Health Physical Education and Recreation.

Table 2. Summary of recommendations for rehabilitation of children and adolescents affected by cancer.

Questions	Recommendations	Level of evidence:	Degree of consent:	Strength of the recommendation:
QUESTION 1: "What are the rehabilitation goals for subjects in developmental age affected by cancer? When should rehabilitation be done?"	"Rehabilitation should aim at preventing and/or improving alterations in sensorimotor, cognitive, and psychosocial functions during and after anticancer treatments."	moderate	average 8.7; range 8–9	strong
	"When indicated, rehabilitation should start as early as possible."	low/ moderate	average 8.7; range 7–9	strong
QUESTION 2: "What characteristics should the individualized rehabilitation plan have?"	"The rehabilitation plan should be carried out by a multiprofessional team and personalized according to the patient's goals."	low	average 8.5; range 1–9	strong
	"The rehabilitation plan (modality, setting, intensity, and duration) should be adapted to the characteristics of the subject, the clinical status, the sensorimotor impairment, and the treatment phase."	low	average 8.6; range 1–9	strong
	"Any ongoing changes to the individualized rehabilitation plan should be made based on the patient's clinical condition, the goals achieved, those to be achieved, and the assessments of the multidisciplinary team."	low	average 8.6; range 1–9	strong
	"Patients and their caregivers should be involved in defining the rehabilitation goals and the individualized rehabilitation plan."	very low	average 8.6; range 1–9	strong
QUESTION 3: "How long should the patient be followed up?"	"Rehabilitation should last as long as required by the subject's clinical condition, regardless of whether in the hospital, community, or home setting."	Low/ moderate	average 8.9 range 8–9	strong

Table 3. Summary of statements for rehabilitation treatment of children and adolescents affected by cancer.

Question 1	What are the rehabilitation goals for subjects in developmental age affected by cancer? When should rehabilitation be done?"	
	Recommendations	• Rehabilitationshould aim at preventing and/or improving alterations in sensorimotor, cognitive, and psychosocial functions during and after anticancer treatments • When indicated, rehabilitation should start as early as possible
	Statements for children/ adolescents affected by leukemia	• In children/adolescents with leukemia, rehabilitation is feasible at all stages of the oncologicalpath and shouldbe modulated according to the clinical condition of the subject • In children/adolescents with leukemia undergoing hematopoietic stem cell transplantation (HSCT), specific physical activity adapted to the needs of the subjectcouldbe carried outduring and after the transplant to prevent or reduce the effects of isolation, immobility (e.g., fatigue) and the complications related to transplantation[11–14]
	Statements for children/ adolescents affected by CNS tumors	• In children/adolescents with CNS tumors, there is no evidence of the utility of initiating rehabilitation in the preoperative period • In children/adolescents with CNS tumors in the immediate postoperative period, a careful evaluation of the cost-benefit ratio for the patient is necessary to establish the appropriate time to start rehabilitation • In children/adolescents with CNS tumors requiring long-term rehabilitation, the frequency and modalities of treatment shouldbe established based on the goals of the individualized rehabilitation plan
	Statements for children/ adolescents affected by bone cancer	• In children/adolescents withbone cancer who are candidatesfor surgery, rehabilitation shouldbegin as soon as possible to improve physical functioning and to reduce postsurgical sequelae13–20 • In children/adolescents with bone cancer, rehabilitation shouldresume as soon as possible after surgery, according to the goals set and the clinical conditions of the subject19–24 • In children/adolescents with bone cancer, post-surgical rehabilitation may continue until the subject has reached the maximum possible autonomy[19,21,23–26]
Question 2	What characteristics should the individualized rehabilitation plan have?	
	Recommendations	• The rehabilitation plan should be carried out by a multiprofessional team and personalized according to the patient's goals • The rehabilitation plan (modality, setting, intensity, and duration) should be adapted to the characteristics of the subject, the clinical status, the sensorimotor impairment, and the treatment phase • Any ongoing changes to the individualized rehabilitation plan should be made based on the patient's clinical condition, the goals achieved, those to be achieved, and the assessments of the multidisciplinary team • Patients and their caregivers should be involved in defining the rehabilitation goals and the individualized rehabilitation plan
	General statements	• In children/adolescents with cancer, to improve compliance with exercise programs or preventive indications, caregivers and siblings shouldbe involved, and the proposed activities shouldhave an age-appropriate playful connotation[27,28] • Structured and routine information, educational and rehabilitation consultationsshouldbe planned to strengthen adherence to the rehabilitation intervention

	Statements for children/ adolescents affected by leukemia	• Children/adolescents with leukemia undergoing treatment or maintenance should engage in physical activity which includes: – aerobic training – stretching and strengthening exercises – balance and coordination exercises[15,17,28–45]
	Statements for children/ adolescents affected by CNS tumors	• In children/adolescents with CNS tumors, the initiation ofrehabilitation in the pre-surgical phase may be considered • The rehabilitation of children/adolescents with CNS tumors in the early post-operative period requires careful evaluation of the benefits for the patient
	Statements for children/ adolescents affected by bone cancer	• In children/adolescents with bone cancer of the lower limbs, post-operative rehabilitation shouldbe plannedincluding: – ROM recovery exercises and strengthening exercises, with a specific focus on the knee extensor muscles – Proprioceptive, motor control and balance exercises24,26,29,43–54 – Strengthening exercises for the muscles of the joints adjacent to the operated one and for those of the contralateral limb to recover the correct gait pattern. • In children/adolescents with bone cancer of the upper limbs, post-operative rehabilitation shouldbe planned including: – ROM recovery and strengthening exercises – Recovery and maintenance exercises forfunctional skills and activities of daily living.[16–25]
Question 3	How long should the patient be followed up?	
	Recommendations	• Rehabilitation should last as long as required by the subject's clinical condition, regardless of whether in the hospital, community, or home setting
	General statements	• The integration of hospital-, community-, and home rehabilitation is useful for reducing the period of hospitalization. The home environment can incentivize the performance of the subject[55,56]

Description

Rehabilitation goals should be defined according to the biopsychosocial model of the World Health Organization (WHO) International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY),[46] which include Body Function and Structure, Activity, Participation, Environmental Factors, and Personal Factors. This model emphasizes the need to support individuals to achieve optimal capacity and participation in all aspects of life.[57] The ICF-Childhood cancer (ICF-CC) model[29] identifies body impairments, activity limitations, and participation restrictions amenable to rehabilitation in children and adolescents with cancer. Setting individual rehabilitation goals is a collaborative process between child, parents, and HCPs. Rehabilitation goals vary according to the subject's age, cancer types, treatment's phases, and clinical settings.

Rehabilitation interventions for infants and young children diagnosed with cancer should aim to support neuro-psychomotor development. Environmental enrichment strategies can be considered for behavior modification, especially for very young children (less than 3 years old) and in the rehabilitation of complex cognitive functions.[58]

"Early rehabilitation" is a widely accepted concept. In oncology, it has been demonstrated that functional recovery is better in patients who start rehabilitation as soon as possible, with some precautions:[30,59–62] exercise should be avoided when hemoglobin level is <8 g/dL, and/or temperature ≥38 °C, and only therapeutic exercise without resistance is recommended with platelets counts less than 20,000/mm^3.[63] Recent studies documented the safety of physical exercise in pediatric patients affected by thrombocytopenia and undergoing intensive chemotherapy,[64,65] if a symptoms-based approach is used in collaboration with interprofessional team to determine appropriateness for physical activity (PA).[66] When rehabilitation treatment is not feasible, it may be useful to structure an indirect intervention, based on rehabilitation counseling for both children/adolescents, parents, and other HCPs.

Preventive counseling during and after anticancer treatment can be useful for all children/adolescents with cancer, to maintain their motor performance. Available evidence and consensus from a team of international experts support that movement is safe, beneficial, and recommended for all children and adolescents affected by cancer.[67]

Leukemia

Children/adolescents affected by leukemia may need to start a rehabilitation intervention at any time in their care path due to the onset of specific problems, including low bone mineral density, loss of lean muscle mass, neuropathy, muscle weakness and impaired cardiorespiratory capacity.[68]

In fact, during ALL induction and later stages of treatment, many children experience chemotherapy-induced peripheral neuropathy and steroid induced myopathy contributing to distal and proximal motor weakness, respectively.[69]

The start of rehabilitation should be modulated according to the characteristics of the different treatment protocols. Some authors suggest introducing physical therapy in the care of subjects with Acute Lymphoblastic Leukemia (ALL) within the first few

weeks after diagnosis, with instructions for stretching and maintaining motor activities, and starting more intensive interventions 1 to 2 months after the beginning of cancer treatment.[65] A recent review found that low to moderate intensity exercises were feasible and safe for children with leukemia during the acute phase of treatment, limiting the subject's functional decline.[31]

Several studies have evaluated the impact of various exercise programs on different physical and psychosocial variables in children/adolescents with leukemia. These studies were performed immediately after diagnosis, during intensive treatments,[32–34,70,71] and up to the maintenance[35–38,47,48,72–76] and off-therapy phase.[30,77–79] A Cochrane Systematic Review examined the effects of physical exercise interventions in children and adolescents with ALL, finding benefits related to body composition, flexibility, and cardiorespiratory function.[5] Unfortunately the literature does not provide a clear indication regarding the treatment parameters for this population.

CNS tumors

Intensive rehabilitation is usually recommended in children/adolescents with CNS tumors. Although no contraindications to early rehabilitation treatment in patients with brain tumors are reported, the CC participants shared some conditions that could limit treatment to cautious passive mobilization and postural hygiene or sometimes even just caregiver counseling, such as the presence of external ventricular or spinal drainages, or the presence of intense psychomotor agitation crises related to cerebellar mutism syndrome.

Various studies have shown that in the acute rehabilitation phase these patients achieve functional gains comparable to pediatric stroke patients.[80] The multidisciplinary rehabilitation plan should be integrated into the oncological setting to complement the intensive cancer treatment.[29] It can continue even after discharge from the hospital, and, if necessary, it can be carried out for long periods,[60,62,81,82] to obtain the best possible recovery. For long-term survivors of pediatric brain tumors, exercise training should be included in neuro-rehabilitation treatments.[27] Additionally, emerging literature supports exercise training, especially in a group setting, to aid brain recovery after radiation treatment.[39]

Bone cancer

In children/adolescents affected by bone cancer, inpatient rehabilitation treatment is feasible, safe, and well tolerated, as demonstrated by the high adherence rate reported in several studies.[5,24,40] In the first year after surgery there was a progressive improvement of all physical outcomes in this population, even when rehabilitation was performed during chemotherapy.[26] After the first year, rehabilitation can also be combined with PA under the supervision of an exercise physiologist.[22,25]

Question 2: "What characteristics should the individualized rehabilitation plan have?"

Recommendations

- "The rehabilitation plan should be carried out by a multiprofessional team and personalized according to the patient's goals."

- “The rehabilitation plan (modality, setting, intensity, and duration) should be adapted to the characteristics of the subject, the clinical status, the sensorimotor impairment, and the treatment phase."
- "Any ongoing changes to the individualized rehabilitation plan should be made based on the patient’s clinical condition, the goals achieved, those to be achieved, and the assessments of the multidisciplinary team."
- “Patients and their caregivers should be involved in defining the rehabilitation goals and the individualized rehabilitation plan."
- Statements are reported in Table 2.

Description

It is not possible to establish a single rehabilitation approach, and several modalities of rehabilitation treatment seem to provide benefits.[48,83] Rehabilitation treatment in this population is complex and multidisciplinary. Physical therapy is often required to maximize motor function, independence, and participation.[7] Occupational therapy (OT) can help children/adolescents to improve their ability to perform meaningful activities.[7] Speech therapy and orthoptic treatment are offered to subjects with CNS tumors to restore swallowing, communication, and visual impairments, respectively.[7]

The FITT (Frequency, Intensity, Time, and Type) principles are recommended in the reporting of physical rehabilitation interventions.[84] Referring to the pediatric oncological population, the intensity parameter is the most challenging to define, especially for preschoolers and for those with neurological impairments, as the exercise is carried out on problem-based tasks. It would be useful to develop a modified version of the FITT principles capable of describing the whole rehabilitation intervention in children/adolescents with cancer.

Rehabilitation for children/adolescents with cancer should be individualized,[17,21,36,38,42,44,48,85–87] the proposed activities should be enjoyable, and should involve parents and siblings to improve compliance.[28] Some recent studies have investigated the role of peer support and have shown that there is a positive influence on PA levels and self-efficacy.[88]

Adherence to rehabilitation is greater when the program is supervised by a physiotherapist.[33] When rehabilitation is unsupervised, it is recommended that treatment be monitored by filling in a diary, and through scheduled phone calls and outpatient visits.[83,89] Exercise intensity ranges from low to moderate to high, and is based on the subject’s clinical condition and treatment phase.[38,42,44,51] In children/adolescents with cancer-related fatigue, physical and relaxation activities are strongly recommended. Rehabilitation for these subjects should include aerobic, strengthening, and balance exercises.[12,14]

Leukemia

For patients with leukemia, both preventive and rehabilitation treatments are possible, depending on the phase of anticancer treatment:

Prevention in the phase of active therapy phase: the physiotherapist could carry out an interview to inform the patient and his parents about the possible onset of

physical problems and the beneficial effect of PA. An active lifestyle should be recommended both during hospitalization and at home, based on the interest of the child/adolescent. The information may be supported by informative material. When a long hospitalization is expected [e.g. patients undergoing hematopoietic stem cell transplantation (HSCT)], an exercise program is indicated to maintain the functional abilities and muscle strength of the patient.[85] This program should be individualized, involve caregivers, and patient adherence should be monitored. During the induction and consolidation phases of treatment, patients should perform regular low-intensity PA, including aerobic training,[36,38,41–44] stretching,[36] and strengthening exercises,[36,38,42–45] to reduce late side effects of treatment.[28]

Prevention in the maintenance and off-therapy phases: an interview should be scheduled at the end of treatment to share information on possible physical impairments and the beneficial effects of PA. Physiotherapist should encourage the patient to gradually start or resume PA and sport as well as to maintain a lifestyle as active as possible. Children/adolescents may be referred to an exercise physiologist, if possible, with specific expertise and knowledge of pediatric oncology, to define a specific individualized exercise program. During the maintenance phase of leukemia treatment, most studies suggest a regular adapted PA program that includes aerobic training, stretching, balance training, and strengthening exercises[30,35,86] under the supervision of an exercise physiologist may be proposed.[76]

Children/adolescents can do light-to-moderate activity (e.g. walking to school, biking, helping with housework or gardening) for as many days as possible during the week. In this phase the goal may be to perform PA daily to progressively reach the activity levels suggested by the guidelines for healthy children/adolescents (Table 1).[28] Once a child is ready for vigorous activity, the increments should be small (5–10 min to begin with), working for periods up to 15 min.[28]

Prevention during HSCT is strongly recommended, with endurance and strengthening exercises to minimize immobility and HSCT side effects and to improve QoL.[13]

During the pre-transplant phase, it is recommended that a physiotherapist: explain to the child/adolescent and his/her parents the benefits of a structured physical activity program during hospitalization and make recommendations for specific rehabilitation, if necessary.[13]

The exercise program during the hospitalization phase of HSCT and after discharge should be of low to moderate intensity, be individualized, and be supervised. The exercise program should include:

- endurance training
- strengthening, balance, coordination, and stretching exercises
- relaxation exercises
- rehabilitation counseling to promote functional mobility, with reference to body moving, walking, and climbing stairs.[13]

Children/adolescents undergoing allogenic transplantation may develop chronic graft-versus-host-disease, in which involvement of the skin, joints/fascia, and lungs has a significant negative impact on physical function and QoL.[87]

In children/adolescents affected by chemotherapy-induced peripheral neuropathy, rehabilitation should focus on correcting postural control deficits, gait abnormalities, muscle weakness, loss of fine motor skills,[90] on supporting motor control skills (jumping, running, climbing stairs), and on the promotion of regular PA. Ankle-foot orthoses can be used to address loss of range of motion (ROM), weakness, and associated gait abnormalities, with possible weaning of the orthoses after the end of treatment.[91] The custom foot orthosis could be prescribed to treat pain[92] and avoid ankle injuries. Based on the expertise of the CC members, functional gloves can be used to support manual dexterity. Furthermore, patient/family education should also address the loss of sensory function. In children who develop hypersensitivity to light touch, desensitization treatments may also be helpful.[93]

In children affected by leukemia the rates of symptomatic osteonecrosis range from < 1% to 18%, with a mayor incidence in adolescence[94] and in femoral head.[95] In children/adolescents with osteonecrosis, rehabilitation during nonsurgical treatment should focus on load protection, pain reduction, and addressing functional impairments that limit mobility or exacerbate pain.[96]

If necessary, the therapist provides and trains the child/adolescent in the use of an assistive device, such as crutches or wheelchair.[29] For patients with shoulder osteonecrosis, physical therapy should include complete passive ROM and pendulum exercises without active exercises with overload, to prevent joint stiffness caused by disuse.[95] Patients with painful osteonecrosis can be treated with bracing, custom orthoses, or slings.[92]

CNS tumors

The literature does not report any standard rehabilitation interventions for children/adolescents with CNS tumors; various treatments appear to provide benefit. Some authors also report the benefits of recreational-rehabilitative activities such as hippotherapy (a form of physical, occupational and speech therapy in which a therapist uses the characteristic movements of a horse to provide carefully graded motor and sensory input), hydrokinetic therapy, active videogames, and aerobic PA.[39,48,97,98] In general, neuromotor rehabilitation treatment of children/adolescents with CNS tumors is similar to that performed in other types of acquired brain injury.

In children/adolescents with ataxia, conventional physical therapy (e.g. strengthening exercises, balance training, practicing functional tasks) has been shown to be beneficial.[98] Problem-based task training can help children/adolescents with CNS tumors achieve functional improvements by facilitating motor control and the learning process.[99]

Long-term communicative, cognitive, and emotive sequelae are described in children/adolescents with cerebellar mutism syndrome. Therefore, multimodal rehabilitation is often required, integrating physical therapy with speech and neuropsychological rehabilitation.[100]

For children/adolescents with hemiplegia, research shows that constraint-induced movement therapy in the post-acute phase may be helpful in improving motor function.[98,101]

For children/adolescents with upper limb neuromotor deficits, a study found promising results of a rehabilitation therapy program based on action observation.[102]

Bone cancer

During the pre-surgical phase, the physiotherapist deals with the functional rehabilitation of the patient, identifying any preexisting impairments providing recommendations, and carrying out a specific treatment to improve function.

In addition, the physiotherapist should help the children/adolescents and their parents to identify achievable post-surgical treatment goals, as the achievement of long-term goals depends on the patient's participation and compliance with rehabilitation.[15]

The most frequent localization of bones cancer (60%) is in the distal femur and proximal tibia; various authors have investigated post-surgical rehabilitation after reconstruction with a modular prothesis, although most of these studies are observational studies with a small sample size. There are rehabilitation treatment protocols for the first month after surgery based on the localization of the tumor and the different surgical approaches. One study[23] reported satisfactory results in most patients at 12 months after surgery based on the Musculoskeletal Tumor Society (MSTS) score. The rehabilitation protocol included ROM, strengthening, proprioceptive, and autonomy recovery exercises. There is a correlation between knee extensor muscle strength recovery, knee flexion ROM, and functional recovery.[52] The subjects with the best ROM recovery are those with the best functional performance and quality of life outcomes.[78] There are two treatment phases based on weight concession. In the first phase, active and passive mobilization, strengthening, and proprioceptive exercises are proposed. In the second phase, with the progressive concession of weightbearing, treatment focuses on exercises in the standing position, weight transfers, neuromotor control of the knee, and quadricep strengthening exercises in a closed kinetic chain.[26] Various studies have also considered gait analysis,[48,49,53,54] highlighting how frequent these patients develop asymmetric gait patterns with obvious compensatory strategies. It is necessary to define a rehabilitation plan that also enhances the strengthening of the contralateral healthy limb.[49,53]

Surgery that determines an extensive resection of bone and muscle tissues causes sensorimotor shock with loss of proprioceptive afferents. In the long term there is no difference between the deep sensitivity of the healthy limb and the contralateral limb.[103] Other authors have underlined that this post-surgical condition determines the loss of motor control with a deficit of postural automatisms and the need for patients to relearn a correct gait pattern.[29,55] These results confirm the importance of balance, proprioceptive, and motor control exercises in post-surgical rehabilitation.

The literature does not provide common standards for the rehabilitation treatment. The different approaches include:[55]

- exercises three times/week for a maximum of 60 minutes per session, for at least 10 weeks before the intervention and for 10–12 weeks post-intervention.[17]
- two-four sessions/week in the first six weeks, then one or two sessions per week for the next six weeks.[22]
- two sessions of 45 minutes per day during chemotherapy treatment (in this case, the literature reports high rates of adherence to rehabilitation).[40]

There are no standardized rehabilitation protocols available in the literature for patients affected by bone tumors of the upper limb. Two rehabilitation treatment

schemes have been proposed for localization in the humerus, in the area surrounding the elbow, and in the scapula. Both treatments aim to recover ROM, muscle strength, and upper limb function.[15,22] There are no studies that indicate an optimal rehabilitation modality, either during hospitalization or in the community. Many authors agree on the importance of personalized intervention.[21,22]

Question 3: "How long should the patient be followed up for?"

Recommendation

- "Rehabilitation should last as long as required by the subject's clinical condition, regardless of whether in the hospital, community, or home setting."
- The Statement is reported in Table 3.

Description

The panel of experts strongly recommend the continuity of rehabilitation between hospital, community, and home, at least for the duration of chemotherapy treatment.[41,60,62,81] Rehabilitation is required in the acute phase, before or after surgery, after discharge, and for those admitted to specialized rehabilitation centers close to home. Rehabilitation should continue in the community and should be integrated with the hospital rehabilitation service.[56] To facilitate the monitoring of patients over time, even during survivorship, it is advisable to provide them with a concise and comprehensive documentation of previous treatments, such as thar reported in the Survivorship Passport (SurPass), elaborated by the Pan-European Network for Care of Survivors after Childhood and Adolescent Cancer (PanCare) and by The European Society for Pediatric Oncology (SIOP Europe), in collaboration with CINECA and European organizations of parents, patients, and survivors.[104]

Discussion

It is difficult to provide evidence-based rehabilitation guidance for pediatric patients with cancer given the paucity and poor quality of currently available literature. In this context, expert opinions mediated by the CC methodology are important to inform clinical practice.

Some key points regarding rehabilitation interventions have already been established, such as the importance of early multimodal rehabilitation and the need to perform both preventive and rehabilitation interventions. The preventive intervention could also address neuro-psychomotor development, with the involvement of the family as a fundamental aspect. PA should be integrated with rehabilitation to promote overall physical and psychosocial health in this population. Rehabilitation care should be supervised, individualized, and aimed at achieving both clinical outcomes and significant goals for the patient. Rehabilitation tools should be age-appropriate, with an emphasis on play-based interventions for children and respect for adolescents' personal interests. Rehabilitation is provided according to the indications of the multidisciplinary team, and in the acute phase it can be intensive.

The lack of strong evidence regarding physical therapy, OT, and speech therapy interventions in children and adolescents with cancer, other than general physical exercise interventions, remains a limitation of our work.

There is a need to define some core outcome sets and related outcome measures for different rehabilitation issues for future studies, and to allow a comparison between different studies. Preschoolers and patients with a diagnosis other than ALL should be included in future clinical research. The relevance of a case series study design should also be considered for future higher quality research. Finally, appropriate reporting checklists may be followed to improve the quality of reporting and, when a control group exists, usually described only as "care as usual"; it needs to be better defined.

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