KNEE-ANKLE-FOOT ORTHOSIS TREATMENT IN CHILDREN WITH SPASTIC CEREBRAL PALSY

J. C. MAAS

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This thesis was prepared within the Amsterdam Public Health research institute (previously EMGO+ Institute for Health and Care Research) and Amsterdam Movement Sciences (previously MOVE Research Institute Amsterdam) at the Department of Rehabilitation Medicine, VU University Medical Center, Amsterdam, the Netherlands.

The studies presented in this thesis are part of the Splint study which is financially supported by a grant from the Phelps Stichting voor Spastici, Bussum, the Netherlands [grant number: 2008032]. In addition to funding, the Splint study is financially supported by a donation of Ultraflex Europe, Ternat (Brussel), Belgium on behalf of Ultraflex Systems, Inc, Pottstown, Pennsylvania, USA. The "temperature sensor-data-loggers" were partly sponsored by PEDAK Meettechniek BV, Heythuysen, the Netherlands. Financial support for printing this thesis is generously provided by Dirame Ortho, Ternat (Brussel), Belgium; D.H. Heine stichting, Zaandam, the Netherlands; Nederlands Paramedisch instituut, Amersfoort, the Netherlands; Lode B.V., Groningen, the Netherlands; OIM orthopedie, Assen, the Netherlands; Phelps Stichting voor Spastici, Bussum, the Netherlands; ProCare B.V., Groningen, the Netherlands; TulipMed B.V., Nieuwegein, the Netherlands and Twente Medical Systems International B.V., Enschede, the Netherlands.

ISBN: 978-94-028-0646-5
Cover design and lay-out: B. Plak & J.C. Maas
Printed by: Ipskamp Printing

VRIJE UNIVERSITEIT

KNEE-ANKLE-FOOT ORTHOSIS TREATMENT IN CHILDREN WITH SPASTIC CEREBRAL PALSY

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor aan
de Vrije Universiteit Amsterdam,
op gezag van de rector magnificus
prof.dr. V. Subramaniam,
in het openbaar te verdedigen
ten overstaan van de promotiecommissie
van de Faculteit der Geneeskunde
op donderdag 6 juli 2017 om 9.45 uur
in de aula van de universiteit,
De Boelelaan 1105

door
Josina Catharina Maas
geboren te Eindhoven

promotoren:	prof.dr. J.G. Becher
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	dr. R.T. Jaspers

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ABBREVIATIONS

Abbreviations and symbols in text

A_f	physiological cross-sectional area
A-Fdf	ankle-foot dorsiflexion
AFO	ankle-foot orthosis
CP	cerebral palsy
Δ	changes between consecutive 3 monthly assessments
EMG	electromyography
$\varphi_{foot\text{-}4Nm}$	angle between footplate of the foot fixation of the hand-held dynamometer and tibia at 4Nm ankle dorsiflexion moment
$\varphi_{foot\text{-}clin}$	angle between hind foot sole and tibia by non-instrumented clinical assessment
$\varphi_{foot\text{-}MST}$	angle between foot sole and fibula at mid stance of gait
$\varphi_{foot\text{-}TSW}$	angle between foot sole and fibula at terminal swing of gait
$\varphi_{knee\text{-}LOW}$	lowest angle between fibula and femur in terminal stance phase of gait
$\varphi_{knee\text{-}MST}$	angle between fibula and femur at mid stance of gait
$\varphi_{knee\text{-}TSW}$	angle between fibula and femur at terminal swing of gait
$\gamma_{(f\text{-}t)}$	angle between footplate of the foot fixation of the hand-held dynamometer and tibia
GAS	m. gastrocnemius
GL	m. gastrocnemius lateralis
GM	m. gastrocnemius medialis
GMFCS	gross motor function classification system
GMFM-66	gross motor function measure 66 item set
ICF-CY	international classification of functioning, disability and health in children and youth
KAFO	knee-ankle-foot orthosis
MRI	magnetic resonance image
MVC	maximal voluntary muscle contraction
RCT	randomized controlled trial
ROM	range of motion
SOL	m. soleus
TA	m. tibialis anterior
WT_{parent}	parent-reported wearing time
WT_{obj}	objectively measured wearing time

Additional abbreviations and symbols in tables and figures

β	regression coefficients
CI	confidence interval
fem	femur
$\gamma_{(fasc)}$	pennation angle (angle between fascicle and aponeurosis)
ℓ_{a}	length of the aponeurosis
ℓ_{Af}	length of physiological cross-sectional area
$\ell_{(fasc)}$	fascicle length
ℓ_{m}	muscle belly length
$\ell_{(m\ th)}$	muscle thickness
ℓ_{t}	tendon length
MST	mid stance
n_{exp}	number of participants in the experimental group
n_{con}	number of participants in the control group
r^2	explained variance
SUB	subcutis
tib	tibia
Tx	measurement at x months

Standardized abbreviations and symbols

C	Celsius
cm	centimeter(s)
h	hour(s)
kg	kilogram(s)
m	meter(s)
m.	musculus
(M)Hz	(mega)Hertz
min	minute(s)
mm	millimeter(s)
n	number
Nm	newton-meter
s	second(s)
SD	standard deviation
p	probability
wk	week
%	percent
°	degree(s)

1 INTRODUCTION

INTRODUCTION

Neuromuscular disorders are the main cause of physical disabilities of children. The most common cause of such disabilities is cerebral palsy (CP) [1]. CP may become manifest as different movement disorders, of which the most common one is a spastic paresis, causing disturbed muscle function and over-activity of the stretch reflex for particular muscles [1, 2]. Children with spastic paresis often develop contractures considered to be due to muscle shortening or increased muscle stiffness. Such contractures may lead to limitations in joint range of motion (ROM) [3]. When the spastic paresis concerns muscles of the lower leg, movement limitation are apparent in gait.

Prevention of possible muscle shortening and contracture requires adequate treatment. Orthoses are commonly used for such treatment. Orthoses are *"externally applied devices used to modify the structural and functional characteristics of the neuromuscular and skeletal system"* [ISO 8549-1:1989]. The most common developing contracture is the reduction of ankle-foot dorsiflexion (A-Fdf), affecting walking [3]. One of the treatments is treatment with an ankle-foot orthosis (AFO). An AFO is applied to prevent reduction in A-Fdf ROM presumably due to shortening and/or enhanced stiffness of the mm. triceps surae, i.e. m. soleus (SOL) and m. gastrocnemius (GAS) [4]. The AFO is used to assist gait whereas a knee-ankle-foot orthosis (KAFO) is worn at rest [4]. The latter type of orthosis, including knee fixation, is used with the goal to maintain or increase muscle length of the GAS. Although these KAFO's are prescribed commonly in clinical care, very little is known regarding their efficacy and the underlying working mechanisms. Therefore the primary aim of this thesis is to quantify effects of treatment of KAFO's over time in children with spastic CP.

Cerebral palsy

In developed countries, the prevalence of CP is about 2 per 1000 live born children [1, 5]. Over the years, the definition of CP has been adapted with the latest update in 2007: *"Cerebral palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems"* [2]. In the Netherlands, to be diagnosed as CP, the onset of brain disturbance in CP has to be before the first birthday [5].

The World Health Organization has developed a method to describe the consequences of a chronic disease on the health status of children, the ICF-CY (international classification of functioning, disability and health in children and youth). In this model, the consequences of a disease have been described at the level of body function (*"physiological functions of body systems, including psychosocial functions"*) as well as structure (*"anatomical parts of the body such as organs, limbs and their components"*), activities (*"execution of a task or action by an individual"*) and participation (*"involvement is a life situation"*) [6]. For the diagnosis CP, the motor disorder should cause limitations in activities like walking and/or participation.

Based on the diversity in the type of motor disorder, CP is generally classified into three subtypes [7]:

- *"Spastic CP is characterized by at least two of the following:*
  - *abnormal pattern of posture and/or movement;*
  - *posture and movement dependent muscle tone regulation disorder;*
  - *pathological reflexes (increased reflexes: hyperreflexia and/or pyramidal signs like Babinski response)."*
- *"Ataxic CP is characterized by both:*
  - *abnormal pattern of posture and/or movement;*
  - *loss of orderly muscular coordination so that movements are performed with abnormal force, rhythm, and accuracy."*
- *"Dyskinetic CP is dominated by both:*
  - *abnormal pattern of posture and/or movement;*
  - *involuntary, uncontrolled, recurring, occasionally stereo typed movements."*

Also, mixed criteria CP is possible if there is mixture of motor disorders without a dominant component. In about 80% of children with CP, the spastic form is present [1]. In this thesis, only children with spastic CP are involved. Within the spastic CP group, the degree of limitation in mobility and consecutive effects on activity and participation differs widely.

In addition to the classification according to motor disorder, there is also a classification with regard to the limbs that are affected. The motor disorder can be unilateral if only on one side an arm and/or leg is involved, or bilateral if both legs are involved [8]. In walking children, the arms may be involved but to a lesser degree than the legs. In this thesis, patients with unilateral spastic CP and patients with bilateral spastic CP will be taken into account.

Gait in children with spastic cerebral palsy

Children with spastic CP may show an abnormal gait pattern. Two potential mechanisms causing an abnormal gait pattern are distinguished [9]: 1) effects due to altered muscle activation and 2) changes in passive biomechanical properties of the muscle-tendon complex.

1) With regard to the altered muscle activation, two groups of symptoms are distinguished: a) deficit symptoms (change of normal muscle activity) as paresis, decreased selectivity in activation of muscles and enhanced muscle fatigability, and b) excess symptoms (signs of abnormal muscle (hyper)activity) such as spasticity, hypertonia due to tonic stretch reflex activity, postural reflexes, mirror movements, co-contraction and involuntary synergies [9].

2) The changes in passive biomechanical properties of the are reported to include shortness and/or increased stiffness of the muscle [10, 11], or hypothesized to be related to altered myofascial connections and force transmission [12].

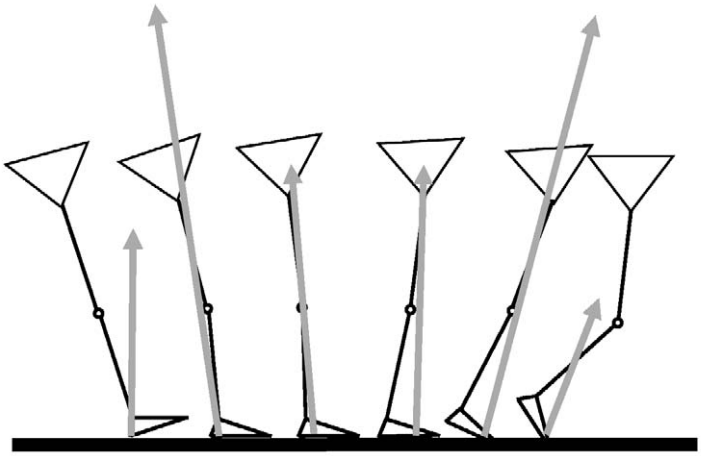

Figure 1.1: Vector alignment in the sagittal plane in normal walking

The grey line shows vector of the ground reaction force during stance phase of gait. After initial contact, the m. soleus slows down the forward inclination of the tibia. The vector of the ground reaction force aligns through the hip and knee joint, stabilizing the hip and knee joint. At the end of stance phase, m. soleus an m. gastrocnemius are active to provide acceleration, causing a forward inclination of the vector with alignment just before the knee joint rotation and behind the hip joint rotation.

If activation and/or biomechanical properties of the GAS are affected, this will have also effects on the ability to walk. In normal walking, the SOL and GAS are very important to control the sagittal plane vector alignment around hip and knee, as well as to control propulsion [13]. After initial contact (heel strike in normal walking) an eccentric contraction of the SOL slows down the forward inclination of the tibia with advancement of the vector from the heel to the midfoot in mid stance. After mid stance, both SOL and GAS are active to provide acceleration. The vector inclines forward and as knee and hip also move forward, the external knee and hip extension moment are stabilized (figure 1.1) [13].

Abnormal properties of the SOL and GAS (e.g. spasticity, paresis, shortness, increased stiffness) will change the gait pattern and reduce the efficiency of walking by abnormal mechanical effects like increase of joint moments caused by altered muscle activation patterns. Muscle hyperactivity, muscle shortening and increased muscle stiffness will each have similar effects on the gait pattern. The impact of limitations in mobility that children with spastic CP experience is classified using the gross motor function classification system (GMSFCS). Children in GMFCS level I-III are able to walk with (GMFCS III) or without walking aids (GMFCS I-II) [14]. Beside the classification of limitations in standing and walking, a classification of gait deviations within the sagittal plane has been described in which the dysfunction of the SOL and GAS is one component [9, 15]. It classifies gait patterns according to 5 subtypes (see figure 1.2):

1. insufficient foot lift in swing, no abnormality in stance;
2. knee (hyper)extension in mid stance without heel rise;
3. knee (hyper)extension in mid stance with heel rise;
4. knee flexion in mid stance with heel rise;
5. knee flexion in mid stance without heel rise.

In spastic CP, type 2 gait in spastic CP is considered to be related to hyperactivity and/or shortness/increased stiffness of the SOL after initial contact: there is reduced tibia inclination in loading response and mid stance [9, 15]. In type 3 gait, hyperactivity and/or shortness/increased stiffness of the SOL and GAS are present; only these muscles are considered to cause the combination of hyperextension of the knee in mid stance combined with heel rise [9, 15]. In type 4 gait, weakness of the SOL is considered to cause increased tibia inclination in loading response [9, 15]. When this weakness of the SOL is combined with hyperactivity and/or increased stiffness/shortness of the GAS, this is considered to cause heel rise in mid stance with knee flexion [9, 15].

Other factors may contribute to the preferred posture of flexion of hip and knee in mid stance, such as reduced hip extension (by weakness or limited ROM) and reduced body balance. Weakness of both the SOL and GAS may cause type 5 gait [9, 15].

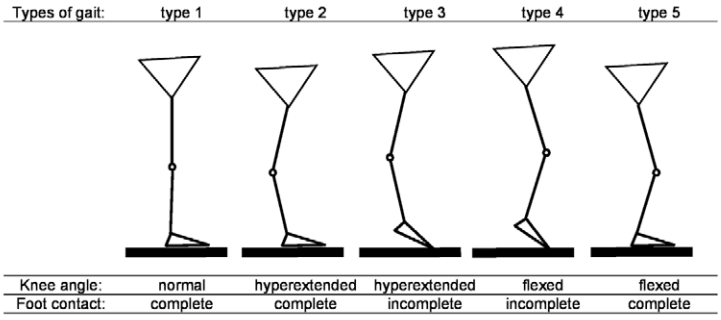

Figure 1.2: classification of gait deviations in the sagittal plane

Gait types based on dysfunction of the m. soleus and m. gastrocnemius, leading to differences in ankle-foot and knee angle in mid stance.

In line with the cause for type 4 gait due to muscle dysfunction of SOL and GAS, children walking with increased knee flexion with heel rise in mid stance often show reduced A-Fdf ROM in physical examination with full knee extension [16]. In children with spastic paresis, walking with reduced A-Fdf in stance, muscle belly length of the GAS has been shown to be shorter compared to that in typically developing children [17-19]. Muscle shortness in children with spastic CP is reported to develop during growth [20]. However, the tendency to develop muscle shortness varies substantially among children with CP and the pathophysiology is still undetermined [10].

During growth, deterioration of walking is seen in children with spastic CP [15]. Prevention of muscle shortening is presumed to prevent development of contractures and maintain walking ability. However the scientific evidence for beneficial effects of treatments preventing a reduction of A-Fdf ROM in children with spastic CP is lacking.

Treatment to improve the ankle-foot dorsiflexion range of motion

Several therapies (e.g. AFO wearing) are applied to prevent or treat presumed shortening or increased stiffness of the GAS. In children with CP, AFO's are prescribed when they start to walk [http://richtlijnendatabase.nl/richtlijn/spastische_cerebrale_parese_bij_kinderen/planning_van_de_behandeling_in_de_tijd_bij_cp/fases_in_ontwikkeling_loopvaardigheid_bij_cp.html]. An AFO is used to keep the ankle in an imposed position in gait. If full knee extension occurs in terminal stance phase during gait, the GAS will be stretched. There are indications that wearing AFO's during gait is effective to prevent shortening of the GAS [21, 22]. However, some children are not able to reach full knee extension in stance phase. As a result, the GAS is not strained fully during stance. In the long run, some of these children may develop progressive shortening of GAS. A commonly used therapy in growing children is successive intramuscular injections with botulinum toxin A, sometimes in combination with serial casting treatment with the goal to improve GAS length and maximum ankle dorsiflexion ROM. Surgical lengthening of the GAS has to be avoided, in particular in children bilaterally involved, because the capacity to generate a plantar flexion moment is considered to be reduced [23] by this procedure [24].

Figure 1.3: knee-ankle-foot orthosis

KAFO's are often custom made by certified orthotists using polyethylene or polypropylene and foam (as a cover inside). A circular foot fixation, made of leather or soft polyethylene is used for foot fixation. Deformity of the patient's foot is corrected by the use of an internal three point pressure system. Static KAFO's are configured with both fixed ankle and knee angles. A dynamic KAFO is configured with variable joint angles. The KAFO as shown in the figure is configured with a fixed knee angle and a variable ankle angle using a spring that provides variable ankle-foot dorsiflexion force.

Despite treatment with an AFO and serial casting, with or without botulinum toxin A, some children show relapses in shortening of the GAS. In such cases, as a treatment of the GAS, a knee-ankle-foot orthoses (KAFO) to be used at rest (in sitting and/or sleeping) is prescribed with the aim of preventing further shortening of the GAS [4]. The KAFO can be manufactured with a fixed knee and dynamic ankle. This KAFO keeps the child's foot in a maximal dorsal flexed position at rest while the knee is extended in order to strain the GAS (figure 1.3).

Although KAFO treatment in children with spastic CP is widely used [25, 26], little is known about the working mechanisms and efficacy of this treatment in preventing a further reduction in A-Fdf ROM or whether it even increases the ROM. Critical determinants of maximum dorsiflexion with full knee extension is the GAS muscle tendon complex length. The length of the muscle belly is considered to be determined by the optimum length of the muscle fibers (i.e. the number of sarcomeres in series), the pennation angle and the cross-sectional area of the muscle fibers [27]. Slack length and stiffness of the tendon are considered to be important factors as well [27].

In this thesis, the rationale behind the use of a KAFO in children with spastic CP is considered to be mainly based on experimental results of joint immobilization in animals (rodents and cats). Immobilization of the ankle in a position in which the plantar flexor muscles are maintained at an high length is shown to increase SOL belly length or SOL tendon length such that optimum muscle length was attained at muscle length in the immobilized position [28, 29]. Conversely, immobilization of rat, mouse and cat SOL in a shortened position results in a reduction in the muscle belly length accompanied by a decrease in the number of serial sarcomeres within muscle fibers [29-32]. There are indications that 30 minutes daily intermitted stretching of mouse SOL that is immobilized in a shortened position for extended time, will prevent a decrease in serial sarcomere number [33]. These results suggest that the number of sarcomeres in series within muscle fibers is regulated such that a muscle attains its optimum length in the joint position in which the muscle (fiber) is frequently active [33]. This regulatory mechanism has also been postulated by Herring et al. (1994) based on sarcomere lengths in rabbit masseter muscle [34].

If the mechanisms of adaptation of muscle length also apply to spastic muscles, it is conceivable that an overly active stretch reflex in children with spastic CP contributes to maintaining the plantar muscles at low length. Due to the enhanced stretch reflex in children with CP, muscles are active in positions at ankle plantar flexion, which may cause reduction in longitudinal growth (i.e. reduction of increase in number of sarcomeres during growth)

or at least in an insufficient longitudinal growth stimulus. The reduction of longitudinal growth should be counteracted by stimulation of addition of sarcomeres in series, or at least prevent decrease of serial sarcomeres numbers. Based on the abovementioned mechanisms in animals, it may be hypothesized that this may be achieved by subjecting the GAS to a continuous strain or to intermitted periods of strain.

If the effects of muscle strain on adaptation of sarcomeres in mouse muscle are similar to those in humans, this may be a promising approach to treat patients with CP. Very little is known regarding the effects of muscle strain in humans and in particular not in children with CP. However, the use of intramedullary distraction to lengthen the tibia bone of a 16-year old girl showed that a human muscle has the ability to synthesize about 350 sarcomeres in series per day [35]. To the best of our knowledge, no studies have been performed that focused on effects of applying muscle strain on adaptations in SOL or GAS sarcomere numbers in children with CP, but effects of muscle strain on adaptations in SOL or GAS due to AFO's or serial casting treatment on A-Fdf ROM have been reported [22, 36-38]. In addition, children with CP of whom the SOL muscle was subjected for at least 6h to muscle strain showed no decline of A-Fdf ROM [39]. These studies suggest that in children with CP, the potential for adaptation of muscle length is likely similar as described in animals. This thesis hypothesizes that treating children with CP, by applying of strain at the GAS muscle for several hours a day, is sufficient to maintain A-Fdf ROM or even to increase GAS length and to shift the ankle-foot ROM towards dorsiflexion.

Since it is unknown whether treatment with a KAFO in children with CP is effective, it is important to investigate the efficacy of this treatment. Investigating the efficacy should focus on effects on A-Fdf ROM / GAS length and related effects on the gait pattern. KAFO wearing time should also be taken into account. From clinical practice it is known that applying strain to spastic muscles is cumbersome as patients suffer from pain and other complaints which may refrain patients from wearing the KAFO. Research on orthoses in scoliosis patients indicates that patient-reported wearing times have been reported as more positive than they actually were [40, 41]. The use of valid measurement methods to measure KAFO wearing time are necessary to interpret results correctly. Therefore, it is a secondary aim of this thesis to investigate whether parent reports of KAFO wearing time are valid indicators.

AIMS OF THIS THESIS

The primary aim of this thesis is to quantify potential effects of treatment with knee-ankle-foot orthoses over time in children with spastic CP. In addition, we aimed 1) to investigate whether parent reported KAFO wearing time can be considered as a valid indicator and 2) to assess effects of affected A-Fdf ROM on gait kinematics in children with CP walking with plantar flexion in the ankle and flexed knees.

OUTLINE OF THIS THESIS

The outline of this thesis is as follows:

Chapter two describes the design of a randomized controlled trial (RCT) to study the efficacy of KAFO treatment in preventing reduction in dorsiflexion ROM in children with spastic CP. In this RCT, the effects on A-Fdf ROM of a group of children with spastic CP has been compared with a group of children with spastic CP who did not receive KAFO treatment.

Results of the RCT are described in in chapter three. The efficacy of the KAFO with respect to A-Fdf ROM is presented and discussed. In addition, the effects of KAFO's on the children's gait pattern and gross motor function have been evaluated. Since it is conceivable that outcome of the RCT was dependent on wearing time of the KAFO, complaints and KAFO wearing time were taken into account.

The outcome of the RCT was likely co-determined by the KAFO wearing time. Chapter four compares parent-reported KAFO wearing time with objectively measured KAFO wearing time.

Chapter five addresses the effects of changed ankle-foot ROM on gait kinematics in children with spastic CP.

Finally, in chapter six, the findings and conclusions of the studies described in the previous chapters are summarized and integrated in a discussion regarding clinical implications and the use of KAFO's. In addition, suggestions for further research are made.

2

Splint: The efficacy of orthotic management in rest to prevent equinus in children with cerebral palsy, a randomized controlled trial (protocol)

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BMC Pediatrics, 2012. 12:38
doi:10.1186/1471-2431-12-38

ABSTRACT

Background

Range of motion (ROM) deficits of the lower extremity occur in about the half of the children with spastic cerebral palsy (CP). Over time, these impairments can cause joint deformities and deviations in the children's gait pattern, leading to limitations in mobility. Preventing a loss of ROM is important in order to reduce secondary activity limitations and joint deformities. Sustained muscle stretch, imposed by orthotic management in rest, might be an effective method of preventing a decrease in ROM. However, no controlled study has been performed.

Methods

A single blind randomized controlled trial (RCT) will be performed in 66 children with spastic CP, divided over three groups with each 22 participants. Two groups will be treated for 1 year with orthoses to prevent a decrease in ROM in the ankle (either with static or dynamic knee-ankle-foot orthoses (KAFO's)) and a third group will be included as a control group and will receive usual care (physical therapy, manual stretching). Measurements will be performed at baseline and at 3, 6, 9 and 12 months after treatment allocation. The primary outcome measure will be ankle-foot dorsiflexion (A-Fdf) ROM at full knee extension, measured with a custom designed hand held dynamometer. Secondary outcome measures will be 1) A-Fdf and knee flexion during gait and 2) gross motor function. Furthermore, to gain more insight in the working mechanism of the orthotic management in rest, morphological parameters like achilles tendon length, muscle belly length, muscle fascicle length, muscle physiological cross sectional area length and fascicle pennation angle of m. gastrocnemius medialis will be measured in a subgroup of 18 participants using a 3D imaging technique.

Discussion

This RCT will provide more insight into the efficacy of orthotic management in rest and the working mechanisms behind this treatment. The results of this study could lead to improved treatments.

Trial Registration Number

Nederlands Trial Register NTR2091

BACKGROUND

Cerebral palsy

"Cerebral palsy describes a group of permanent disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems" [2]. Spastic cerebral palsy (CP) is the most common form of CP (85%) [42]. Muscle spasticity is a clinical symptom characterized by a velocity dependent resistance to passive stretch or movement [43]. At present, in developed countries, about 2 live born children per 1000 have CP [5, 44].

Range of motion (ROM) deficits in one or more limb joints are present in many children with spastic CP with about the half of the children having ROM deficits in the ankle, knee and hip [3]. In clinical practice, it is assumed that a reduced ROM in a joint is caused by a relative shortness of the muscle tendon complex compared to the length of the bone and/or by enhanced stiffness of the muscle tendon complex [10, 11].

The m. gastrocnemius (GAS) is often spastic in children with CP [45]. As the GAS has origin at the femur and his insertion at the calcaneus, this muscle is a major determinant of the ankle and knee ROM. The GAS was found to be shorter and stiffer in children with CP (having reduced ankle-foot dorsiflexion (A-Fdf) ROM) compared to typical developing children [46] and is expected to play a major role in the cause of limited ankle dorsiflexion ROM (measured at full knee extension). This A-Fdf ROM may lead to equinus deformities in the ankle [16]. Furthermore, a short and stiff GAS may lead to a gait pattern with increased ankle plantar flexion and increased knee flexion in mid stance [47, 48]. Compared to children with typical gait patterns, children with deviated gait patterns are impaired in mobility [45] and are metabolically less efficient and less resistant to fatigue during walking [49]. To prevent equinus contractures and less efficient gait patterns, it is important to treat and prevent impaired A-Fdf ROM [45].

Effectiveness of stretch

It is recommended not to use surgical interventions to improve gait (and thus not to treat impaired A-Fdf ROM by using surgical intervention) until gait is matured [45]. Based on joint immobilization studies of animals, it is well known that sustained muscle stretch stimulates an increase in muscle length by addition of sarcomeres in series [29, 50, 51]. In analogy with these results it is expected sustained muscle stretch as treatment of spastic calf muscles, will lengthen these muscles and in particular the GAS. However, a systematic review about the effectiveness of passive stretching shows that there is conflicting evidence on whether passive stretching can increase the ROM in a joint in children with CP [52]. Two types of stretching were investigated: 1) Manual stretching and 2) Sustained muscle stretch. Manual stretching was defined as *"holding the targeting joint to the available end ROM manually for a set amount of time, expressed as seconds, and then releasing it"* [52]. Sustained muscle stretch was defined as *"holding the targeting joint to the available end ROM by mechanical means such as standing tables or position equipment for an extended period, expressed as minutes up to 5h-7h a day"* (a duration of 30min stretching was the most commonly chosen in the analyzed studies) [52]. In this review it was concluded that there appears to be only some indications that sustained muscle stretch is preferable to increase joint ROM in children with CP compared to manual stretching.

Orthotic management in rest

Although sustained stretch is not an evidence based treatment, it is often applied by the use of night splints that are part of the general management of children with CP [25, 26, 45]. "Night splints" are used during night and/or during rest periods during the day. Therefore, we prefer to use the term "orthotic management in rest" instead of "night splinting". Regarding the muscle of interest in this study, the GAS of children with spastic CP, sustained stretch is applied by using knee-ankle-foot orthosis (KAFO). Static KAFO's (with ankle and knee angle fixed) as well as dynamic KAFO's (with ankle angle imposed by a spring allowing movement) are used. These orthoses hold the ankle joint at the maximal angle of dorsiflexion at full knee extension.

Using KAFO's in rest could be more effective compared to using KAFO's during active moments of the day. It might be presumed that a KAFO with fixed knee joints limits mobility, and therefore, will likely not be worn during active moments of the day. Other orthoses, like ankle-foot orthoses (AFO's) that are often used during active parts of the day, do not necessarily stretch the GAS as the knee is allowed to flex. Knee flexion will occur during, for example, walking and sitting.

To the best of our knowledge, Tardieu et al. [39] is the only study that evaluates the efficacy of orthotic management in rest in children with CP. It reports the effectiveness of orthotic treatment at night in two children, but these results are not confirmatory, due to the limited study design: 1) the number of treated subjects (2) was small, 2) there was no control group, and 3) the subject's A-Fdf ROM was measured in knee flexion rather than extension which is more consistent with a measure of the m. soleus (SOL) length instead of the GAS. Therefore, more research is needed to establish whether their conclusions were correct and whether the GAS will adapt in the same way to sustained stretch as the SOL. Despite the reported limited evidence in the literature, the efficacy of orthotic management in rest is probably considered as general knowledge. It is supposed that a KAFO prevents for reduced A-Fdf ROM when the KAFO is worn for 6h or more a day.

The major aim of this study is to obtain insight in the efficacy of orthotic management in rest to prevent a reduction in A-Fdf at full knee extension (clinical part of the study). Differences in the efficacy of static and dynamic KAFO's will be investigated and compared as well.

Morphological properties

Recent literature shows that the morphological properties of muscles in children with CP differ from those in typically developing children [18, 19, 53]. For example, muscle belly length and muscle volume are smaller in children with CP compared to typically developing children [18, 19, 46]. A smaller fascicle length and smaller muscle thickness is found as well in children with CP [46, 53]. Mostly, the m. gastrocnemius medialis (GM) was investigated. However, very little is known about the development of these morphological properties during growth both in typically developing children and children with CP [54], and the mechanisms underlying the decreasing A-Fdf ROM during development in children with CP are unknown. Such insight is required to improve treatments for preventing reduced A-Fdf ROM. Since the ROM of a joint is thought to be determined by the passive slack length (i.e. the smallest length at which any force is exerted) of the muscle tendon complex in relation to bone length and by the muscle tendon complex stiffness, improved knowledge of the changes in muscle morphology will likely provide insight into the etiology of reduced ROM. It is expected that the passive slack length of the muscle tendon complex will be affected by architectural variables, such as fascicle length, muscle belly length, physiological cross- sectional area, angle between fascicle and aponeurosis and tendon length [30, 55-57]. The muscle tendon complex stiffness is determined by the size and length of the muscle belly fibers and by the amount and arrangement of connective tissues (parallel elastic components) of the muscle tendon complex [58].

The KAFO treatments tested in this study are assumed to prevent the development of a reduced A-Fdf ROM at full knee extension by increasing the slack length of the GAS muscle tendon complex and by reducing the muscle tendon complex stiffness. However, even if effective, the question remains whether the muscle tendon complex slack length increases due to muscle architectural changes like increased fascicle length or due to the amount and arrangement of connective tissues of the muscle tendon complex or both (see figure 2.1 for an overview of the different architectural parameters that determine the length of the GM. Therefore, the secondary aim of this study is to evaluate how changes in ankle dorsiflexion are related to morphological changes in the GM.

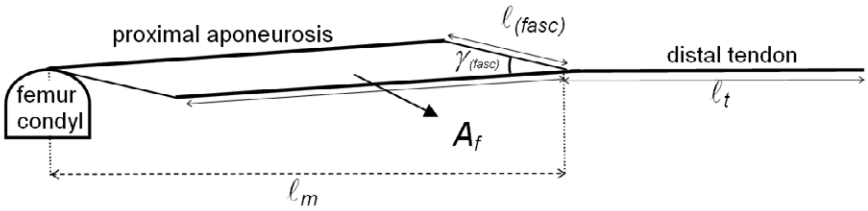

Figure 2.1: Schematic overview of the different architectural parameters that determine the length of the muscle tendon complex of the m. gastrocnemius medialis

Symbols: $\ell_{(fasc)}$: fascicle length, ℓ_m: muscle belly length, A_f: physiological cross-sectional area, $\gamma_{(fasc)}$: pennation angle (angle between fasicle and aponeurosis), ℓ_t: tendon length

Hypotheses

Clinical part

We hypothesize that children with CP who are treated with a KAFO will show a smaller decline in (or even increase in) A-Fdf ROM compared to children not being treated with a KAFO. In addition, we anticipate that children who are treated with a static KAFO will show less of a response (i.e. they will have a larger decline or a smaller increase in A-Fdf ROM) when compared to children being treated with a dynamic KAFO.

We expect that for children with CP, treatment with either KAFO will have a less negative change in gait or even a positive change in gait pattern. A positive change refers to less ankle-foot plantar flexion and less knee flexion in mid stance, compared to no KAFO treatment. The effects are expected to be more positive in children being treated with the dynamic KAFO compared to the children being treated with the static KAFO.

The level of mobility of children who are treated with either KAFO is expected to show a smaller decline or increase compared to children who are not treated with a KAFO. As above, the effects are expected to be larger in children being treated with the dynamic KAFO rather than in children being treated with the static KAFO.

Morphological part

In this study, it is hypothesized that the tendon length, muscle belly length and fascicle length increase and the muscle tendon complex stiffness decreases due to exposure of the GM to sustained stretch.

METHODS

This study is approved by the Medical Ethics Committee of the VU University Medical Center and by the Institutional Review Board of the Washington University in Saint Louis.

Participants

Criteria

The specific inclusion and exclusion criteria are shown in table 2.1. Briefly, participants are children with spastic CP having been treated for reduced A-Fdf ROM in the past, but not needed to be treated at the moment they were included into this study. Children are excluded from the study if they have a history of surgery of the GAS and/or SOL and/or selective dorsal rhizotomy, if they have severe enough morbidity or mobility limitations that prevent them from walking far enough to complete a gait analysis, or if they are being treated with intrathecal baclofen therapy (i.e. they have a current, active pump).

Sample size calculation

Expecting a 5˚ change in A-Fdf ROM (assumed as clinically relevant), with a standard deviation of 4.5˚, a significance level of 0.05 that is corrected for comparisons between three groups using a Bonferroni correction (level of significance=0.0167), and a power level of 80%, 13 children in each group will be sufficient. The calculation takes five repeated measurements with a correlation coefficient of ρ=0.7 into account. In this study, 66 participants (22 in each group) will be recruited to allow drop outs.

Table 2.1: Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Children must have:	**Children must not:**
1. a clinical diagnosis of unilateral or bilateral spastic CP	1. have had surgery of the m. gastrocnemius and/or m. soleus
2. an age between 4-12 years old	2. have had Selective Dorsal Rhizotomy
3. at least 0˚ ankle-foot dorsiflexion with extended knee (physical examination)	3. have had Intrathecal Baclofen therapy
4. a gross motor function classification level I, II or III	4. have had Botulinum toxin A treatment in the lower extremity less than 6 months ago
5. has been treated for reduced ankle-foot dorsiflexion (<5˚ dorsiflexion) before the start of the study by:	5. have had casting of the lower extremity less than 3 months ago
a. and/or serial casting at least 3 months ago	6. have knee contractures (less than 0˚ knee extension)
b. and/or botulinum toxin A injections in the m. gastrocnemius and/or m. soleus at least 6 months ago	7. have more than 20˚ ankle-foot dorsiflexion at full knee extension
c. orthotic management in rest with a knee-ankle-foot orthosis to prevent for decreasing ankle-foot dorsiflexion	8. have behavioral problems (like severe mental retardation)
6. a stable social family situation	9. have significant sleeping problems
	10. be institutionalized
	11. be suffering from co-morbidity interfering with mobility that prevents them from walking adequate distance.
	12. have problems with understanding either the Dutch (for subjects in the Netherlands) or English language

Recruitment procedure

Subjects will be recruited from three centers: 1) the VU University medical center in the Netherlands (n=18), 2) “Rehabilitation Medical Center (RMC) Groot Klimmendaal” in the Netherlands (n=18) and 3) the Pediatric Neurology Cerebral Palsy Center at Washington University School of Medicine and St. Louis Children’s Hospital in the USA (n=30). Eligible subjects will be identified by the physicians during clinical sessions or from review of patient’s charts. The recruited children and their parents will receive a letter about procedures and content of the study, as well as an informed consent form. The potential subjects and their caregivers will be informed by the site investigators and physicians. Both parents/guardians and children being 12 years old are asked to sign and return the informed consent to agree on voluntary participation in the study.

Setting & design

A single blind randomized controlled trial will be performed at the three above mentioned centers. The participants will be assigned into 3 different groups. In addition to their regular treatment, two groups will be treated with a dynamic or static KAFO for one year to prevent for a reduction of A-Fdf ROM at full knee extension and one group will be included as a control group without additional intervention. The morphological measurements will be performed only at Dutch participants at the VU University medical center.

Measurements will be performed at baseline and at 3, 6, 9 and 12 months after treatment allocation. In combination with those measurements, participants of the experimental groups will have a meeting with the orthotist and physician to check for complications with the KAFO.

The assessor and analyzer are blinded for treatment allocation. The trial will be performed between January 2010 and December 2012.

Intervention/comparisons

Patients of the control group will receive their usual care which may include AFO's that are worn during the day (for standing and walking), oral baclofen therapy or other tone-reducing medications, strength training, stretching exercises, physical therapy, occupational therapy etc. Changes in usual care during the study will be monitored using questionnaires. Children will drop out of the study if they need surgical treatment (orthopedic and neurosurgical procedures affecting muscle tone and length), botulinum toxin A injections in the lower extremity or serial casting treatments in the lower extremity.

In addition to their usual care, patients of the experimental groups will be treated for one year with a static KAFO or with a dynamic KAFO using an Ultraflex® ankle power unit. Children will be asked to wear the KAFO at least 6h per night. They will be allowed to remove the KAFO during the night when the child is seriously uncomfortable after wearing the KAFO for at least 20 min or when the child wakes up at night with complaints concerning the KAFO. When children do not wear the KAFO for 6h per night, parents will be asked to increase wearing time by asking the child to wear the KAFO during rest activities in day time. In case of unilateral treatment, patients will sleep one night with and one night without a KAFO. In case of bilateral treatment, patients will wear a KAFO alternating on the right and left side each night.

Manufacturing the KAFO

The KAFO will be custom made by certified orthotists using polyethylene or polypropylene and foam (for a covered inside). Two transverse bars (polyethylene or polypropylene) above and below the knee will be used to reinforce and stiffen the KAFO. Bandages of nylon Velcro straps will be placed at three locations: 1) as high as possible on the thigh, 2) directly above the patella and 3) directly below the patella. A circular foot fixation, made of leather or soft polyethylene, will be used for foot fixation. This circular foot fixation will be closed with two velcro straps. One strap overlaps the patient's most convex part of the ankle and one strap will overlap the patient's foot proximal of the caput ossis metatarsal I and V. Deformity of the patient's foot will be corrected by the use of an internal three point pressure system (see figure 2.2).

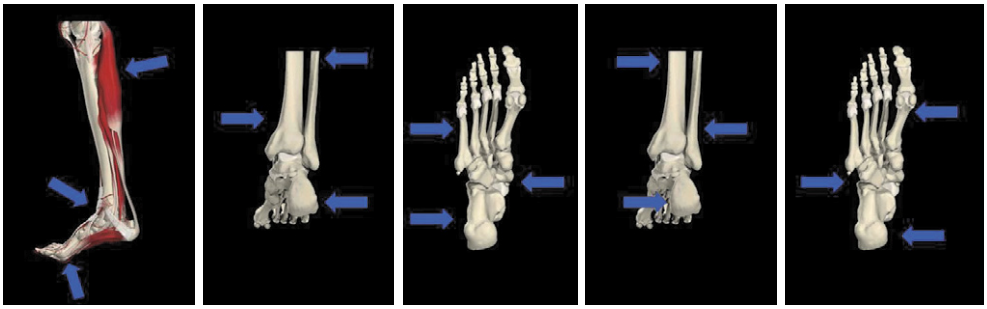

Figure 2.2: Three point's pressure for correction of deformity

a. The equinus correction will be performed by exerting force on the dorsal side of the lower leg (just below the knee), on the instep of the foot and under the ball of the foot.
b. The valgus correction of the calcaneus will be performed by a exerting a force laterally on the heel/calcaneus, laterally on the middle of the lower leg and medially on the lower leg, just above the medial malleolus.
c. The forefoot abduction correction will be performed by exerting a medial stabilization force calcaneus and talus and a lateral force on the calcaneus and the fifth os metatarsi.
d. The varus correction of the calcaneus will be performed by exerting force on the medial part of the calcaneus, medially on the middle of the lower leg and laterally on the lower leg, just above the lateral malleolus.
e. The forefoot adduction will be performed by exerting force on the tuberositas of the fifth os metatarsi, by exerting force laterally on the calcaneus and laterally on the first metatarsal phalangeal joint

Static KAFO specification

The static KAFO will provide a fixed knee extension of 0˚ and a fixed ankle dorsiflexion angle of 0˚.

Dynamic KAFO specification

The dynamic KAFO will also have a fixed knee extension of 0˚, but will use an Ultraflex® ankle power unit (Ultraflex Systems, Pottstown, PA, USA). The force of the power unit that provides variable A-Fdf angles will be set according to the prescription shown in figure 2.3.

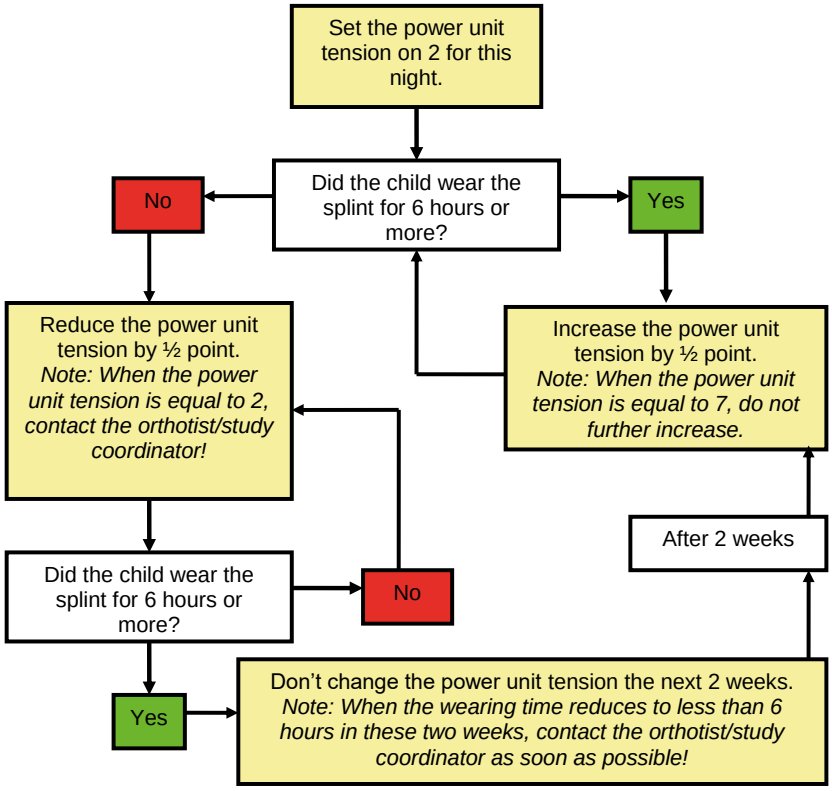

Figure 2.3: Manual for dynamic splint settings

Outcome measures

Primary outcome

To measure the maximal A-Fdf angle at full knee extension, a Single Digital Inclinometer (Model ACU001, Acumar, Lafayette, IN, USA) will be used. This goniometer is attached to a torque wrench (Sensotork 713/6, Stahlwille, Germany). The goniometer-torque wrench combination is attached to an adjustable foot fixation. The foot fixation is constructed with a forefoot part and a calcaneal part. The two parts can be adjusted in rotation and in distance with respect to each other. With the adjustment in rotation, adjustments for fore foot adduction and supination can be made to stabilize instable valgus foot deformity. With the adjustment in distance, foot sizes can be accommodated from 150mm to 240mm. The calcaneal part has a heel support (width: 45mm) and a point to attach the torque wrench. Both parts are equipped with Velcro straps for foot fixation [59]. Figure 2.4 shows a photograph of the measurement device attached to the foot. The A-Fdf angle will be measured as the angle between the footplate of the foot fixation and the tibia ($\gamma_{(f\text{-}t)}$).

The children will be asked to lie prone on a bench, with both feet overhanging the edge. The lower leg will lie in such a way that the fibula head and the lateral malleolus of the fibula are on the same height. The foot will be firmly attached to the adjustable foot plate for fixation. The ankle will be plantar flexed by the researcher, applying an external plantar flexion moment of 4Nm, as measured using the toque wrench. The corresponding $\gamma_{(f\text{-}t)}$ is measured (further described as the 4Nm plantar flexion angle). Subsequently, this procedure is repeated for 1Nm plantar flexion and, 0Nm, 1Nm dorsiflexion, 4Nm dorsiflexion and 6Nm dorsiflexion. All measurements will be repeated six times and each moment will be exerted for 5s. The $\gamma_{(f\text{-}t)}$ will be read out from the inclinometer simultaneously at the end of these 5s at the target ankle joint moment. Positive values refer to an external dorsal flexion moment (Nm) of the dynamometer and dorsal flexion angle (°) of the ankle joint. There will be 5s rest between each repetition and 2min rest between each condition. The conditions will always be applied in the described order.

Children have to relax their muscles and will be asked to lie quietly during the measurements. Muscle activity will be checked using the electromyography (EMG) signals of m. tibialis anterior and m. gastrocnemius lateralis. The maximal voluntary muscle contraction (MVC) will be recorded before the measurements. The EMG signal will be A-D converted at 1000Hz. After sampling, the signal will be high-pass filtered at 20Hz to remove movement artefacts.

Then, the signal will be normalized with respect to the MVC-value and filtered low pass at 5Hz. EMG signals have to remain below 10% MVC during the angle and moment measurements to ensure muscle relaxation. Skin preparation and electrode placement of EMG will be carried out according to SENIAM guidelines [60].

Figure 2.4: Photographic illustration of the hand held dynamometer

The hand-held dynamometer consists of an adjustable foot fixation, a torque wrench and a goniometer. The foot fixation has parts supporting the forefoot and calcaneus. These parts are connected by a rod, allowing independent adjustments in rotation and abduction/adduction. The forefoot part is equipped with a fixation point to the table when needed (*).

The mean of the first 5 measurements for each condition in which the EMG signal remained below 10% MVC will be used for further analysis. The results will be used to create angle-moment plots in which, for example, the muscle tendon complex stiffness can be determined by calculating the slope of the line between the 0Nm and 4Nm (see figure 2.5). A change in A-Fdf ROM will be investigated by analyzing the $\gamma_{(f\text{-}t)}$ measured with 4Nm dorsiflexion.

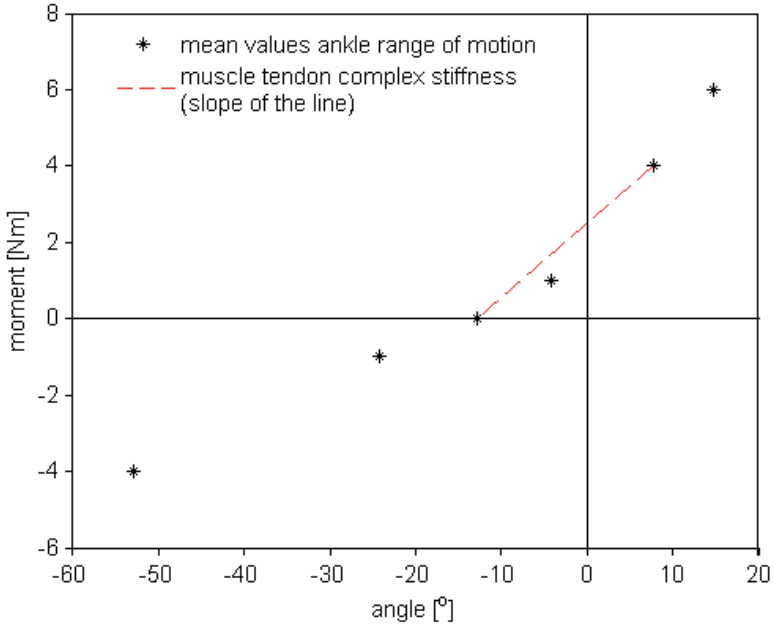

Figure 2.5: Ankle-moment plots

This figure will be created from the values measured with the hand held dynamometer. The dotted line will be used to calculate the muscle tendon complex stiffness by calculating the slope of that line.

In case of potential bilateral treatment, the full procedure will only be performed on the participant's most involved leg. For the other leg, only the 4Nm condition without EMG measurement will be performed to check for exit criteria (see withdrawal paragraph below). In case of potential unilateral treatment, the primary outcome measure will only be measured for the participant's potentially treated leg.

Secondary outcome

Gait analyses

Sagittal and frontal video-recordings of the patient's gait pattern will be made at 50 Hz. The subjects will walk 5 times barefoot and 5 times with shoes and AFO if applicable, along a 10m walkway at self-selected comfortable speed. Walking speed will be calculated from the time to complete a part of the track (5m, measured with infrared detectors or with a stopwatch, depending on measurement location). For follow up measurements, the patient will be requested to walk at baseline walking speed (within a range of ±5%). Video recordings of the involved leg(s) will be taken in the sagittal and frontal plane. Three representative steps

will be chosen for the assessment of the knee angle in mid stance, the minimum knee angle in stance (between mid stance and second bipedal phase of foot contact) and the A-Fdf in mid stance. For the video analysis, a custom-made software package will be used (the Moxie Viewer®, VU University Medical Center, Amsterdam, the Netherlands, www.smalll.nl), and a software tool, allowing on screen video measurements of sagittal lower extremity joint angles [61]. For all participants, the gait related outcome measures will only be measured in the potentially treated legs.

Mobility

The level of mobility will be quantified using the Gross Motor Function Measure 66 Item Set (GMFM-66) [62] by a certified assessor. GMFM-66 scores will be calculated with the corresponding software (Gross Motor Ability Estimator version 1.0) that calculates scores on an interval scale.

Patient Characteristics

Patient characteristics will be recorded using an intake form and will include age, gender, race, ethnicity, weight, length, localization of CP (uni- or bilateral) and Gross Motor Function Classification System (GMFCS) [14] class. To assess problematic behavior of the child, the strength and difficulties questionnaire [63] will be filled in by the parents. In addition, questions will also be asked about the children's sport activities, current therapies and other treatments, as well as preference sleeping positions.

Physical examination

Physical examination will be performed by the assessor to evaluate the physical characteristics of the patient. Variables to be measured are: 1) Position of the foot in standing, 2) trans malleolar axis position [64], 3) gait pattern classification according to Rodda [65] and Becher [9], 4) ROM of the ankle and knee joints, 5) spasticity, by measuring the angle of catch [66] of the ankle and knee, 5) selective motor control, using the selective control assessment of the lower extremity (SCALE) [67] and 6) lower leg length. For all participants, the physical examination related outcome measures will only be measured in the potentially treated legs.

Protocol adherence

Web based diaries will be used to record the protocol adherence and will be collected by a research assistant. These diaries will be filled in during the fourth week of each month and include questions regarding KAFO use, KAFO-related complaints, sleeping problems, the use of an AFO as well as questions regarding stretching exercises performed over the last month.

Problems with KAFO use experienced by patient and/or parents will be monitored by specific diary questions. The research assistant will call the participants at least once a month to check if there are any problems with the KAFO or motor function of the participant. Reported problems will be solved as soon as possible.

Furthermore, to check the reliability of diary reported KAFO wearing time, wearing time of the splints (for a subgroup of 10 children, recruited at VU University Medical Center) will be determined on the basis of KAFO temperature measured using a TidBit temperature data-logger (UTBI-001, Onset Computer Corporation, Bourne, MA). The KAFO temperature will increase due to body heat when the KAFO is worn. A sample of KAFO temperature data will be recorded each 15min during the treatment period. Parents and children are not informed about the purpose of this measurement.

Other

To get an indication of the sustained muscle stretch that is applied by the KAFO's, two measurements will be added. 1) The ankle moment at a $\gamma_{(f\text{-}t)}$ *of* 0˚ to simulate the static KAFO condition. This condition will be performed before the handheld dynamometer protocol. 2) The A-Fdf angle that could be imposed by the dynamic KAFO will be estimated during consultation hours by the physician using a goniometer.

Morphological part

To determine muscle morphology related variables, 3D-ultrasound imaging will be performed on the GM. This muscle, covered with an ultrasound gel, will be scanned along its length (making multiple transverse cross-section images, see figure 2.6) using a 5cm linear array probe (12,5 MHz) of a B-mode ultrasound device (Technos MPX, ESAOTE, Italy). Two sets of recordings of the GM will be made for each session. During 3D-ultrasound measurements, the position of the probe with a cluster marker is recorded using an active 3D marker motion analysis system (Optotrak, Northern Digital, Waterloo, Canada). In addition, 6 anatomical landmarks (lateral malleolus, medial malleolus, medial femur condyle, lateral femur condyle, medial femur epicondyle and lateral femur epicondyle) are recorded before each experiment to gain an anatomical frame of reference for post experimental 3D image reconstruction. In a prone position, the children are lying quietly on a bench. Using the ankle dynamometer, the ankle is fixed at $\gamma_{(f\text{-}t)}$ corresponding to 0Nm, 1Nm and 4Nm net dorsal flexion moment. Muscle activity is checked using EMG during the ultra sound measurements as described above in the primary outcome section.

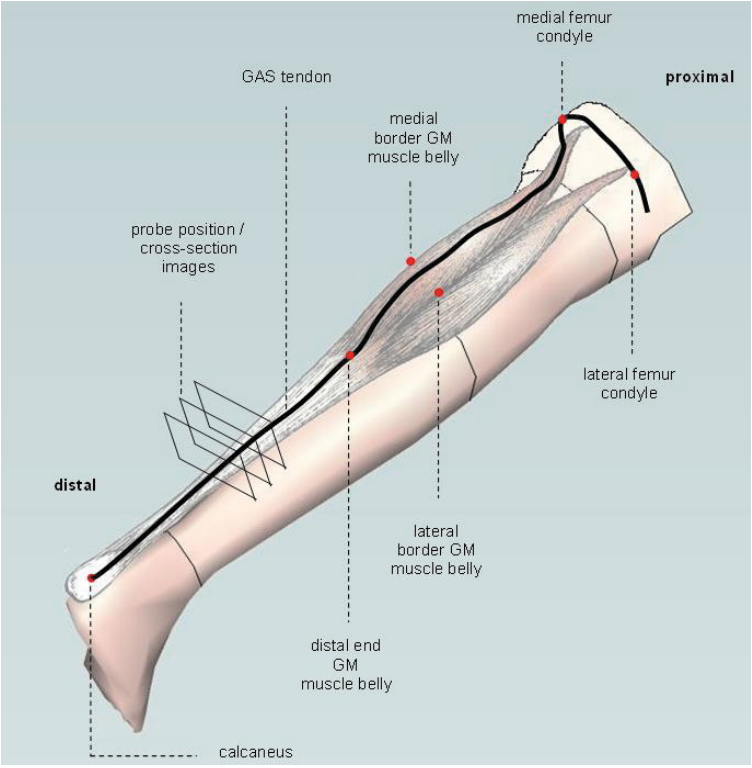

Figure 2.6: Path of the ultrasound probe during scanning the m. gastrocnemius medialis (GM)

The probe follows the path over the black line. It starts proximal, with the probe perpendicular to the path. First, the probe will be guided from lateral to medial over the respectively lateral and medial condyle of the femur. Then the probe will be rotated and moved to distal between the medial and lateral border of GM belly towards the distal end of the muscle belly, the GAS tendon and the calcaneus.

The ultra sound images will be converted into a voxel array and 3D-reconstructions will be calculated using a custom made program in MATLAB software according to the method that was described by Bénard et al [68]. Measurements are performed in the mid-longitudinal fascicle plane of the GM, being perpendicular to (the tangent of) the distal aponeurosis of the GM, selected from the voxel array (see figure 2.7). The use of the correct plane is essential for minimizing measurement errors of fascicle length, fascicle angle and muscle thickness [69]. Measurements are performed five times because this number of repetitions has been shown to yield reliable results [69].

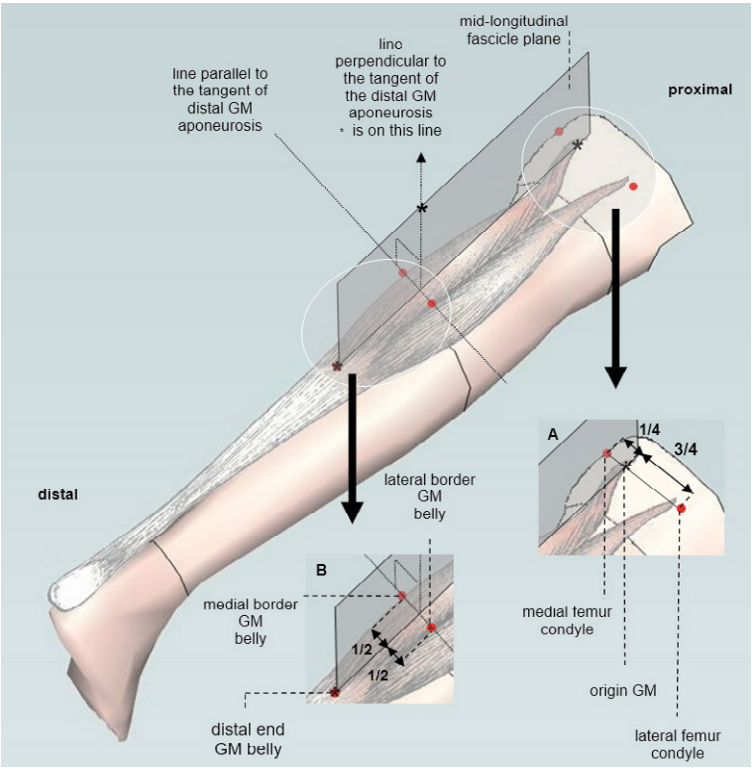

Figure 2.7: The orientation of the mid-longitudinal fascicle plane

Three orientation items (*) were used to define the mid-longitudinal fascicle plane of the m. gastrocnemius medialis (GM), shaded plane and inset): 1) The estimate of the origin of the GM (at 1/4th of the line from medial to lateral condyle of the femur, see inset A) 2) the most distal muscle belly end, and 3) a point on the line perpendicular to tangent to the distal aponeurosis in the transversal plane. The direction of the tangent is determined in the distal part of the GM belly exactly in between the GM borders (see inset B).

The following variables will be measured: tendon length, muscle length, fascicle length, muscle thickness and fascicle angles with the aponeuroses.

Using trigonometry, the following variables will be calculated: length of GM muscle intramuscular distal (i.e. deep) and proximal (i.e. superficial aponeuroses) and length component of the physiological cross-section (the added perpendicular diameters of fascicles within the mid-longitudinal fascicle plane, figure 2.8).

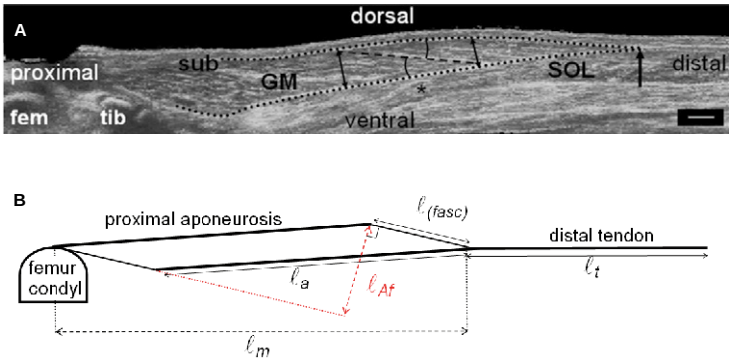

Figure 2.8: Measurement and calculation of muscle geometry of m. Gastrocnemius medialis within its mid-longitudinal fascicle plane

A. The mid-longitudinal fascicle plane, determined with 3D ultrasound. The m. gastrocnemius medialis (GM) is covered by the subcutis (SUB) and supported by m. soleus (SOL). Parts of both femur (fem) and tibia (tib) are shown. The black dotted lines define the outline of the muscle. The most distal muscle belly end is indicated by a black arrow. The length of the target fascicle ($\ell_{(fasc)}$, dashed black line), centered at 2/3rd (*) of muscle belly length (from the origin) is measured. Muscle thickness ($\ell_{(m\ th)}$) was calculated as the distance between the proximal and the distal aponeurosis at the proximal end of the target fascicle (left black double arrow). The fascicle-aponeurosis angle ($\gamma_{(fasc)}$) was calculated as the mean of the angles of the fascicle with the proximal and distal aponeurosis (black arcs). Scale bar depicts 1cm.

B. Schematic overview of morphological muscle parameters in the mid-longitudinal fascicle plane of the GM. The length of the aponeurosis (ℓ_a) and the length of the physiological cross-sectional area (ℓ_{Af}) will be calculated from this model. The muscle belly length (ℓ_m) will be measured from the origin at the femur condyle to the distal end of the muscle belly. The tendon length (ℓ_t) will be measured from the distal muscle belly end to the insertion at the calcaneus.

In case of potential bilateral treatment, the morphological outcome measures will only be measured on the participant's most involved leg. In case of potential unilateral treatment, the morphological outcome measure will only be measured at the participant's potentially treated leg.

Exit criteria

Withdrawal

The investigator and/or clinician can decide to withdraw a subject from the study for urgent medical reasons. First, they have an A-Fdf angle with an extended knee, measured as the angle between tibia and footplate ($\gamma_{(f\text{-}t)}$), of 10° plantar flexion or more when an external ankle dorsiflexion moment of 4Nm is applied. In such a case, the assessor will refer the child to the clinician who will decide whether the reduction in ROM has to be treated or not (note that the net ankle dorsiflexion moment of 4Nm applied by the assessors is lower than is typically applied in a clinical setting). These children will not undergo follow-up measurements as they will receive other treatment for impaired ROM. Second, children have irresolvable problems with KAFO use (pain, pressure sores, sleeping problems). These subjects will be asked to undergo measurements after withdrawal and will be included in the analyses. Third, children can decide to withdraw at any time for any reason. These children will be asked to undergo measurements after withdrawal as well and will also be included in the analyses.

Premature termination of the study

The effects of orthotic management in rest on A-Fdf ROM at full knee extension will be evaluated as soon as measurements have been performed on 30 children regarding follow-up measurement of 6 months. If the children in the control group show significantly larger $\gamma_{(f\text{-}t)}$ reduction compared to the other groups, this group will also be treated with a KAFO. If the KAFO groups (static and/or dynamic) show significantly larger reductions in $\gamma_{(f\text{-}t)}$ than the control group, the study will be terminated.

Randomization

Randomization will be performed by block randomization of 3, 6 or 9 subjects, with pre-stratification by center. A member of the project team (AJD) not being involved in the recruitment/inclusion procedure of the subjects and not being involved in measurements will randomly generate an allocation sequence before the start of the trial to perform the randomization. The order of allocation of treatment will be noted by AJD and kept in numbered sealed envelopes. After checking the inclusion and exclusion criteria by a physician and after receiving informed consent of the participant's parents, treatment allocation will be established by the research assistant after opening the numbered envelope. Subjects will be informed about their allocation after performing their baseline measurement.

Blinding

The researchers performing the measurements and analyzing the data will be blinded with respect to the treatment allocation. The children and their parents will be instructed to give no information about their treatment to the assessors. Blinding will be evaluated at the end of the study by asking the researchers the question: "In which group is the subject allocated and do you know this for sure, or is this a guess?"

Statistics

Statistical analysis will be performed according to an "intention to treat" principle. All relevant subject characteristics, such as age, body weight and length, gender, clinical diagnosis, will be described by their mean value and standard deviation, or percentages. Differences between groups at baseline will be tested using linear regression techniques or Chi-square statistics. The effect of the intervention will be analyzed using a multi-level analysis, with the primary and secondary outcome measures as dependent variables and treatment group and time as independent variables. To test for any differences in the changes of variables between groups, a treatment*time interaction is included as independent variable. Analysis are adjusted for treatment site (Amsterdam, Arnhem or St Louis). Covariates will be: 1) KAFO wearing time, 2) lower leg growth, 3) use of an AFO by day, 4) stretching exercises and 5) level of spasticity. The level of significance will be set at 0.05.

DISCUSSION

This randomized controlled trial (RCT) focuses on the efficacy of orthotic management in rest in children with CP to prevent a decline in A-Fdf ROM at full knee extension. Although orthotic management in rest in children with CP is widely applied, very little is known about the efficacy of this treatment. Therefore, more research on the efficacy of orthotic management in rest is needed. We decided to focus on the efficacy of two types of KAFO's as orthotic management in rest treatment since we expect that KAFO's will be the most effective in preventing loss of A-Fdf ROM. This expectation is based on the fact that a KAFO, in contrast to an AFO, is able to impose both knee extension and ankle-foot dorsiflexion simultaneously. This may lead to more stretch on the GAS which is the target muscle of this study. The GAS is often affected in children with spastic CP, having equinus [45].

To measure the efficacy of orthotic management in rest, the A-Fdf ROM has to be measured in a reliable and valid way. In order to achieve that, a custom designed hand held dynamometer [59] is used to measure the A-Fdf angle. The device allows reproducible measurements of the ankle angle-moment relationships [59]. This is important as A-Fdf ROM depends on the exerted dorsiflexion moment. Standardization of this measurement procedure reduces variability of ankle moment and angle measurements and hence increases the sensitivity to measure changes in ROM. Furthermore, the device allows the investigator to correct for foot deformations by using two separate adjustable foot plates (to stabilize the talonavicular joint) [59]. Foot deformations like equinovarus and equinovalgus [70] can, if not corrected, affect the A-Fdf angle measurement results.

The custom designed hand held dynamometer also allows us to measure morphological parameters of the GM at a standardized ankle position during repeated measurements. By measuring changes in the morphological parameters and changes in A-Fdf ROM simultaneously, we will gain insights into the working mechanisms of orthotic management in rest. As described in the methodological section we obtain the morphological parameters by a 3D ultrasound method. We decided to use this method instead of a 2D ultrasound technique, because 3D ultrasound offers the advantage of measuring the morphological parameters in the mid-longitudinal fascicle plane. Previous research has shown that measuring outside of the mid-longitudinal fascicle plane leads to over or under estimation of the results [69].

The primary outcome measure of this study (A-Fdf ROM) is an impairment parameters at the body-function level of the international classification of function, disability and health (ICF) [6]. Improvements (or less decline) in this parameter do not necessarily lead to improvements in activity level of the ICF model, such as walking [6]). In order to better understand the impact of orthotic management during rest on activity level, this study will also investigate improvements in gait and gross motor function in response to treatment.

In conclusion, this RCT is aimed to provide insight in the efficacy of orthotic management in rest on body function level (A-Fdf ROM) and activity level (gait, gross motor function), and will provide insight in the treatment's underlying myological adaptive mechanisms. The results of this study may provide indications for improved treatment strategies for children with CP and in particular the use of orthoses.

COMPETING INTERESTS

The authors declare that they have no competing interests. Although Ultraflex Europe made a donation to this study on behalf of Ultraflex Systems Inc, and although PEDAK Meettechniek BV sponsored the "Tidbit temperature data loggers" partly, these companies will not have any authority over this study. Measurements and data-analyses will be performed independently by the researchers.

ACKNOWLEDGEMENTS

This study is financially supported by a grant from the Phelps Foundation for spastic disorders, Bussum, the Netherlands. This study is also financially supported by a donation of Ultraflex Europe, Ternat, Belgium on behalf of Ultraflex Systems, Pottstown, Pennsylvania, USA. The "Tidbit temperature data loggers" were partly sponsored by PEDAK Meettechniek BV, Heythuysen, the Netherlands.

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A randomized controlled trial studying efficacy and tolerance of a knee-ankle-foot orthosis used to prevent equinus in children with spastic cerebral palsy (results)

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Clinical Rehabilitation, 2014. 28(10): p.1025 –1039
doi:10.1177/0269215514542355

ABSTRACT

Objective

To examine whether using a knee-ankle-foot orthosis helps maintain ankle-foot dorsiflexion (A-Fdf) range of motion (ROM) over time.

Design

A multicenter randomized controlled trial.

Setting

Two hospitals and one rehabilitation center in the Netherlands and the USA.

Subjects

Children (4-16 years old) with spastic cerebral palsy (CP) who were able to walk.

Intervention

Use of a knee-ankle-foot orthosis, equipped with an Ultraflex® ankle power unit, for at least 6h every other night for one year.

Main measures

Primary outcome measure: ankle-foot dorsiflexion ROM. Secondary outcome measures: ankle-foot and knee angle in gait and gross motor function. Wearing time was also measured. Measurements were taken at baseline and at 3, 6, 9 and 12 months.

Results

28 children (experimental group: n=15, control group: n=13) participated in the study. 11 participants (experimental: n=4, control: n=7) did not complete all 5 measurements, as they needed additional treatment. No significant difference was found in the decrease of A-Fdf ROM between the experimental and control groups (difference: -1.05°, 95% confidence interval: -4.71° – 2.61°). In addition, secondary outcome measures did not show differences between groups. Despite good motivation, knee-ankle-foot orthosis wearing time was limited to a mean±SD of 3.2h±1.9h per prescribed night due to discomfort.

Conclusions

Knee-ankle-foot orthosis with dynamic ankle and fixed knee are poorly tolerated and are not beneficial in preventing a reduction in A-Fdf ROM in children with spastic CP, at least with limited use.

INTRODUCTION

Cerebral palsy (CP) is a common physical disability in children and the spastic subtype is the most common motor disorder [44]. Many children with spastic CP develop limitations in ankle-foot dorsiflexion (A-Fdf) range of motion (ROM) [3]. These limitations are assumed to be caused by shorter and/or stiffer muscle bellies of m. gastrocnemius (GAS) [18, 19]. However, the pathophysiology of this phenomenon is still unclear [11, 71].

Reduced A-Fdf ROM, if measured with an extended knee, is related to changes in gait patterns of children with spastic CP [72-74]. Deviating gait patterns cause higher levels of energy expenditure compared to typical gait patterns and may increase risk of falling [45]. One of the treatment options is to apply muscle strain using orthoses [4]. However, evidence for the effectiveness of this treatment in children with spastic CP is limited [52]. Tardieu et al. [39] suggested that prevention of decreased ankle-foot ROM requires exerting muscle strain for minimally 6h/day.

Orthosis imposed strain in GAS can be applied during daily activities or at rest [4]. Orthoses to be worn during the day are generally prescribed to improve static foot alignment and gait pattern [36]. Particular ankle-foot orthosis treatment is indicated to prevent reduction of dorsiflexion ROM [21, 22, 36]. Although ankle-foot orthoses (AFO's) are also used to strain ankle plantar flexors at rest, no additional effects beyond use during daily activities were reported [22]. It is conceivable that during use at rest insufficient strain is applied to GAS due to shortening effects of knee flexion. Therefore, knee-ankle-foot orthoses (KAFO's) may be more effective in applying strain to GAS than AFO's, since full knee extension is combined with A-Fdf.

To our knowledge, effects of wearing KAFO's at rest on preventing reduction of A-Fdf ROM has not been investigated. Therefore, this study aims to: 1) quantify potential treatment effects of KAFO's over time in children with spastic CP and 2) evaluate effects of such treatment at rest on ankle-foot and knee angles during gait, as well as on gross motor function. We hypothesized children using KAFO's to have smaller reductions in A-Fdf ROM over time compared to peers without such treatment. We also hypothesized that children using such orthoses show more typical ankle-foot and knee angles during gait and show improved gross motor function over time.

METHODS

The Medical Ethics Committees of VU University Medical Center and the Institutional Review Board of Washington University, Saint Louis approved this study.

Settings, design, randomization & blinding

A single blind, randomized controlled trial was performed. Patients agreeing to participate were randomly allocated to either an experimental group (usual care with added knee-ankle-foot orthosis treatment at rest on alternating nights for up to one year) or control group (no knee-ankle-foot orthosis treatment at rest).

A block randomization procedure (block size between 3 and 9) was used. The randomization was computer generated per center before starting the study by an investigator not involved in recruitment or measurement procedures. The assignments were stored in numbered sealed envelopes, and opened by a research assistant after receiving informed consent from the participants and parents. The participant and parents were informed of group allocation after initial measurements. All investigators, data collectors and personnel responsible for patient measurements or data analysis were blinded regarding group allocation until tests and analyses were completed. Measurement sessions were scheduled immediately before treatment and after 3, 6, 9 and 12 months. The protocol is described briefly below.

Participants

Children with spastic CP, aged between 4 and 16 years and able to walk (gross motor function classification system (GMFCS) levels I-III), and treated previously for reductions in A-Fdf ROM were invited to participate in this study. A-Fdf was measured as the angle between hind foot sole and tibia by non-instrumented clinical assessment (further indicated as $\varphi_{foot\text{-}clin}$). Previous treatments included botulinum toxin injections (more than 3 months prior to study initiation), serial casting (more than 2 months prior to study initiation) or knee-ankle-foot orthosis treatment at rest. Exclusion criteria were: 1) previous selective dorsal rhizotomy, 2) intrathecal baclofen therapy, 3) attainable with extended knee, $\varphi_{foot\text{-}clin}$ less than 0˚ (i.e. 90˚ between lower leg and foot while stabilizing the talus bone - for detailed description see below; note that results of instrumented measurement used in the analysis below may differ from clinician's assessment), 4) limitation in knee extension ROM (full knee extension had to be possible), 5) surgical interventions at GAS, as well as planned botulinum toxin injections and/or serial casting and/or surgery on the lower leg within the study period.

Children were recruited during physician's consultation hours at the VU University Medical Center, the Rehabilitation Medical Center Groot Klimmendaal, the Viecuri Medical Center and at the St. Louis Children's Hospital. All participants were informed about procedures, aim and content of the study and parents and children of 12 years and above signed an informed consent.

Sample size calculation

A sample size calculation for comparisons of two groups with 5 repeated measurements [75] was performed at a level of significance smaller than 0.05 and a power level of 0.80. A change of 5˚ was taken to be clinically relevant, and a standard deviation of 4.5˚ was assumed to apply, based on measurement error of previous ankle dynamometry measurements [59]. Sample size calculations indicated that 10 participants per group were required.

Intervention

Participants in the experimental group were prescribed a polyethylene or polypropylene knee-ankle-foot orthosis for one year. Knee joint angle was fixed at full extension (i.e. 0˚) and variable A-Fdf was made possible using a spring ("ankle power unit", Ultraflex Systems, Pottstown, PA, USA). Four types of power units were available, and the type being dependent on body mass of the participant (P1: more than 50kg, P3: between 25kg and 50kg, P5: less than 25kg, PC1: less than 25kg).

Wearing of the orthosis was prescribed for one leg on alternate nights. If a child had orthoses for both legs, an orthosis was worn on each leg on alternating nights, to reduce treatment burden and to increase actual wearing time. To attain similar wearing time per leg for single leg treatment, children were instructed to wear the knee-ankle-foot orthosis on alternate nights. Wearing of the orthosis for at least 6h per night was prescribed for all participants. If participants experienced serious discomfort after a 20min adjustment period, or if they woke up during the night, the orthosis could be removed. Orthosis applied tension at the ankle was set according to a predefined scheme [76]. Briefly, patients started at point 2 on the indicated scale and increased tension settings each night by 0.5 points. Moments exerted corresponding to these settings are reported in tables 3.1-3.4 of the supplement. If children could not tolerate these increased moments, tension was kept constant for two weeks. Following this period, the procedure to increase moments was repeated. If problems with wearing time remained, participants were advised to wear the knee-ankle-foot orthosis during rest periods through the day, for example while watching television. To deal with any problems, participants were intensively monitored by a qualified research assistant.

All children, including the experimental group, received regular treatment including wearing AFO's during the day (for standing and walking) and physiotherapy. Participants were excluded from the study when their physician decided that additional treatment was needed (for example botulinum toxin injections and/or serial casting for reduced $\varphi_{foot\text{-}clin}$) or when they no longer wished to participate. Data that was collected before patients quit, was included in analyses.

Outcome measures

Primary outcome

Ankle-foot dorsiflexion range of motion

To evaluate the efficacy of KAFO treatment, A-Fdf ROM at full knee extension was measured using a single digital inclinometer (Model ACU001, Acumar Lafayette, IN, USA) that was attached to a torque wrench (Sensotork 713/6, Stahlwille, Germany). The torque wrench was attached to an adjustable footplate consisting of a separate forefoot and calcaneal part (figure 3.1). These parts could be fixed in a required position of pronation or supination, as well as abduction or adduction of the forefoot. The aim was to stabilize the talus bone, especially if valgus deformation was present. This was achieved by applying the following corrections, as described by Huijing et al. [77]:

1)*"The calcaneus is rotated to the neutral position within the frontal plane. This brings the calcaneus to a neutral position under the tibia."*

2)*"Adduction of the forefoot is applied with the aim of bringing the calcaneus midline to pointing between the 2nd and 3rd ray of the forefoot. This will cause the talus to protrude under the skin. If the talocalcaneal joint is sufficiently stable, the skin over the most medial part of the caput of the talus will wrinkle on imposing dorsal flexion."*

3*)"If the talocalcaneal joint is not sufficiently stable as yet, the fore- and midfoot is supinated until sufficient stability is reached."*

During measurements, participants lay prone on a bench with their knees extended and both feet overhanging the edge. The lower limb was positioned in such a position that the line connecting the fibula head and lateral malleolus was horizontal. The assessor exerted a 4Nm dorsiflexion moment on the footplate that was maintained for 5s ('holding' phase). At the end of the holding phase, the angle between the footplate and tibia ($\varphi_{foot\text{-}4Nm}$) was read and recorded. This procedure was repeated 6 times, at 5s intervals.

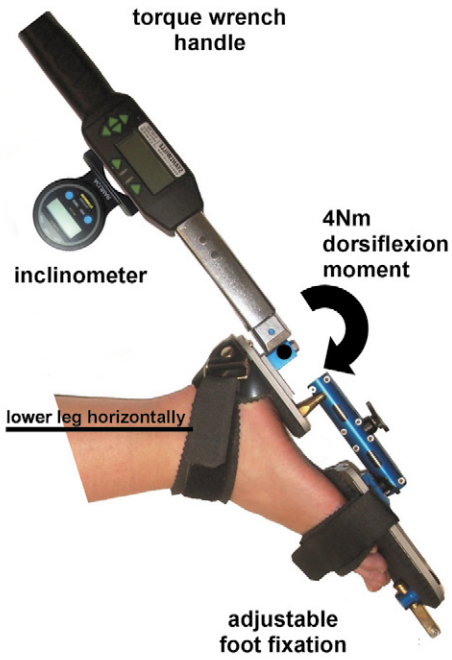

Figure 3.1: The hand-held dynamometer

The hand-held dynamometer consists of a torque wrench, inclinometer and an adjustable foot fixation in order to stabilize the talus bone in case of valgus or varus deformations. The dorsiflexion moment is exerted at the location of the black dot. During measurements, the lower leg is in a horizontal position.

Table 3.1: Moments exerted by power unit P1.

	Moment exerted (Nm) for degree of ankle-foot dorsiflexion (˚)													
settings	**60**	**40**	**30**	**20**	**10**	**0**	**-10**	**-20**	**-30**	**-40**	**-50**	**-60**	**-70**	**-75**
7	7.91	8.22	8.53	8.84	9.15	9.46	9.77	10.08	10.39	10.70	11.01	11.32	11.63	11.94
6	6.78	7.09	7.40	7.71	8.02	8.33	8.64	8.95	9.26	9.57	9.88	10.19	10.50	10.81
5	5.65	5.96	6.27	6.58	6.89	7.20	7.51	7.82	8.13	8.44	8.75	9.06	9.37	9.68
4	4.52	4.83	5.14	5.45	5.76	6.07	6.38	6.69	7.00	7.31	7.62	7.93	8.24	8.55
3	3.39	3.70	4.01	4.32	4.63	4.94	5.25	5.56	5.87	6.18	6.49	6.80	7.11	7.42
2	2.26	2.57	2.88	3.19	3.50	3.81	4.12	4.43	4.74	5.05	5.36	5.67	5.98	6.29
1	1.13	1.44	1.75	2.06	2.37	2.68	2.99	3.30	3.61	3.92	4.23	4.54	4.85	5.16
0	0.00	0.31	0.62	0.93	1.24	1.55	1.86	2.17	2.48	2.79	3.10	3.41	3.72	4.03

This table presents moments exerted by power unit type P1 (for children with a body weight of more than 50kg).
The first column represents power unit settings. Moments exerted (Nm) for each setting are displayed for different ankle-foot dorsiflexion angles.
Data provided by Ultraflex Systems Inc., Pottstown, Pennsylvania, USA.

Table 3.2: Moments exerted by power unit P3.

	Moment exerted (Nm) for degree of ankle-foot dorsiflexion (˚)													
settings	**60**	**40**	**30**	**20**	**10**	**0**	**-10**	**-20**	**-30**	**-40**	**-50**	**-60**	**-70**	**-75**
7	4.63	4.84	5.05	5.26	5.47	5.68	5.89	6.10	6.31	6.52	6.73	6.94	7.15	7.36
6	3.84	4.05	4.26	4.47	4.68	4.89	5.10	5.31	5.52	5.73	5.94	6.15	6.36	6.57
5	3.16	3.37	3.58	3.79	4.00	4.21	4.42	4.63	4.84	5.05	5.26	5.47	5.68	5.89
4	2.49	2.70	2.91	3.12	3.33	3.54	3.75	3.96	4.17	4.38	4.59	4.80	5.01	5.22
3	2.03	2.24	2.45	2.66	2.87	3.08	3.29	3.50	3.71	3.92	4.13	4.34	4.55	4.76
2	1.13	1.34	1.55	1.76	1.97	2.18	2.39	2.60	2.81	3.02	3.23	3.44	3.65	3.86
1	0.57	0.78	0.99	1.20	1.41	1.62	1.83	2.04	2.25	2.46	2.67	2.88	3.09	3.30
0	0.00	0.21	0.42	0.63	0.84	1.05	1.26	1.47	1.68	1.89	2.10	2.31	2.52	2.73

This table presents moments exerted by power unit type P3 (for children with a body weight of between 25kg and 50kg).
The first column represents power unit settings. Moments exerted (Nm) for each setting are displayed for different ankle-foot dorsiflexion angles.
Data provided by Ultraflex Systems Inc., Pottstown, Pennsylvania, USA.

Table 3.3: Moments exerted by power unit P5.

	Moment exerted (Nm) for degree of ankle-foot dorsiflexion (˚)													
settings	**60**	**40**	**30**	**20**	**10**	**0**	**-10**	**-20**	**-30**	**-40**	**-50**	**-60**	**-70**	**-75**
7	3.39	3.52	3.65	3.78	3.91	4.04	4.17	4.30	4.43	4.56	4.69	4.82	4.95	5.08
6	2.83	2.96	3.09	3.22	3.35	3.48	3.61	3.74	3.87	4.00	4.13	4.26	4.39	4.52
5	2.37	2.50	2.63	2.76	2.89	3.02	3.15	3.28	3.41	3.54	3.67	3.80	3.93	4.06
4	2.03	2.16	2.29	2.42	2.55	2.68	2.81	2.94	3.07	3.20	3.33	3.46	3.59	3.72
3	1.47	1.60	1.73	1.86	1.99	2.12	2.25	2.38	2.51	2.64	2.77	2.90	3.03	3.16
2	0.90	1.03	1.16	1.29	1.42	1.55	1.68	1.81	1.94	2.07	2.20	2.33	2.46	2.59
1	0.45	0.58	0.71	0.84	0.97	1.10	1.23	1.36	1.49	1.62	1.75	1.88	2.01	2.14
0	0.00	0.13	0.26	0.39	0.52	0.65	0.78	0.91	1.04	1.17	1.30	1.43	1.56	1.69

This table presents moments exerted by power unit type P5 (for children with a body weight of less than 25kg).
The first column represents power unit settings. Moments exerted (Nm) for each setting are displayed for different ankle-foot dorsiflexion angles.
Data provided by Ultraflex Systems Inc., Pottstown, Pennsylvania, USA.

Table 3.4: Moments exerted by power unit PC1.

	Moment exerted (Nm) for degree of ankle-foot dorsiflexion (˚)													
settings	**60**	**40**	**30**	**20**	**10**	**0**	**-10**	**-20**	**-30**	**-40**	**-50**	**-60**	**-70**	**-75**
7	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.39	3.40
6	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.25
5	2.37	2.37	2.37	2.37	2.37	2.37	2.37	2.37	2.37	2.37	2.37	2.37	2.37	3.10
4	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	2.95
3	1.47	1.47	1.47	1.47	1.47	1.47	1.47	1.47	1.47	1.47	1.47	1.47	1.47	2.80
2	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	0.90	2.65
1	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	0.45	2.50
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.35

This table presents moments exerted by power unit type PC1 (for children with a body weight of less than 25kg).
The first column represents power unit settings. Moments exerted (Nm) for each setting are displayed for different ankle-foot dorsiflexion angles.
Data provided by Ultraflex Systems Inc., Pottstown, Pennsylvania, USA.

During $\varphi_{foot\text{-}4Nm}$ measurements, surface electromyography (EMG) of the mm. gastrocnemius lateralis and tibialis anterior was collected during the final 1.5s of the holding phase. EMG signals were recorded with a sampling rate of 1000Hz and then high-pass filtered at 20Hz. Off-line, recorded signals were filtered with a 50Hz 5th order band pass Butterworth filter, then full wave rectified and finally low-pass filtered with a 5Hz 5th order low pass Butterworth filter using a custom software package programmed in Matlab (version 7.1, The MathWorks Inc., Natick, MA, USA). The processed signals of each muscle were normalized for identically treated signals of maximal voluntary muscle contractions (MVC). To include $\varphi_{foot\text{-}4Nm}$ in the analyses, any differences in values of normalized EMG between measurements and between measurement sessions had to be smaller than 10% of the MVC.

For $\varphi_{foot\text{-}4Nm}$, the mean of 5 acceptable measurements was used in the analyses. This method yields a smallest detectable difference in $\varphi_{foot\text{-}4Nm}$ of 2.45˚ [59]. For participants who wore a KAFO on both legs, $\varphi_{foot\text{-}4Nm}$ was measured for the most involved leg only.

Secondary outcome

Ankle-foot and knee angle in gait

To evaluate ankle-foot and knee angle in barefoot gait, video images of participant's were recorded, with a sample rate of 50Hz, when walking on a 10m walkway at a self-selected comfortable walking speed. Sagittal images were used for measuring ankle-foot and knee angles using custom-made software (the MoXie Viewer®, VU University Medical Center, Amsterdam, the Netherlands, http://www.smalll.eu) with an integrated digital goniometer for on-screen measurements [61]. Frontal images were used to check if sagittal joint angles could be measured reliably, for example with less than 20˚ hip endo- or exorotation present [61]. Walking speed was calculated over 5m of the track, using infrared sensors or a stopwatch. For measurement sessions at 3, 6, 9 and 12 months, participants were asked to walk at similar speed as their first measurement session. Each measurement session consisted of 5 walking trials.

At mid stance (instant that the swing leg passes by the stance leg), ankle-foot angle ($\varphi_{foot\text{-}MST}$, angle between tibia and foot sole below the calcaneus) as well as knee angle ($\varphi_{knee\text{-}MST}$, angle between tibia and femur) were measured. The lowest knee angle ($\varphi_{knee\text{-}LOW,}$ maximal knee extension) in stance between mid stance and pre-swing (floor contact of the contralateral leg) was also measured. The mean of three selected trials was used in further analyses. Neutral ankle-foot angle (lower leg and foot sole perpendicular) was designated as 0˚. Positive values are referred to as dorsiflexion and negative values as plantar flexion. For knee angle, an extended knee, lower and upper leg aligned, was designated as 0˚. Positive values were referred to as knee flexion and negative values as knee hyperextension.

For those children in the experimental group receiving treatment on both legs and for children in the control group with bilateral CP, measurements were performed on both legs.

Mobility

Mobility was measured using the gross motor function measure 66 Item Set (GMFM-66). Scores on a 0–100 scale were calculated using gross motor ability estimator software (Gross Motor Ability Estimator version 1.0) [62].

Knee-ankle-foot orthosis wearing time and tension settings

In a subgroup of patients, wearing time was measured by recording temperature, using a temperature sensor-data-logger (UTBI-001, Onset Computer Corporation, Bourne, MA) that was incorporated in the shelf of the KAFO. Temperature was recorded every 15min. Using this data, mean KAFO wearing hours per prescribed night were calculated for each interval between measurement sessions. Because it was not possible to provide all patients wearing a KAFO with a temperature sensor-data-logger, additional information regarding wearing time was collected using self-report questionnaires. These questionnaires were also used to collect information on tension settings of the power unit. Tension settings were used to estimate the maximum moment exerted on the ankle by the power unit at 0° dorsiflexion, using power unit specifications as described in the supplement (tables 3.1-3.4).

Complaints

Using questionnaires, participants were asked about occurrence, location and causes of pain during wearing of the KAFO. They were also asked to report KAFO-related sleeping problems.

Changes of Protocol with respect to an earlier description

The original protocol has been described in detail [76]. Some changes from the original protocol were necessary due to recruitment problems. 1) The static KAFO group (constant knee flexion at 0° and constant ankle foot angle at 0°, n=2) was removed from the experiment (March 2011). We decided to focus on efficacy of dynamic KAFO's exclusively. 2) The minimum time interval between botulinum toxin treatment and the start of the study was reduced from 6 to 3 months. 3) The upper age range limit was increased to 16 instead of 12 years of age.

As some children showed higher than expected levels of muscle activity during measurements, new EMG levels were chosen, allowing inclusion in A-Fdf ROM analyses. The maximum difference in EMG levels must be less than 10% of MVC between measurements and between measurement sessions.

Statistics

The efficacy of orthotic management at rest on A-Fdf ROM was tested by multilevel analyses [75]. This method takes into account repeated measurements within one subject and conceivable differences in treatment effect between different treatment centers. It also allows a variable number of observations per subject, allowing participants quitting the study before last measurements, also be included in analyses. The dependent variable was $\varphi_{foot\text{-}4Nm}$, and group allocation (experimental or control) was used as independent variable. Analyses were carried out with a nested structure with measurements as level 1, clustered within subjects as level 2, and subjects clustered within centers as level 3. The model was corrected for the initial or first available $\varphi_{foot\text{-}4Nm}$ result. KAFO treatment effect was represented by the regression coefficient of group allocation. This regression coefficient represents difference in change in $\varphi_{foot\text{-}4Nm}$ between the experimental and control groups between consecutive measurement sessions. To assess whether drop outs affected results of treatment effect, an additional analysis was performed including only measurements up to 6 and 9 months. To evaluate the effects of orthotic management at rest on gait and mobility, similar analyses were performed for dependent variables $\varphi_{foot\text{-}MST}$, $\varphi_{knee\text{-}MST}$, $\varphi_{knee\text{-}LOW}$ and GMFM-66 score. All analyses were performed according to intention to treat principles.

An additional analysis was performed to determine whether the control group showed a reduction in $\varphi_{foot\text{-}4Nm}$ over time. The same procedure as described above was applied, with as independent variable time (moment of measurement in numbers) and no correction for the initial or first available $\varphi_{foot\text{-}4Nm}$ result. In this analysis, the regression coefficient represents change in $\varphi_{foot\text{-}4Nm}$ between consecutive measurement sessions.

Another analysis was performed to investigate the effects of KAFO wearing time on change in $\varphi_{foot\text{-}4Nm}$ between consecutive measurement sessions (experimental group only). The dependent variable for this analysis was $\varphi_{foot\text{-}4Nm}$, and wearing time per prescribed night was included as independent variable. The model was corrected for the initial or first available $\varphi_{foot\text{-}4Nm}$ result. The regression coefficient is indicative of a possible relation between changes in $\varphi_{foot\text{-}4Nm}$ between consecutive measurement sessions and KAFO wearing time per prescribed night.

Analyses were performed using MLWin (version 2.21, Center for Multilevel Modelling, University of Bristol) and alpha level was set to 0.05.

RESULTS

All patients were recruited between February 2010 to April 2012 and measurement sessions were performed between March 2010 and April 2013. A flow chart of the number of participants is shown in figure 3.2. Some patients declined to participate because their preference for a specific treatment led them to object to the randomization process, or because they considered the additional visits to the hospital for the measurement sessions to be a burden. Reasons for drop out after initial measurement were serious illness of a mother (n=1), contact lost (n=1), disagreement with group allocation (n=1) or logistical problems (n=1). Reasons for drop out later in the study were need for additional treatment for reduced $\varphi_{foot\text{-}clin,}$ such as botulinum toxin injections or serial casting (exit criteria, n=11), foot bone fracture (n=1), contact lost (n=1), or being unavailable for the final measurement (n=3). Characteristics of patients who were included in analyses are shown in table 3.5.

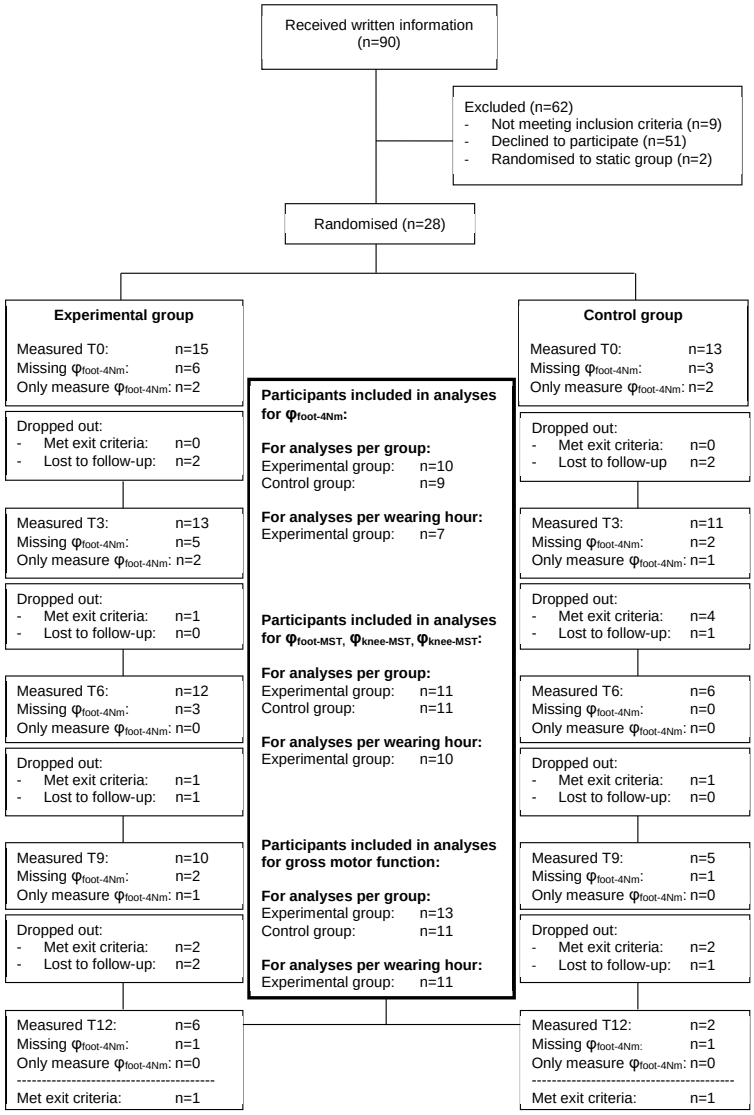

Figure 3.2: Participants flow diagram

Diagram showing flow of participants during the study. N represents the number of participants, $\varphi_{foot\text{-}4Nm}$ represents outcome parameters for ankle-foot dorsiflexion range of motion and T0, T3, T6, T9 and T12 represent measurements at 0, 3, 6, 9 and 12 months resp. 'Missing $\varphi_{foot\text{-}4Nm}$' represents the number of measurements that could not be included in the analyses for $\varphi_{foot\text{-}4Nm}$ due to not meeting electromyography criteria or because measurements could not be performed due to pain. 'Only measure $\varphi_{foot\text{-}4Nm}$' represents the number of measurements that could not be included in the analyses because there was only one $\varphi_{foot\text{-}4Nm}$ for that participant.

Table 3.5 Participants characteristics at baseline.

	Experimental group		Control group	
Analysis (number of participants)	**Total (n=13)**	**$\varphi_{foot\text{-}4Nm}$ (n=10)**	**Total (n=11)**	**$\varphi_{foot\text{-}4Nm}$ (n=9)**
Age (mean±SD)	8.6±3.2	8.8±3.4	10.0±2.9	9.0±2.0
Gender female/male	3/10	2/8	6/5	5/4
GMFCS I/II/III	7/4/2	6/3/1	6/4/1	4/4/1
Uni/Bilateral	7/6	6/4	5/6	3/6
Catch m. gastrocnemius yes/no	8/5	6/4	7/4	5/4
Knee flexion in MST >10˚ yes/no	10/1	9/1	10/3	8/2
Foot: varus/valgus/neutral	2/9/2	1/7/2	2/7/2	2/6/1
Physiotherapy yes/no	8/5	6/4	8/3	8/1
AFO (day) treatment yes/no	10/3	7/3	8/3	7/2
Stretching exercises yes/no/missing	7/4/2	5/3/2	9/0/2	8/0/1
One/Two sided treatment	10/3	N/A	N/A	N/A

Abbreviations:
φfoot-4Nm : Ankle-foot dorsiflexion range of motion angle, measured with hand-held ankle dynamometer at 4Nm dorsiflexion; GMFCS: gross motor function classification system; MST: mid stance; AFO: ankle-foot orthosis.

Primary outcome: Ankle-foot dorsiflexion range of motion

For $\varphi_{foot\text{-}4Nm}$, data were available for 10 participants in the experimental group (table 3.6A) and 9 participants in the control group (table 3.6B). Patient characteristics for both groups are shown in table 3.5 and mean changes (from initial measurement session) in $\varphi_{foot\text{-}4Nm}$ at each time interval are shown in table 3.7. The patient groups did not statistically differ at baseline. Multilevel analyses showed that change in $\varphi_{foot\text{-}4Nm}$ was not significantly different between groups (see table 3.8). Changes in $\varphi_{foot\text{-}4Nm}$ were also not statistically different between the control and experimental groups when only 0–6 months data (regression coefficient=-2.01, confidence interval=-4.69–0.67) or 0–9 months data (regression coefficient =-1.65, confidence interval=-5.03–1.73) were taken into account.

Although we hypothesized that $\varphi_{foot\text{-}4Nm}$ would reduce over time for children in the control group, $\varphi_{foot\text{-}4Nm}$ did not decline significantly over one year (regression coefficient=-0.35, confidence interval=-1.51–0.81). No significant reduction of $\varphi_{foot\text{-}4Nm}$ was seen between 0–9 months (regression coefficient =-0.20, confidence interval=-1.50–1.11), although there was a significant reduction for 0–6 months (regression coefficient =-1.90, confidence interval=-3.22–-0.57).

Secondary outcome: Ankle-foot and knee angle in gait

For ankle-foot and knee angles in gait, data were available for 22 participants (control group: n=11; experimental group: n=11). No treatment effect was seen for either $\varphi_{foot\text{-}MST}$, $\varphi_{knee\text{-}MST}$, or $\varphi_{knee\text{-}LOW}$ (see table 3.8).

Secondary outcome: Mobility

For GMFM-66, data were available for 24 participants (control group: n=11; experimental group: n=13). No significant KAFO treatment effects could be shown (table 3.8).

Secondary outcome: knee-ankle-foot orthosis wearing time and tension settings

KAFO wearing time data were available for 12 participants, and tension settings of the power unit were available for 10 participants. Mean±SD wearing hours per prescribed night were 3.0h±0.9h, with values ranging from 0.9h–6.8h. Only one participant (305) was able to wear the KAFO for the required 6h per prescribed night. From reported tension settings, it was calculated that the mean±SD maximum moment exerted by the power unit was 5.0Nm±1.8Nm, with values ranging from 2.1Nm–7.8Nm at 0° A-Fdf.

As mentioned above, data on wearing time were available for 12 participants. For 5 of these participants, temperature sensor data were also available. For the other participants, actual wearing time data were obtained only from the self-report questionnaires.

Since low KAFO wearing time may have contributed to lack of effects of KAFO treatment, we tested if change in $\varphi_{foot\text{-}4Nm}$ over time was related to mean wearing hours per prescribed night per time interval. For this analysis, data regarding KAFO wearing hours was available for 7 participants. Their mean±SD wearing time per night was 2.4h±1.6h (range: 0.9h-4.8h). From reported tension settings, it was calculated that the mean±SD maximum moment exerted by the power unit was 5.3Nm±1.5Nm (range: 3.0Nm–7.2Nm, n=6) at 0° A-Fdf. Multilevel analyses showed that change in $\varphi_{foot\text{-}4Nm}$ was not related to KAFO wearing time (table 3.8).

Table 3.6: Outcome of ankle-foot dorsiflexion range of motion measurements.

A: Experimental group

Participant	T0	T3	T6	T9	T12
102	3.8˚		-0.4˚	2.8˚	3.6˚
103	7.8˚	3.4˚	1.0˚	-5.2˚	3.4˚
109	6.2˚	5.0˚	2.8˚	1.6˚	3.2˚
110	3.0˚	-6.3˚	-6.4˚		
201	3.4˚		-2.8˚	-0.4˚	
207	-0.2˚	3.0˚	-1.0˚	0.0˚	0.8˚
301			5.0˚	16.2˚	12.3˚
303		20.2˚	12.0˚		
305			7.4˚	2.8˚	
306	2.0˚	-3.8˚			

B: Control group

Participant	T0	T3	T6	T9	T12
101	0.4˚	1.6˚	-4.6˚	0.2˚	
105	-7.2˚	-12.6˚			
106		11.8˚	6.8˚		
111	5.8˚	9.4˚			
112	3.2˚	0.0˚	0.8˚	9.4˚	0.8˚
202	14.6˚		11.8˚	10.8˚	
204	-0.4˚	-1.0˚	-5.8˚		
206	19.0˚	11.8˚	16.6˚	19.8˚	
208	11.6˚	7.6˚			

Outcome of ankle-foot dorsiflexion range of motion measurements at 0 (T0), 3 (T3), 6 (T6), 9 (T9) and 12 (T12) months for experimental (A) and control (B) groups.

Table 3.7: Outcome ankle-foot dorsiflexion range of motion measurements, corrected for initial value

Group	T0	T3	T6	T9	T12
Experimental group	0.0±0.0	-2.9±4.5	-4.3±3.6	-2.2±7.3	0.1±4.5
Control group	0.0±0.0	-2.0±3.6	-3.8±1.4	0.8±4.1	-2.4

Outcome of ankle-foot dorsiflexion range of motion measurements per group (mean±SD) at 0 (T0), 3 (T3), 6 (T6), 9 (T9) and 12 (T12) months, when corrected for initial values.

Table 3.8: Multilevel analyses outcome

Dependent variable	Intention to treat				KAFO wearing time		
	n_{exp}	n_{con}	β	95% CI	n_{exp}	β	95% CI
$\varphi_{foot\text{-}4Nm}$	10	9	-1.05	-4.71–2.61	7	-0.01	-1.15–1.14
$\varphi_{foot\text{-}MST}$	11	11	-2.62	-5.80–0.57	10	-0.27	-1.78–1.24
$\varphi_{knee\text{-}MST}$	11	11	-0.04	-4.24–4.17	10	1.06	-0.27–2.39
$\varphi_{knee\text{-}LOW}$	11	11	-1.35	-5.19–2.48	10	0.25	-1.23–1.72
GMFM-66	13	11	0.21	-3.26–3.68	11	-0.84	-1.72–0.06

Regression coefficients (β) and 95% confidence intervals (95% CI) for ankle-foot dorsiflexion range of motion (φfoot-4Nm), ankle-foot angle in mid stance (φfoot-MST), knee angle in mid stance (φknee-MST), the lowest knee angle (φknee-LOW) between mid stance and following initial contact of the contralateral leg and gross motor function measure (GMFM-66) are reported as outcome random coefficient analyses. β indicates the change between initial and repeated measurements. Numbers of participants that could be included in analyses are given for experimental (nexp) and control (ncon) groups. Analyses were performed to test for differences between groups (intention to treat analyses) and to test the relation between dependent variables and knee-ankle-foot orthosis (KAFO) wearing time. Wearing time analyses could only be performed for the experimental group.

For a similar analysis of gait variables and GMFM-66 scores (experimental group only), data on KAFO wearing hours were available for 10 and 12 participants, respectively. Mean±SD wearing time per night was 2.9h±1.9h (range: 0.9–6.8) for participants included in analyses regarding gait parameters, and 3.0h±1.9h (range: 0.9–6.8) for participants included in analyses regarding GMFM-66 score. From reported tension settings, it was calculated that the mean±SD maximum moment exerted by the power unit at 0° A-Fdf was 5.0Nm±1.9Nm (range: 2.1Nm–7.7Nm, n=9) and 5.0Nm±1.8Nm (range: 2.1Nm–7.8Nm, n=10) for patients included in analyses of gait parameters and GMFM-66 score, respectively. Neither the change in gait variables nor the change in GMFM-66 score was related to KAFO wearing time per prescribed night (table 3.8).

Secondary outcome: knee-ankle foot orthosis complaints

Data regarding complaints about KAFO wearing were available for all participants. Data was extracted from questionnaires and from notes of the research assistants. Seven participants reported pain ascribed to muscle strain and 9 to pressure spots. In addition, participants complained of a hot or sweating leg (n=4), itch (n=3), cramp (n=1), stiffness (n=1) or hitting or rubbing against their contralateral leg by the KAFO (n=1). Pain locations included the heel (n=8), other parts of foot and ankle (n=8), lower leg (n=4), upper leg (n=2) and knee (n=3). One participant reported bedwetting because the participant could not get out of bed quickly enough due to the KAFO, and all 13 participants reported sleeping problems. Although reasons for sleeping problems were not always indicated, the reasons described were mostly related to the above mentioned complaints or to general discomfort.

DISCUSSION

We investigated the efficacy of KAFO treatment at rest in preventing reduction in A-Fdf ROM. Our hypothesis that KAFO treatment at rest would prevent reduction of A-Fdf ROM could not be confirmed. A likely contributing factor for this lack of treatment effect is the low wearing time per prescribed night. However, it may be questioned if KAFO's need to be worn for at least 6h per night to be effective. This recommendation is based on a study [39] suggesting that m. soleus (SOL) contractures would not develop if the ankle-foot joint of children with spastic CP is kept at peak dorsiflexion for 6h each day. The results of this study have not been duplicated to date. In the present study, we could not show any relation between orthosis wearing time and changes in A-Fdf ROM. However, it should be noted that our results cannot be taken as unequivocal evidence against wearing of KAFO's because, for all but one subject, orthosis wearing time was considerably less than the recommended 6h. Children and parents agreed to KAFO treatment as a means to prevent (further) reduction of A-Fdf ROM and as possible means to avoid additional treatments such as serial casting and/or botulinum toxin injections. Despite this clear motivation, children were unable to wear the KAFO for the recommended 6h due to excessive discomfort.

In order to be effective, orthotic treatment may need to be modified to improve comfort and tolerability. Many participants reported pain or discomfort caused by pressure spots and/or muscle strain. Despite intensive support from clinicians and orthotists, the complaints proved to be unavoidable. A cause of discomfort may be insufficient fixation of the foot in the orthosis. Heel rise within the KAFO was observed clinically, resulting in pressure on the dorsal side of the calcaneus and consequent pain.

Another cause of discomfort may be high levels of muscle strain. Despite exerted external moments being relatively low, patients experienced perceptible muscle strain that resulted in discomfort and pain. This problem may be related to very high local strains imposed within plantar flexor muscles [78, 79]. In addition to strain, involuntary muscle activation such as dystonic contractions or reflex muscle spasm may contribute to discomfort. Some children woke due to pain, but without notable pressure spots on calf or foot.

It may be interesting to test the efficacy of KAFO's allowing more knee flexion. Children who are allowed some knee flexion during treatment may have less discomfort. It is conceivable that allowing motion into partial knee flexion may increase wearing time of KAFO's due to lower discomfort. Conversely, if pain associated with wearing KAFO's with fixed extended knee is caused by strain imposed on GAS, the absence of pain due to allowing some knee flexion may indicate lack of adequate strain on plantar flexor muscles.

This could then negate treatment effect on the A-Fdf ROM. On the other hand, strain distributions within plantar flexor muscles and from externally applied strain on GAS were found to differ [78, 79], and are unknown for the type of KAFO used in the present study. Therefore, investigation of effects of different strain distributions induced by KAFO treatments on muscular properties is indicated.

KAFO treatment should, theoretically, be effective due to strain imposed on plantar flexor muscles resulting in adaptation of the strained muscles. Long-term increases in numbers of serial sarcomeres within fibers would yield higher muscle fiber slack and optimum lengths, and might enhance joint ROM. However, it is quite conceivable that KAFO's impose lower than expected strains on plantar flexor muscles. During dorsiflexion, substantial fractions of angular changes of the foot sole, or plate, derive from movements and deformations within tarsus and metatarsus joints, rather than from movement at the talocrural joint [77, 80]. As plantar flexor muscles insert on the calcaneus, they strain less than expected from foot sole or plate movements. Through efforts to maximize fixation of the subtalar joints, movement at these joints can be minimized, particularly for our dynamometry measurements. However, it is not feasible to fix joints of tarsus and metatarsus in such a way that change in footplate angle is a valid estimator of change of talocrural joint angle. The clinically noted heel rise described above indicates that the situation may actually be even worse within the KAFO.

As mentioned, it is very difficult to precisely determine the straining conditions of muscles: externally applied strain on GAS (global strain) has been shown to be very dissimilar to local strains found within the globally strained muscle [78, 79]. Some parts of GAS showed, locally, very high positive strains relative to global strain, while high negative strains and groups of shortened serial sarcomeres were encountered in some parts of the muscle.

These studies also showed that strain applied only to GAS (by movement of the knee) yielded strains of similar magnitude in SOL, as well as in all other muscles (including antagonistic muscles) of the lower leg that cross the ankle. These observations indicate that local strains within muscles are not homogenously distributed along muscle fibers and that intermuscular force transmission via connective tissues is omnipresent within a body segment. Despite the fact that adaptations (e.g. increased serial sarcomere numbers) are expected to play a major role in adaptive processes, types of strain distributions inducing these effects within muscle fibers are currently unknown [81].

Effects of global strain may be different for muscles with low and high degrees of pennation. In highly pennate muscles, as GAS, muscle fiber strain may be considerably lower than imposed muscle strain due to the fact that decreases in the muscle fiber angle with the line of pull of the muscle will take up some of the imposed strain [68]. This may have consequences for adaptation of muscle fiber length by addition of sarcomeres in series. An additional important difference between muscles with different degree of pennation is that muscles with a low degree of pennation can only increase their length by increasing fiber lengths (increased number of sarcomeres series), whereas in highly pennate muscles length can also be increased by increasing the cross-sectional area of the muscle fibers [68, 82, 83]. If hypertrophy is induced, for example by high imposed strain [84], muscle length would increase as a consequence. It should be taken into consideration that, for a given ankle joint angle, increased muscle-tendon complex length would lead to lower mean strain within muscle fibers, as well with possible consequences for the number of sarcomeres in series [81].

To improve treatment methods using orthoses at rest, further research of muscular mechanisms resulting from knee-ankle-foot and other orthoses is indicated, as well as other treatments in children with spastic CP. Future studies should focus on which types of strain distributions in plantar flexor muscles are effective in increasing muscle length and how deformations within the foot affect the conditions imposed. This will enhance insight into pathological and physiological mechanisms underlying treatment and may allow improvement of treatment.

As a limitation of this study, several A-Fdf ROM results could not be taken into account because EMG data did not meet inclusion criteria. Although these missing data points reduced the power of the study, sufficient participants could be included to meet our estimate of sample size requirements. Moreover, the results of the present study do not suggest that a larger sample size would have shown beneficial effects for the KAFO, as no positive trends were found. Regarding secondary outcome measures, a limitation of this study is the use of 2D video-analyzing techniques instead of a 3D motion analyses system. This was done to reduce the burden of participants as by the set of extensive measurement. For reliable on-screen analyses, movements had to be performed within the prescribed plane. Although we used data only when hip rotations were less than 20°, it is difficult to assess such rotations adequately. However, visual on-screen measurements, are reported to yield detectable relevant changes [61].

Another limitation of on-screen video measurements was that only two specific points of gait cycle (mid stance and terminal stance) were analyzed. It may be that kinematics of ankle and knee joints changed at other moments of gait cycle. However, as no effect on A-Fdf ROM was found from the intervention, it is not expected that changes in kinematics will be major.

In conclusion, this study could not show that KAFO treatment, with ankle power unit and knee fixed in extension, at rest in children with spastic CP is beneficial in preventing reduction in A-Fdf ROM compared to regular treatment, at least with limited wearing times due to poor tolerance.

COMPETING INTERESTS

The authors declare that they have no competing interests. Although Ultraflex Systems, made a donation to this study, they had no authority over this study or its publication. Measurements, data-analyses and interpretation were performed independently by the researchers.

FUNDING

This study was financially supported by a grant from the Phelps Stichting voor spastici, Bussum, the Netherlands [grant number: 2008032].

ACKNOWLEDGEMENTS

In addition to the funding described below, the Dutch arm of this study was also financially supported by a donation from Ultraflex Europe, Ternat, Belgium, on behalf of Ultraflex Systems, Inc, Pottstown, Pennsylvania, USA. The US arm of this study was financially supported by a donation from Ultraflex Systems, Inc, Pottstown, Pennsylvania, USA and the Correction and Ortho-Prosthetic Research and Charity Fund, Heusden, Belgium. In addition, the “Tidbit temperature data loggers” were partly sponsored by PEDAK Meettechniek BV, Heythuysen, the Netherlands. We thank all participants and their parents for their participation in this study. We also thank the Pediatric Clinical Research Unit at the Department of Pediatrics at Washington University School of Medicine, Saint Louis, Missouri,

USA; the Department of Rehabilitation Medicine of the VU University Medical Center, Amsterdam, the Netherlands; the Rehabilitation Medical Center Groot Klimmendaal, Arnhem, the Netherlands; the Department of Rehabilitation of Viecuri Medical Center, Venlo, the Netherlands; Orthotic and Prosthetic Lab, Inc., Saint Louis, Missouri, USA; Noppe Orthopedie, Noordwijkerhout, the Netherlands; Kamer Orthopedie, Amsterdam, the Netherlands; OIM, Arnhem, the Netherlands, Orthopedie Heckert & van Lierop, Venlo, the Netherlands, as well as Freda Branch, Ruben Hernandez, Rogier Plas, Marieke Vervoort and Bodil Oudshoorn for their assistance during organization and measurements and/or manufacturing the KAFO's.

4

Measuring wearing time of knee-ankle-foot orthoses in children with cerebral palsy: comparison of parent-report and objective measurement

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Disability and Rehabilitation, 2016.
doi:10.1080/09638288.2016.1258434

ABSTRACT

Purpose State

Orthotic wearing time may be an important confounder in efficacy studies of treatment in children with spastic cerebral palsy (CP). Most studies measure parent-reported wearing time (WT_{parent}) with questionnaires, but it is questionable whether this yields valid results. This study aims to compare WT_{parent} with objectively measured wearing time (WT_{obj}) in children with spastic CP receiving orthotic treatment.

Method

Eight children with spastic CP participated in this observational study. For one year, they received knee-ankle-foot orthosis (KAFO) treatment. WT_{parent} was measured using questionnaires. WT_{obj} was measured using temperature sensor-data-loggers that were attached to the KAFO's. The 2.5^{th} and 97.5^{th} percentiles and median of differences between methods (per participant) were used to calculate limits of agreement and systematic differences.

Results

There was no systematic difference between WT_{parent} and WT_{obj} (0.1h per week), but high inter-individual variation of the difference was found, as reflected by large limits of agreement (lower limit/2.5^{th} percentile: -1.7h per week; upper limit/97.5^{th} percentile: 11.1h per week).

Conclusions

WT_{parent} of a KAFO differs largely from WT_{obj} using temperature sensors. Therefore, WT_{parent}) of KAFO's should be interpreted with utmost care.

INTRODUCTION

According to the International Society for Prosthetics and Orthotics consensus document [36, 85], orthotic treatment is applied in efforts to prevent deformities and muscle shortening in children with spastic cerebral palsy (CP). Applying a high tensile strain onto muscles by stretching the muscle tendon complex using orthoses is presumed to increase joint range of motion (ROM) or prevent its loss [36]. Wearing time is an important factor in determining effectiveness, as efficacy of treatment with orthoses is suggested to be dependent on duration that muscles are strained [39]. Two recent studies [22, 76, 86], investigating the efficacy of ankle-foot orthoses (AFO's) and knee-ankle-foot orthoses (KAFO's) straining the calf muscles, used questionnaires filled in by the participant's parents to assess wearing time. However, it is questionable whether such parent-reported wearing time is a valid measure.

Research focusing on objective methods to measure wearing time has been reported for patients with scoliosis, wearing spine orthoses. Several objective methods are available, such as data acquisition using temperature sensors [87-90] or using force transducers [89, 91] attached to the orthoses. These methods yielded reliable and valid wearing time estimates [87-91]. Temperature sensors have been mentioned as most feasible with good agreement with actual wearing time, with no reported mechanical problems and the sensors being easy to use [89].

Objective measures have been used for comparison of self-reported wearing time and actual wearing time (further referred to as objectively measured wearing time). Previous studies assessing the reliability and validity of self-reported wearing time measurements in patient with spine orthoses showed that, in general, self-reports by patients or parents led to overestimation [40, 41, 88, 92-94]. In particular cases, patient-reported wearing time was twice the objectively measured wearing time [40, 41]. Also children with clubfoot deformities, who were wearing a foot abduction orthosis, patient-reported wearing time (by parents) was overestimated [95]. In efficacy studies, such overestimation may lead to erroneous conclusions if orthoses were not worn long enough to be effective.

To the best of our knowledge, in children with spastic CP who wear KAFO's or other orthoses to prevent loss of ankle-foot ROM, parent-reported wearing time has not been compared to objectively measured wearing time. Because wearing instructions, aim of treatment and design of orthoses are different from patients wearing spine orthoses, validity of parent-reported orthotic wearing time may vary from the above described studies.

Therefore, we aim to compare parent-reported wearing time in children with spastic CP, collected using questionnaires, and objective wearing time, measured using temperature sensor-data-loggers attached to the KAFO. It is hypothesized that parent-reported wearing time differs from objective measurements.

METHODS

This observational study is part of a randomized controlled trial that tested the efficacy of KAFO treatment. Approval for this study was obtained from the Medical Ethics Committee of VU University Medical Center [76, 86]. All participants (if older than 12 years) and their parents signed an informed consent form.

Participants and study design

All children participating in this study were also participants in the experimental group of a multi-center study investigating the efficacy of KAFO's to prevent equinus in children with spastic CP (Splint study [76, 86]). In the Splint study, 30 children were recruited and 17 of them were randomized to the KAFO group. They were recruited between February 2010 to April 2012. The KAFO's of children who were recruited in Amsterdam or Venlo (8 children, allocation was determined by the child's residence) were equipped with a temperature sensor-data-logger to measure wearing time (figure 4.1). These 8 children were included in the present study. Although the sensor-data-logger was visible for the participants, they were not informed about the actual aim of the device. Besides that wearing time was measured objectively, parents of participants were asked to report KAFO wearing time for their child. The participants were aged between 4 and 16 years and were able to walk independently (gross motor function classification system (GMFCS) level of I-II) or with walking aids (GMFCS level III) [14]. All participants were instructed to wear KAFO's for at least 6h every other night.

Measurements

Parent-reported wearing time (WT_{parent}) in h per week, was collected using questionnaires. For all days of the 4^{th} week of each month during the treatment period, parents of participants were asked to complete online questionnaires. These questionnaires were sent to the parents by email (Netquestionnaire Nederland B.V., Utrecht, The Netherlands). A reminder was sent after two weeks if parents did not respond. The following multiple choice question was asked: 'How many hours did your child wear his/her KAFO?'. Answers were given as seven categories, ranging from 0h-1h to 6h or more.

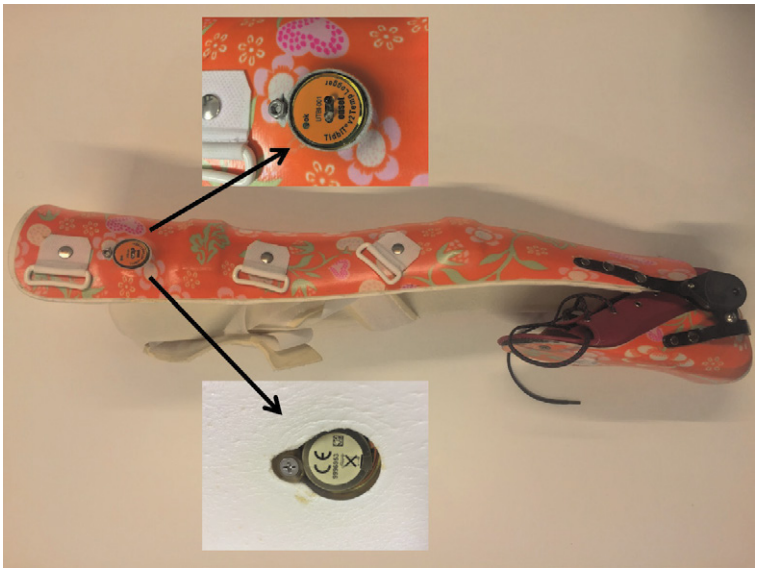

Figure 4.1: The temperature sensor-data-logger attached to the KAFO

The KAFO as shown in the figure is configured with a fixed knee angle and a variable ankle angle using a spring that provides variable ankle-foot dorsi-flexion. The temperature sensor-data-logger was attached to the KAFO with a nut (upper inset) and bolt (lower inset). The flat side (lower inset) of the sensor-data-logger touched the participants skin while wearing the KAFO.

Objectively measured wearing time (WT_{obj}) in h per week, was measured with a temperature sensor-data-logger (UTBI-001, Onset Computer Corporation, Bourne, MA, USA) during the treatment period. The sensor-data-logger was embedded in the shelf of the KAFO, touching upper-leg skin of the participant. Temperature was recorded every 15min. KAFO wearing time was derived from time-temperature data. An increase of at least 3°C in temperature within 45min, indicated that the KAFO was put on. As KAFO temperature is not expected to increase over normal body temperature (37˚C), periods with higher temperatures were ignored, because it was assumed that these temperature increases were artefacts caused by external heating (e.g. KAFO exposed to direct sunlight or heater radiation). The KAFO was assumed to be removed if temperature decreased to values similar to previous periods that KAFO was not worn.

Analyses

For each participant, WT_{parent} and WT_{obj} per week were calculated for all weeks that data of both methods were available. A week was only analyzed if WT_{parent} and WT_{obj} measurements were available for at least 4 days. If only 4-6 days of a week were available, wearing time of those days was used to estimate total wearing time of 7 days. For WT_{parent}, the center value of each time category (i.e. 0.5 for 0h-1h, 1.5 for 1h-2h up to 6.5h for 6h or more) was used to calculate total wearing time of the week.

Agreement between the two methods was assessed according to the non-parametric Bland and Altman method [96]. The non-parametric method was used because of violation of normal distribution of data due to some extreme values for differences in wearing time between measurement methods. For each participant, median of the differences between both measurement methods per week was determined. In addition, the group median of differences and 2.5^{th} and 97.5^{th} percentile score were determined, reflecting the systematic difference between methods and limits of agreement respectively.

RESULTS

Temperature sensor data were available for 8 participants of the Splint study (mean age: 8.7±1.9 years; gender: 6 males, 2 females; GMFCS: level I (n=2), level II (n=4), III (n=2)). The period of KAFO treatment of 4 participants was shorter than one year because other treatment (e.g. botulinum toxin treatment) was indicated clinically (n=3) or the KAFO caused too much discomfort (n=1) and therefore the protocol was not finished. As a consequence, KAFO treatment varied from 2 months to 1 year. Individual response to questionnaires ranged from 22 to 100% with a median of 87%. For about 25% of the sent questionnaires, reminders had to be sent. Acceptable time-temperature data that was available per participant ranged from 10 to 100% (median: 66%). Missing time-temperature data was caused by 1) too high air temperature because of weather conditions, leading to a too small increase in temperature if the KAFO was worn (3% of total missing time-temperature data), or 2) technical problems with sensor-data-loggers (due to sensor failure that was not related to KAFO wearing), leading to empty data-files (97% of total missing time-temperature data). The period that data of both WT_{parent} and WT_{obj} were available ranged from 1 to11 weeks per participant, with a median of 3 weeks.

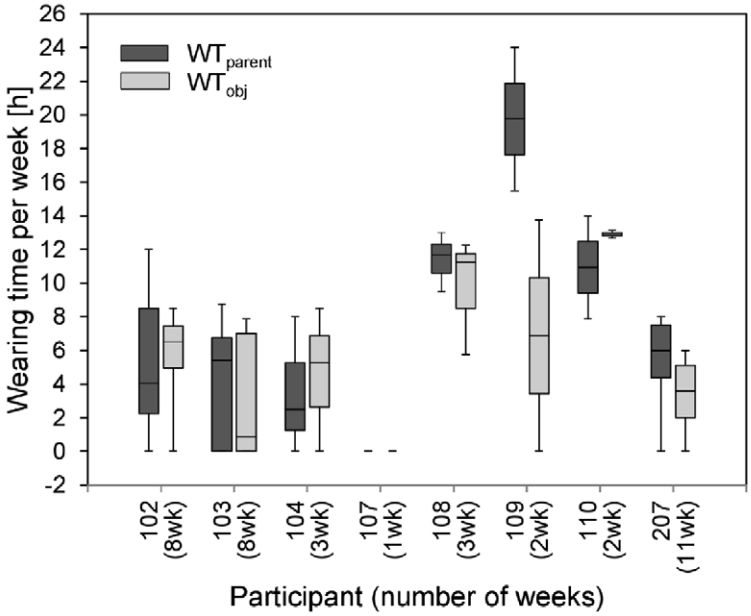

Figure 4.2: Box-and-whisker plots of wearing time per week per participant

Comparison of parent-reported wearing time per week (WT_{parent}) and objectively measured wearing time per week (WT_{obj}) per participant. Numbers of weeks included in analyses are for each participant noted on the x-axis. For participant 107, WT_{parent} and WT_{obj} was reported and measured as 0h per week. The middle line of each box shows the median wearing time. The outer lines of each box show the 25th and 75th percentile of the wearing times and the end of the whiskers show the maximum and minim values.

Individual median, interquartile range, minimum and maximum values of WT_{parent} and WT_{obj} are presented in figure 4.2. Temperature data show that KAFO wearing time was lower than prescribed and in one case, KAFO wearing time was 0h. In addition, data show that, in some participants, there were large differences between WT_{parent} and WT_{obj}. The median of these differences per week are shown per participant in figure 4.3. This figure shows that there was no systematic difference between both methods (median: 0.13h per week), but that differences between methods show large variability between participants (ranging from -2.0h to 12.9h per week), resulting in large limits of agreement (lower limit/2.5th percentile: -1.7h per week; upper limit/97.5th percentile: 11.1h per week), This indicates that agreement between methods is low.

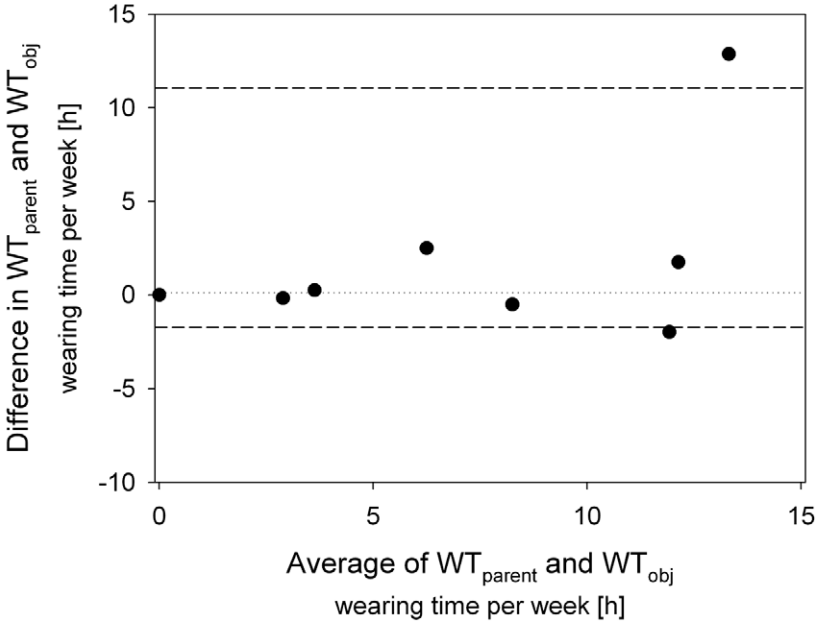

Figure 4.3: Bland-Altman plot: median differences per participant

Bland-Altman plot of parent-reported wearing time per week (WT_{parent}) and objectively measured wearing time per week (WT_{obj}). Upper and lower dotted lines indicate limits of agreement (2.5th and 97.5th percentile). Dotted line in middle indicates median of the difference between WT_{parent} and WT_{obj} for all participants.

Comparing measurements within participants, a high variability in differences between the two methods was shown as well. Individual data of weekly measurements of two participants is shown in figure 4.4. For participant 102, WT_{parent} ranged from 0h to 12h per week, while WT_{obj} ranged from 0h to 8.5h per week (figure 4.4A). Differences between WT_{parent} and WT_{obj} ranged from -5.5h to 5.5h per week with a median of 0h per week (figure 4.4B). For participant 207, WT_{parent} ranged from 0h to 16.5h per week, while WT_{obj} range from 0h to 8.5h per week (figure 4.4C). Differences between WT_{parent} and WT_{obj} ranged from -1h to 10h per week with a median of 2.5h per week (figure 4.4D). The wide range of within participant difference between WT_{parent} and WT_{obj} was also expressed in high individual limits of agreement (see figure 4.4B and 4.4D, participant 102: lower limit/2.5th percentile: -5.4h per week, upper limit/97.5th percentile: 5.2h per week; participant 207: lower limit/2.5th percentile: -0.9h per week, upper limit/2.5th percentile: 9.4h per week).

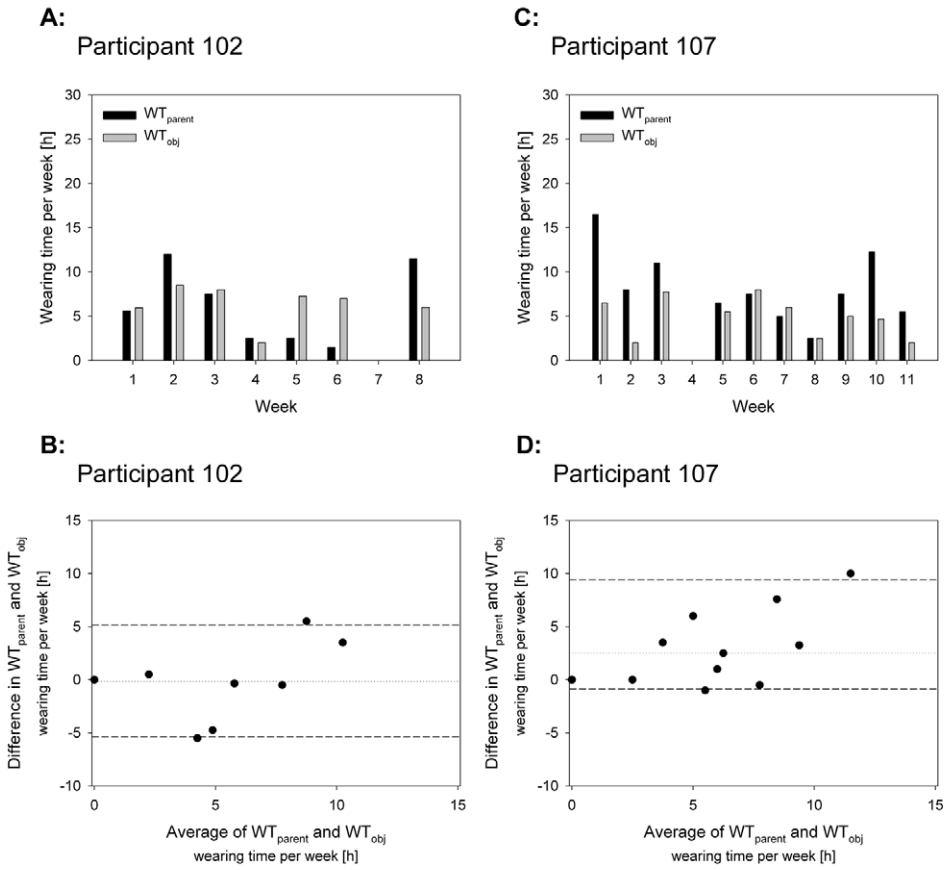

Figure 4.4: Individual data: examples

A+C: Comparison of parent-reported wearing time per week (WT_{parent}) and objectively measured wearing time per week (WT_{obj}) for two participants. If no column is visible, wearing time is 0h.

B+D: Bland-Altman plot of parent-reported wearing time per week (WT_{parent}) and objectively measured wearing time per week (WT_{obj}) for the same participants as in A and C. Upper and lower dotted lines indicate limits of agreement (2.5^{th} and 97.5^{th} percentile). Dotted line in middle indicates median of the difference between WT_{parent} and WT_{obj} for all measurements.

DISCUSSION

The present study shows that parent-reported wearing time of KAFO's differs from objective measurements. The differences in reported wearing time between methods vary considerably per participant: some parents reported higher wearing times than what was measured by temperature sensor-data-loggers while others reported lower wearing times. In literature regarding spine orthoses, mostly overestimation of self/parent-reported wearing time is reported (differences range from 0-150%) [40, 41, 88, 92-94]. It should be noted that these conclusions are often based on means of all participants. In accordance with the reported range of differences between wearing time measurement methods, the present study found no systematic difference or at most a small overestimation of parent-reported wearing time. The large range of overestimation reported in literature may indicate a similar trend as found in this study that self/parent-reported wearing time and objectively measured wearing time varies considerably between participants. Therefore it may be concluded that parent-reported wearing time and objectively measured wearing time are not comparable.

In the present study, high values of limits of agreement between parent-reported and objectively measured wearing times were found. If the objectively measured wearing time method is considered as a golden standard, the limits of agreement reflect the error of parent-reported wearing time. In the present study, the limits of agreement indicate that only if parents reported that the KAFO was worn for more than 11h per week, it can be concluded with certainty that the KAFO was worn for at least a short period. However, participants often did not wear their KAFO for such long period in general (i.e. figure 2 shows that participant 102 and 207 did wear their KAFO not more than 8.5h per week). This indicates that parent reported wearing time cannot distinguish whether participants wore their KAFO or not. It should be noted that one outlying value (participant 109, figure 1) affected error of parent-reported outcome considerably. However, sub-analyses excluding this outlier still showed an upper limit of agreement of 2.4h per week. Taking into account that the median of objectively measured wearing time of the remaining 7 participants was about 5h per week, agreement between methods is still very low.

The response rate of questionnaires was relatively high (approximately 85%). Additional correlation analysis showed that there was no correlation between response rate and agreement between parent-reported and objectively measured wearing times (Spearman's rho=0.252, p=0.5). Another factor possibly affecting agreement was delayed response to questionnaires: it was often necessary to send reminders to parents after 2 weeks.

This may indicate that parents did not complete questionnaires on the day of KAFO wearing and may explain the variability in response. However, uncertainty about delayed responses and therefore variable recall time will always be part of any parent report method. In this study, WT_{parent} could not be influenced by the results of WT_{obj} when WT_{parent} response was delayed because parents and children were not informed about the actual aim and results of the temperature sensor-data-logger. Overestimation in WT_{parent} was larger compared to under estimation: some parents reported KAFO wearing for periods that the temperature-data-logger did not register any higher temperatures. This may be the result of a more general phenomenon that people adjust their answers according to socially desired answers. It is unknown whether other methods of self-reporting may yield more accurate results.

Due to validity problems of parent-reported wearing time, we recommend the use of objective techniques to measure KAFO wearing time. We agree with Hunter [89] et al, that it is feasible to use temperature sensor-data-loggers to measure KAFO wearing time. However, the high percentage of missing data with the current device indicates that technical failures can occur and need to be solved. In this study, we were able to collect data for each participant after replacing the non-functioning sensors. In most datasets, it was straightforward to distinguish KAFO wearing from non-KAFO wearing using criteria described above. However, at high ambient temperatures (about 25˚C), it is more difficult to determine KAFO wearing time because differences in temperature with or without a leg in the KAFO was smaller. Comparison of data from temperature sensors inside the KAFO and additional outside temperature sensors [97] may solve this problem.

Limitations of the study

A limitation of this study is the low number of participants. Non-parametric Bland Altman plots are less reliable in small sample sizes [96]. However, because of the large intra-individual variation, we believe that research using larger samples will yield similar conclusions. A second limitation is that parent-reported wearing time was assessed by only one method and cannot be generalized to other self/parent-reporting wearing time methods. We chose to send online questionnaires during each day. This was only done for every 4th week of the month to decrease burden on participants.

Applications to clinical practice

Measuring parent-reported orthotic wearing time with online daily questionnaires for one week per month does not show to agree with objective measurements using a temperature sensor-data-logger. Outcome of parent-reported questionnaires has to be interpreted with extreme care.

CONCLUSION

Wearing time of a KAFO assessed by questionnaires is not in agreement with of wearing time assessed by temperature sensor-data-loggers and should therefore be interpreted with utmost care. Using objective measurement methods are preferred. Regarding temperature sensors, we recommend to use a more sophisticated method then used in this study to measure orthotic wearing time with temperature sensor-data-loggers, like the method described by Bus et al [97], in order to overcome difficulties in determining orthotic wearing time at high ambient temperatures.

DISCLOSURE STATEMENT

The authors report no declarations of interest

FUNDING

The Splint study is financially supported by a grant from the Phelps Stichting voor Spastici, Bussum, the Netherlands [grant number: 2008032]. In addition to funding, the Splint study is financially supported by a donation of Ultraflex Europe, Ternat, Belgium on behalf of Ultraflex Systems, Inc, Pottstown, Pennsylvania, USA. The “temperature sensor-data-loggers” were partly sponsored by PEDAK Meettechniek BV Heythuysen, the Netherlands. The authors declare that there is no conflict of interest. Although we received financial support from Ultraflex Europe, Ultraflex Systems Inc. and PEDAK Meettechniek, they did not have authority over this study.

ACKNOWLEDGEMENT

We thank all participants and their parents for their participation in this study. We also thank OIM/Noppe orthopedie, Noordwijkerhout, the Netherlands; Kamer orthopedie, Amsterdam, the Netherlands and Orthopedie Heckert & van Lierop, Venlo, the Netherlands for their cooperation.

5

Decrease in ankle-foot dorsiflexion range of motion is related to increased knee flexion during gait in children with spastic cerebral palsy

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Journal of Electromyography and Kinesiology, 2015. 25: p. 339–346
doi:10.1016/j.jelekin.2014.10.015

ABSTRACT

Purpose

To determine the effects of decreased ankle-foot dorsiflexion (A-Fdf) range of motion (ROM) on gait kinematics in children with spastic cerebral palsy (CP).

Methods

All participants were children with spastic CP (n=10) who walked with knee flexion in mid stance. Data were collected over 2-5 sessions, at 3-monthly intervals. A-Fdf ROM was quantified using a custom-designed hand-held ankle dynamometer that exerted 4Nm at the ankle. Ankle-foot and knee during gait were quantified on sagittal video recordings. Linear regression (cross-sectional angles analysis) and general estimation equation analysis (longitudinal analysis) were performed to assess relationships between (change in) A-Fdf ROM and (change in) ankle-foot and knee angle during gait.

Results

Cross-sectional analysis showed a positive relationship between A-Fdf ROM and both ankle-foot angle in mid stance and terminal swing. Longitudinal analysis showed a positive relationship between individual decreases in A-Fdf ROM and increases of knee flexion during gait (lowest knee angle in terminal stance and angle in terminal swing).

Conclusion

For this subgroup of spastic CP children, our results indicate that while changes in ankle angles during gait are unrelated to changes in A-Fdf ROM, changes in knee angles are related to changes in A-Fdf ROM.

INTRODUCTION

Limitations in ankle-foot dorsiflexion (A-Fdf) range of motion (ROM) are common in children with spastic cerebral palsy (CP) [3, 59, 98] and frequently result in altered gait patterns such as equinus gait, characterized by increased ankle plantar flexion at the ankle-foot [9, 45, 65]. As walking with equinus gait results in higher than normal levels of energy expenditure [49], several treatment strategies have been developed to reduce equinus at the ankle during gait. These strategies focus on lengthening the calf muscles to increase A-Fdf ROM, as physicians assume that increasing A-Fdf ROM leads to an increase in A-Fdf during gait [36]. However, this assumption has received relatively little scientific attention and the few cross-sectional studies available have reported rather low correlation coefficients between these variables [72, 73]. Currently, a possible relationship between changes in A-Fdf ROM and ankle angle in gait is unknown.

As the m. gastrocnemius (GAS) exerts forces and moments at both ankle and knee joints, it is likely that its length and stiffness probably affect ROM of both A-Fdf and knee extension. Lengthening and/or reducing stiffness of GAS is therefore expected to affect both joint angles. Surprisingly, earlier studies failed to show any relationship between A-Fdf ROM and knee angles during gait [72-74].

At least three factors could potentially explain a failure to show a relationship between A-Fdf ROM and gait knee angles. One factor may be the specific gait patterns seen in children with equinus gait. These children show distinguishable gait patterns. For instance, in some children the gait pattern is characterized by walking with knee hyperextension in mid stance [9], which is presumably related to a prematurely active, short or stiff m. soleus (SOL). Additional shortness, stiffness or hyperactivity of the GAS may yield excessive plantar flexion in the ankle-foot [9, 47]. Another pattern is characterized by walking with knee flexion in mid stance [9]. Changes in A-Fdf ROM in this pattern may not only affect the ankle-foot angle during gait, but may also change knee flexion [9, 47]. Therefore, effects of altered A-Fdf ROM on ankle-foot and knee angles during gait may vary for both patterns. It is important to clearly distinguish these gait patterns, because gait type differences may be confounding the relationship between A-Fdf ROM and the ankle-foot and knee angle during gait research.

A second important factor is the sizable inter-individual variation in factors, besides gait type and A-Fdf ROM, that affects knee angle during gait. Confounding factors such as hip flexion ROM and the length and stiffness of the hamstring muscles may affect the relationship between A-Fdf ROM and knee angle during gait [45, 73]. Longitudinal analysis of this relationship will help reduce confounding.

A third important factor is the very large variation due to measurement errors. Further improvements in measurement methods for A-Fdf ROM are therefore essential: 1) Rather than using simple goniometry for joint angle measurement (for limitations, see studies by Kim et al. and Rome & Cowieson [99, 100]), joint angular measurement should be combined with techniques that standardize externally applied moments [101, 102]. 2)) Particular attention should be paid to stabilization of the foot joints, as the measured A-Fdf ROM is a combination of talocrural and other foot bone joint movements rather than talocrural joint movement alone [77, 80]. For example, in the case of flexible valgus deformations, talonavicular movement should be prevented by supinating and adducting the forefoot. Applying these methods yields higher levels of precision (of up to 3˚ [59]) compared to use of simple goniometry to determine A-Fdf ROM.

The present study was designed to investigate relationships between longitudinal changes in A-Fdf ROM and concomitant changes in ankle-foot and knee angles during gait in children walking with equinus and flexed knees. These longitudinal results will be compared to results from a cross-sectional study for the same subjects and variables. It is hypothesized that: 1) A-Fdf ROM changes over time and is related to changes in A-Fdf and knee flexion angles during gait, and 2) children with smaller A-Fdf ROM walk with less A-Fdf and enhanced knee flexion.

MATERIALS AND METHODS

This study, being part of a larger study [76], was approved by the Medical Ethics Committee of VU University Medical Center. The parents of all participants provided written informed consent.

Participants and ethics

Ten children with spastic CP (9.2±1.8 years old, range: 5.9-11.2) took part in a randomized controlled trial assessing the effects of orthotic treatment at rest [76]. Participant characteristics included: 1) a clinical diagnosis of spastic CP, 2) aged between 4 and 12 years old and 3) a GMFCS (gross motor function classification system) class of I-III. In addition, 4) a non-instrumented clinical assessment of at least 0˚ A-Fdf was attainable, also described as 90˚ between lower leg and foot, with extended knee (note that the result with instrumented measurement, used in the analysis below, may differ from this clinical assessment), 5) the knee joint could be fully extended on clinical examination, and 6) participants walked with knee flexion in mid stance. Furthermore, participants 7) had been previously treated for reduced A-Fdf ROM, 8) participated in at least two consecutive sessions, and 9) were able to relax during measurements (meaning that electromyography (EMG) levels of m. gastrocnemius lateralis (GL) and m. tibialis anterior (TA) had to be lower than 10% of maximum voluntary muscle contraction (MVC) values).

Experimental procedures

The participants were tested 2-5 times, at intervals of 3 months (see table 5.1). Testing was performed at the VU University Medical Center, Department of Rehabilitation Medicine, Amsterdam and at the Medical Rehabilitation Center Groot Klimmendaal, Arnhem, the Netherlands.

Experimental protocols

Dynamometry

A hand-held ankle dynamometer (figure 5.1, for details see Bénard et al [59]) was used to quantify A-Fdf ROM at each testing session. This hand-held dynamometer enables correction for mobile valgus or varus deformity of the foot (for details see Huijing et al [77]). During quantification of A-Fdf ROM, participants were prone on a bench with extended knees, both feet overhanging the edge. The lower leg was positioned horizontally by alignment of fibula head and lateral malleolus. Using the dynamometer handle, the foot was dorsiflexed slowly until a 4Nm external dorsiflexion moment was exerted. This was maintained for 5s ('holding' phase). The measurement was acceptable only if participants did not move during holding. The procedure was repeated 5 times, with 5s intervals between trials.

The angle between footplate and tibia at the end of holding was used to quantify A-Fdf ROM ($\varphi_{foot\text{-}4Nm}$). Means of 5 trials were used as individual data points. Standard error of the mean is 1.36˚ [59]. Longitudinal changes of A-Fdf ROM ($\Delta\varphi_{foot\text{-}4Nm}$) were quantified by calculating the differences in $\varphi_{foot\text{-}4Nm}$ between consecutive sessions.

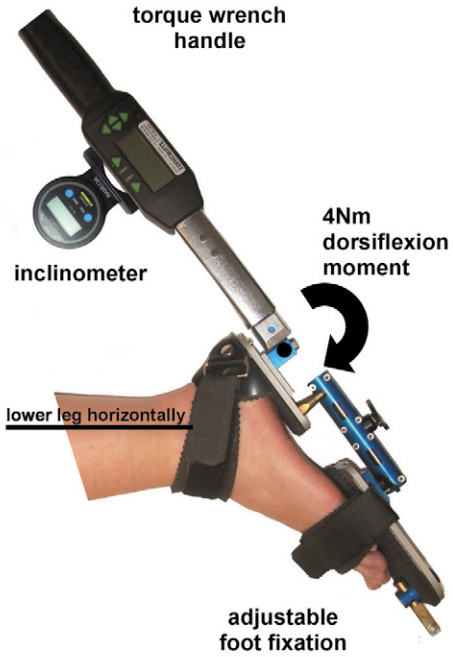

Figure 5.1: The hand-held dynamometer

The hand-held dynamometer consists of a torque wrench, inclinometer and an adjustable foot fixation designed to stabilize the talus bone in case of valgus or varus deformations. The indicated dorsiflexion moment is exerted at the location of the black dot. The lower leg is in a horizontal position.

To quantify muscle activation during dynamometry measurements (i.e. determination of A-Fdf ROM), surface EMG levels of GL and TA were recorded using a Porti 5 system (TMS-International, the Netherlands). Only EMG data from the last 1.5s of the holding phase were analyzed. EMG signals were recorded at a sampling rate of 1000Hz using Portilab (TMS International, the Netherlands). According to Seniam Guidelines [103] and De Luca et al [104], raw EMG signals were filtered at 20Hz using a 5^{th} order high pass Butterworth filter. In addition, a 50Hz 5^{th} order band stop Butterworth filter was used to eliminate hum (from 50Hz power line interference) and signals were full wave rectified for further processing. Subsequently, for visual inspection, the signals were filtered with a 5Hz 5^{th} order low pass Butterworth filter. To quantify possible events during holding phase, the moving average of a 200ms timeframe [105] around the maximum of the rectified signal during the last 1.5s of the holding phase was calculated.

Processing was performed using a custom software package programmed in Matlab (version 7.1, The MathWorks Inc., Natick, MA, USA). To express the EMG activity of dynamometry measurements as a percentage of MVC, MVC of plantar- and dorsiflexion at the ankle was measured (with the ankle slightly plantar flexed and the knee almost extended) and recorded for each participant while the assessor provided resistance. This was performed twice. After processing MVC EMG signals of GL and TA (similar to EMG processing during dynamometry measurements), EMG signals recorded during dynamometry measurements were expressed as percentages of MVC values. A-Fdf ROM measurements were excluded from the analysis if processed normalized EMG was higher than 10% MVC.

Angles during gait

For each participant, 5 trials of walking barefoot over a 10m walkway at self-selected, comfortable speed were recorded using frontal and sagittal video cameras with a sampling rate of 50Hz. Frontal videos were used only to exclude cases of hip endo- or exorotation, preventing reliable sagittal angular measurements [61]. With sagittal videos, A-Fdf and knee angle during gait were measured using a custom-made software package (the MoXie Viewer®, VU University Medical Center, Amsterdam, the Netherlands, www.smalll.eu) and an integrated digital goniometer for on-screen measurements of sagittal joint angles. The standard error of the mean ranges between 1.68˚ and 3.46˚ [61]. Using infrared sensors or a stopwatch (infrared sensors were unavailable for 3 testing sessions), walking speed was calculated from the time required to traverse 5m of track. This result was used to determine whether subjects walked at similar speeds during consecutive visits.

Three steps per session were selected for analysis. For each step selected, A-Fdf ($\varphi_{foot,}$ angle between foot sole and fibula) was measured: 1) at mid stance (MST, the instant passing of contralateral ankle by the target leg) and 2) at terminal swing (TSW, just prior to target leg initial contact). Over selected steps, mean values of variables $\varphi_{foot\text{-}MST}$ and $\varphi_{foot\text{-}TSW}$ were used to characterize A-Fdf angle during gait for each selected step. In addition, knee angle (φ_{knee}, angle between fibula and femur) was measured: 1) at mid stance, 2) at terminal swing, and 3) at its lowest (LOW) angle in terminal stance (the phase that ends when the opposite leg makes initial contact). Over selected steps, mean values of variables $\varphi_{knee\text{-}MST}$, $\varphi_{knee\text{-}TSW}$ and $\varphi_{knee\text{-}LOW}$ were used to characterize the knee angle during gait. The reference angle for ankle-foot was 90˚, also referred to as neutral ankle-foot angle. The reference angle for knee was 180˚, also referred to as the angle at which the knee is fully extended. Longitudinal changes, which will be indicated as Δ-values, of ankle-foot and knee angles during gait were quantified by calculating changes in all variables between consecutive 3 monthly assessments.

Statistical analyses

Cross-sectional data sets for dynamometry and gait (obtained at t=0 months) were analyzed using linear regression analysis. The regression coefficients for relationships between dynamometry and gait were tested for significance and explained variances were calculated. The independent variable was $\varphi_{foot\text{-}4Nm}$ (A-Fdf ROM) and dependent variables were φ_{foot} and φ_{knee} during gait.

When analyzing longitudinal datasets (within subject effects), a general estimation equation analysis with an independent correlation structure [75] was used to test the regression coefficients for significance. The independent variable was $\Delta\varphi_{foot\text{-}4Nm}$ (ΔA-Fdf ROM) and dependent variables were $\Delta\varphi_{foot}$ and $\Delta\varphi_{knee}$ during gait.

Statistical analyses were performed using SPSS (PASW Statistics, release 20, SPSS Inc., Chicago, IL, USA), and $p<0.05$ was selected as a level of significance.

RESULTS

Ten children were included in the study (6 girls, 4 boys, 6 bilateral spastic CP, 4 unilateral spastic CP, 9.2±1.8 years old). All walked with knee flexion at mid stance (16.6±6.9˚, see table 5.1). Nine walked with $\varphi_{knee\text{-}MST}>10^{\circ}$ at first measurement (see figure 5.2C). Note that not all patients participated in 5 consecutive sessions, either due to late admission to the program or because more urgent treatment for reduced A-Fdf ROM was clinically indicated. During analysis, 3 out of 32 measurement sessions were excluded because participants did not meet the EMG criterion during dynamometry measures.

Table 5.1 shows group mean values of the ankle-foot angles and EMG levels during dynamometry measurements and group mean values of the ankle-foot and knee angles during gait for the initial measurement session (t=0 months). For consecutive sessions, changes in these values relative to their previous session are shown. Although mean group changes in angles of dynamometry and gait measures are small, there is a large inter-individual variation as indicated by the large standard deviations. For muscle activity, mean group changes, as well as inter-individual variations between consecutive measurement sessions were small.

Smaller peak ankle-foot angles during gait occurred than measured with the dynamometer. Actually at mid stance, mean $\varphi_{foot\text{-}MST}$ was -6.4˚, while $\varphi_{foot\text{-}4Nm}$ measured with dynamometer was +5.3˚ dorsiflexion.

Inter-individual relationships (cross-sectional analysis) of joint angles during dynamometry and gait

Significant and positive regression coefficients for the relationships between $\varphi_{foot\text{-}4Nm}$ and $\varphi_{foot\text{-}TSW}$ and between $\varphi_{foot\text{-}4Nm}$ and $\varphi_{foot\text{-}MST}$ were found (figure 5.2A&B). This indicates that A-Fdf angles during gait are smaller in spastic CP children with more limited 4Nm A-Fdf ROM. In addition, $\varphi_{foot\text{-}4Nm}$ explains 82% and 48% of the variances of $\varphi_{foot\text{-}TSW}$ and $\varphi_{foot\text{-}MST,}$ respectively.

Regression coefficients between $\varphi_{foot\text{-}4Nm}$ and the three different φ_{knee} variables were not significantly different from zero (figure 5.2C-E). This result from the cross-sectional analyses suggests that a more limited 4Nm A-Fdf ROM does not necessarily indicate altered knee angles during gait.

Table 5.1: Ankle-foot and knee angles during dynamometry and gait (0 month values and 3-month changes).

	Variables	0 months (n=10)		Δ0-3 months (n=10)		Δ3-6 months (n=5)		Δ6-9 months (n=3)		Δ9-12 months (n=1)
		SD	Mean	SD	Mean	SD	Mean	SD	Value	
dyn	$\varphi_{foot\text{-}4Nm}$ [°]	5.3	7.6	-3.4	4.2	-1.6	4.4	-0.6	5.5	8.6
	$_{EMG\ level\ TA}$ [% MVC]	2.7	1.9	-0.3[a]	2.2	-0.7[a]	0.8	1.0[a]	2.3	0.3
	$_{EMG\ level\ GL}$ [% MVC]	3.1	1.5	1.0[b]	1.2	-0.3[b]	1.0	-0.7[b]	1.3	-1.7
gait	$\varphi_{foot\text{-}TSW}$ [°]	-12.1	6.6	-2.1	2.4	1.2	5.3	-1.2	4.9	-1.3
	$\varphi_{foot\text{-}MST}$ [°]	-6.4	9.2	1.7	3.2	-1.6	8.3	0.8	0.8	0.7
	$\varphi_{knee\text{-}TSW}$ [°]	32.1	12.9	-1.3	5.6	1.9	8.1	0.8	4.8	-4.0
	$\varphi_{knee\text{-}MST}$ [°]	16.6	6.9	-1.0	6.1	2.5	5.1	0.6	4.3	-4.3
	$\varphi_{knee\text{-}LOW}$ [°]	11.6	9.8	-1.1	5.2	-1.8	4.0	2.6	3.6	-22.7

Dynamometry (dyn): φfoot-4Nm: angle foot sole with fibula at an applied dorsiflexion moment of 4Nm.
TA: m. tibialis anterior; GL: m. gastrocnemius lateralis.
[a] ranges of changes in TA EMG levels were -4.6% to 3.6%, -2.0% to -0.1% and -0.4% to 3.6% for Δ0-3, Δ3-6 and Δ6-9 months, respectively.
[b] ranges of changes in GL EMG levels were -0.9% to 2.4%, -1.4% to 0.8% and -2.1% to 0.4% for Δ0-3, Δ3-6 and Δ6-9 months, respectively.
During gait: φfoot-TSW: angle of foot sole with fibula at terminal swing; φfoot-MST: angle foot sole with fibula at mid stance during gait; φknee-TSW: angle between fibula and femur at terminal swing during gait; φknee-MST: angle between fibula and femur at mid stance; φknee-LOW: minimum angle between fibula and femur between instants of mid-stance and terminal stance.
Δ: 3 months change in angles over period indicated.

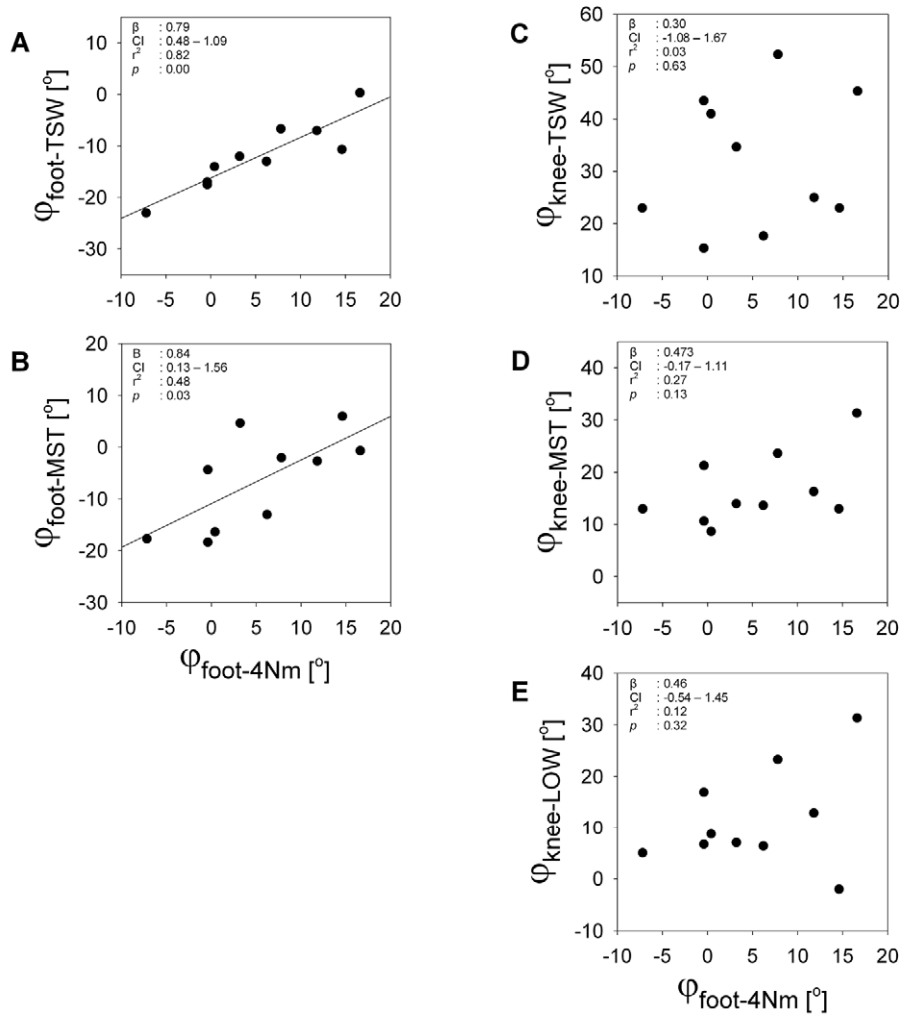

Figure 5.2: Cross-sectional relationships between angles during dynamometry and gait

Scatter plots of the investigated cross-sectional relationships are shown:
A, Ankle-foot angle at 4Nm (dynamometry: $\varphi_{foot\text{-}4Nm}$) and at terminal swing (gait, $\varphi_{foot\text{-}TSW}$). B, Ankle-foot angle at 4Nm (dynamometry: $\varphi_{foot\text{-}4Nm}$) and at mid stance (gait, $\varphi_{foot\text{-}MST}$). C, Ankle-foot angle at 4Nm (dynamometry: $\varphi_{foot\text{-}4Nm}$) and knee angle at terminal swing (gait, $\varphi_{knee\text{-}TSW}$). D, Ankle-foot angle at 4Nm (dynamometry: $\varphi_{foot\text{-}4Nm}$) and knee angle at mid stance (gait, $\varphi_{knee\text{-}MST}$). E, Ankle-foot angle at 4Nm (dynamometry: $\varphi_{foot\text{-}4Nm}$) and knee angle at minimal knee flexion in stance (gait, $\varphi_{knee\text{-}LOW}$). All values were obtained during the initial session (t=0). Positive values represent ankle-foot dorsiflexion (90˚ being reference value) and knee flexion (180˚ being reference value). Regression lines are plotted only for regression coefficients differing significantly from zero. Values for regression coefficient (β) and 95% confidence interval (CI), explained variance (r^2) and probability (p) are indicated. Signs of these regression coefficients are positive.

Intra-individual relationships (longitudinal analysis) of joint angles during dynamometry and gait

Regression coefficients for the relationship between $\Delta\varphi_{foot\text{-}4Nm}$ and $\Delta\varphi_{foot}$ (figure 5.3A&B) did not differ significantly from zero. This indicates that if 4Nm A-Fdf ROM decreases from one session to the next, it does not follow that A-Fdf will also be more limited during gait. In fact, figure 5.3A&B indicate that ankle-foot angles during gait remain fairly constant, even if a more limited range of dorsiflexion (A-Fdf ROM) is found. In contrast, regression coefficients for the relationship between $\Delta\varphi_{foot\text{-}4Nm}$ and $\Delta\varphi_{knee\text{-}TSW}$ and between $\Delta\varphi_{foot\text{-}4Nm}$ and $\Delta\varphi_{knee\text{-}LOW}$ were significantly different from zero (figure 5.3C&E). The signs of these regression coefficients were negative, indicating that a more limited 4Nm A-Fdf ROM becomes evident as enhanced knee flexion during gait, at least for its minimum value during stance and at the instant of terminal swing. Regression coefficients did not differ from zero for the relationship between $\Delta\varphi_{foot\text{-}4Nm}$ and $\Delta\varphi_{knee\text{-}MST}$ (figure 5.3D).

Taken together, these results indicate that during gait changes of 4Nm A-Fdf ROM appear not to be expressed as changes in ankle-foot angle, but rather as changes of knee angle.

DISCUSSION

The major finding of this study is that in children with spastic CP and walking with knee flexion during mid stance, longitudinal changes of 4Nm A-Fdf ROM are not expressed as longitudinal changes in the ankle-foot angle during gait, but rather as longitudinal changes of knee angle during gait. This finding is in accordance with the results of longitudinal analyses for manipulated healthy adults [47], but contrasts with our cross-sectional results and previous cross-sectional studies [72-74]. However, in our opinion, longitudinal analyses are of greater value to clinicians due to the focus on individual changes over time.

Relationship of ankle-foot dorsiflexion range of motion to ankle-foot angle during gait

No relationship between longitudinal changes in A-Fdf ROM and longitudinal changes in ankle-foot angle during gait could be demonstrated. As the explained variance of this relationship in the cross-sectional dataset was high (up to 82%), this was a surprising finding. A potential factor that may have obscured a longitudinal relation is variation across consecutive measurement sessions in the degree of muscle excitation during dynamometry measurements. However, we attempted to avoid this by including only measurements with EMG activity below 10% MVC. As a consequence, within participants, differences in muscle activity of GL and TA between measurement sessions were quite limited (table 5.1).

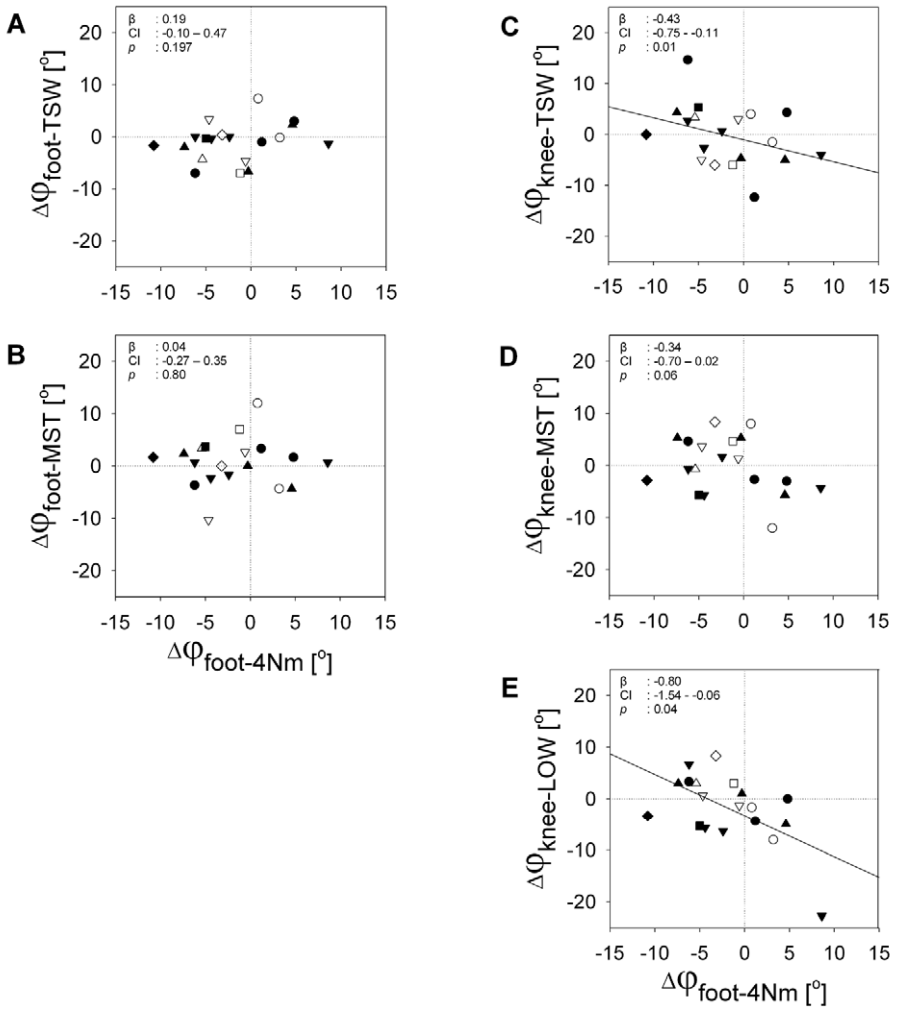

Figure 5.3: Longitudinal relationship between 3-month angular changes during dynamometry and during gait

Scatter plots of the investigated longitudinal relationships are shown: A, Changes of ankle-foot angle at 4Nm (dynamometry: $\Delta\varphi_{foot\text{-}4Nm}$) and at terminal swing (gait, $\Delta\varphi_{foot\text{-}TSW}$). B, Changes of ankle-foot angle at 4Nm (dynamometry: $D\varphi_{foot\text{-}4Nm}$) and at mid stance (gait, $\Delta\varphi_{foot\text{-}MST}$). C, Ankle-foot angle at 4Nm (dynamometry: $\Delta\varphi_{foot\text{-}4Nm}$) and changes of knee angle at terminal swing (gait, $\Delta\varphi_{knee\text{-}TSW}$). D, Changes of ankle-foot angle at 4Nm (dynamometry: $\Delta\varphi_{foot\text{-}4Nm}$) and changes of knee angle at mid stance (gait, $\Delta\varphi_{knee\text{-}MST}$). E, Ankle-foot angle at 4Nm (dynamometry: $\Delta\varphi_{foot\text{-}4Nm}$) and changes of knee angle at minimal knee flexion in stance (gait, $\Delta\varphi_{knee\text{-}LOW}$). Angular values are plotted as changes from their previous value at each 3-month period. Positive values represent enhanced ankle-foot dorsiflexion and knee flexion. Each symbol represents a participant. Regression lines are plotted exclusively if the regression coefficient differed significantly from zero. Values for regression coefficient (β) and 95% confidence interval (CI), explained variance (r^2) and probability (p) are indicated. Regression coefficients significantly different from zero were found for the relationship between change in dynamometry ankle-foot angle and change in knee angle at terminal swing and for lowest stance knee angle during gait. Both regression coefficients are negative.

Based on the discrepancy between cross-sectional and longitudinal data-sets, we hypothesize that the observed relationship within the cross-sectional dataset regarding A-Fdf ROM and ankle-foot angle during gait is not a causal one.

It is conceivable that the relationship in the cross-sectional dataset regarding A-Fdf ROM and ankle-foot angle during gait is affected by deformations within the foot, because A-Fdf ROM and the ankle-foot angle may be separately affected by that foot deformation. Regarding A-Fdf ROM, Huijing and colleagues [77] showed that the foot fixation which was used during dynamometry measurements in this study allows this kind of deformation. Iwanuma et al [80] showed sizable deformation within the foot at higher levels of muscle activity. Such higher levels of muscle activity are present during gait and thus may have occurred during gait measurements. Because the amount of deformation within the foot differs between persons [77], it may be that some children show larger A-Fdf ROM and A-Fdf angles during gait than others, without individual differences in GAS length. In that case, a relationship (with high explained variance) between A-Fdf ROM and ankle-angle in gait will be found in the cross-sectional relationship, while a causal (longitudinal) relationship between both variables does not exist.

A lower explained variance in mid stance than in terminal stance may be related to higher loading due to body mass effects during stance phase of gait compared to swing phase and dynamometry measurements. Body mass probably had no effect on the relation between A-Fdf ROM and ankle angle in terminal swing, as loading conditions of the ankle in terminal swing were quite similar to those during dynamometry measurements. For the subjects under study, we conclude that A-Fdf ROM and A-Fdf angle during gait, and the longitudinal changes in these variables, are unrelated. Therefore, we do not expect that enhancing A-Fdf ROM by clinical interventions aimed at increasing A-Fdf during gait will be effective.

In general, even if the potential ROM as measured during dynamometry is decreased, the ankle-foot angle during gait remains constant (longitudinal analysis) and the children use a higher fraction of the available A-Fdf angle range. This will affect sarcomere lengths within muscle fibers and increase the forces exerted. It seems likely that unchanged A-Fdf angles during gait are due to specific mechanical conditions of gait, such as projection of center of mass within the support plane or clearance of the foot during swing.

Ankle-foot dorsiflexion range of motion and knee angles during gait

The relationship between (change in) A-Fdf ROM and (change in) knee angle during gait, that was only found in the longitudinal dataset, may be due to factors confounding the cross-sectional analysis. Potential confounders include: 1) Lower push off force during the end of stance phase may yield decreased knee extension in terminal swing due to lower swing velocities [45], 2) Enhanced excitation of hamstring muscles may increase knee flexion [45], 3) Premature contraction of the SOL may cause decreased tibia rotation and, as a consequence, enhanced knee extension in mid stance and terminal stance [45]. This indicates that the knee angle during gait is dependent on many factors other than A-Fdf ROM. If a clinical aim is to achieve an increase in A-Fdf ROM in order to decrease knee flexion during gait, one must ensure that other factors are not simultaneously causing opposite effects during gait.

Although actual ankle-foot and knee angles were smaller during gait than during dynamometry, it was possible to detect the relationship between A-Fdf ROM and knee angle during gait, even though joint moments, and probably muscle activation, during gait were higher than during the dynamometer measurements (i.e. for children between 20-30kg, joint moments in the ankle-foot are 10Nm-15Nm in mid stance [106] and approximately 4Nm during ankle dynamometry). When A-Fdf ROM is reduced, a possible effect of increased knee flexion angles during gait may be the wider dispersion of knee loads over tissues due to enhanced myofascial force transmission. For effects, see review [12] and further literature [107].

Limitations of the study

The potential limitations of our study include:
1) A relatively low number of participants. However, study power was partially compensated by data from up to 5 sessions per participant, and the children in the study were selected for unimpaired knee ROM and a gait pattern with knee flexion in mid stance. Despite the low numbers, we were able to show a relationship between A-Fdf ROM and knee angle in gait.

2) Some participants did not complete all five testing sessions due to clinical treatment for reduced A-Fdf ROM (e.g. botulinum toxin-A injections or serial casting). While this may have reduced power at particular time points, the general estimation equation (which does not require equal numbers of intervals per participant) increased the power of the study due to the inclusion of more than one interval per participant. In addition, participants unable to complete the 5 testing sessions are more likely to show a reduction in A-Fdf ROM, which may have increased variation in change values and thus increased the strength of the association (i.e. larger regression coefficient).

3) Deformation within the foot has been shown to be an important factor in dynamometry, affecting differences between ankle-foot angle and actual ankle joint angle in children with spastic CP [77]. The use of ankle-foot angles is necessary because talocrural angles cannot be measured directly. Deformation of the foot also occurs in healthy subjects, but is likely to be increased in spastic CP [77]. However, applying imaging techniques to quantify deformation within the foot simultaneously with dynamometry and gait does not seem feasible, particularly in children with spastic CP.

Anatomically, it is clear that any movement at the ankle within the sagittal plane will involve some pronation and supination movement at the talocalcaneal joint. Although we attempted to limit this movement by fixation of the foot during dynamometry, foot deformation is expected to increase during gait compared to dynamometry. In longitudinal analysis, foot deformation is probably less variable between subsequent sessions within participants compared to the individual variation seen in cross-sectional analysis.

Clinical applications

The results of the present study indicate that a change in A-Fdf ROM of spastic CP children walking with knee flexion in mid stance, with an unimpaired knee ROM, is unrelated to changes in ankle-foot kinematics in gait. Rather, an increase in A-Fdf ROM is related to reduced knee flexion in gait. This may implicate that treatment to increase A-Fdf ROM in spastic CP children walking with knee flexion in mid stance aimed to improve ankle-foot kinematics in gait should be reconsidered. Based on the current study, it seems unlikely that ankle kinematics in gait improve due to increased A-Fdf ROM. However, knee kinematics in gait may be improved.

Conclusion

The results of the present study show that, for children with spastic CP walking with knee flexion in mid stance and with unimpaired knee ROM, changes in A-Fdf angles during gait are not related to changes in A-Fdf ROM. Rather, changes in knee angles during gait are related to changes in A-Fdf ROM. These results therefore suggest that treatment of A-Fdf ROM should aim to influence the knee angle during gait.

CONFLICT OF INTEREST

There is no conflict of interest.

ACKNOWLEDGEMENTS

The Splint study, of which this study is a part, was financially supported by a grant from the Phelps Foundation for spastic disorders, Bussum, the Netherlands. We also acknowledge a donation (as a contribution to the Splint study), allowing full academic freedom, by Ultraflex Europe, Ternat, Belgium on behalf of Ultraflex Systems, Pottstown, Pennsylvania, USA.

DISCUSSION 6

DISCUSSION

The primary aim of this thesis was to quantify potential effects of treatment with knee-ankle-foot orthoses (KAFO's) over time in children with spastic cerebral palsy (CP). In addition, we aimed to investigate whether parent reported KAFO wearing time can be considered as a valid indicator. Also, we aimed to assess effects of affected ankle-foot dorsiflexion (A-Fdf) range of motion (ROM) on gait kinematics in children with CP walking with plantar flexion in the ankle-foot and flexed knees.

The intervention study (chapter 2 and 3), shows that wearing a KAFO designed with a fixed knee at 0˚ flexion and a dynamic ankle joint was not effective in preventing a decrease of A-Fdf ROM. Ankle-foot and knee angles in gait and gross motor function of children also did not change after treatment. Despite a high level of motivation of the participants and their parents, the KAFO was poorly tolerated, resulting in low wearing times that may be contributing to the lack of effect of treatment. In chapter 4 it is concluded that wearing time as reported by parents proved to be an invalid measure as shown by objectively measured KAFO wearing time. Chapter 5 shows that within subject, improvement in A-Fdf during gait was not related to changes in A-Fdf ROM (determined at standardized low EMG activity), while improvement in knee extension angle during gait significantly correlated with changes in A-Fdf ROM.

KAFO treatment effects

Based on results of joint immobilization experiments in animals and studies showing positive effects of treatment on A-Fdf ROM in children with spastic CP with serial casting or ankle-foot orthoses (AFO's), this thesis was initiated on the expectation that KAFO treatment would be effective. It was assumed that the muscle–tendon complex of the m. gastrocnemius (GAS) would adapt to the conditions imposed by knee and ankle angle maintained by the KAFO. As a consequence, A-Fdf ROM was expected either to increase or to be prevented for decrease. In children with CP, who often show a decreasing A-Fdf ROM during growth, it was expected that strain imposed on the GAS by the KAFO would promote an increase of its optimum muscle-tendon complex length and would therefore prevent a decrease in A-Fdf ROM. In contrast to these expectations, the present study shows no effect of KAFO treatment on A-Fdf ROM.

Assumption of decrease of ankle-foot dorsiflexion range of motion over time if not treated

Based on the results of the randomized controlled trial (RCT) described in chapter 2 and 3, it is not proved that a decrease in A-Fdf can be prevented by KAFO treatment. Although participants were selected because they had been treated previously for a decrease in A-Fdf ROM over time and were therefore considered to be at high risk, children of the control group, who did not receive KAFO treatment, did not show decreases in A-Fdf ROM over the present experimental period. This means that additional advantages of KAFO treatment over the regular treatment including wearing AFO's during the day (for standing and walking) and physiotherapy (i.e. stretching exercises at home supervised by physiotherapists) could not be shown. Almost all participating children wore AFO's during the day for which it was reported that it induced an increase in A-Fdf ROM [36]. Note that 6 children of the control group dropped out of the study as it was judged clinically they had to be treated with botulinum toxin A combined with serial casting. Nevertheless, while still subjects in the present study, only 2 of these 6 control group subjects dropping-out later, showed A-Fdf ROM lower than 0˚ at 4Nm. The reasons for the clinical judgement were increased knee flexion in stance phase of gait and/or complaints of pain while wearing AFO's. Differences in clinical judgement and dynamometric measurement of A-Fdf ROM can be explained by the fact that increased knee flexion in stance phase of gait is considered to be caused by several reasons, for example reduced A-Fdf ROM (as showed in chapter 5) and reduced knee extension ROM [45]. In such cases, clinicians need to be aware that different treatment options are suitable for the different cases. It is conceivable that if children participating in the present study were not treated with botulinum toxin A, they would have shown a reduced A-Fdf ROM. An indication in support of this assumption is the significant reduction in A-Fdf ROM of this group of children between measurements at baseline and 6 months (at which some children who had to drop out later in the study because of additional treatment were still included). However, the RCT study could not show a treatment effect over the period from baseline to 6 months as well (see chapter 2 and 3), indicating inefficacy of the investigated KAFO to prevent for decreased A-Fdf ROM.

There are at least three possible explanations for the lack of efficacy of the KAFO treatment: 1) Related to low tolerance of the KAFO, the orthosis may not have been worn long enough by the children, 2) The strain applied onto GAS muscle fibers was insufficient possibly due caused by myofascial interactions of the GAS with its surrounding muscles and connective tissues, and 3) Applied strain by the footplate of the KAFO was absorbed by deformity of the structures of the mid- and hind-foot (as also described in [77]). Because of that, it is unknown to what extend the imposed strain really strained the GAS.

Low wearing time and tolerance of the KAFO

In the present study, despite being overestimated and/or quite variable (see chapter 4), reported wearing time was low. In children participating in the study, KAFO's were poorly tolerated. They experienced pain and discomfort. With a mean KAFO wearing time of 3h every other night, KAFO treatment turned out not to be effective. It is unlikely, if the KAFO would have been worn longer, that the treatment would have been effective. Although wearing time varied largely within the treatment group, the present study could not show any relation between KAFO wearing time and A-Fdf ROM. This may be related to the fact that for all but one subject, KAFO wearing time was lower than 6h per night (on alternating nights). Previously, some indications were reported [39] that for effective treatment an orthosis should be worn at least 6h per night. In any case, to increase wearing time, the problems with discomfort for the subjects need to be solved.

Low tolerance due to KAFO design

The KAFO was not worn long mainly due to complaints of pain. Wearing the KAFO many participants were reported to complain of pain around the knee, ankle, heel and/or other parts of the foot, as well as lower and upper leg due to muscle strain or pressure spots. Pain remained despites intensive support of professionals to correct for pressure sores near bony structures. Originally, the RCT study planned to investigate the efficacy of treatment using static KAFO's (chapter 2, KAFO with ankle fixed at 0^{o} ankle dorsiflexion and knee fixed at full knee extension(0°)), as well as that of treatment with dynamic KAFO's (KAFO with fixed knee at 0° extension and dorsiflexion adjustable spring ankle joint Ultraflex® power unit). However, participants randomized to the static KAFO group reported so many complaints that they were not able to tolerate their KAFO during the night. Therefore, the comparison between efficacy of treatments with the static and dynamic KAFO was abandoned. Recently, also a French research group at a conference reported that in a group of 30 patients the use of static KAFO's was tolerated less than dynamic KAFO's [108]. From this it is clear that a majority of complaints is dependent on the design of the KAFO.

For the dynamic KAFO that was used in the present study, the use of a fixed knee joint instead of a fixed ankle joint may have affected tolerance as well. A spring was attached to the ankle joint of the KAFO to impose A-Fdf and to strain the GAS, but still allowing movement. In clinical practice, KAFO's are tolerated more if the spring is on the knee joint. In the present study, it was decided to strongly limit knee flexion because it was assumed that the GAS would not be strained sufficiently if knee flexion movement was allowed. However, in contrast to such expectations there is a conference report [108] that showed that 6-8 months wearing at rest of a KAFO with dynamic knee was able to increase A-Fdf ROM in patients with spastic CP. In that study, 50% of the children were ambulant.

The results from this study [108] should be interpreted with caution, because of only manual, goniometric measurements of joint angles were made (i.e. not as reliable and precise as measurements with an ankle dynamometer [59]). Nevertheless, it seems worthwhile to investigate further the potential efficacy of KAFO's with a dynamic knee joint. Such KAFO's with dynamic knee joint may be better tolerated and therefore worn longer. However, the question if sufficient strain is imposed remains as the need for at least some degree of knee extension to strain the GAS was suggested [22, 109].

Comparison of effects on A-Fdf ROM by AFO's worn during the day with those on AFO's worn during day and night, showed no beneficial effect of the latter condition [22]. Such lack of additional effect is likely to be caused by the knees not being extended while sleeping. Another study supports the idea that knee extension is needed by showing that GAS muscle-tendon complex length did not change after wearing an AFO at night [109]. However, the minimum knee flexion angle that is tolerated and yet to strain the GAS sufficiently is not clear as yet. To estimate the effects of knee flexion on ankle dorsiflexion ROM, an OpenSim model [110], disregarding potential effects of changes in relative position on myofascial force transmission, is often used in studies calculating muscle origin to insertion distances in children with CP. Results of using such a model show that that if the knee is flexed by 20˚, ankle dorsiflexion angle should be increased by about 10˚ to obtain similar GAS origin to insertion distances as obtained with fully extended knees (figure 6.1, unpublished, additional analyses). With the given limitations, it is derived that for children being able to gain ±10˚ ankle dorsiflexion with 20˚ knee flexion, the GAS may be strained sufficiently to expect effects of adaptation.

Low tolerance due to postural reflexes

Participants in the present study were mostly complaining about pressure spots and strained muscles. It may be that a KAFO is not well tolerated with full knee extension due to overactivated postural reflexes. The positive support reflex [111] may be activated as the footplate of the KAFO applies a force at the foot sole of the forefoot. This pressure on the forefoot can cause activation of the plantar flexion muscles, resulting in plantar flexion of the ankle and extension of the knee, possibly being experienced as very comfortable. It is conceivable that the positive support reflex will be inhibited while wearing a KAFO that allows some knee flexion.

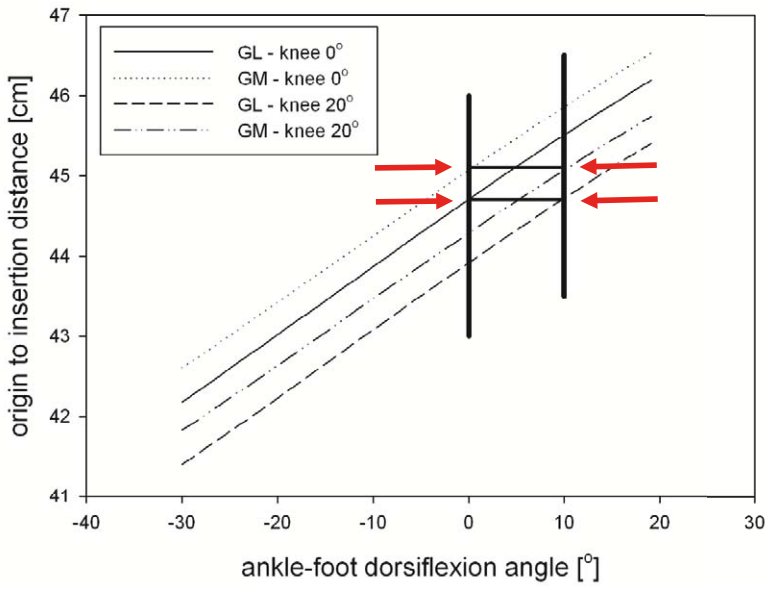

Figure 6.1: Predictions of m. gastrocnemius origin to insertion distances at different ankle and knee angles

Knee flexion of 20˚ requires about 10˚ ankle dorsiflexion to obtain similar m. gastrocnemius origin to insertion distances as with fully extended knees (between two opposite arrows). Lengths are derived from an OpenSim model [110]. Abbreviations: GM: m. gastrocnemius medialis, GL: m. gastrocnemius lateralis.

Low tolerance due to strain distribution in and around the m. gastrocnemius

The fact that a KAFO is not well tolerated with full knee extension may also be due to locally high strains in the GAS causing pain and discomfort. These high local strains may be caused by inhomogeneous distribution of sarcomere strains within the muscle. For GAS at different knee and ankle-foot angles, analysis of magnetic resonance images showed that strains are not uniform [78, 79]. In some regions of the GAS very high positive strains were found while other regions of the GAS are unstrained or even shortened. Such very local stains are expected if epi-muscular myofascial force transmission between the GAS and surrounding muscles and tissues via inter- or extra-muscular connective tissue is present. It may cause forces exerted within the GAS to be transferred to other muscles [78, 79] or structures, for example onto the neurovascular tract passing by this muscle. Such force transmission may explain why children wearing a KAFO complain about strain at different locations (near both ankle and knee joint). Straining the GAS by knee extension compared to dorsiflexion may result in differences in extra-muscular loads on the GAS and, as such may have different effects on the sarcomere strain distributions within its muscle fibers and force transmission, to other muscles and structures.

Insufficient applied strain on the m. gastrocnemius by knee-ankle-foot orthoses due to myofascial interactions

By a KAFO with a dorsiflexion spring in the ankle joint, force is applied by the footplate. The force is supposed to strain the target muscle, the GAS. If force is transferred myofascially from one muscle to another or to other tissues, this may contribute to the inefficacy of KAFO treatment. Force can be transferred via inter- or extra-muscular connective tissue [78, 79] and the residual strain on the GAS may be too small to provoke adaptation of serial sarcomere numbers. It is unknown how the muscle strain distribution is affected by the type of KAFO that is worn. In addition, it is unknown which specific distribution(s) of strains within the muscle fibers (serial distribution) and/or within the muscle (parallel distribution) are needed to optimally stimulate addition of serial sarcomeres. Further insight in strain distributions within the GAS at different combinations of ankle and knee angles is needed to allow potential improvements of treatment methods for children with spastic CP needing to be prevented for decrease of ankle dorsiflexion ROM. It may be interesting to investigate strain distribution of the GAS and surrounding muscles and connective tissues when wearing a KAFO by analysis of high resolution 3D magnetic resonance image (MRI) and using Demons algorithm (non-rigid and non-parametric image analyses technique) [112] or other analyzing techniques. Changes in strain per voxel can be calculated [78, 79] as in above described studies regarding strain distributions in healthy subjects. This will enhance insight to what extent GAS and/or surrounding muscles are strained by wearing a KAFO and how strain is distributed within the muscle and it muscle fibers.

Insufficient applied strain on the m. gastrocnemius by knee-ankle-foot orthoses due to deformity of structures in the foot

Another cause for applying insufficient strain on the GAS may be that applied strain by the footplate of the KAFO was absorbed by deformity of the structures of the mid- and hindfoot because resistance to movement in these structures was lower than the resistance to lengthen the GAS. The movements and deformations of the tarsal and metatarsal joints lead to less dorsiflexion at the talocrural joint and thus lower strain on the GAS. In addition, in the present study it was observed that some children showed heel-rise within the KAFO, leading to a lower ankle dorsiflexion angle and thus lower strain on the GAS as well. The movements and deformations of the tarsal and metatarsal joints are expected based on a comparison between changes in GAS origin and insertion distance and the change in foot plate angle [77]. Analysis was performed on X-rays of ankle and foot of a child with CP wearing the hand-held dynamometer at positions corresponding two different external applied dorsiflexion moments. The rotation between foot sole and tibia proved almost twice as large as the rotation at the talocrural joint.

The other 50% of the movement of foot sole was explained by deformation of the foot (i.e. movements between foot bones, particularly at the midfoot). Because of this result, showing that foot plate angle is not a good estimator of ankle joint angles, within this thesis the term ankle-foot dorsal flexion (A-Fdf) has been used.

Although in the RCT there was special attention (i.e. use of three points pressure technique as described in chapter 2) to stabilize the talocalcaneal joint while bringing the foot into ankle dorsiflexion by the KAFO's, it is unknown whether there were movements of bones within the foot. Note that attempts to stabilize subtalar joints by using our handheld dynamometer and presumably the KAFO are not always fully successful [77]. Potential foot deformation is an important confounder of how much strain is applied to the GAS when the footplate is moved into dorsiflexion. To allow improvement of the design of the KAFO, it would be helpful to quantify the effect of foot deformation on the dorsiflexion ROM of the foot sole within a KAFO. Such assessments require state-of-the-art imaging techniques. In this regard, the application of recently developed 4D-CT imaging techniques may be suitable to learn how the bones of the foot and ankle move with respect to each other [113, 114]. This may provide information on how the orthosis can be modified individually such that stable talocalcaneal and foot bone joint are achieved and on how muscle strain is actually imposed on the calf muscles.

Evidence for effects of sustained muscle strain on muscle morphology of the m. gastrocnemius is lacking

The hypothesis that a KAFO would be effective to prevent A-Fdf ROM was based on the assumption that adaptation to strain applied to the GAS would yield an increase of the optimum and slack muscle-tendon complex length, as there are several indications that muscle fibers add serial sarcomeres when the muscle is strained (see chapter 1). However, these indications were found from animal studies focusing on m. soleus (SOL, in those species a muscle of much smaller degree of pennation than the GAS). It is unknown whether the GAS, as a highly pennate muscle, does adapt to the applied muscle strain in the lengthened immobilized position by an increase in muscle belly length in a similar way as the less pennate SOL. Studies focusing on the effect of such high muscle strains could not be found in literature. It is assumed that GAS increases its length like SOL and according the principle that a muscle fiber regulates its optimum length to the joint position most frequently active, but other mechanisms may play a role as well. Such a mechanism has been shown in a study focusing on immobilization in shortened position, in which GAS showed shortening of the muscle belly length, but due to atrophy of the muscle fibers, rather than by break down of sarcomeres in series and decreased fiber length [31, 82, 115].

Although it was intended that effects of the KAFO on muscle morphological variables would be analyzed in the RCT (chapter 2), these analyses have not been performed due to the lack of effect of KAFO treatment on A-Fdf ROM.

Adverse effect of muscle strain on the m. gastrocnemius physiological cross-sectional area

Although the present study does not bring clarity regarding potential effects of muscle strain on muscle adaptation of morphology variables, the past few years studies were performed that may be helpful to increase our understanding of how strain applied onto the GAS may yield increases of optimum muscle-tendon complex length. Effects of growth on the GAS morphology in typical developing children have been investigated by using 3D ultrasound techniques similar to described in chapter 2. In adolescents, GAS increased its length exclusively by trophy (i.e. an increase in the physiological cross-sectional area (A_f) of the muscle belly) [116], while in young children also fascicle (muscle fiber) and tendon length increased [68]. See figure 6.2 for explanation of effects of increase of fascicle length and cross-sectional area on muscle belly length. A major difference in studies focusing on changes in GAS due to growth and potential changes in GAS due to KAFO treatment, is that in studies focusing on KAFO treatment, immobilization effects may play a role (i.e. KAFO immobilizes the muscle by limiting knee flexion).

It has been shown that in contrast to typical developing children, muscle volume of children with spastic CP increased less during growth compared to that of typical developing children [117]. For children wearing a KAFO, it is conceivable that the longitudinal growth of the very pennate GAS will be decreased further than in children without wearing a KAFO because of the daily temporary immobilization which attenuates muscle trophy. In rodents it has been shown that joint immobilization at low, neutral and extended length leads to substantial decreases in muscle volume and A_f [118]. In addition, in children with CP it was shown that muscle thickness decreased after about 16 weeks of AFO wearing [109]. Muscle thickness of the GAS is determined by A_f, the angle of pennation and muscle fiber length. It is therefore likely that, in adaptation to wearing a AFO, the A_f of the GAS decreases as well. For children with CP, such decrease in muscle volume due to immobilization may be problematic as they already show problems with muscle growth. The reduced trophy of the GAS in children with spastic CP (small A_f) who also wear a KAFO may result in a further decrease in A_f and consequently decrease in muscle belly length. Such decrease in A_f and muscle belly length may be compensated by an increase in tendon length, but will affect the length-force characteristics of the muscle-tendon complex.

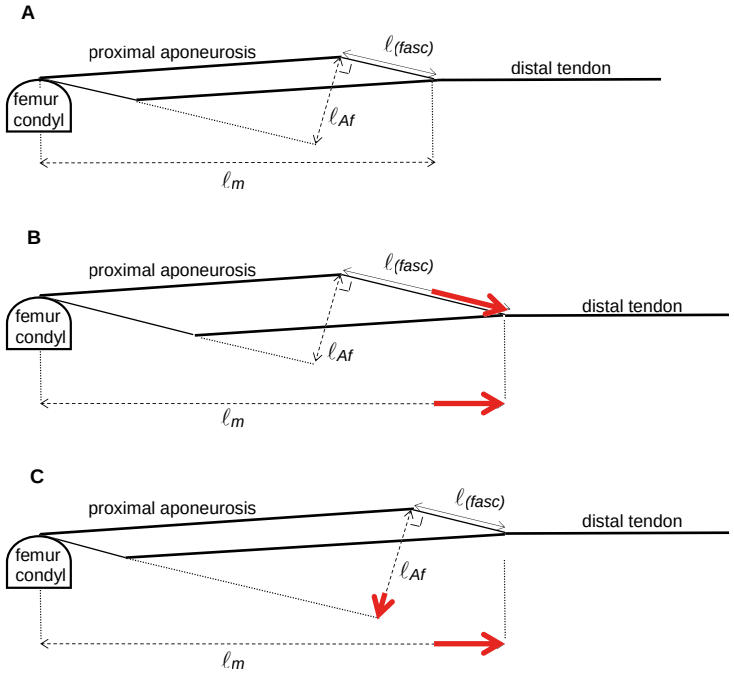

Figure 6.2: Schematics showing of the effect of changes in muscle architecture on muscle belly length

Schematic view of the mid-longitudinal plane of a pennate muscle. Muscle belly length (ℓ_m), fascicle length ($\ell_{(fasc)}$) and length component of pyhsiological cross-sectional area are given (ℓ_{Af}). A: Schematic view without lenghtening. B: Schematic view with increase in ℓ_m due to increase in $\ell_{(fasc)}$. C: Schematic view with increase in ℓ_m due to increase in (ℓ_{Af}). Figure adapted from [68, 76].

Decrease of muscle fiber length when applying muscle strain on m. gastrocnemius of young children

Effects of wearing an AFO on muscle morphology have been studied [109] in children with CP who were able to walk without crutches or a walker. This study shows that due to AFO wearing in addition to a reduction in m. gastrocnemius medialis (GM) muscle thickness, GM muscle fiber length (as a percentage of tibia length at minimum, maximum and mid muscle-tendon complex length) decreases, instead of increases. This reduction in fiber length is remarkably different from what is expected on the basis of morphological changes in GM reported during growth in children in range of 7-12 years (i.e. no change in morphological parameters after normalization for tibia length at negative, zero and positive net ankle dorsiflexion moments considering to yield minimum and extended muscle-tendon complex lengths) [46].

Based on that study and on morphological changes in SOL reported during immobilization in mature animals (i.e. increase of serial sarcomere numbers) [28, 29] it was expected that fiber length as a percentage of tibia length would be similar post AFO treatment compared pre AFO treatment. It not clear whether the decrease in fiber length leaded to lower numbers or lower lengths of serial sarcomeres. If the number of sarcomeres in series is reduced, the length-force characteristics of the muscle may be affected (i.e. the length range over which the muscle is able to exert force will be smaller). This adaptation will affect physical performance such as effective force generation during gait.

A decrease in fiber length due to a decrease in number of sarcomeres in response to conditions in which strain is applied onto a muscle has also been reported to occur within SOL of young mice [28, 29, 51, 119]. In several studies, it has been suggested that in muscles of young animals, contractions are needed to stimulate the addition or to prevent the loss of sarcomeres in series and so to increase or at least remain muscle fiber length [28, 29, 51, 119]. In rat undergoing tenotomy, it was shown that isometric contractions prevented sarcomere loss [120]. It is unknown whether young healthy immobilized rats or children with CP wearing a KAFOs already perform regular isometric contractions. Therefore, it would be worthwhile to consider a training program that stimulates GAS, while wearing a KAFO because muscle activation is likely needed to stimulate the addition of sarcomeres in series and therewith an increase in optimum length of GAS muscle belly. This may be performed by isometric contractions or by voluntarily moving their knee and/or ankle joint actively (i.e. possible when the KAFO joint is dynamic) while applying resistance and subject them to a sort of strength training. Such training may enhance (hyper)trophy as well [121, 122] and therefore prevent a reduction in A_f due to immobilization.

Adaptive effects on passive muscle and tendon stiffness by applying muscle strain

Another effect of straining muscles may be that passive muscle belly and tendon stiffness is reduced. In the present study, it was planned to measure the ankle angle at 0Nm and 4Nm ankle dorsiflexion moment to obtain an indication of the stiffness of the plantar flexor muscles. However, as recent research showed that the applied net ankle moment was absorbed partly by other structures [77] and thus it was unknown whether the GAS was strained, this analyses would not give valid results and was not performed. In recent literature, increased extensibility (as an indicator of stiffness) of the tendon as an adaptation to AFO treatment has been showed in children with spastic CP and decreased A-Fdf ROM, although this tendon extensibility was suggested to be overestimated due to the used measurement methods [109]. Studies focusing on stretching exercises in children with CP as

well as in healthy volunteers did not find indications for increased tendon extensibility, but did find indications of reduced GAS muscle belly stiffness (i.e. calculated as the slope from dynamometer torque – elongation curves) [123, 124]. The presumed reduction of muscle belly stiffness was suggested to be caused by altered/more compliant intra/extra-muscular connective tissues [123, 124] as strain at fascicles was increased at maximal A-Fdf ROM measurements [124].

In children with spastic CP, it is suggested for hamstrings that their muscle stiffness is increased compared to typical developing children due to an increased amount of connective tissues in these muscles [125]. It is conceivable that quantity of intramuscular connective tissues increases to protect muscle tissue, for example to protect sarcomeres from being overstretched as there have been found some indications that they are longer than in typical developing children [125]. Whether this also applies to the GAS is unknown. The amount of connective tissues are considered to be variable in different muscles [126]. In upper limb muscles (tested in m. flexor carpi ulnaris), only an increase of connective tissue around intramuscular neurovascular structures (i.e. tertiary perimysium) penetrating the muscle in children with CP compared to typical developed subjects was found [126]. This tissue may interact mechanically with extra-muscular connective tissues and from that muscle stiffness is considered to be enhanced in children with CP [126]. If strain applied to the muscle is able to adapt the stiffness of tertiary perimysium and extra-muscular connective tissues, this is an interesting side effect the KAFO as stiffness of the GAS possibly may be reduced after treatment. However, if muscle tissue has to be protected for overstretching and stiffness of intramuscular tissue would be reduced by KAFO treatment, this would be not eligible. Further research should reveal whether wearing a KAFO affects GAS intra- and/or extra-muscular connective tissues and whether this results in injuries on GAS.

Expected effects of KAFO treatment on gait

Besides quantifying effects of KAFO treatment on A-Fdf ROM, this thesis also studied effects of changed A-Fdf ROM on gait. The effects of changes in A-Fdf ROM, as assessed by dynamometry on gait, were investigated in a subgroup of participants in the KAFO study. Although A-Fdf ROM did not change over time on group level, there were individual fluctuations in A-Fdf ROM over time. These individual changes were expected to be correlated with ankle-foot angle in mid stance of gait. However, results in chapter 5 showed that not the ankle-foot angle, but rather knee angle in gait did change if A-Fdf ROM measured at 4Nm dorsiflexion moment was altered. These results indicate that equinus gait may not be prevented even when A-Fdf ROM is unaltered. This may be caused by the effects of myofascial force transmissions [12, 107].

If A-Fdf ROM is reduced and the ankle-foot angle in stance phase of gait is unaltered, the higher strains on plantar flexors may be transferred to knee flexors. Consequently, knee extension in gait may be limited. Children walking with knee flexion are at risk for knee and hip contractures [15]. If an increase in A-Fdf ROM leads to increased knee extension in gait, then knee contractures may be prevented. Further research should verify effects of myofascial force transmission in gait when A-Fdf ROM is changed. Note that since KAFO treatment is not suitable yet to increase the A-Fdf ROM, other treatment methods should be applied for such studies.

CONCLUSIONS

Based on the data presented, it is concluded that effects of wearing a KAFO at rest as investigated in this thesis are not beneficial in preventing reduction of A-Fdf ROM at least with limited wearing times due to poor tolerance. The mechanism which causes complaints and subsequent poor tolerance are unclear. Prevention of reduction in A-Fdf ROM will be helpful in preventing deterioration of gait by progressive knee flexion in children with a gait pattern characterized by increased knee flexion in the stance phase.

To improve tolerance and wearing time, a design of a KAFO allowing 20 degrees fixed knee flexion with an ankle dorsiflexion spring may be a solution. The joints of the hind- and midfoot need to be stabilized to apply sufficient strain onto the GAS. Whether a KAFO with a modified design can be effective in preventing reduction in A-Fdf ROM is unknown. Future studies testing new KAFO designs, should include objective control of wearing time.

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SUMMARY

SUMMARY

Children with spastic cerebral palsy (CP) often develop contractures in joints due to muscle shortening or increased muscle stiffness. This may lead to limitations in joint range of motion (ROM). The most common contracture developing in children with CP is the reduction of ankle-foot dorsiflexion (A-Fdf) ROM (measured with extended knees) due to a shortened or stiffer m. gastrocnemius (GAS). The reduced dorsiflexion ROM results in an impaired gait. In particular children walking with excessive ankle-foot plantar flexion and flexed knees show decreased A-Fdf ROM. A knee-ankle-foot orthosis (KAFO) worn at rest, which includes ankle and knee fixation to apply strain on the GAS, is commonly prescribed in clinical care. It is expected that GAS length can be maintained or even increased by the strain because a muscle may be able to adapt its optimum length to the joint position in which the muscle is frequently active. However, very little is known regarding the efficacy of wearing a KAFO at rest and whether the assumptions regarding the underlying working mechanisms are correct. The primary aim of this thesis is to quantify potential effects of treatment with knee-ankle-foot orthoses over time in children with spastic CP. In addition, we aimed 1) to investigate whether parent reported KAFO wearing time can be considered as a valid indicator and 2) to assess effects of affected A-Fdf ROM on gait kinematics in children with CP walking with plantar flexion in the ankle and flexed knees. The aims are discussed in chapter 1.

Chapter 2 describes the protocol of a single blinded randomized controlled trial investigating the efficacy of wearing KAFO's in children with spastic CP to prevent a decrease in A-Fdf ROM. It was aimed to follow three groups of children with spastic CP for one year. One group was treated with a static KAFO (fixed knee at 180° extension and fixed ankle at 0° dorsiflexion) and usual care and one group was treated with a dynamic KAFO (fixed knee at 180° extension and a dynamic ankle applied with an Ultraflex® power unit) and usual care. The third group was included as a control group and received usual care only (physical therapy, manual stretching). KAFO's had to be worn for at least 6h every other night. For all children participating, KAFO treatment to prevent a decrease in A-Fdf ROM was indicated because they were at risk for reduction of A-Fdf ROM due to their medical history. At baseline and after 3, 6, 9 and 12 months, A-Fdf ROM was measured using a custom designed hand-held dynamometer. In addition, measurements to obtain information about gait kinematics, gross motor function, wearing time and complaints were performed. In a subgroup of patients, information about morphological parameters was collected using a 3D imaging technique. Results of morphological measurements are not presented in this thesis.

Chapter 3 describes results of the randomized controlled trial. 28 children (15 in the dynamic KAFO group and 13 in control group) with spastic CP and an age between 4 and 16 years old participated in the study. The static KAFO group had to be removed from the study design after the inclusion of some participants as they were not able to wear the KAFO because they experienced too much pain during wearing. Regarding the comparison between the control group and dynamic KAFO group, no effect was found in the decrease of A-Fdf ROM, gait kinematics and gross motor function. Other interesting outcomes were that: 1) the expected reduction of A-Fdf ROM over time in the control group was only statistically significant at 6 months, but not at 9 or 12 months, 2) 11 participants (4 in the experimental group and 7 in the control group) did not complete all five measurements, as they needed additional treatment, 3) wearing time of the dynamic KAFO was low and 4) all participants of the experimental group complained about pain and/or sleeping problems while wearing the KAFO. It was concluded that a dynamic KAFO was poorly tolerated and not beneficial in preventing a reduction in A-Fdf ROM, at least with limited use.

Chapter 4 presents the results of a study comparing the measurements of parent-reported wearing time (collected by questionnaires) and those of objectively measured wearing time (collected by temperature sensor-data-loggers attached to the KAFO's). Although mean difference between the two measured wearing times was low, there was a high inter-individual variation between parent-reported and objectively measured wearing time. Therefore, objective measurement methods to measure KAFO wearing time are recommended. Differences in parent-reported wearing time may bias results of efficacy studies and hinder the possibility to investigate the relation between wearing time and treatment efficacy.

The study described in chapter 5 investigated effects of changes in A-Fdf ROM on gait kinematics in 10 children with spastic CP, walking with knee flexion and ankle-foot plantar flexion in mid stance. Although an effect of KAFO treatment could not be shown, participants of the randomized controlled trial showed large individual variation in A-Fdf ROM over time. This study showed that when A-Fdf ROM changed over time, this resulted in changed knee extension in mid stance of gait, rather than a change in A-Fdf in mid stance of gait. This finding is likely due to the fact that the GAS (which length change causes decreased A-Fdf ROM) is a bi-articular muscle generating a moment over both ankle and knee. This study shows that effects of involved muscles have to play a role when selecting treatment options improving gait pattern of children with spastic CP. The effect of the GAS needs to be taken into account when treating patients with excessive ankle-foot plantar flexion and knee flexion.

Chapter 6 includes a discussion of the findings of the research as a whole. Based on the results of the different studies it is concluded that the lack of effect of the dynamic KAFO may be caused by the low KAFO wearing time due to low tolerance and/or by the inability of the KAFO to apply a sufficient high strain on the GAS. It is therefore suggested that that a KAFO with modified design will be more effective. A KAFO allowing 20° knee flexion is presumed to be better tolerated. However, to be able to assess whether such a KAFO strains the GAS sufficiently, requires further research. It should be evaluated whether the KAFO stabilizes the foot bones of hind- and midfoot sufficiently to allow application strain on the GAS, but also whether there are local stain amplifications which may be necessary for lengthening of the muscle fibers (i.e. to increase the number of sarcomeres in series). In addition, it is presumed that strength training during KAFO wearing is required to stimulate addition of sarcomeres in series within muscle fibers and to prevent atrophy (i.e. reduction in the physiological cross-sectional area). In children with spastic CP, the rate of addition of sarcomeres in series may be reduced compared to that in typical developing children. Moreover, physiological cross-sectional area may be reduced due to immobilization of the GAS due to fixed knee flexion while wearing a KAFO. Strength training may prevent this atrophy as well. The efficacy of treatment with a modified treatment needs to be tested while measuring wearing time using with objective measurement techniques. If the suggested modified KAFO is better tolerated and more effective than the KAFO tested in the present study, it may be a promising approach to improve A-Fdf ROM and to reduce knee flexion in gait in children walking with excessive knee flexion and ankle-foot plantar flexion.

SAMENVATTING

BEHANDELING MET KNIE-ENKEL-VOET ORTHESEN BIJ KINDEREN MET SPASTISCHE CEREBRALE PARESE

Kinderen met spastische cerebrale parese ontwikkelen vaak contracturen door spierverkortingen en/of toegenomen spierstijfheid. Dit kan leiden tot afname van de bewegingsmogelijkheden in de gewrichten. De meest voorkomende contractuur bij kinderen met cerebrale parese is de reductie van de enkel-voet dorsaal flexie (gemeten met gestrekte knie) door een verkorte of stijvere m. gastrocnemius. De gereduceerde dorsaal flexie resulteert in een afwijkend looppatroon. Vooral kinderen die lopen met toegenomen enkel-voet plantairflexie en knieflexie laten een afgenomen maximale enkel-voet dorsaalflexie zien. De behandelend arts kan een knie-enkel-voet orthese, gedragen in rust, voorschrijven om de knie en enkel in een positie te fixeren zodat de m. gastrocnemius wordt gerekt. Men verwacht dat de lengte van de m. gastrocnemius behouden of zelfs vergroot kan worden door rek, omdat een spier zijn optimale lengte kan aanpassen aan de lengte waarin de spier zich het meest bevindt. Echter, er is nog weinig bekend over de effectiviteit van deze behandeling en of de aannames betreffende het onderliggende werkingsmechanisme correct zijn. Het primaire doel van dit proefschrift is om de potentiële effecten van een behandeling met een knie-enkel-voet orthese te evalueren. Aanvullend wordt onderzocht of de door ouders gerapporteerde draagtijd van de knie-enkel-voet orthese een valide indicator is van de werkelijke draagtijd. Ook wordt bekeken wat de effecten zijn van een verminderde enkel-voet dorsaal flexie op het looppatroon van kinderen met cerebrale parese die lopen met toegenomen plantairflexie in de enkel en flexie in de knie. Deze doelen zijn beschreven in hoofdstuk 1.

Hoofdstuk 2 beschrijft het onderzoeksprotocol van een enkelvoudig geblindeerd, gerandomiseerd en gecontroleerd onderzoek dat kijkt naar de effectiviteit van het dragen van knie-enkel-voet orthesen door kinderen met spastische cerebrale parese om een afname van de maximale enkel-voet dorsaalflexie te voorkomen. Eén groep kinderen werd behandeld met een statische knie-enkel-voet orthese met een gefixeerde knie op 180° extensie en gefixeerde enkel op 0° dorsaalflexie (statische groep) en één groep werd behandeld met een dynamische knie-enkel-voet orthese met gefixeerde knie op 180° extensie en dynamische enkel uitgevoerd met een Ultraflex® power unit (dynamische groep). De knie-enkel-voet orthese behandeling was aanvullend op de reguliere behandeling (fysiotherapie, rekoefeningen). De derde groep werd geïncludeerd als een controle groep en ontving alleen de reguliere behandeling. De knie-enkel-voet orthese moest om de nacht 6 uur gedragen worden. De behandeling met knie-enkel-voet orthesen was voor alle deelnemers geïndiceerd omdat zij vanwege hun medische historie een verhoogd risico hadden om een afname van de enkel-voet dorsaalflexie te ontwikkelen.

Bij de start van het onderzoek en na 3, 6, 9 en 12 maanden werd de enkel-voet dorsaalflexie mogelijkheid gemeten met behulp van een speciaal ontwikkelde dynamometer. Daarnaast werden metingen verricht om informatie te verzamelen met betrekking tot de kinetica van het looppatroon, het grof motorisch functioneren, de draagtijd van de knie-enkel-voet orthese en eventuele klachten naar aanleiding van het dragen van de knie-enkel-voet orthese. Bij een deel van de deelnemers werd ook informatie verzameld over morfologische parameters van de m. gastrocnemius met behulp van een 3D echo. Resultaten van het onderzoek gericht op deze morfologische parameters worden niet gepresenteerd in dit proefschrift.

Hoofdstuk 3 beschrijft de resultaten van het enkelvoudig geblindeerde, gerandomiseerde en gecontroleerde onderzoek. 28 kinderen (15 in de dynamische groep en 13 in de controle groep) met spastische cerebrale parese en een leeftijd tussen 4 en 16 jaar oud hebben deelgenomen aan de studie. De statische groep is na de inclusie van enkele patiënten verder niet meegenomen in het onderzoek omdat de deelnemers door klachten (pijn, ongemak) niet in staat waren om de knie-enkel-voet orthese te dragen. Voor de controle en dynamische groep werd geen verschil gevonden in afname van de enkel-voet dorsaalflexie. Andere interessante uitkomsten waren dat:

1) er zoals verwacht een statistisch significante reductie van de maximale enkel-voet dorsaalflexie over de tijd was na 6 maanden, maar niet na 9 en 12 maanden.
2) 11 deelnemers (4 in de experimentele groep en 7 in de controle groep) niet alle 5 de metingen ondergingen omdat zij aanvullende therapie nodig hadden en de behandeling met knie-enkel-voet orthesen moesten staken.
3) de draagtijd van de dynamische knie-enkel-voet orthese laag was.
4) alle deelnemers van de experimentele groep klaagden over pijn en slaapproblemen wanneer zij de knie-enkel-voet orthese droegen.

Er werd geconcludeerd dat de knie-enkel-voet orthese slecht werd verdragen en dat deze, bij een gelimiteerde draagtijd, een reductie van de enkel-voet dorsaalflexie mogelijkheid niet kan voorkomen.

Hoofdstuk 4 presenteert de resultaten van een studie waarin door ouders gerapporteerde draagtijd van knie-enkel-voet orthesen (verzameld door middel van vragenlijsten) wordt vergeleken met een objectief gemeten draagtijd door middel van temperatuursensoren. Hoewel er weinig verschil was in de gemiddelde draagtijd gemeten met beide methoden, was er wel een grote individuele variatie voor het verschil tussen beide meetmethoden binnen de individuen.

Daarom wordt aangeraden een objectieve meetmethode te gebruiken om de draagtijd van knie-enkel-voet orthesen te meten in wetenschappelijk onderzoek naar de effectiviteit van zo'n behandeling. Afwijkingen in de door ouders gerapporteerde draagtijd kan de resultaten van onderzoek naar de effectiviteit van orthesen vertekenen.

De studie beschreven in hoofdstuk 5 onderzoekt het effect van verandering in de maximale enkel-voet dorsaalflexie op de kinematica van het lopen bij 10 kinderen met spastische cerebrale parese die lopen met knieflexie en enkel-voet plantairflexie in de middenstandsfase van het lopen. Hoewel er geen effect van behandeling met knie-enkel-voet orthesen aangetoond kon worden, was er wel grote individuele variatie in de verandering van enkel-voet dorsaalflexie bij de deelnemers van het eerder beschreven gerandomiseerde onderzoek. De resultaten beschreven in dit hoofdstuk lieten zien dat wanneer de maximale enkel-voet dorsaalflexie verbetert over de tijd, ook de knie extensie in de middenstandsfase van het lopen verbetert, terwijl er geen verandering plaats vindt in de enkel-voet dorsaalflexie in de middenstandsfase. Dit kan vermoedelijk worden verklaard door het bi-articulaire karakter van de m. gastrocnemius, waarbij een toegenomen lengte een verbeterde maximale enkel-voet dorsaalflexie, gemeten met gestrekte knie, toe laat. Deze studie laat zien dat bij een keuze voor behandeling voor het verbeteren van looppatronen ook rekening gehouden moet worden met het effect van de m. gastrocnemius op zowel de enkel als de knie.

Hoofdstuk 6 betreft een algemene discussie over de bevindingen van de studies beschreven in dit proefschrift. Op basis van de resultaten van de verschillende studies wordt geconcludeerd dat het uitblijven van effect van de dynamische knie-enkel-voet orthese waarschijnlijk veroorzaakt is door een lage draagtijd omdat de deelnemers de orthese niet konden verdragen. Een andere oorzaak zou kunnen zijn dat het dragen van de orthese niet leidde tot rek van de m. gastrocnemius. Mogelijk dat een knie-enkel-voet orthese met een ander design, bijvoorbeeld een design dat 20° knieflexie toe laat, beter verdragen wordt. Echter, of zo'n knie-enkel-voet orthese de m. gastrocnemius effectief kan rekken moet verder onderzocht worden. Er moet bekeken worden of de voetbeenderen van de midden en achtervoet gestabiliseerd kunnen blijven ten tijde van het dragen van een knie-enkel-voet orthese zodat de dorsaalflexie ook daadwerkelijk kan leiden tot rek van de m. gastrocnemius. Ook moet bekeken worden of rek in de m. gastrocnemius op specifieke plaatsen in de spier hoog moet zijn om de spiervezels te verlengen (door toename van het aantal sarcomeren in serie). Daarnaast zou krachttraining tijdens het dragen van een knie-enkel-voet orthese nodig kunnen zijn om de aanmaak van sarcomeren in serie te stimuleren. Bij kinderen met spastische cerebrale parese is de aanmaak van sarcomeren in serie mogelijk verminderd in vergelijking met kinderen zonder spastische cerebrale parese.

Bij het dragen van een knie-enkel-voet orthese zou daarnaast de fysiologische doorsnede af kunnen nemen vanwege een immobilisatie effect op de m. gastrocnemius doordat de knie gefixeerd wordt. Krachttraining zou, naast dat het de toename van het aantal sarcomeren in serie kan stimuleren, ook reductie van de fysiologische doorsnede van de spiervezel kunnen voorkomen.

De effectiviteit van behandeling met een aangepaste knie-enkel-voet orthese moet getest worden terwijl de draagtijd wordt gemeten met behulp van objectieve meettechnieken. Als de voorgestelde aangepaste knie-enkel-voetorthese beter verdragen wordt en meer effectief is dan de orthese onderzocht in dit proefschrift zou dit een hoopvolle methode kunnen zijn om de maximale enkel-voet dorsaalflexie te verbeteren en om knie flexie tijdens lopen te laten verminderen bij kinderen met spastische cerebrale parese.

DANKWOORD

WORD OF THANKS

DANKWOORD, WORD OF THANKS

Op de basischool vertelde één van mijn leraren: “Als je gaat promoveren schrijf je een boek over een onderwerp waar nog nooit iemand over geschreven heeft”. Ik was diep onder de indruk en vroeg mij af wat er zou gebeuren als iemand tegelijkertijd een zelfde soort boek zou schrijven. Had je dan gewoon pech en alles voor niets gedaan? Inmiddels begrijp ik dat het schrijven van een proefschrift draait om het uitvoeren en rapporteren van onderzoek. Dat onderzoek is uniek en daarmee ook het boek. Ik ben trots dat ik zo’n uniek onderzoek heb kunnen afronden en mijn proefschrift nu voor u ligt.

Het schrijven van mijn proefschrift ging gepaard met de nodige pieken en dalen. Gelukkig waren er vele mensen die de pieken met mij vierden en mij hielpen om uit de dalen op te klimmen. Graag wil ik iedereen die een bijdrage heeft geleverd aan mijn proefschrift (hoe klein ook) hartelijk bedanken. Een aantal mensen wil ik graag persoonlijk noemen.

Alle deelnemende kinderen en hun ouders

Zonder *deelnemende kinderen en hun ouders* had dit onderzoek simpelweg niet plaats kunnen vinden. Ik voel me vereerd dat jullie kostbare tijd en moeite in mijn onderzoek wilden steken. Jullie moeten al zo vaak in het ziekenhuis zijn, en nu kwamen jullie nog een paar keer extra voor metingen die soms wel een halve dag duurden. Sommigen van jullie moesten ook nog eens een spalk dragen tijdens het slapen, terwijl die spalk helemaal niet lekker zat. Toch waren jullie allemaal gemotiveerd en vrolijk. Ik hoop dat jullie genoten hebben van de films en van de uitjes naar Artis, Nemo en/of TunFun. Ik vond het fijn met jullie te werken. Ook dank aan de kinderen op wie ik mijn metingen mocht oefenen. Ik heb veel van jullie geleerd!

All participants and their parents

Without *participants and their parents,* this study could not have been performed. I feel honored that you invested your spars time in participating my study. It took you a lot of time to travel to the hospital and to undergo the measurements. In addition, some of you had to wear uncomfortable splints. However, you all did. Thank you! I also would like to thank the children on who we could practice the measurements. We learned a lot from you!

Promotoren en co-promotoren

Mijn promotie-traject is begonnen doordat ik het vertrouwen kreeg van mijn begeleiders om dit project uit te voeren.

Jules Becher, ondanks dat je altijd een enorm volle agenda had, kon ik altijd bij je aankloppen en kon je snel een plekje in je agenda voor mij vrij maken. Het was prettig je altijd aan te treffen in een vrolijke bui. Desalniettemin waren we altijd serieus aan het werk. Naast aandacht voor het werk had jij ook aandacht voor mij als persoon. Dankjewel voor je inzet en betrokkenheid!

Annet Dallmeijer, jij was mijn rots in de branding. Naast inhoudelijke begeleiding kon ik altijd bij je terecht voor een persoonlijk gesprek. Ik vond het heel fijn met je samen te werken. Bedankt voor alles!

Peter Huijing, ik heb diep respect voor jouw enorme hoeveelheid aan kennis en ervaring. Dank voor je inzet om die kennis aan mij over te dragen!

Richard Jaspers, ondanks dat jouw kantoor @VU op een paar minuten lopen afstand lag van mijn kantoor @VUmc, hield je regelmatig een vinger aan de pols door even te bellen of te emailen over hoe het er voor stond. Ik heb je leren kennen als een enorm bevlogen wetenschapper met veel oog voor detail. Ik heb veel van je kunnen leren. Bedankt voor je hulp en betrokkenheid!

Overige leden van de Splint onderzoeksgroep

Naast bovengenoemde personen zijn er nog vele mensen die een bijdrage hebben geleverd om het Splint onderzoek tot een succes te maken. Graag wil ik speciaal benoemen:

Petra van Kampen, dank dat je de samenwerking met *Groot Klimmendaal* in Arnhem hebt mogelijk gemaakt en ingevuld, en dat je mij hebt wegwijs gemaakt in het looplab. Dank ook aan je collega's die een bijdrage hebben geleverd aan onze samenwerking.

Viecuri medisch centrum, dank dat jullie wilden meewerken aan het vergroten van onze groep deelnemers.

In het begin *Karen Lagendijk* en later *Eline Bolster,* jullie hebben een grote bijdrage aan mijn onderzoek geleverd als onderzoeksassistent. Dank voor al jullie planwerk en het onderhouden van de contacten met deelnemers. Jullie waren onmisbaar!

Rogier Plas, Marieke Vervoort en *Bodil Oudshoorn,* dank voor jullie hulp en input bij het uitvoeren van de metingen. Het was prettig met jullie samenwerken. Bodil, ook bedankt voor je inzet bij het tot stand komen van hoofdstuk 4! Het was een leuke ervaring om je te mogen begeleiden als stagair. Dat laatste geldt ook voor *Guido Weide*. Ik ben trots dat ik co-auteur ben geworden van jouw artikel en vind het leuk dat ik je later nog eens tegen kwam in het VUmc als je metingen verrichtte voor je huidige onderzoek.

Orthopedisch instrumentmakers: mensen van *Heckert en van Lierop, Kamer orthopedie* en *OIM (vestigingen Noordwijkerhout en Arnhem)*, dank dat jullie de spalken die gebruikt werden voor ons onderzoek wilden maken.

Other members of the Splint researchgroep

Besides the above mention persons, a lot of other people helped me to finish this research. I would like to thank all colleagues at *St. Louis Children's Hospital* and *Pediatric Clinical Research Unit at the Department of Pediatrics at Washington University School of Medicine* for their cooperation and the warm welcome they gave me during my visits. I would like to thank specificly: *Janice Brunstrom-Hernandez*, thank you for giving us the possibility to collaborate with St. Louis Children's Hospital. It was impressive to see what you managed in St. Louis.

Kelly Moffat and Freda Branch, thank you for organizing all measurements and having contact with the participants in USA.

Kathy Herndon and Courtney Dunn, thank you for collecting study-data.

Ruben Hernandez, thank you for your assistance.

Orthotic and Prosthetic Lab Inc., thank your for producing the orthoses that were used in this study.

Mark DeHarde, thank you for your support and advice.

Collega's

Ik had vele *collega's* bij VUmc, EMGO en MOVE. Jaren lang zat ik in de kelder van de polikliniek, bij de afdeling revalidatiegeneeskunde van VUmc. Bijna iedereen kende elkaar daar. Het was een prettige plek om mijn onderzoek te mogen uitvoeren. Dank voor alle gezelligheid, gezamenlijke lunches, werkbesprekingen, adviezen, medewerking en getoonde interesse. Een speciaal woord van dank aan de collega's die mij steunden in mindere tijden met een bezoek, goed gesprek, kaartje en/of cadeautje. Ik heb dit heel erg gewaardeerd. Een aantal mensen wil ik graag nog in het bijzonder noemen:

Kamergenoten van PK-1Y158, dank dat ik met jullie onze kamer mocht delen. Op onze kamer was er altijd tijd voor het delen van ervaringen, maar werd er ook hard en serieus gewerkt. Dank voor jullie interesse, luisterend oor, tips en adviezen.

Leontien van Wely, met jou heb ik deze kamer 4,5 lang mogen delen. Wij hoorden bij het meubilair. Het was wel even wennen toen daar een einde aan kwam. Bedankt voor de fijne tijd!

Secretariaat, back-office en technische ondersteuning, Met jullie had ik regelmatig contact omdat ik weer eens 'iets' nodig had. Vaak volgde een bijklets momentje. Dank voor jullie ondersteuning en interesse.

Caroline Doorenbosch, met jou heb ik vaak op de rode banken plaats genomen om mijn hart te luchten. De gesprekken waren altijd waardevol en hielpen om weer verder te kunnen. Bedankt daarvoor!
Jaap Harlaar, dank voor je adviezen en voor je bijdrage aan hoofdstuk 5! Dank ook dat je in mijn opposite wilt plaatsnemen.
Menno Bénard, jij was degene die mij wegwijs kon maken in alle meetapparatuur en bijbehorende protocollen. Ook hebben we veel gediscussieerd over de gebruikte software en meetmethodes. Dank voor de fijne samenwerking!
Helga Haberfehlner, met jou kreeg ik er niet alleen een collega bij, maar ook een vriendin. Het is fijn om met jou ervaringen te kunnen uitwisselen met betrekking tot ons onderzoek, maar ook gezellig uit eten te gaan. Ik ben heel blij dat jij mij straks als paranimf bijstaat op het podium!

Promotiecommissie

De verdediging van mijn proefschrift kan niet plaatsvinden zonder promotiecommissie. Graag wil ik de leden van de *oppositie* bedanken voor hun deelname. In het bijzonder wil ik de leden van de *leescommissie* (*prof. dr. Gemke, prof. dr. van Bennekom, prof. dr. Nollet, dr. Buizer* en *dr. Meijer*) bedanken voor het lezen en beoordelen van mijn proefschrift.

NCDR

Sinds 3,5 mag ik werken voor *NCDR*. Vanaf het begin van mijn aanstelling stelden jullie je enorm flexibel op, waardoor ik de kans heb gekregen om mijn proefschrift af te ronden. Dank daarvoor, en voor de goede samenwerking!

Vrienden en familie

Naast werken aan mijn proefschrift kon ik de laatste jaren gelukkig ook nog mijn tijd besteden aan *vrienden en familie*. Dank voor alle interesse die jullie toonden in mijn werk en voor de leuke, gezellige en ontspannen momenten. Ook dank voor het luisteren naar mijn soms minder leuke verhalen en de hulp en steun die jullie gegeven hebben. Ik vind het leuk dat jullie nu een glimp kunnen opvangen van waar ik de afgelopen 8 jaren mee bezig ben geweest.
Scouting- en roeimaatjes, dank voor de geboden afleiding tijdens onze activiteiten. *Danita de Baat,* jij wilde mijn promotie zo graag meemaken. Het is niet te beschrijven wat jij en jouw familie moeten doormaken. Gelukkig strijden je ouders en zussen voor het beste voor jou.
Bianca Plak, dankjewel voor het opmaken van mijn proefschrift en het ontwerpen van de omslag en het Splint-logo!
Ineke Janssen, dank dat jij mijn verdediging wilt vastleggen op de gevoelige plaat!

Gerard Maas, wat ben ik blij dat ik nog aan jou kon vertellen dat jij 6 juli 2017 je toga aan mag trekken. Ik ben heel benieuwd hoe hij je staat! Dank voor je hulp en adviezen bij het afronden van mijn proefschrift.

Paul Roos en *Tess van de Wal*, als zwager en 'vriendin van' hebben jullie veel meegekregen van de hordes die ik moest nemen om tot dit punt te komen. Dank voor jullie medeleven en aanmoediging.

Bas Maas, al zien we elkaar niet zo vaak, ik zou je niet willen missen als broer! Ook jij bedankt voor je getoonde interesse.

Ankie Roos-Maas, jij hebt aan één woord genoeg om mij te begrijpen. Het is heel fijn dat jij mij zus bent en dat jij mij bijstaat als paranimf tijdens mijn verdediging.

Els Maas-Janssen, mama, als er iemand altijd voor mij klaar staat, dan ben jij het wel. Zelfs als je het zelf moeilijk hebt. Wat ben ik trots op jou om wie je bent en waar je staat, en wat ben ik blij dat jij mijn moeder bent.

Bart Maas, papa, het is een gemis dat jij er niet meer bent. Gelukkig weet ik dat jij trots op me was. Je bent er straks bij in mijn hart.

ABOUT THE AUTHOR

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José (Josina Catharina) Maas was born on the 26th of September 1982 in Eindhoven, the Netherlands. She finished elementary school in 1995 at Basisschool De Windroos in Geldrop and secondary school in 2000 at Strabrecht College in Geldrop. In 2000-2004 she studied Human Kinetic Technology at The Hague University in The Hague and attained her Bachelor of Engineering degree with a thesis focusing on the effect of lower flexibility of joints on risk of back injuries in the cricket fast bowler. She also completed a study focusing on the effects of wedges under the horse hoof on muscle tension of the m. vastus medialis for an internship at the department of Veterinary Medicine at Utrecht University in Utrecht. From 2005 to 2006, José participated on voluntary basis on projects of the Expertise Center of Human Kinetic Technology in The Hague (designing a coupling between wheelchairs) and the department of Rehabilitation Medicine of the Academic Medical Center Amsterdam (investigating lower extremity dynamics of walking in neuropathic diabetic patients wearing a forefoot offloading shoe). In 2006 she started with the (pre)master Human Movement Sciences at the VU University in Amsterdam. She performed a study regarding mechanical efficacy and perceived discomfort during arm crank ergometry at the Swiss Paraplegic Center in Nottwil, Switzerland and she performed a study regarding outlining ankle-foot orthosis in children with cerebral palsy at the department of Rehabilitation Medicine of the VU University Medical Center in Amsterdam. With this latest study, José was nominated for the ISPO-NL graduation price 2009. Upon completing her Master's degree in 2009, José started with her PhD-trajectory at the department of Rehabilitation Medicine of the VU University Medical Center in Amsterdam. She joined the Splint study group investigating the efficacy of knee-ankle-foot orthosis in children with spastic cerebral palsy. Currently, José is working at the National Cardiovascular Data Registry (NCDR) in Utrecht.

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Children with spastic cerebral palsy often develop reduction in ankle-foot dorsiflexion range of motion due to a shortened or stiffer m. gastrocnemius. This results in impaired gait. A knee-ankle-foot orthosis worn at rest is commonly prescribed in clinical care. Very little is known regarding the efficacy of wearing a knee-ankle-foot orthosis at rest and whether the assumptions regarding the underlying working mechanisms are correct. The aim of this thesis is to quantify potential effects of treatment with knee-ankle-foot orthoses over time in children with spastic cerebral palsy. In addition, it is aimed to investigate whether parent reported knee-ankle-foot orthosis wearing time can be considered as a valid indicator and it is aimed to assess effects of affected ankle-foot dorsiflexion range of motion on gait kinematics in children with cerebral palsy.

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