The sooner the better?!

Providing ankle-foot orthoses
in the rehabilitation after stroke

Corien Nikamp-Simons

THE SOONER THE BETTER?!

PROVIDING ANKLE-FOOT ORTHOSES IN THE REHABILITATION AFTER STROKE

Corien Nikamp-Simons

Address of correspondence

Corien Nikamp-Simons
Roessingh Research and Development
PO Box 310
7500 AH Enschede
The Netherlands
+31 (0)88 087 5777
c.nikamp@rrd.nl

The work in this thesis was supported by grants from the Ministry of Health, Welfare and Sport (Innovatiecentrum) and Stichting Hulpfonds Het Roessingh, Enschede, the Netherlands. The ankle-foot orthoses used in this thesis were provided by Basko Healthcare, Zaandam, the Netherlands.

The publication of this thesis was generously supported by:

Basko Healthcare/D.H. Heijne Stichting

Cover by Kelly Wichers Schreur, Studio KWS

Print by Gildeprint - the Netherlands

ISBN: 978-90-365-4747-5

DOI: 10.3990/1.9789036547475

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PROEFSCHRIFT

ter verkrijging van
de graad van doctor aan de Universiteit Twente,
op gezag van de rector magnificus,
prof. dr. T.T.M. Palstra,
volgens besluit van het College voor Promoties
in het openbaar te verdedigen
op woensdag 29 mei 2019 om 16.45 uur

door

Corien Diana Maria Nikamp-Simons
geboren op 14 mei 1984
te Heeten

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Chapter 1

General introduction

Approximately 43.000 people are affected by a first stroke in the Netherlands every year, which equates to around 2,6 per 1.000 inhabitants.¹ In 2016, more than 320.000 people in the Netherlands lived with the consequences of stroke. Strokes are responsible for 25% of the mortality from cardiovascular diseases,¹ are one of the most important causes of mortality in general and is the most important cause of disability in the Netherlands.² In stroke, the blood circulation in the brain is affected, being either ischemic (approximately 80%) or hemorrhagic (around 20%).² The effects can vary widely, depending on the location of the lesion. A combination of motor, sensory, cognitive and emotional impairments are often present, leading to limitations in performing activities of daily living.³

Post-stroke gait dysfunction is among the most investigated neurological gait disorders.⁴ Initial walking function is limited in approximately two-third of the patients with acute stroke and regaining walking ability is one of the major goals in rehabilitation.⁵ Insufficient foot-clearance is an important alteration in the gait pattern often seen following stroke. This can be caused by decreased dorsiflexion at the ankle, or decreased flexion of the knee and/or hip. At the ankle level the limited flexion is often referred to as a “foot-drop”, categorized as “an inability to dorsiflex the foot, with or without excessive inversion” and is most commonly caused by weakness in the dorsiflexors (and evertors) and/or overactivity in the plantar flexors (and invertors).⁶ Drop-foot is estimated to be present in 20-30% of people with a stroke.⁶ Together with decreased knee⁷⁻⁹ and hip flexion¹⁰, drop-foot causes foot-clearance problems during swing phase and also affects initial contact at the start of the stance phase. Insufficient foot-clearance is associated with high risks for stumbling and falling.¹¹

Ankle-foot orthoses (AFOs) are commonly used to correct foot-drop after stroke.^{12,13} They can provide mediolateral stability in stance, facilitate toe-clearance in swing phase and promote heel strike.¹⁴ Many different AFO-designs are available, divided into prefabricated or so-called off-the-shelf orthoses and custom-made AFOs. Furthermore, three categories can be defined: passive, semi-active and active AFOs.¹⁵ Passive AFOs do not consist of any electronic elements or power source. Mechanical elements like springs or dampers to control ankle-foot motion during gait may be included. Semi-active AFOs use computer control to vary flexibility of the ankle joint, while active AFOs include a power source, control system, sensors and actuators.¹⁵ Of these three categories, passive AFOs are most commonly used in daily clinical practice because of the compactness, durability and simple design.^{15,16} Currently, semi-active and active orthoses are mainly used within research-projects and are not general available for patient care. Within the passive AFOs, two different types can be distinguished: non-articulated and articulated. The non-articulated AFOs are usually made of one piece, covering the dorsal aspect of the calf or the ventral part of the tibia, and the bottom of the foot. They are often made of lightweight polypropylene or polyethylene, and more recently also of carbon material. Articulated AFOs include an articulated ankle joint, with hinges, flexion stops and elements like springs or oil dampers to control stiffness.¹⁵ Overall, there is a large variability in designs and accompanying stiffness, from highly rigid

to more flexible AFOs.

There are many scientific studies on the effects of AFOs after stroke. Within these studies a variety of in- and exclusion criteria from the selected subjects are found. Furthermore, many different types of AFOs are studied and a broad range of outcome measures are included. These outcome measures vary from kinematics, kinetics and EMG to effects on balance, clinical scales, falls and fear of falling. Positive effects of AFOs after stroke are reported on aspects of mobility and balance,¹⁷ ankle kinematics,^{16,18} and walking speed.^{17,19} Furthermore, self-confidence²⁰ and fear of falling²¹ are reported to improve because of AFO-use. However, within the existing literature on effects of AFOs after stroke, there seems to be a gap between the patients that are included in trials, and the patients for which AFOs are considered necessary in daily clinical practice. Important aspects in the included subjects within the trials that study the effects of AFOs hinder the transfer of scientific knowledge into the clinic. Primarily, the majority of the studies included subjects already provided with AFOs in daily life.¹⁷ In most studies, effects of walking with and without AFO were compared. Since these subjects were already accustomed to walking with AFOs, these studies actually measured the effect of removing an AFO, instead of the effect of providing one. The latter is relevant for clinical practice, in which patients directly following a stroke have no experience in walking with AFOs. Secondly, most subjects included in the research on AFOs after stroke were able to walk independently, with or without AFO.¹⁷ This implies that more severely affected subjects, the ones that might benefit from AFO-use the most (and are often admitted into the clinic) are not well studied. Thirdly, transfer from scientific literature to clinical practice may be limited because of “a misalignment between the timing of randomized controlled trials and the real-world delivery of stroke rehabilitation”.²² For studies on effects of AFOs, this appears to be the case since previously conducted studies mainly included chronic patients,¹⁷ while AFOs are often considered in the more (sub-)acute phase. Fourthly, most studies assessed the immediate or short-term effects and effects were assessed within one or two sessions.^{16–18,23} As a result, long-term studies are limited. This is in contrast to clinical practice, in which AFOs are often prescribed for long-term use.¹⁹ In a systematic review, Tyson et al. concluded that studies assessing immediate or short-term effects are important, as they show that an AFO works. However, the information is insufficient and therefore does not fully inform clinicians in daily practice.¹⁷ Important questions like which type of AFO should be prescribed for a specific patient, the optimal time to prescribe an AFO and for how long should it be used remains unanswered in scientific literature^{17,23} and are pointed out as implications for further research.²⁴

Guidelines on stroke management also lack clear information on when to start with AFOs and for how long.^{24–27} A best practice statement on AFO-use states that AFOs may help to avoid development of abnormal patterns, or prevent such patterns becoming established.²⁵ It was recommended that they should be considered for early intervention rather than as a last resort. However, guidelines and literature also state that there is insufficient evidence to determine the impact of AFOs on long-term outcomes.^{16,26} This also accounts

for the long-term effects of AFO-use early after stroke. It was questioned whether early orthotic interventions would affect the time to require rehabilitation milestones and/or discharge dates.²⁴ In contrast to the possible beneficial effects of early AFO-use on reducing the development of abnormal gait patterns, or on the functional benefits resulting in earlier discharge, possible negative effects of AFOs are also found in literature. They are mentioned in relation to aesthetics and comfort, which impacts on compliance and satisfaction.^{6,21} One of the main reasons why clinicians are reluctant to use AFOs early after stroke is that AFOs are suggested to induce muscle weakness, especially of the tibialis anterior muscle,^{14,28–30} thereby worsening the existing loss of strength, delaying recovery and prolonging dependence on AFOs.

General aim and the EVOLUTIONS-project

The aforementioned considerations show that there are a lack of studies examining the effects of AFOs early after stroke. This lack includes studying the effects of AFOs in more severely affected subjects and in subjects that have no experience in previous AFO-use. Furthermore, there are a lack of studies including long-term effects and studies focusing on timing of AFO-provision in rehabilitation after stroke. This results in insufficient evidence on the use of AFOs and AFO-provision after stroke in clinical practice.

The general aim of this thesis is to increase the understanding of the effects of providing AFOs early after stroke. Therefore, the **EVOLUTIONS**-project (**EV**idence based applications **f**or **L**ower extremity **f**unction **I**n **S**troke) was conducted, a randomized controlled trial in which the effects of AFO-provision on two different time points in the rehabilitation post-stroke were studied.

Within the EVOLUTIONS-project, subjects with and without independent walking ability were included within six weeks after stroke and randomized for the timing of AFO-provision. The early group was provided with AFOs at inclusion of the study (in week 1), while subjects in the delayed group did not use an AFO in the first period of the study, as they were provided with AFOs eight weeks later (e.g. in week 9 of the study). All subjects were provided with one of three commonly used types of off-the-shelf, non-articulated, posterior leaf design polyethylene or polypropylene AFOs: flexible, semi-rigid or rigid, see Figure 1.1. The type of AFO was chosen in week 1 (early group) or week 9 (delayed group), according to a custom-developed protocol based on the prerequisites of gait.³¹ Within the protocol, it was determined whether the main walking problem was related to stability in stance, foot-clearance in swing, and/or prepositioning at heel strike, see Figure 1.2.

AFO-fitting was performed by a licensed orthotist, and the effect of the prescribed AFO was verified and confirmed by the responsible physician. The effects of AFO-provision were studied up to 17 weeks with (bi)weekly intervals. Follow-up measurements up to 26 and 52 weeks were included, see Figure 1.3. The effects were studied by including a wide range of outcome measures, mainly on the level of “body functions and structures” and “activities” from the International Classification of Functioning, Disability and Health (ICF) framework

Figure 1.1: Three types of AFOs used in the study.

From left to right: 1) polyethylene, non-articulated AFO with two crossed posterior steels and open heel, most flexible type; 2) semi-rigid, polypropylene, non-articulated AFO with two crossed posterior steels and open heel, larger posterior steel compared to type 1; 3) rigid, polypropylene, non-articulated AFO with closed posterior steel and closed heel.

of the World Health Organization.³²

Functional tests related to balance, walking and activities of daily living (like turning, walking stairs) were included. Based on previous literature (which mainly included chronic stroke patients already using an AFO), we expected that on a functional level, early AFO-provision would also be beneficial for patients after stroke without previous AFOexperience. It was unknown as to whether early AFO-provision would also be beneficial on the ICF-level of “body functions and structures”. On the one hand, AFOs were expected to improve ankle kinematics by improving drop-foot. Early AFO-provision therefore was expected to positively affect proximal joints as well, and decrease the development of possible compensatory walking patterns. On the other hand, the literature suggested increase in muscle weakness due to AFO-use, which could impede recovery. To study these aspects, 3D gait analysis and muscle electromyography measurements were included. Another aspect related to AFOs are falls, which are commonly reported after stroke. AFOs are often provided to improve safety and walking after stroke and therefore might be beneficial in reducing falls. However, the effect of AFOs on falls after stroke is unknown. Therefore, a diary to register (near) falls was included in the outcome measurements.

Summarizing, this thesis aims to answer the following research questions regarding the provision of AFOs after stroke:

With respect to outcomes on balance, walking and activities of daily living:

- What are the effects of actual AFO-provision, and does timing of AFO-provision (early or delayed) influences these effects?
- What are the long-term effects of providing AFOs at different moments (early or delayed) after stroke, and does the timing of AFO-provision influence the effects?

Figure 1.2: Protocol used for selecting the type of AFO.

Figure 1.3: Overview of measurements performed during the randomized controlled trial. Measurements performed by the early group (left), provided with an AFO in study week 1, and performed by the delayed group (right), provided with an AFO in study week 9 are shown. In the week of AFO-provision, the functional tests were performed without AFO as a baseline-measurement. After provision, functional tests were performed with AFO, and gait analysis was performed with and without AFO.

With respect to outcomes on gait kinematics:

- What are the short-term kinematic effects of AFO-provision, and does the timing of AFO-provision (early or delayed) influence these effects?
- What are the long-term kinematic effects of AFO-provision at different moments (early or delayed) after stroke, and is there a difference in the pattern of recovery over time in terms of kinematics between both groups?

With respect to outcomes on muscle activity:

- What is the effects of AFO-use on tibialis anterior muscle activity within a single measurement session?
- What is the long-term effects of AFO-use on muscle activity of the tibialis anterior muscle, and does the timing of AFO-provision (early or delayed) influence these effects?

With respect to outcomes related to falls:

- What are the effects of AFO-provision on the occurrence and circumstances of falls and near falls in patients after stroke?

Outline of the thesis

The results of the randomized controlled trial are reported in this thesis. In **chapter 2**, the effect of the actual AFO-provision is described, including outcome measures related to balance, walking and activities of daily living (like turning and walking stairs). Subsequently, **chapter 3** describes the effects of early or delayed AFO-provision on a functional level in the long-term, over a period of 26 weeks. Furthermore, in this chapter survival analysis was used to study whether clinically relevant cut-off points related to independence and safety of walking were affected by a different timing of AFO-provision post-stroke. In analogy of **chapter 2**, **chapter 4** describes the short-term effects of the actual AFO-provision, including 3D gait-analysis in one single session. Kinematic and spatiotemporal parameters were measured to describe movement of the affected ankle and foot, knee, hip and pelvis. In addition, the effects of timing on AFO-provision were studied. In **chapter 5**, the kinematic effects of early versus delayed AFO-provision in week 26 of the study are described. This chapter addresses the topic as to whether early AFO-provision decreases the development of compensatory movements in proximal joints, when foot-drop is limited by AFO-use early after stroke. **Chapter 6** addresses the effect of AFO-provision on muscle activity of the tibialis anterior. Both the effects over a period of 26 weeks, as well as the effects of timing of AFO-provision (early or delayed) were studied. **Chapter 7** describes the effects of AFO-provision on the occurrence and circumstances of falls and near falls after stroke using diaries. This thesis concludes with a summary and general discussion of the results in **chapter 8**. This includes the implications of the present thesis for daily clinical practice.

Chapter 2

Early or delayed provision of an ankle-foot orthosis in patients with acute and subacute stroke: A randomized controlled trial

Corien DM Nikamp
Jaap H Buurke
Job van der Palen
Hermie J Hermens
Johan S Rietman

Published in Clinical Rehabilitation 2017;31(6):798-808.

ABSTRACT

Objective 1) To study the effects of providing ankle-foot orthoses (AFOs) in subjects with (sub)acute stroke; and 2) to study whether the point in time at which an AFO is provided post-stroke (early or delayed), influences these effects.

Design Randomized controlled trial.

Setting Rehabilitation centre.

Subjects Unilateral hemiparetic stroke subjects with indication for use of an AFO and maximal six weeks post-stroke.

Interventions Subjects were randomly assigned to: early provision (at inclusion; week 1) or delayed provision (eight weeks later; week 9).

Outcome measures 10-meter walk test, 6-minute walk test, Timed Up and Go Test, stairs test, Functional Ambulation Categories, Berg Balance Scale, Rivermead Mobility Index and Barthel Index; assessed in week 1, 3, 9 and 11.

Results A total of 33 subjects were randomized (16 early, 17 delayed). Positive effects of AFOs were found two weeks after provision, both when provided early (significant effects on all outcomes) or delayed (Berg Balance Scale $p=0.011$, Functional Ambulation Categories $p=0.008$, 6-minute walk test $p=0.005$, Timed Up and Go Test $p=0.028$). Comparing effects after early and delayed provision showed that early provision resulted in increased levels of improvement on Berg Balance Scale (+5.1 points, $p=0.002$), Barthel Index (+1.9 points, $p=0.002$) and non-significant improvements on 10-Meter walk test (+0.14m/s, $p=0.093$) and Timed Up and Go Test (-5.4 sec, $p=0.087$), compared to delayed provision.

Conclusions We found positive effects of providing AFOs in (sub)acute stroke subjects that had not used these orthoses before.

INTRODUCTION

Ankle-foot orthoses (AFOs) are often applied during stroke rehabilitation and may provide mediolateral stability in stance, facilitate toe-clearance in swing, and promote heel strike.¹⁴ Despite the frequent application of AFOs, there is little scientific evidence available to guide provision of AFOs early after stroke. The majority of trials studying the effects of AFOs included subjects that were already using their orthosis in everyday life and subjects were measured while walking both with and without the orthosis.^{20,33–37} In this situation, the effect of removing the orthosis is tested, rather than effects of providing AFOs, which does not completely reflect the kind of knowledge clinicians need. To our knowledge, no previous studies looked at the effects of the actual provision of AFOs itself on functional outcome measures early after stroke.

Another limitation in the current body of evidence with respect to clinical practice is that “a misalignment between timing of RCTs (randomized controlled trials) and the real-world delivery of stroke rehabilitation may be an important aspect of the evidence base that limits its translation to clinical practice”.²² Many previously conducted studies included chronic stroke patients,¹⁷ which does not correspond to daily practice where AFOs are often prescribed in the (sub)acute phase.

Another important consideration in studying the literature of use of AFOs after stroke is that effects in more severely affected subjects are not well studied, since most studies included subjects that were able to walk independently with or without walking aid.¹⁷ Only four studies included subjects with no walking ability in everyday life.^{34,38–40}

The aforementioned considerations show that there is a lack of studies examining the effects of the provision of AFOs and the timing of this provision to patients in their early rehabilitation post-stroke.¹⁷ Therefore, we conducted an explorative randomized controlled trial to study the effects of providing AFOs on two different time points post-stroke. Both patients with and without independent walking ability were included. The primary aim of the current article was to investigate the effects of the actual provision of AFOs on balance, walking, and activities of daily life. The secondary aim was to study whether the point in time (early or delayed) at which the AFO was provided post-stroke influenced these effects. We hypothesised that early provision is more beneficial.

METHODS

We designed a single centre, randomized, controlled, parallel group study. The study was approved by the Medical Ethical Committee Twente and registered in the ‘Netherlands Trial Register’, number NTR1930. All subjects provided written informed consent. Subjects were allocated by an independent person, using stratified block randomization with sealed envelopes (strata based on Functional Ambulation Categories (FAC) levels⁴¹ 0-2 vs. 3-5, en-

velopes filled in blocks of four with a ratio 1:1), to either: (1) AFO-provision at inclusion in the study, in study week 1 (early group); or (2) delayed AFO-provision after eight weeks, in study week 9 (delayed group). Effects were assessed two weeks after provision, in study weeks 3 and 11 for the early and delayed group, respectively.

Baseline measurements were performed without orthosis in week 1 for the early group (Figure 2.1). Subjects were provided with the AFO after these measurements and effect of the provision was studied two weeks later, in week 3. Natural recovery is expected in this period and this will interfere with the effects of orthosis provision. Therefore, the delayed group (not using an AFO in this period) was also measured in weeks 1 and 3 and can serve as a control group in this period. In week 9 the delayed group was measured without AFO and subjects were provided with the orthosis after the measurements. Two weeks later, in week 11, the effect of the provision was measured. In weeks 9 and 11 the early group (already provided with an AFO) was also measured as a reference. Besides the different timing of the provision of the orthosis, all subjects received usual care from experienced physiotherapists according to the Dutch guidelines for physiotherapy after stroke.⁴²

Subjects

Subjects were recruited by the main researcher between December 2009 and March 2014 from the Roessingh, Centre for Rehabilitation in Enschede, the Netherlands. Inclusion criteria were: (1) unilateral ischemic or hemorrhagic stroke leading to hemiparesis (single and first-ever stroke or history of previous stroke with full physical recovery); (2) at least 18 years of age; (3) maximal six weeks post-stroke; (4) receiving inpatient rehabilitation care at inclusion; (5) able to follow simple verbal instructions; and (6) indication for use of an AFO (i.e. abnormal initial floor contact and/or problems with toe-clearance in swing and/or impaired ability to take bodyweight through the paretic lower limb in stance) determined by the treating rehabilitation physician and physiotherapist. Exclusion criteria were: (1) suffering from severe comprehensive aphasia or neglect; and (2) complicated medical history, such as cardiac, pulmonary, or orthopaedic disorders, that could interfere with testing.

Ankle-foot orthosis protocol

No standard practice for providing AFO regarding timing and type of orthosis is available in the Netherlands. Subjects were provided with one of three commonly used types of off-the-shelf, non-articulated, posterior leaf design, polyethylene, or polypropylene AFO: flexible, semi-rigid, or rigid (Basko Healthcare, Zaandam, the Netherlands), see Figure 2.2. All orthoses included a proximal calf strap. Fitting was performed by a licensed orthotist. Type of orthosis was chosen in week 1 (early group) or week 9 (delayed group) according to a custom-developed protocol based on the prerequisites of gait³¹ determining whether the main walking problems were related to stability in stance, foot clearance in swing, and/or prepositioning at heel strike (see Figure 2.3). In all subjects the effect of the prescribed AFO was verified and confirmed by the responsible physician.

Figure 2.1: CONSORT Flowchart.

Outcome measures

At inclusion, basic demographic data were recorded and subjects completed the Mini-Mental State Examination,⁴³ Erasmus MC modifications to the Nottingham Sensory Assessment, lower-limb part,⁴⁴ and the Motricity Index, lower-limb part.⁴⁵ The primary outcome measure was comfortable walking speed, assessed with the 10-metre walk test (10MWT).⁴⁶ Secondary, balance was assessed using the Berg Balance Scale (BBS),⁴⁷ walking ability with the 6-minute walk test (6MWT),⁴⁸ functional mobility with the Timed Up and Go Test (TUG)⁴⁹ and Stairs Test (ST),²⁰ and independence of walking with the FAC.⁴¹ The Rivermead Mobility Index (RMI)⁵⁰ and Barthel Index (BI)⁵¹ were used to assess mobility during activities of daily life.

All tests were administrated by trained research physiotherapists and measurements were performed at the rehabilitation centre. Blinding of the assessor to use of the orthosis or early or delayed provision was not possible. For all walk tests, subjects were allowed to

Figure 2.2: Three types of AFOs used in the study.

From left to right: 1) polyethylene, non-articulated AFO with two crossed posterior steels and open heel, most flexible type; 2) semi-rigid, polypropylene, non-articulated AFO with two crossed posterior steels and open heel, larger posterior steel compared to type 1; 3) rigid, polypropylene, non-articulated AFO with closed posterior steel and closed heel.

use their usual assistive device (cane or quad cane) and actual use was recorded. Changes in assistive devices between the measurements were allowed. All functional tests that included walking were only performed in case subjects could walk without physical support (minimum FAC level 3 required) at the time of the measurement.

Data analysis

A power calculation was not performed as data of previous studies measuring timing effects of providing ankle-foot orthoses early or later after stroke were not available. IBM SPSS Statistics version 19 (IBM SPSS Statistics, Chicago, USA) was used for data-analysis. Continuous data are presented as mean (standard deviation (SD)) or median (interquartile ranges (IQR)), as appropriate. The level of significance for all analyses was set at $p < 0.05$. In case walk tests could not be performed because $FAC < 3$, the 10MWT and 6MWT were set at 0.0 m/s and 0 m, respectively, while the TUG and ST were treated as missing values since using 0 seconds for these outcome measures would mean an infinite fast performance of the test. In order to answer the primary research question, the effects of AFOs were determined comparing differences of weeks 1-9 for the early group and weeks 9-11 for the delayed group using the Wilcoxon signed rank test. Since natural recovery is expected during the period of measurements (especially in weeks 1-3), the effect of the orthosis provision is expected to be mixed with effects of natural recovery. Therefore, the Wilcoxon signed rank test was also used to compare scores for weeks 1-3 in the delayed group (indicating natural recovery). The Wilcoxon rank sum test was used in weeks 1-3 to compare scores of the early (orthosis-effect and natural recovery) and delayed group (only natural recovery). For weeks 9-11 an additional Wilcoxon signed rank test was performed to indicate progress in the early group with ankle-foot orthosis. The Wilcoxon rank sum test was not performed, as in this period the early group was already using an AFO for an extended period of time. The secondary research question was whether or not the point in time at which an orthosis

Figure 2.3: Guideline for AFO-selection.

is provided (early or delayed) influences the effects of provision. We used analysis of covariance (ANCOVA) and analysed whether the effects of providing an orthosis are different for the early and delayed group. This implies looking at the outcomes at week 3 for the early group and week 11 for the delayed group (measurement with orthosis). The independent variables were group assignment (early or delayed) and values of the outcome of interest at weeks 1 and 9 for the early and delayed group, respectively (measurement without orthosis). To check whether the assumptions for ANCOVA analysis were fulfilled, we checked the distribution of the regression standardised residuals.

RESULTS

Baseline characteristics

In total 33 subjects were included; 16 in the early group, 17 in the delayed group. There were no significant differences at baseline between both groups (Table 2.1). Figure 2.1 details the participant flow through the study. Five subjects dropped-out (one early, four delayed) and data of two additional subjects (one early, one delayed) were unavailable in week 11.

Table 2.1: Subject characteristics.

	Total (n=33)	Early (n=16)	Delayed (n=17)
Sex (male/female)	20/13	10/6	10/7
Age (years, mean $\pm$ SD)	57.2 (9.2)	56.9 (9.6)	57.5 (9.1)
Time since stroke at Week 1 (days, mean $\pm$ SD)	31.4 (6.3)	32.0 (6.2)	30.8 (6.5)
Affected body side (left/right)	16/17	8/8	8/9
Type of stroke (ischemic/hemorrhagic)	27/6	14/2	13/4
Type of AFO (flexible/semi-rigid/rigid/no orthosis)	27/0/3/3	14/0/2/0	13/0/1/3
Sensation ^a Tactile (normal/impaired/absent)	26/4/3	13/1/2	13/3/1
Proprioception (normal/impaired/absent)	26/6/1	13/2/1	13/4/0
Mini-Mental State Examination (mean $\pm$ SD)	25.5 (4.1)	25.4 (4.5)	25.5 (3.8)
Motricity Index, lower limb (mean $\pm$ SD)	30.3 (20.0)	32.0 (17.8)	28.8 (22.3)

^atested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part.

Effects of ankle-foot orthosis provision

Mean time since stroke (SD) at provision of the AFO was 32.0 days (6.2) for the early group (n=16) and 88.1 days (6.1) for the delayed group (n=13). Table 2.2 shows the median scores of both groups for weeks 1 and 9, and the improvements after providing AFOs in the early (weeks 1-3) and delayed group (weeks 9-11). Furthermore, effects of only natural recovery are shown for the delayed group (improvement weeks 1-3), as are the results of weeks 9-11 for the early group. In the early group, median improvements after orthosis provision from week 1 to week 3 were significant for all outcome measures (all $p \leq 0.028$). In the same

period the delayed group not using an orthosis) also showed significant improvements on all outcome measures ($p \leq 0.037$), except for the ST ($p=0.068$). However, comparing the median improvements of the early group (using the orthosis) and the delayed group (only natural recovery) showed that improvements were numerically larger in the early group, except for FAC and RMI. The BBS (+8.5 points, $p=0.017$) and the 10MWT (+0.23 m/s, $p=0.025$) showed statistically significant larger median improvements in the early group, the 6MWT showed non-significant improvements (+62.5 m, $p=0.076$). Provision of the orthosis in week 9 in the delayed group resulted in median improvements on all outcome measures, except for RMI and BI. The BBS ($p=0.011$), FAC ($p=0.008$), 6MWT ($p=0.005$) and TUG ($p=0.028$) increased statistically significantly. The RMI and ST showed non-significant improvements ($p=0.066$ and $p=0.075$, respectively). As a reference, median improvements from weeks 9 to 11 of the early group (already using an orthosis) are also presented, showing only a significant median improvement of the RMI of 0.5 points ($p=0.016$).

Effect of early or delayed provision

Table 2.3 shows the results of the ANCOVA comparing the effects of early or delayed provision of the AFO, thereby correcting for differences in week 1 and week 9 scores, respectively, at the time the orthosis was provided. Adding “time after stroke” or “time in the rehabilitation center” as independent variables did not result in improvement of the model and therefore were left out. Except for FAC and ST, effects two weeks after provision were higher in the early group compared with the delayed group. Correcting for differences in baseline values at the two time points of provision of the orthosis, the early group improved 5.1 points more on the BBS ($p=0.002$) and 1.9 points more on the BI than the delayed group two weeks after provision ($p=0.002$). The 10MWT and TUG showed non-significant improvements of 0.14 m/s extra increase in walking speed ($p=0.093$) and 5.4 seconds faster performance ($p=0.087$), respectively, in the early group compared with the delayed group two weeks after provision.

DISCUSSION

This study showed positive effects of providing AFOs on functional outcomes, whether provided early (on average 32.0 days (6.2) after stroke) or delayed by eight weeks in subjects that did not use an AFO before. These positive effects were more pronounced in the early group, suggesting that providing AFOs early after stroke may be beneficial.

Our primary aim was to study the effects of the actual provision of AFOs early after stroke. When orthoses were provided in week 1 we found significant improvements on all outcome measures for the early group. In the same period, all but one (ST) outcome measures improved in the delayed group. This delayed group was not using an orthosis and therefore the improvements in this group are indicative for the natural recovery occurring

Table 2.2: Effect of providing AFOs comparing week 1-3 and week 9-11.

Early							Early versus Delayed			
	N	Week 1	Improvement week 1-3 (without vs with orthosis) ^a	N	Week 9	Improvement week 9-11 (with vs with orthosis) ^a				
BBS	16	8.5	+11.5 (5.3;17.8)*	14	49.5	0.0 (0.0;1.3)				
FAC	16	2.0	+1.0 (0.0;1.0)*	14	4.0	0.0 (0.0;0.0)				
RMI	16	5.0	+2.0 (1.0;3.8)*	14	12.0	+0.5 (0.0;2.0)*				
10MWT (m/s) ^c	16	0.00	+0.23 (0.08;0.34)*	14	0.56	+0.01 (-0.02;0.07)				
6MWT (m) ^c	16	0.0	+67.5 (7.0;108.5)*	12	176.3	+6.5 (-5.5;22.9)				
BI	16	12.0	+2.5 (1.0;3.8)*	14	18.0	0.0 (0.0;0.3)				
TUG (sec) ^c	7	23.8	-9.1 (-14.3;-3.1)*	14	25.2	-0.1 (-1.2;1.4)				
ST (sec) ^d	6	85.9	-20.1 (-22.5;-8.6)*	12	53.0	-1.1 (-4.4;4.2)				
Delayed							Early versus Delayed			
	N	Week 1	Improvement week 1-3 (without vs without orthosis) ^a	N	Week 9	Improvement week 9-11 (without vs with orthosis) ^a	Week 1-3 difference early - delayed ^b			
BBS	17	25.0	+3.0 (1.5;11.5)*	12	46.5	+3.0 (0.0;4.0)*	+8.5*			
FAC	17	2.0	+1.0 (0.0;1.0)*	12	4.0	+1.0 (0.0;1.0)*	0.0			
RMI	17	6.0	+2.0 (0.0;4.0)*	12	12.0	0.0 (0.0;1.0)	0.0			
10MWT (m/s) ^c	17	0.00	0.00 (0.00;0.18)*	12	0.36	+0.02 (-0.04;0.18)	+0.23*			
6MWT (m) ^c	17	0.0	+5.0 (0.0;58.8)*	12	121.3	+38.0 (10.9;60.5)*	+62.5			
BI	17	12.0	+2.0 (0.0;3.5)*	12	18.0	0.0 (0.0;0.8)	+0.5			
TUG (sec) ^c	8	30.3	-5.6 (-16.9;-3.5)*	9	24.0	-3.8 (-5.9;-0.8)*	-3.5			
ST (sec) ^d	4	51.3	-14.9 (-31.3;-7.1)	6	45.8	-3.8 (-16.2;-0.1)	-5.2			

* $p < 0.05$; Median scores and median improvements (interquartile range) are presented; ^aWilcoxon signed rank (within group); ^bWilcoxon rank sum test (between group); ^c10MWT was set at 0.0m/s, 6MWT set at 0m and TUG was missing in case subjects scored FAC < 3. In the early group, this was the case in nine and three subjects in week 1 and 3, all subjects were able to perform the test in week 9 and 11. For the delayed group this was the case in: nine, seven and two subjects in week 1, 3 and 9 respectively. All subjects were able to perform the test in week 11. In week 9-11 6MWT was missing in two additional subjects (early) and TUG was missing in one additional subject (delayed); ^dIn the early group ten, six, two and one subjects were not able to perform the ST in week 1, 3, 9 and 11 respectively. This was the case in thirteen, eight, five and four subjects in the delayed group. In week 9-11 additional data of one subject was missing (delayed). BBS: Berg Balance Scale; FAC: Functional Ambulation Categories; RMI: Rivermead Mobility Index; 10MWT: 10-meter walk test; 6MWT: 6-minute walk test; BI: Barthel Index; TUG: Timed Up and Go; ST: Stairs test. Note that negative results of TUG and ST indicate faster performance of the test.

Table 2.3: Analysis of covariance of the effects of providing AFOs comparing the early and delayed group.

	N	Difference	95% confidence interval for difference	
			Lower	Upper
BBS	28	-5.1 *	-8.052	-2.134
FAC	28	0.1	-0.420	0.590
RMI	28	-0.9	-2.179	0.284
10MWT (m/s)	28	-0.14	-0.295	0.024
6MWT (m)	28	-30.4	-82.980	22.259
BI	28	-1.9 *	-2.972	-0.760
TUG (sec)	16	5.4	-0.909	11.799
ST (sec)	12	-0.9	-9.592	7.806

* $p < 0.05$.

Note that for all outcome measures (except TUG and ST) negative results indicate that the early group improved more compared to the delayed group, two weeks after providing the orthosis. For TUG and ST, negative results indicate that the delayed group improved more compared to the early group, two weeks after providing the orthosis. BBS: Berg Balance Scale; FAC: Functional Ambulation Categories; RMI: Rivermead Mobility Index; 10MWT: 10-Meter Walk Test; 6MWT: 6-Minute Walk Test; BI: Barthel Index; TUG: Timed Up and Go; ST: Stairs Test.

after stroke and can be useful in the interpretation of the improvements in the early group. This is of importance, as the differences in the early group have a mixed origin: they are made up of both natural recovery and the effect of providing the orthosis. Comparing the median improvement of the early group with the delayed group at weeks 1-3, we found that improvements in the BBS and the 10MWT were significantly larger in the early group. On other outcomes, no significant differences were found in median improvement between the early and delayed group for weeks 1-3. We believe that these results are indicative for the short-term effect of providing the AFO in the early group.

When orthoses were provided to the delayed group in week 9 and effects were measured in week 11, we found significant improvements on the BBS, FAC, 6MWT and TUG. In the same period, the early group was already using an orthosis and showed only a significant improvement on the RMI. The early group cannot be compared with the delayed group, as indication for the amount of natural recovery in weeks 9-11 since the early group was provided with the orthosis eight weeks earlier.

When looking at the magnitude of the effects, we found a striking improvement on walking speed of +0.23 m/s for provision in weeks 1-3 for the early group. This improvement, which can be considered clinically relevant,⁵²⁻⁵⁴ is higher compared with a previous review reporting improvements of around 0.06 m/s (95% CI 0.03-0.08) for walking speed.¹⁷ The difference in effect could not be explained by the fact that we also included subjects without independent walking ability, as post-hoc analysis including only patients with independent walking ability in weeks 1-3 (early $n = 7$; delayed $n = 8$) resulted in median improvements of

+0.28 m/s (early; $p=0.018$) and +0.06 m/s (delayed; $p=0.123$). Furthermore, the difference could not be explained by the short stroke onset time in our study (a phase after stroke in which improvements are known to be highest⁵⁵) or our measurement protocol that included a two-week interval between the measurements (in which natural recovery may take place). This can be concluded from the fact that the large improvements on walking speed were only found in the early group that was provided with an orthosis, and not in the delayed group. The delayed group can serve as a control group as they had comparable stroke onset time and measurement protocol. Apparently, including subjects with FAC level <3 and the early onset time after stroke in our study cannot explain our results for walking speed. Therefore, we assume that the effects can be contributed to the early provision of the AFO, suggesting that the positive results of AFO on walking speed in chronic stroke reported previously may be more pronounced when the orthosis is provided early after stroke. Another striking improvement of providing the orthosis in weeks 1-3 between the early and delayed group was the result of the BBS (+8.5 points, $p=0.017$). This improvement is clinically relevant^{56,57} and more pronounced than improvements of around 1-2 points previously reported.^{36,58} Balance performance of the included subjects in the two previous studies was higher compared with our study. Ceiling-effects are well known for the BBS⁵⁹ and may explain why smaller effects were reported in those studies.

Our secondary aim was to study whether or not the point in time at which an orthosis is provided influences the effects of the provision. The ANCOVA showed a significantly higher improvement for early provision on the BBS and BI (extra median improvement of +5.1 and +1.9 points, respectively). These results are around the clinical meaningful changes reported for the BBS⁵⁷ and BI.⁶⁰ In addition, we found a trend in improvements on the 10MWT and TUG, indicating that early provision may be beneficial on aspects of balance, activities of daily living, and walking ability.

Our finding that the effects of AFOs may be more pronounced when provided early after stroke adds new insights to the available literature, as hardly any knowledge about the effects of the timing of providing orthoses after stroke is available. Only Wang et al.⁵⁸ studied effects of AFOs in stroke subjects with hemiparesis of different durations before. They found that the orthosis improved symmetry in quiet standing, dynamic standing balance, speed, and cadence in subjects less than six months after stroke, whereas only weak effects in subjects over 12 months post-stroke were found.

An important strength of this study is that this is the first study that takes timing of providing AFOs after stroke into account. Furthermore, the intervention is studied in a time frame and subject population that reflects clinical practice. We recruited subjects early after stroke and without experience in walking with an orthosis. The relation to the clinical practice is further strengthened since we also included subjects without independent walking ability. The majority of the subjects received a flexible AFO because of problems with drop-foot. This type of walking problem is often seen in stroke rehabilitation. Therefore, we think that our results are representative for daily clinical practice.

Five subjects dropped-out in the study (one early, four delayed) for various reasons (see Figure 2.1). We have no reasons to believe that drop-out rates were related to the intervention. Since data of previous studies measuring timing effects were not available, no valid power calculations could be performed to determine the sample size for this explorative RCT. Together with a small sample size, this is a limitation of our study. Despite the lack of a power calculation and the small sample size of our study, we are convinced that our sample size was sufficient since we were able to detect statistically significant effects. Another limitation is that it was not possible to blind subjects and assessors for early or delayed provision of the orthosis, which is a potential risk of bias.

This report focused on the effects of providing AFOs and whether or not early or delayed provision influences these effects. Functional outcomes were included and effects were studied two weeks after provision. Effects on the long-term follow-up need further study. A possible long-term adverse effect of early provision often mentioned by therapists is that use of an AFO would enhance disuse of the tibialis anterior muscle.³⁰ However, one might also speculate about positive effects of early use of an orthosis, as the AFO is reported to limit foot-drop in the distal segment, which may diminish the need of developing compensatory movements in more proximal segments. Therefore, future analysis of kinematics and muscle activation patterns is necessary to give insight in these effects of AFOs after stroke. Whether or not the early provision leads to benefits, like higher levels of mobility in an earlier stage of the rehabilitation or shortening of length of stay in the rehabilitation centre, was not studied in this current research and should be investigated in a next study.

Clinical messages

- There are considerable positive effects of providing an AFO on balance, walking ability and activities of daily life in subjects with (sub)acute stroke that have not used an orthosis before.
- The positive effects of providing an AFO are more pronounced when the orthosis is provided early (on average 32.0 (6.2) days) after stroke.

Chapter 3

Six-month effects of early or delayed provision of an ankle-foot orthosis in patients with (sub)acute stroke: A randomized controlled trial

Corien DM Nikamp
Jaap H Buurke
Job van der Palen
Hermie J Hermens
Johan S Rietman

Published in Clinical Rehabilitation 2017;31(12):1616-1624.

ABSTRACT

Objective 1) Study the six-month clinical effects of providing ankle-foot orthoses (AFOs) at different moments (early or delayed) in (sub-)acute stroke; 2) Study whether different timing affects functional improvement over time and whether reaching levels of independent and safe walking differed between early and delayed provision. This is a follow-up to a published trial.

Design Randomised controlled trial.

Setting Rehabilitation centre.

Subjects Unilateral hemiparetic stroke subjects maximal six weeks post-stroke with indication for AFO-use.

Interventions Subjects were randomly assigned to early (at inclusion; week 1) or delayed provision (eight weeks later; week 9).

Outcome measures Functional tests assessing balance and mobility were performed bi-weekly for 17 weeks and at 26 weeks.

Results Thirty-three subjects were randomised. No differences at week 26 were found between both groups for any of the outcome measures. However, results suggest that early provision leads to better outcomes in the first 11-13 weeks. Berg Balance Scale ($p=0.006$), Functional Ambulation Categories ($p=0.033$) and 6-Minute Walk Test ($p<0.001$) showed significantly different patterns over time. Clinically relevant but non-significant differences of 4-10 weeks in reaching independent walking with higher balance levels were found, favouring early provision.

Conclusions No six-month differences on functional outcomes of providing AFOs at different moments in the early rehabilitation after stroke were found. Results suggest that there is a period of 11-13 weeks in which early provision may be beneficial, possibly resulting in earlier independent and safe walking. However, our study was underpowered, therefore further research including larger numbers of subjects is warranted.

INTRODUCTION

Ankle-foot orthoses (AFOs) are often used to minimize gait deviations and to improve walking after stroke. Despite the frequent use of AFOs, clinical relevant questions, such as long-term effects of using an orthosis after recent stroke, and when to start treatment, remain unanswered.¹⁷ Most studies investigating effects of AFO-use after stroke reported the direct or short-term effects and included chronic patients with independent walking ability. Most of them were already using an orthosis in everyday life.¹⁷ Studies including longer follow-up periods of three to six months did not investigate the actual provision of orthosis early after stroke but compared different orthosis designs with each other,⁴⁰ or orthosis use was compared with functional electrical stimulation,^{61–63} conventional physical therapy³⁹ or no orthosis.⁶⁴ Studies investigating when to start using AFOs are scarce. Wang et al.⁵⁸ found that an orthosis improved balance, gait speed and cadence in patients less than six months after stroke, whereas effectiveness was minimal in patients more than 12 months after stroke.⁵⁸

We previously reported the short-term results of an explorative randomised controlled trial to study the effects of providing off-the-shelf AFOs on two different moments post-stroke.⁶⁵ We included patients within six weeks post-stroke and provided them with an AFO in week 1 (early) or 9 (delayed) of the study. The effects of provision were studied after two weeks. We found that the positive effects were more pronounced in the early group compared to the delayed group. This suggests that early provision may be beneficial. This article reports on the six-month outcomes of the randomized controlled trial. Our primary aim was to investigate the six-month clinical effects of providing AFOs at different moments (early or delayed) in the rehabilitation post-stroke. The secondary aim was to study whether different timing affects functional improvement over time and whether reaching levels related to independence and safety of walking differed between the two groups. We hypothesized that early provision is more beneficial.

METHODS

We designed a single centre, randomized, controlled, parallel group study. The study was approved by the Medical Ethical Committee Twente and registered in the “Netherlands Trial Register”, number NTR1930. A detailed description of our study design and patient inclusion can be found in our previous paper.⁶⁵ In summary, we recruited unilateral ischemic or hemorrhagic stroke subjects from the Roessingh, Centre for Rehabilitation in Enschede, the Netherlands. Subjects were maximal six weeks post-stroke and had an indication for use of an AFO. Subjects were randomised to either: 1) AFO-provision at inclusion, in study week 1 (early group); or 2) delayed provision after eight weeks, in study week 9 (delayed group). Subjects were provided with one of the three commonly used types of off-the-shelf, non-

Figure 3.1: Three types of AFOs used in the study.

From left to right: 1) polyethylene, non-articulated AFO with two crossed posterior steels and open heel, most flexible type; 2) semi-rigid, polypropylene, non-articulated AFO with two crossed posterior steels and open heel, larger posterior steel compared to type 1; 3) rigid, polypropylene, non-articulated AFO with closed posterior steel and closed heel.

articulated, posterior leaf design, polyethylene or polypropylene AFOs: flexible, semi-rigid or rigid (Basko Healthcare, Zaandam, the Netherlands) (see Figure 3.1). The type of orthosis was chosen in week 1 (early group) or week 9 (delayed group). A full description of the orthosis-selection was published previously.⁶⁵

Baseline measurements were performed without orthosis in week 1 for both groups. Measurements were repeated every other week until week 17, with follow-up measurements in week 26 (see Figure 3.2). Subjects in the early group were provided with the orthosis after the measurements of week 1, and subjects in the delayed group did not use an orthosis in this period and were provided with the orthosis eight weeks later, after the measurements in week 9. After provision, all measurements were performed with AFO.

At inclusion demographic data were recorded. The primary outcome measure was comfortable walking speed, assessed with the 10-Meter Walk Test (10MWT).⁴⁶ Secondary, balance was assessed using the Berg Balance Scale (BBS),⁴⁷ independence of walking with the Functional Ambulation Categories (FAC),⁴¹ walking ability with the 6-Minute Walk Test (6MWT),⁴⁸ and functional mobility with the Timed Up and Go (TUG)⁴⁹ and Stairs Test (ST).²⁰ Selective muscle control and isometric contraction were assessed with the Motricity Index (MI), lower-limb part.⁴⁵ The Rivermead Mobility Index (RMI)⁵⁰ and Barthel Index (BI)⁵¹ were used to assess mobility during activities of daily life. All tests that included walking were only performed in subjects who could walk without physical support (minimum FAC-level 3 required) at the time of the measurement.

Data analysis

IBM SPSS Statistics version 19 (IBM SPSS Statistics, Chicago, USA) was used for data analysis. The level of significance for all analyses was set at $p < 0.05$. Normality was checked using the Shapiro-Wilk test in all analyses. In case walk tests could not be performed because the FAC-level is less than three, the 10MWT and 6MWT were set at 0.0 m/s and 0 m, respectively,

Figure 3.2: Consort Flowchart.

The grey areas indicate previously published data.

while the TUG and ST were treated as missing values because using 0 second for these outcome measures would mean an infinitely fast performance of the test.

Baseline data are presented as mean (SD) or median (interquartile ranges (IQR)) and tested as appropriate. Six-month effects were studied by comparing outcome results of the early and delayed group at week 26 using independent samples *t*-tests (normal distribution) or Mann-Whitney *U* tests (non-normal distribution), as appropriate. Secondary, Generalized Estimating Equation analyses were performed to compare group by time interactions, using data from all functional tests from week 1 to 17 (measured every other week) and week 26. Survival-analyses (log-rank test) were performed to compare both groups in reaching clinical relevant cut-off points related to independence and safety of walking. One minus survival functions were used for depicting results. The following cut-off points were used: FAC ≥ 3 , which relates to the ability to walk without physical support of another person; BBS ≥ 45 points, which relates to a decreased fall risk;⁶⁶ ≥ 0.27 m/s for walking speed, which relates to the functional walking category “unlimited household walker” as defined by Perry et al.⁵⁴

RESULTS

In all, 33 subjects were included, 16 in the early group, 17 in the delayed group (see Table 3.1). There were no significant differences at baseline between both groups. Figure 3.2 details the participant flow through the study. Six subjects dropped-out (one early, five delayed). In addition, data of six of the included subjects were unavailable in one of the measurement weeks due to practical reasons (holiday, illness; see Figure 3.2).

At week 26, no significant differences were found between the early and delayed group for any of the outcome measures (Table 3.2).

Figure 3.3 shows the mean (SE) scores of both the early and delayed group for all outcome measures during the study. In general, both groups improved over time. Furthermore, the early group showed better outcomes on most functional tests in the first 11-13 weeks of the study compared to the delayed group, except for the MI and the ST. The BBS ($p=0.006$), FAC ($p=0.033$) and 6MWT ($p<0.001$) showed significantly different patterns over time.

Results of the survival-analyses are shown in Figure 3.4. All subjects reached FAC levels ≥ 3 within the follow-up period of the study (early: latest in week 5; delayed: latest in week 15). The cut-off points of ≥ 45 points for BBS and ≥ 0.27 m/s for walking speed were reached by all subjects in the early group (both by week 11), while three subjects in the delayed group did not reach these levels. None of the outcomes reached statistical significance (FAC $p=0.101$; BBS $p=0.102$; walking speed $p=0.183$).

Table 3.1: Subject characteristics.

	Total (n=33)	Early (n=16)	Delayed (n=17)
Sex (male/female) ^a	20/13	10/6	10/7
Age (years) ^b	57.2 (9.2)	56.9 (9.6)	57.5 (9.1)
Time since stroke at week 1 (days) ^b	31.4 (6.3)	32.0 (6.2)	30.8 (6.5)
FAC level at inclusion (0/1/2/3/4/5) ^c	0/7/14/11/1/0	0/3/7/6/0/0	0/4/7/5/1/0
Affected body side (left/right) ^a	16/17	8/8	8/9
Type of stroke (ischemic/haemorrhagic) ^c	27/6	14/2	13/4
Type of AFO ^d (flexible/semi-rigid/rigid/no orthosis) ^c	27/0/3/3	14/0/2/0	13/0/1/3
Sensation ^e Tactile (normal/impaired/absent) ^c	26/4/3	13/1/2	13/3/1
Proprioception (normal/impaired/absent) ^c	26/6/1	13/2/1	13/4/0
Mini-Mental State Examination ^f	27.0 (23.5-28.0)	27.0 (25.3-28.0)	27.0 (22.5-28.0)

Mean (SD) or median (interquartile range (IQR)) are presented. ^aPearson chi-square test (two-tailed); ^bIndependent samples *t*-test; ^cFisher exact test; ^dThree subjects were not provided with an orthosis: one dropped out before orthosis provision (week 5); one preferred wearing high mountain shoes instead of an orthosis, and one had not indication any longer at the moment of provision in week 9. Furthermore, two subjects (both early) changed from a flexible to a semi-rigid type during the study (in week 4 and 8, respectively) since support provided by the flexible type appeared to be insufficient. ^etested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part; ^fMann-Whitney *U* test with median (IQR).

Table 3.2: Results at week 26.

	N	Early	N	Delayed	Independent samples <i>t</i> -test Early group - Delayed group (95% CI)	<i>p</i>
10MWT (m/s)	14	0.72 (0.37;0.93)	12	0.82 (0.26;0.87)		0.700 ^a
BBS	14	52.5 (48.8;55.3)	12	53.0 (44.5;53.8)		0.534 ^a
FAC	14	5.0 (4.0;5.0)	12	4.5 (3.3;5.0)		0.256 ^a
6MWT (m) ^b	14	234 (126)	11	244 (134)	-10.2 (-118;98)	0.846
ST ^c	13	50.6 (23.9)	8	49.8 (19.5)	0.8 (-20.3;21.8)	0.942
TUG (sec)	14	16.9 (11.8;27.8)	12	14.3 (12.3;40.8)		0.837 ^a
RMI	14	13.0 (12.0;14.0)	12	13.5 (9.3;14.0)		1.000 ^a
BI	14	19.5 (18.5;20.0)	12	19.5 (14.8;20.0)		0.562 ^a
MI	14	49.8 (17.9)	12	56.8 (24.7)	-7.0 (-24.3;10.3)	0.414

Mean (SD) or median (interquartile range) are presented. ^aMann-Whitney *U* test; ^bData of 1 subject (delayed) is missing; subject was too tired to perform the test; ^cData of 1 (early) and 4 (delayed) subjects are missing; subjects were not able to walk the stairs. 10MWT: 10-Meter Walk Test; BBS: Berg Balance Scale; FAC: Functional Ambulation Categories; 6MWT: 6-Minute Walk Test; ST: Stairs Test; TUG: Timed Up and Go; RMI: Rivermead Mobility Index; BI: Barthel Index; MI: Motricity Index.

Figure 3.3: Generalized estimating equation-analysis to compare the early and delayed group over time. Generalized estimating equation-analysis for all functional tests is shown to compare group by time interactions. Early (blue line) and delayed (red line) group are depicted. Means (SE) are shown during all measurement weeks. Note that the early group was provided with an AFO after the measurements in week 1, the delayed group after the measurements in week 9. Increasing scores represent better performance on a particular test, except for the Stairs test and the Timed Up and Go test, where decreasing scores represent better (faster) performance of the test.

Figure 3.4: Survival analysis reaching clinical relevant cut-off points.

The vertical axis represents the proportion of subjects that reached the cut-off point: Functional Ambulation Categories: ≥ 3 points; Berg Balance Scale: ≥ 45 points; walking speed during 10m walk test: ≥ 0.27 m/s. The horizontal axis represents the measurement weeks of the study. Solid line: early group; dashed line: delayed group. ^aLog-rank test. For Berg Balance Scale and walking speed, data of three subjects (all delayed) is censored (marked with +) as they did not reach the cut-off point within the measurement period. The last subject in the delayed group who did reach the cut-off point for Berg Balance Scale and walking speed reached this in week 15 and 17, respectively.

DISCUSSION

This study showed no differences in functional outcomes after 26 weeks of early compared to delayed provision of an AFO after recent stroke. However, we must emphasise that our study has included only a limited number of patients and is therefore underpowered. Despite the small number of patients, we were able to find trends with respect to the pattern of functional improvement over time and with respect to reaching levels of independence and safety of walking. We found that the early group had higher scores in the beginning of the study (during the first 11-13 weeks) for most outcome measures compared to the delayed group. In addition, the early group could walk up to 10 weeks earlier without physical support of another subject compared to the delayed group. Balance levels related to less fall risk and walking speed related to household walking were reached four to six weeks earlier, respectively. The differences were non-significant, but these trends suggest that there may be a period of time in which early provision may be beneficial. This is valuable information for clinicians because early orthosis provision may therefore increase the ability to perform task-specific rehabilitation exercises with high repetitions and in a meaningful context –conditions known to be important for better outcomes.⁶⁷ Furthermore, this may also affect the length of in-clinic stay. Therefore, a new study with larger number of patients is warranted.

An important strength of this study is that we took the timing of providing AFOs into account. We included subjects early after stroke, also in case they had no independent walking

ability. This strengthens the transfer of our results to daily clinical practice. We found indications that there is a period of time in which early provision is beneficial. These results match with observations by Stinear et al.²² who stated that “the benefits of treatments delivered in the early stage could go undetected if the primary outcome is ≥ 3 months after stroke, by which time the control group may have caught up.”

The main limitation of our study is the small sample size as discussed. Furthermore, six subjects dropped-out in the study (one early, five delayed) for various reasons. We have no reasons to believe that drop-out was related to the intervention. The contrast of our intervention could have been larger in case we included a control group that was not provided with an AFO, instead of a delayed provision. This would increase the prospects of detecting differences. Within the generalized estimating equation analysis, missing data are assumed to be “missing at random”. However, this was not the case for missing data of the TUG and the ST (FAC < 3 or not able to negotiate stairs). Since no other options were available, we chose to perform the generalized estimating equation analysis, including the non-random missing data, so these results should be interpreted with caution.

Clinical messages

- Early provision of an AFO after stroke was associated with a better functional outcome at about 12 weeks, but at 26 weeks there were no detectable differences. The study was not powered to detect differences at six months.
- Patients with early provision of AFOs showed a general trend towards earlier independence in mobility, warranting further and larger trials.

Chapter 4

A randomized controlled trial on providing ankle-foot orthoses in patients with (sub-)acute stroke: Short-term kinematic and spatiotemporal effects and effects of timing

Corien DM Nikamp
Marte SH Hobbelink
Job van der Palen
Hermie J Hermens
Johan S Rietman
Jaap H Buurke

Published in Gait & Posture 2017;55:15-22.

ABSTRACT

Initial walking function is often limited after stroke, and regaining walking ability is an important goal in rehabilitation. Various compensatory movement strategies to ensure sufficient foot-clearance are reported. Ankle-foot orthoses (AFOs) are often prescribed to improve foot-clearance and may influence these strategies. However, research studying effects of actual AFO-provision early after stroke is limited. We conducted an explorative randomized controlled trial and aimed to study the short-term effects of AFO-provision on kinematic and spatiotemporal parameters in patients early after stroke. In addition, we studied whether timing of AFO-provision influenced these effects. Unilateral hemiparetic patients maximal six weeks post-stroke were randomly assigned to AFO-provision: early (at inclusion) or delayed (eight weeks later). Three-dimensional gait-analysis with and without AFO in randomized order was performed within two weeks after AFO-provision. Twenty subjects (8 early, 12 delayed) were analyzed. We found significant positive effects of AFO-provision for ankle dorsiflexion at initial contact, foot-off and during swing ($-3.6^{\circ}(7.3)$ vs $3.0^{\circ}(3.9)$; $0.0^{\circ}(7.4)$ vs $5.2^{\circ}(3.7)$; and $-6.1^{\circ}(7.8)$ vs $2.6^{\circ}(3.5)$, respectively), all $p < 0.001$. No changes in knee, hip and pelvis angles were found after AFO-provision, except for knee ($+2.3^{\circ}$) and hip flexion ($+1.6^{\circ}$) at initial contact, $p \leq 0.001$. Significant effects of AFO-provision were found for cadence ($+2.1$ steps/min, $p=0.026$), stride duration (-0.08 sec, $p=0.015$) and single support duration ($+1.0\%$, $p=0.002$). Early or delayed AFO-provision after stroke did not affect results. In conclusion, positive short-term effects of AFO-provision were found on ankle kinematics early after stroke. Timing of AFO-provision did not influence the results.

INTRODUCTION

Initial walking function is limited in two-thirds of patients with acute stroke⁵ and regaining this walking ability is an important goal in rehabilitation.⁶⁸ Important kinematic changes observed after stroke are decreased ankle dorsiflexion^{7,8,69,70} and decreased knee⁷⁻⁹ and hip flexion¹⁰ in swing, contributing to insufficient foot-clearance. Various compensatory movement strategies to ensure sufficient foot-clearance after stroke are reported,¹⁰ including pelvic hiking^{9,71} or pelvic obliquity,⁷² both in the frontal plane, and circumduction.^{9,71} Furthermore, increased hip flexion⁷⁰ and a hip abductor pattern⁷³ are reported. However, kinematic strategies to achieve sufficient foot-clearance are reported to differ between subjects^{70,71,73} and are thought to be linked with self-selected walking speed.⁷¹

Ankle-foot orthoses (AFOs) are often prescribed to improve walking. Literature states that AFOs may provide mediolateral stability in stance, facilitate toe-clearance in swing and promote heel strike.¹⁴ In a review on the effects of AFO-use after stroke, Tyson et al. reported improvements on ankle kinematics in early stance, swing phase and toe-off and knee kinematics in stance.¹⁸ No effects on knee kinematics in swing or hip kinematics were found. Most studies in this review included chronic stroke patients, of which many were already using AFOs in everyday life and walked independently. One may argue that in these subjects the effect of removing an AFO is tested. Studying effects of the actual AFO-provision early after stroke to patients that are not used to walk with an AFO is more in line with daily clinical practice and therefore could provide more relevant information to clinicians. Measuring the biomechanical effects of AFO-provision early after stroke is relevant, as one may speculate that the development of compensatory movement patterns in proximal lower limb segments may decrease when foot-drop in the distal segment is limited in an early stage because of early AFO-provision. However, studies measuring kinematic and spatiotemporal effects of AFO-provision in subjects with recent stroke are limited.⁷⁴⁻⁷⁶ In total 37 subjects were included in these three studies, with a mean time since stroke between 24.5⁷⁶ and 67⁷⁴ days. Positive effects on sagittal ankle kinematics were reported,^{74,75} as well as effects on walking speed,^{74,75} cadence,⁷⁴⁻⁷⁶ step length^{74,76} and stride length.⁷⁵ No effects on sagittal knee and hip kinematics were found. Effects of early AFO-provision on frontal plane kinematics and effects on the pelvis were not studied. However, these are considered to be relevant because compensatory strategies in the frontal plane and around the pelvis are reported to be important to achieve toe clearance in the absence of sufficient dorsiflexion provided by the AFO.⁷⁰⁻⁷²

The aforementioned considerations show that there is a lack of studies examining kinematic and spatiotemporal effects of the actual provision of AFOs and the timing of this provision early after stroke. Therefore, we conducted an explorative randomized controlled trial to study the effects of providing AFOs on two different moments in the rehabilitation early post-stroke. Effects of AFO-provision on functional outcome measures like balance,

walking ability and activities of daily-life were reported previously.⁶⁵ The primary aim of the current paper was to study the short-term effects of the AFO-provision on kinematic and spatiotemporal parameters in patients in the early rehabilitation phase post-stroke. The secondary aim was to study whether timing of AFO-provision post-stroke (early or delayed) influenced these effects. We hypothesize that early provision is more beneficial.

METHODS

We designed a single center, randomized, controlled, parallel group study. The study was approved by the Medical Ethical Committee Twente, registered in “the Netherlands Trial Register”, number NTR1930 and followed the CONSORT guidelines.⁷⁷ All subjects provided written informed consent. This paper contains a brief description of the study methods; a full description can be found in a previous publication.⁶⁵

Subjects

We recruited subjects from the Roessingh, Center for Rehabilitation in Enschede, the Netherlands. Inclusion criteria were: 1) unilateral ischemic or hemorrhagic stroke leading to hemiparesis (single and first-ever stroke or history of previous stroke with full physical recovery); 2) at least 18 years of age; 3) maximal six weeks post-stroke; 4) receiving in-patient rehabilitation care at inclusion; 5) able to follow simple verbal instructions; and 6) indication for AFO-use (i.e. abnormal initial floor contact and/or problems with toe-clearance in swing and/or impaired ability to take bodyweight through the paretic lower limb in stance) determined by the treating rehabilitation physician and physiotherapist. Subjects suffering from severe comprehensive aphasia or neglect or with cardiac, pulmonary or orthopedic disorders that could interfere with gait were excluded.

Randomization

Participants were allocated to one of two intervention-groups using stratified block-randomization: 1) AFO-provision at inclusion, in study week 1 (early group); or 2) AFO-provision eight weeks later, in study week 9 (delayed group). Stratification was based on the Functional Ambulation Categories (FAC).⁴¹ Walking with (FAC 0-2) and without (FAC 3-5) physical support of another person at inclusion were used as stratification categories.

AFO-provision

Subjects were provided with one of three commonly used types of off-the-shelf, non-articulated, posterior leaf design, polyethylene or polypropylene AFOs: flexible, semi-rigid or rigid (Basko Healthcare, Zaandam, the Netherlands (Figure 4.1). All AFOs were worn inside the shoe and included a proximal calf strap. AFO-fitting was performed by a licensed orthotist. AFO-type was chosen according to a custom developed protocol,⁶⁵ based on the

Figure 4.1: Three types of AFOs used in the study.

From left to right: 1) polyethylene, non-articulated AFO with two crossed posterior steels and open heel, most flexible type; 2) semi-rigid, polypropylene, non-articulated AFO with two crossed posterior steels and open heel, larger posterior steel compared to type 1; 3) rigid, polypropylene, non-articulated AFO with closed posterior steel and closed heel.

prerequisites of gait,³¹ determining whether the main walking problems arise in stance, foot-clearance in swing and/or prepositioning at heel strike. The effect of the prescribed AFO was verified and confirmed by the responsible physician in all subjects.

Procedures

Measurements included 3D gait-analysis in one single session, with and without AFO in random order. Measurements were performed after AFO-provision in week 1 or 9 of the study, for the early and delayed group, respectively. The measurements required that subjects were able to walk without physical support of another person ($FAC \geq 3$) and had sufficient endurance to complete a measurement. If this was not the case, the measurement was postponed until subjects complied with these conditions. We defined that short-term effects of the actual AFO-provision could only be assessed in case measurements could be performed within two weeks after AFO-provision. Therefore, subjects were only included in the analysis in case measurements were performed in week 1-3 (early group) or week 9-11 (delayed group). Besides the AFO-intervention, all subjects received usual care from experienced physiotherapists according to the Dutch guidelines for physiotherapy after stroke.^{42,67}

Data collection and processing

At inclusion, basic demographic data were recorded. Kinematic and spatiotemporal data were collected in a gait laboratory at 100 Hz using a six-camera Vicon MX13+ motion-analysis system (Vicon, Oxford, UK) for capturing marker trajectories. Reflective 25-millimeter markers were placed directly on the skin and shoes according to the modified Helen Hayes marker set. Additional to this marker set, two markers were placed on each shoe at metatarsal I and V to assess in/eversion movements. Subjects walked on a level walkway at self-selected walking speed wearing their own shoes. Measurements with and without AFO were performed in random order, without removing the reflective markers. Assistive de-

vices (such as a cane or quad stick) were permitted and it was allowed to rest between the trials to prevent effects of fatigue.

Data processing was performed using the lower-body Plug-In-Gait model from Vicon and custom in-house software, developed in Matlab (MathWorks, Natick, Massachusetts). Initial contact and foot-off were determined manually. Marker trajectories were time-normalised to stride duration and averaged, with 0% representing initial contact and 100% representing the next initial contact of the same foot. Eight to ten representative strides were used for further analysis.

Outcome measures

The primary outcome measure was sagittal ankle movement (dorsiflexion), measured at initial contact and foot-off and values in stance (max) and swing (min and max). Secondary, frontal ankle movement (in/eversion), foot-progression angle, sagittal knee movement (flexion/extension), sagittal (flexion/extension) and frontal (abd/adduction) hip movement and sagittal (tilt) and frontal (obliquity) pelvic movement were measured. Angles were calculated at initial contact and foot-off. Furthermore, minimal and maximal angles in stance and/or swing phase were calculated for knee, hip and frontal pelvic movement. Results of the affected side are presented in this paper. Besides, spatiotemporal parameters were calculated. See Table 4.1 for definitions.

Statistical analysis

We did not perform a power-calculation since no data of previous studies measuring timing effects of AFO-provision was available. SPSS version 19 (IBM SPSS Statistics, Chicago, USA) was used for data-analysis. The level of significance for all analyses was set at $p < 0.05$ and normality was checked using the Shapiro-Wilk test. Basic demographic data of the early and delayed group at inclusion were compared: continuous variables were tested using independent samples *t*-tests (normal distribution) or Mann-Whitney *U* tests (non-normal distribution); categorical variables were tested with chi-squared tests or Fisher exact tests, as appropriate. Furthermore, kinematic and spatiotemporal parameters without AFO of the early (week 1) and delayed group (week 9) were compared to detect possible differences between both groups. Independent samples *t*-test or Mann-Whitney *U* test were used, as appropriate.

To calculate effects of AFO-provision, measurements with and without AFO were compared, combining the data of both the early and delayed group. Paired samples *t*-tests were used for normally distributed variables with the kinematic and spatiotemporal parameters as dependent variables and AFO-condition (with and without AFO) as independent variable. Wilcoxon signed-rank tests were conducted for non-normally distributed variables. To study whether timing of AFO-provision (week 1 or 9) influenced the effects, differences between measurements with and without AFO were calculated for both groups separately and these differences were compared. Independent samples *t*-tests were conducted with the differ-

ences (with - without AFO) as dependent variable and group as independent variable for normally distributed differences, otherwise, a Mann-Whitney *U* test was conducted.

RESULTS

Baseline

In total 33 subjects were included. Twenty subjects (eight early, 12 delayed) were included in the analysis as measurements were performed within two weeks after AFO-provision. Figure 4.2 details the participant flow through the study. Table 4.2 shows no statistically significant differences in patient characteristics at inclusion between both groups. On average, measurements were performed 39.8 (9.1) and 90.2 (6.4) days after stroke in the early and delayed group, respectively. Median time between AFO-provision and gait analysis was 10.5 and 2.0 days in the early and delayed group, respectively. The shortest duration between AFO-provision and gait analysis was 1 (early) and 0 (delayed) days. Baseline comparison between the early and delayed group without AFO revealed no significant differences on outcome parameters at the ankle, foot or hip-level or for spatiotemporal parameters (see Table 4.3). Significant differences were found for minimal knee flexion during stance (9.2 vs 16.2°; $p=0.031$), pelvic tilt at initial contact (7.2 vs -1.4°; $p=0.031$) and foot-off (12.0 vs 6.0°; $p=0.030$) and pelvic obliquity at initial contact (0.8 vs 4.0°; $p=0.017$) for the early and delayed group, respectively.

Effect of AFO-provision

Effects of AFO-provision are shown in Table 4.4 and visually presented in Figure 4.3. Significant effects of AFO-provision were found on the ankle-level for all outcome parameters, except for maximal dorsiflexion in stance, see Table 4.4. Furthermore, foot-progression at initial contact increased significantly after AFO-provision, as did knee and hip flexion at initial contact. Other parameters at the knee and hip-level did not change. No effects on the pelvis were found. Statistically significant effects of AFO-provision were found for cadence (+2.1 steps/min, $p=0.026$), stride duration (-0.08 sec, $p=0.015$) and single support duration (+1.0%, $p=0.002$) (Table 4.4).

Effect of timing

No significant kinematic effects of the timing of AFO-provision were found when effects were compared between the early and delayed group, see Table 4.5. Furthermore, no effects of timing were found for the spatiotemporal parameters, except for a significant effect on single support phase ($p=0.026$; increase of 0.3% (SD 1.3) from 21.5% to 21.8% (early) vs increase of 1.5% (SD 1.0), from 19.7% to 21.2% (delayed)).

Figure 4.2: CONSORT Flowchart.

DISCUSSION

Our primary aim was to study the short-term kinematic and spatiotemporal effects of the actual AFO-provision early after stroke. We found significant positive effects on sagittal ankle movement, our primary outcome measure, as plantarflexion angles at initial contact and during swing significantly improved into dorsiflexion angles. Furthermore, inversion angles improved significantly. These changes are clinically relevant because foot-clearance in swing and prepositioning of the foot at initial contact were improved by the AFO. Both phases are considered important prerequisites of gait.³¹ Our results show that the indication for AFO-use was correct in our included population and that the AFO corrected the ankle as expected. Our findings are in line with a review studying effects of AFOs in mainly chronic stroke patients familiar to walking with AFO¹⁸ and literature studying effects of recent AFO-provision on ankle kinematics after recent stroke.^{74,75} Walking speed with and without AFO did not change in our study, so this did not confound our results.

On the knee- and hip level, we found increased flexion angles at initial contact after AFO-provision. Most studies including hip kinematics did not report any effects.^{7,74–76,78} On the knee-level effects of AFOs are inconclusive: both no effects after recent stroke,^{74–76} and increased knee flexion at initial contact after chronic stroke are reported.⁷⁹ Kobayashi et al. used an experimental AFO in patients after stroke to demonstrate that increasing levels of plantarflexion resistance result in increased knee flexion angles in early stance phase.⁸⁰ These findings may explain our results, since applying an AFO increases plantarflexion resistance, thereby changing ankle angles at initial contact from plantar flexion to dorsal flexion. This induces forward rotation of the shank pushing the knee joint forward,⁸⁰ resulting in increased knee flexion at initial contact and also effecting hip flexion.

This is the first randomized controlled trial on effects of early AFO-provision including frontal plane hip kinematics and effects on the pelvis. No effects were found on hip ab/adduction or pelvic tilt (sagittal plane) and obliquity (frontal plane). This means that in our study AFO-provision did not affect possible compensatory movement strategies around hip and pelvis, often mentioned after stroke.^{9,71–73} In correspondence with our results, Cruz et al. also reported no effects of AFOs on hip ab/adduction, but they found effects on the pelvis.⁷² Chronic stroke patients (50.2 (39.9) months post-stroke) used to wearing AFOs daily were included in their study. Perhaps effects of removing AFOs in habitual AFO-users after chronic stroke are larger than effects of providing AFOs in subjects after early stroke, or possible compensatory movement patterns were not (yet) developed in our recent stroke subjects. Future analysis of the long-term effects of early AFO-provision on the gait pattern is necessary to give insight in this.

Previous studies often reported positive effects of AFOs on walking speed. This result may be explained by the fact that these studies included chronic stroke patients already using AFOs in daily-life.^{17,23} Walking without AFO is probably an unfamiliar situation for

Figure 4.3: Effect of providing AFOs. This figure shows the mean kinematics (°) of the affected pelvis, hip, knee, ankle and foot, as % of the gait cycle (n=20). The data with AFO are shown as a solid black line, the data without AFO are shown as a solid grey line. Anterior pelvic tilt, up pelvic obliquity, hip flexion, hip adduction, knee flexion, ankle dorsiflexion, ankle eversion and internal foot-progression are defined as positive (+).

Table 4.1: Definitions of kinematic and spatiotemporal parameters.

Kinematics parameters	Movement in
Ankle dors/plantar flexion	sagittal plane
Ankle in/eversion	frontal plane
Foot-progression	transverse plane
Knee flexion/extension	sagittal plane
Hip flexion/extension	sagittal plane
Hip ab/adduction	frontal plane
Pelvic tilt	sagittal plane
Pelvic obliquity	frontal plane
Spatiotemporal parameters	Definition
Walking velocity (m/s)	The mean speed of the anterior superior iliac spine markers along the axis of progression
Cadence (steps/min)	The number of steps per minute
Stride length (m)	The horizontal distance between the ankle joint centers of two consecutive initial contacts of the same foot
Step length (m)	The horizontal distance between the ankle joint center at initial contact of the contralateral foot and the subsequent initial contact of the ipsilateral foot
Step width (m)	The mediolateral distance between the ankle joint centers of two consecutive initial contacts
Stride duration (s)	The time between two consecutive initial contacts of the ipsilateral foot
Stance duration (% gait cycle)	The time between ipsilateral initial contact and ipsilateral foot-off, relative to the duration of the gait cycle
First double support duration (% gait cycle)	The time between ipsilateral initial contact and contralateral foot-off, relative to the duration of the gait cycle
Single support duration (% gait cycle)	The time between contralateral foot-off and contralateral initial contact, relative to the duration of the gait cycle
Second double support duration (% gait cycle)	The time between contralateral initial contact and the ipsilateral foot-off, relative to the duration of the gait cycle
Swing duration (% gait cycle)	The time between ipsilateral foot-off and ipsilateral initial contact, relative to the duration of the gait cycle

Table 4.2: Patient characteristics at inclusion.

	Total (n=20)	Early (n=8)	Delayed (n=12)
Sex (male/female) ^a	10/10	4/4	6/6
Age (years) ^b	56.0 (9.8)	57.3 (11.1)	55.2 (9.3)
Height (cm) ^c	170.8 (165.6-175.0)	173.0 (164.0-177.3)	170.3 (167.6-174.8)
Weight (kg) ^b	75.8 (14.0)	80.1 (11.7)	72.9 (15.1)
Time since stroke at week 1 (days) ^b	30.0 (6.3)	27.1 (6.1)	31.9 (5.9)
Affected body side (left/right) ^a	12/8	5/3	7/5
Type of stroke (ischemic/hemorrhagic) ^a	16/4	7/1	9/3
Type of AFO (flexible/semi-rigid/rigid) ^a	18/0/2	7/0/1	11/0/1
Sensation* Tactile (normal/impaired/absent) ^a	18/0/2	7/0/1	11/0/1
Propriocepsis (normal/impaired/absent) ^a	18/1/1	7/0/1	11/1/0
Mini-Mental State Examination ^c	27.0 (24.5-28.0)	27.0 (27.0-28.0)	27.5 (22.3-28.0)
Motricity Index, lower limb ^c	42.0 (17.5-45.8)	42.0 (42.0-53.0)	42.0 (0-42.0)

Mean (SD) or median (interquartile range) are presented. ^aFisher exact test (2-tailed); ^bindependent samples *t*-test;

^cMann-Whitney *U* test with median (IQR). *tested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part.

Table 4.3: Baseline comparison early and delayed group, without AFO.

	Without AFO		Independent samples <i>t</i> -test	
	Early group (week 1, n=8)	Delayed group (week 9, n=12)	Early group - Delayed group (95% CI)	<i>p</i>
Kinematics (°)				
Ankle				
Dorsiflexion at initial contact	-3.3 (8.0)	-3.7 (7.1)	0.4 (-6.8;7.6)	0.911
Max. dorsiflexion during stance	14.1 (8.2)	14.0 (5.5)	0.1 (-6.3;6.5)	0.973
Dorsiflexion at foot-off	-3.7 (9.2)	2.4 (4.8)	-6.1 (-14.1;1.8)	0.115
Min dorsiflexion during swing	-7.9 (7.8)	-4.8 (7.9)	-3.1 (-10.7;4.5)	0.402
Max. dorsiflexion during swing	2.4 (7.4)	3.5 (5.5)	-1.1 (-7.2;4.9)	0.706
Inversion at initial contact	5.4 (6.3)	9.3 (5.8)	-3.8 (-1.9;9.6)	0.175
Inversion at foot-off	8.1 (7.8)	7.9 (5.1)	0.2 (-6.2;5.8)	0.948
Foot				
Foot-progression at initial contact	-9.5 (-13.2;-8.3)	-12.3 (-16.7;-7.1)		0.487 ^a
Foot-progression at foot-off	-12.1 (-24.0;-7.4)	-21.6 (-45.8;-14.3)		0.247 ^a
Knee				
Flexion at initial contact	15.7 (5.7)	19.7 (5.4)	-3.9 (-9.2;1.4)	0.135
Min. flexion during stance	9.2 (4.0)	16.2 (7.7)	-7.0 (-13.2;-0.7)	0.031
Flexion at foot-off	46.0 (21.5;56.9)	36.8 (34.0;44.8)		0.589 ^a
Max. flexion during swing	45.7 (16.9)	40.3 (8.8)	5.4 (-9.1;20.0)	0.424
Hip				
Flexion at initial contact	31.2 (11.3)	22.3 (9.2)	8.9 (-0.7;18.5)	0.068
Min. flexion during stance	5.6 (14.3)	2.0 (10.2)	3.7 (-7.8;15.1)	0.508
Flexion at foot-off	13.2 (8.0;29.4)	8.4 (1.8;16.0)		0.123 ^a
Max. flexion during swing	34.9 (10.6)	26.7 (9.6)	8.2 (-1.4;17.7)	0.090
Adduction at initial contact	0.9 (2.8)	0.0 (3.8)	0.9 (-2.4;4.2)	0.570
Max. adduction during stance	4.8 (2.7)	2.4 (3.1)	2.4 (-0.5;5.2)	0.096
Adduction at foot-off	-1.6 (-3.6;-0.7)	-3.5 (-4.7;0.1)		0.817 ^a
Max. adduction during swing	1.9 (2.1)	1.0 (3.9)	0.9 (-2.0;3.7)	0.527
Pelvis				
Tilt at initial contact	7.2 (1.2;15.3)	-1.4 (-3.8;4.4)		0.031^a
Tilt at foot-off	12.0 (6.8)	6.0 (4.7)	6.0 (0.6;11.4)	0.030
Obliquity at initial contact	0.8 (3.0)	4.0 (2.5)	-3.3 (-5.9;-0.6)	0.017
Max. obliquity during stance	2.2 (2.7)	4.6 (2.6)	-2.4 (-4.9;0.1)	0.056
Obliquity at foot-off	0.3 (3.9)	3.2 (3.1)	-2.9 (-6.1;0.4)	0.080
Max obliquity during swing	3.0 (3.3)	5.9 (3.5)	-2.8 (-6.0;0.4)	0.086

CI: confidence interval. Mean (SD) or median (interquartile range) is presented. Independent samples *t*-test were used to compare early - delayed group, unless otherwise noted; ^aMann-Whitney *U* test was used. *Table continues on the next page.*

Table 4.3: Baseline comparison early and delayed group, without AFO. (*continued*)

	Without AFO		Independent samples <i>t</i> -test	
	Early group (week 1, n=8)	Delayed group (week 9, n=12)	Early group - Delayed group (95% CI)	<i>p</i>
Spatiotemporal				
Walking velocity (m/s)	0.46 (0.21)	0.42 (0.23)	0.04 (-0.17;0.25)	0.705
Cadence (steps/min)	65.4 (14.4)	68.2 (25.2)	-2.8 (-23.6;17.9)	0.779
Stride length (m)	0.80 (0.22)	0.71 (0.14)	0.10 (-0.07;0.27)	0.240
Step length (m)	0.44 (0.09)	0.39 (0.07)	0.05 (-0.02;0.13)	0.175
Step width (m)	0.17 (0.03)	0.20 (0.05)	-0.03 (-0.07;0.02)	0.193
Stride duration (s)	1.93 (0.51)	2.00 (0.76)	-0.07 (-0.72;0.58)	0.822
Stance duration (% gait cycle)	69.8 (6.2)	67.5 (7.9)	2.4 (-4.6;9.3)	0.486
First double support (% gait cycle)	16.3 (4.5)	15.8 (3.8)	0.4 (-3.5;4.4)	0.817
Single support (% gait cycle)	21.5 (6.8)	19.7 (6.8)	1.8 (-4.7;8.3)	0.565
Second double support (% gait cycle)	32.1 (13.6)	32.0 (13.4)	0.1 (-12.8;13.0)	0.989
Swing duration (% gait cycle)	30.2 (6.2)	32.5 (7.9)	-2.4 (-9.3;4.6)	0.486

CI: confidence interval. Mean (SD) or median (interquartile range) is presented. Independent samples *t*-test were used to compare early - delayed group.

Table 4.4: Effect of providing AFOs.

	Effect (n=20)			
	Without AFO	With AFO	With AFO - Without AFO	<i>p</i>
Kinematics (°)				
Ankle				
Dorsiflexion at initial contact	-3.6 (7.3)	3.0 (3.9)	6.6 (4.0;9.1)	< 0.001^a
Max. dorsiflexion during stance	14.1 (6.5)	14.6 (5.6)	0.5 (-1.0;2.0)	0.464 ^a
Dorsiflexion at foot-off	0.0 (7.4)	5.2 (3.7)	5.2 (2.9;7.6)	< 0.001^a
Min. dorsiflexion during swing	-6.1 (7.8)	2.6 (3.5)	8.7 (5.9;11.5)	< 0.001^a
Max. dorsiflexion during swing	3.1 (6.2)	6.7 (3.9)	3.7 (2.0;5.3)	< 0.001^a
Inversion at initial contact	7.7 (6.1)	5.5 (2.9)	-2.3 (0.1;4.5)	0.043^a
Inversion at foot-off	7.9 (6.1)	4.7 (3.5)	-3.2 (0.9;5.5)	0.009^a
Foot				
Foot-progression at initial contact	-10.0 (-15.5;-8.3)	-13.2 (-18.2;-5.6)	-1.6 (-5.2;-0.9)	0.014^b
Foot-progression at foot-off	-16.5 (-31.4;-11.1)	-18.8 (-28.6;-10.1)	-2.3 (-3.8;3.9)	0.478 ^b
Knee				
Flexion at initial contact	18.1 (5.7)	20.4 (6.4)	2.3 (1.6;3.0)	< 0.001^a
Min. flexion during stance	13.4 (7.3)	14.6 (7.4)	1.2 (-0.3;2.7)	0.112 ^a
Flexion at foot-off	39.2 (11.8)	40.6 (9.7)	1.3 (-0.7;3.3)	0.179 ^a
Max. flexion during swing	42.5 (12.6)	42.8 (10.3)	0.3 (-1.5;2.1)	0.711 ^a
Hip				
Flexion at initial contact	25.9 (10.7)	27.4 (10.5)	1.6 (0.7;2.4)	0.001^a
Min. flexion during stance	3.4 (11.8)	3.1 (11.8)	-0.3 (-1.5;0.8)	0.572 ^a
Flexion at foot-off	11.1 (6.0;17.6)	11.1 (3.7;17.6)	-0.3 (-1.5;1.2)	0.601 ^a
Max. flexion during swing	30.0 (10.5)	30.3 (10.6)	0.3 (-0.9;1.6)	0.592 ^a
Adduction at initial contact	0.4 (3.4)	0.2 (3.1)	-0.2 (-0.6;0.3)	0.426 ^a
Max. adduction during stance	3.4 (3.1)	2.8 (3.1)	-0.6 (-1.2;0.0)	0.061 ^a
Adduction at foot-off	-2.6 (3.4)	-2.7 (3.6)	-0.2 (-0.7;0.4)	0.577 ^a
Max. adduction during swing	1.4 (3.3)	1.1 (3.0)	-0.2 (-0.6;0.1)	0.106 ^a
Pelvis				
Tilt at initial contact	1.8 (-2.9;8.6)	2.3 (-2.0;9.7)	0.0 (-0.5;1.4)	0.478 ^b
Tilt at foot-off	8.4 (6.2)	8.2 (6.5)	-0.2 (-0.7;0.4)	0.541 ^a
Obliquity at initial contact	2.7 (3.1)	2.6 (2.9)	-0.2 (-0.7;0.4)	0.563 ^a
Max. obliquity during stance	3.7 (2.8)	3.5 (2.7)	-0.2 (-0.6;0.3)	0.517 ^a
Obliquity at foot-off	2.0 (3.6)	1.7 (3.2)	-0.4 (-1.0;0.2)	0.190 ^a
Max obliquity during swing	4.7 (3.6)	4.1 (3.0)	-0.6 (-1.3;0.0)	0.067 ^a

Mean (SD) or median (interquartile range) is presented. ^aPaired samples *t*-test (mean, 95% confidence interval) is presented; ^bWilcoxon signed-rank test (median (interquartile range)) is presented. *Table continues on the next page.*

Table 4.4: Effect of providing AFOs (*continued*).

	Effect (n=20)			
	Without AFO	With AFO	With AFO - Without AFO	<i>p</i>
Spatiotemporal				
Walking velocity (m/s)	0.44 (0.22)	0.46 (0.22)	0.02 (-0.01;0.05)	0.112 ^a
Cadence (steps/min)	67.1 (21.1)	69.2 (21.1)	2.1 (0.3;3.9)	0.026^a
Stride length (m)	0.75 (0.18)	0.76 (0.17)	0.01 (-0.1;0.05)	0.345 ^a
Step length (m)	0.41 (0.08)	0.40 (0.08)	-0.01 (-0.03;0.01)	0.332 ^a
Step width (m)	0.19 (0.16;0.21)	0.17 (0.15;0.21)	-0.01 (-0.02;0.00)	0.052 ^b
Stride duration (s)	1.97 (0.66)	1.89 (0.58)	-0.08 (-0.14;-0.02)	0.015^a
Stance duration (% gait cycle)	68.4 (7.2)	68.5 (6.4)	0.1 (-1.4;1.6)	0.877 ^a
First double support (% gait cycle)	16.0 (4.0)	16.7 (3.6)	0.7 (-0.3;1.7)	0.149 ^a
Single support (% gait cycle)	20.4 (6.7)	21.4 (6.3)	1.0 (0.4;1.6)	0.002^a
Second double support (% gait cycle)	26.5 (22.4;45.8)	26.9 (21.8;41.5)	-1.2 (-2.6;0.8)	0.070 ^b
Swing duration (% gait cycle)	31.6 (7.2)	31.5 (6.4)	-0.1 (-1.6;1.4)	0.877 ^a

Mean (SD) or median (interquartile range) is presented. ^aPaired samples *t*-test (mean, 95% confidence interval) is presented; ^bWilcoxon signed-rank test (median (interquartile range)) is presented.

Table 4.5: Effect of providing AFOs: early and delayed group separately.

	Early (n=8)		Delayed (n=12)				Δ early - Δ delayed	p
	Without AFO	With AFO	Δ early	Without AFO	With AFO	Δ delayed		
Kinematics (°)								
Ankle								
Dorsiflexion at initial contact	-3.3 (8.0)	3.6 (4.4)	6.9 (5.7)	-3.7 (7.1)	2.6 (3.7)	6.3 (5.5)	0.6 (-4.7;6.0)	0.810 ^a
Max. dorsiflexion during stance	14.1 (8.2)	14.9 (6.2)	0.8 (4.1)	14.0 (5.5)	14.4 (5.3)	0.4 (2.6)	0.4 (-2.7;3.6)	0.780 ^a
Dorsiflexion at foot-off	-3.7 (9.2)	4.1 (3.8)	7.9 (6.7)	2.4 (4.8)	5.9 (3.6)	3.5 (2.4)	4.4 (-1.3;10.1)	0.112 ^a
Min. dorsiflexion during swing	-7.9 (7.8)	2.4 (3.6)	10.3 (6.3)	-4.8 (7.9)	2.7 (3.6)	7.6 (5.7)	2.8 (-2.9;8.5)	0.321 ^a
Max. dorsiflexion during swing	2.4 (7.4)	6.5 (4.2)	4.1 (4.3)	3.5 (5.5)	6.9 (3.8)	3.3 (3.0)	0.8 (-3.1;4.6)	0.677 ^a
Inversion at initial contact	5.4 (6.3)	4.4 (3.0)	-1.0 (4.6)	9.3 (5.8)	6.2 (2.8)	-3.1 (4.8)	2.1 (-2.4;6.6)	0.340 ^a
Inversion at foot-off	8.1 (7.8)	3.7 (2.7)	-4.4 (6.8)	7.9 (5.1)	5.4 (3.9)	-2.5 (3.4)	-1.9 (-7.7;3.9)	0.482 ^a
Foot								
Foot-progression at initial contact	-12.9 (13.8)	-14.9 (13.9)	-2.0 (4.3)	-12.2 (7.9)	-14.4 (8.7)	-2.1 (3.3)	0.1 (-3.5;3.6)	0.960 ^a
Foot-progression at foot-off	-20.9 (24.9)	-23.3 (20.8)	-2.5 (4.9)	-25.6 (19.2)	-24.8 (18.6)	0.8 (6.2)	-3.3 (-8.8;2.3)	0.229 ^a
Knee								
Flexion at initial contact	15.7 (5.7)	17.3 (6.6)	1.6 (1.7)	19.7 (5.4)	22.4 (5.7)	2.8 (1.3)	-1.2 (-2.6;0.2)	0.087 ^a
Min. flexion during stance	9.2 (4.0)	11.9 (6.3)	2.7 (3.5)	16.2 (7.7)	16.3 (7.8)	0.2 (2.6)	2.6 (-0.3;5.4)	0.075 ^a
Flexion at foot-off	46.0	43.4	-1.9	36.8	39.8	1.9		0.165 ^b
	(21.5;56.9)	(26.7;53.3)	(-3.2;1.9)	(34.0;44.8)	(38.4;45.0)	(0.2;4.4)		
Max. flexion during swing	45.7 (16.9)	44.9 (14.0)	-0.8 (3.3)	40.3 (8.8)	41.4 (7.4)	1.1 (4.2)	-1.9 (-5.6;1.8)	0.302 ^a

Mean (SD) or median (interquartile range) is presented. ^aIndependent samples t-test (mean, 95% confidence interval); ^bMann-Whitney U test. *Table continues on the next page.*

Table 4.5: Effect of providing AFOs; early and delayed group separately (*continued*).

Kinematics (°)	Early (n=8)		Delayed (n=12)				p
	Without AFO	With AFO	Δearly	Without AFO	With AFO	Δdelayed	
Hip							
Flexion at initial contact	31.2 (11.3)	32.3 (11.7)	1.1 (2.0)	22.3 (9.2)	24.1 (8.7)	1.8 (1.7)	-0.7 (-2.5;1.1)
Min. flexion during stance	5.6 (14.3)	6.2 (14.0)	0.6 (2.9)	2.0 (10.2)	1.1 (10.2)	-0.9 (2.1)	1.5 (-0.9;3.8)
Flexion at foot-off	17.8 (12.3)	16.2 (12.0)	-1.6 (3.9)	9.5 (7.5)	9.3 (8.2)	-0.1 (2.0)	-1.5 (-4.8;1.9)
Max. flexion during swing	34.9 (10.6)	34.7 (12.0)	-0.2 (2.4)	26.7 (9.6)	27.4 (8.9)	0.6 (2.8)	-0.8 (-3.4;1.8)
Adduction at initial contact	0.9 (2.8)	0.6 (2.4)	-0.3 (0.8)	0.0 (3.8)	-0.1 (3.6)	-0.1 (1.0)	-0.2 (-1.1;0.7)
Max. adduction during stance	4.8 (2.7)	3.8 (2.9)	-1.0 (1.1)	2.4 (3.1)	2.1 (3.2)	-0.3 (1.4)	-0.7 (-1.9;0.6)
Adduction at foot-off	-2.6 (2.8)	-2.9 (2.8)	-0.4 (1.0)	-2.6 (3.9)	-2.6 (4.1)	0.0 (1.4)	-0.4 (-1.5;0.8)
Max. adduction during swing	1.9 (2.1)	1.7 (1.7)	-0.2 (0.6)	1.0 (3.9)	0.7 (3.6)	-0.3 (0.7)	0.1 (-0.5;0.8)
Pelvis							
Pelvic tilt at initial contact	7.7 (7.7)	7.8 (7.5)	0.2 (1.7)	0.7 (6.0)	1.0 (5.9)	0.3 (1.0)	-0.1 (-1.4;1.2)
Pelvic tilt at foot-off	12.0 (6.8)	11.7 (7.2)	-0.3 (1.5)	6.0 (4.7)	6.0 (5.0)	-0.1 (1.1)	-0.3 (-1.5;0.9)
Pelvic obliquity at initial contact	0.8 (3.0)	0.6 (2.6)	-0.1 (1.5)	4.0 (2.5)	3.9 (2.3)	-0.2 (0.9)	0.0 (-1.1;1.1)
Max. obliquity during stance	2.2 (2.7)	1.9 (2.4)	-0.3 (1.3)	4.6 (2.6)	4.6 (2.5)	-0.1 (0.9)	-0.2 (-1.3;0.8)
Pelvic obliquity at foot-off	1.2 (-1.7;2.6)	0.5 (-2.5;1.8)	-0.8 (-1.4;0.3)	2.6 (1.0;6.0)	2.3 (0.1;6.0)	-0.2 (-1.4;0.5)	-0.2 (-1.4;0.5)
Max obliquity during swing	3.3 (0.0;5.6)	2.8 (1.0;4.6)	-0.9 (-1.3;-0.1)	5.2 (2.9;8.8)	3.9 (2.6;8.3)	-0.7 (-1.3;0.3)	-0.7 (-1.3;0.3)

Mean (SD) or median (interquartile range) is presented. ^aIndependent samples t-test (mean, 95% confidence interval); ^bMann-Whitney U test. *Table continues on the next page.*

Table 4.5: Effect of providing AFOs; early and delayed group separately (*continued*).

	Early (n=8)		Delayed (n=12)				Δ early - Δ delayed	p
	Without AFO	With AFO	Δ early	Without AFO	With AFO	Δ delayed		
Spatiotemporal								
Walking velocity (m/s)	0.46 (0.21)	0.46 (0.19)	0.00 (0.05)	0.42 (0.23)	0.46 (0.25)	0.04 (0.07)	-0.03 (-0.09;0.02)	0.217 ^a
Cadence (steps/min)	69.9 (52.4;76.3)	68.6 (55.0;78.6)	-1.3 (-2.1;4.0)	66.2 (45.7;96.5)	67.3 (52.0;98.2)	2.5 (1.2;7.0)		0.217 ^b
Stride length (m)	0.80 (0.22)	0.80 (0.21)	0.00 (0.07)	0.71 (0.14)	0.73 (0.15)	0.03 (0.06)	-0.03 (-0.10;0.03)	0.311 ^a
Step length (m)	0.44 (0.09)	0.42 (0.10)	-0.02 (0.04)	0.39 (0.07)	0.39 (0.07)	0.00 (0.04)	-0.02 (-0.06;0.02)	0.336 ^a
Step width (m)	0.17 (0.03)	0.17 (0.02)	0.00 (0.02)	0.20 (0.05)	0.19 (0.05)	-0.01 (0.02)	0.01 (-0.01;0.02)	0.487 ^a
Stride duration (s)	1.72 (1.57;2.30)	1.75 (1.53;2.18)	0.03 (-0.18;0.05)	1.81 (1.25;2.63)	1.79 (1.23;2.31)	-0.09 (-0.22;-0.02)		0.189 ^b
Stance duration (% gait cycle)	69.8 (6.2)	69.9 (5.2)	0.0 (2.5)	67.5 (7.9)	67.6 (7.1)	0.2 (3.7)	-0.1 (-3.2;3.0)	0.937 ^a
First double support (% gait cycle)	16.3 (4.5)	17.4 (3.4)	1.1 (1.9)	15.8 (3.8)	16.3 (3.8)	0.4 (2.2)	0.7 (-1.3;2.7)	0.465 ^a
Single support (% gait cycle)	21.5 (6.8)	21.8 (6.2)	0.3 (1.3)	19.7 (6.8)	21.2 (6.6)	1.5 (1.0)	-1.2 (-2.3;-0.2)	0.026^a
Second double support	26.2 (23.6;46.3)	26.3 (21.9;44.0)	-1.5 (-1.9;0.8)	26.7 (20.5;45.8)	27.1 (21.5;41.5)	-1.0 (-2.8;0.8)		0.938 ^b
Swing duration (% gait cycle)	30.2 (6.2)	30.1 (5.2)	0.0 (2.5)	32.5 (7.9)	32.4 (7.1)	-0.2 (3.7)	0.1 (-3.0;3.3)	0.937 ^a

Mean (SD) or median (interquartile range) is presented. ^aIndependent samples t-test (mean, 95% confidence interval); ^bMann-Whitney U test.

these patients. Another explanation may be that subjects in our study may not be completely familiar with walking with AFO, as they were recently provided. Other studies reported positive effects on walking speed in subjects after recent stroke.^{75,76} However, differences in study design are observed compared to our study, as anterior and posterior AFO-use while walking barefoot,⁷⁵ and subjects measured in two different sessions with seven days between measurements using different shoes were studied.⁷⁶ Another explanation is that most studies included 5 or 10m timed walking tests, whereas we used 3D gait-analysis to measure walking speed. It is our clinical observation that walking speed is lower during 3D gait-analysis measurements compared to timed walking tests. This could be explained because subjects were measured in a specialized gait laboratory wearing all kinds of equipment. We speculate that these factors affect walking speed probably more than AFO-provision will affect walking speed, as both Gök et al.⁷⁴ and our results show no effects of recent AFO-provision when walking speed is measured during 3D gait-analysis.

Our secondary aim was to study whether timing of AFO-provision post-stroke influenced the short-term effects. We hypothesized that early AFO-provision may be beneficial since the development of compensatory movement patterns in the proximal limb segments may decrease when foot-drop is limited early in the rehabilitation because of early AFO-provision. However, no effects of timing were found for any of the kinematic or spatiotemporal parameters, except for a very small but significant effect on single support phase. Apparently, short-term effects were not influenced by the timing of AFO-provision. Whether or not long-term effects are present is subject for future studies.

An important strength of this study is that we included subjects early after stroke who were not yet used to walking with an AFO. We provided them with an AFO during the study and measured effects within two weeks after provision. These conditions match with AFO-provision in daily clinical practice. Furthermore, to our knowledge, this is the first study on effects of early AFO-provision that included frontal plane hip kinematics and effects on the pelvis. Our findings add new insights to the literature as hip- and pelvis-movements are often mentioned as important compensatory strategies in the absence of sufficient dorsiflexion after stroke.⁷⁰⁻⁷² However, in our study no effects of AFOs were found with respect to these compensatory strategies.

There are some limitations to this study. The order of testing with and without AFO was randomized, but unfortunately, it was not possible to blind subjects and assessor for AFO-use or early or delayed provision. We found some kinematic differences at baseline between both groups without AFO. However, these differences did not involve our primary outcome measures. Our sample size was limited and not all included subjects could be included in the data-analyses since they were not able to perform the measurements within two weeks after AFO-provision. We could not perform a valid power-calculation to determine sample size because data of previous studies measuring timing-effects of AFO-provision were not available. Therefore, we performed a post-hoc power calculation. For outcome measures with p-values between 0.05 and 0.2 in Table 4.4 and 4.5, we calculated that between 39

and 92 subjects would be needed to find significant differences. However, we would like to point out that it is doubtful whether these effects would be clinically relevant, as in our calculations the kinematic differences were very small (up to 1.3° differences comparing with and without AFO). Power calculation for outcome measures with p-values >0.2 showed that over hundred(s) of subjects would be needed to find significant differences. Therefore, we conclude that for these outcome measures it is unlikely that differences of AFO-provision or timing of AFO-provision exist.

In conclusion, this study showed positive short-term effects of AFO-provision on ankle kinematics in patients early after stroke. Minor effects on knee and hip flexion and spatiotemporal parameters were found. Hip ab/adduction and pelvis movement were not affected. Furthermore, no differences in effects of AFO-provision were found when early and delayed provision (39.8 (9.1) vs. 90.2 (6.4) days) after stroke were compared.

Chapter 5

The influence of early or delayed
provision of ankle-foot orthoses on
pelvis, hip and knee kinematics in
patients with sub-acute stroke:
A randomized controlled trial

Corien DM Nikamp
Job van der Palen
Hermie J Hermens
Johan S Rietman
Jaap H Buurke

Published in Gait & Posture 2018;63:260-267.

ABSTRACT

Background Compensatory pelvis, hip- and knee movements are reported after stroke to overcome insufficient foot-clearance. Ankle-foot orthoses (AFOs) are often used to improve foot-clearance, but the optimal timing of AFO-provision post-stroke is unknown. Early AFO-provision to prevent foot-drop might decrease the development of compensatory movements, but it is unknown whether timing of AFO-provision affects post-stroke kinematics.

Research questions 1) To compare the effect of AFO-provision at two different points in time (early versus delayed) on frontal pelvis and hip, and sagittal hip and knee kinematics in patients with sub-acute stroke. Effects were assessed after 26 weeks; 2) To study whether possible changes in kinematics or walking speed during the 26-weeks follow-up period differed between both groups.

Method An explorative randomized controlled trial was performed, including unilateral hemiparetic patients maximal six weeks post-stroke with indication for AFO-use. Subjects were randomly assigned to AFO-provision early (at inclusion) or delayed (eight weeks later). 3D gait-analysis with and without AFO was performed in randomized order. Measurements were performed in study-week 1, 9, 17 and 26.

Results Twenty-six subjects (15 early, 11 delayed) were analyzed. After 26 weeks, no differences in kinematics were found between both groups for any of the joint angles, both for the without and with AFO-condition. Changes in kinematics during the 26-weeks follow-up period did not differ between both groups for any of the joint angles during walking without AFO. Significant differences in changes in walking speed during the 26-weeks follow-up were found ($p=0.034$), corresponding to the first eight weeks after AFO-provision.

Significance Results indicate that early or delayed AFO-use post-stroke does not influence pelvis, hip and knee movements after 26 weeks, despite that AFO-use properly corrected drop-foot. AFOs should be provided to improve drop-foot post-stroke, but not with the intention to influence development of compensatory patterns around pelvis and hip.

INTRODUCTION

Insufficient foot-clearance is an important alteration in the gait pattern often seen after stroke. It can be caused by decreased hip¹⁰ and knee flexion^{9,10} and decreased ankle dorsiflexion.^{10,70} To overcome foot-clearance problems, individual stroke patients may use compensatory movement strategies like circumduction,^{9,71} increased hip flexion⁷⁰ and pelvic hiking^{9,71,72} depending on the patient's specific impairments and chosen strategy. Ankle-foot orthoses (AFOs) are often used to improve walking and are reported to facilitate, amongst others, toe-clearance in swing.¹⁴ In a review, AFOs were found to prevent foot-drop (i.e. plantarflexion) in early stance, swing and toe-off.¹⁸ Most of the included studies investigated chronic subjects (>6 months).

With respect to daily clinical practice, studying effects of AFOs earlier after stroke is relevant, since the optimal timing of AFO-provision after stroke is still unclear¹⁷ and a topic for debate amongst clinicians. On the one hand, AFO-use early post-stroke is reported to improve early mobilization.⁷⁶ On the other hand, papers reported that clinicians might fear (early) AFO-use, as this could lead to muscle-disuse. Consequently, delays in recovery and permanent gait impairments are feared.^{14,28,30} Clear evidence of the long-term effects of timing of AFO-provision on gait kinematics after stroke is missing.

3D gait-analysis is a powerful tool to quantify joint kinematics during gait⁸¹ and studies assessing kinematic effects of AFOs early post-stroke may contribute to the debate about the optimal timing of AFO-provision. By capturing kinematics, the effects of AFOs on the gait pattern can be quantified. This includes the direct effects on the ankle, but also on more proximal joints like pelvis, hip and knee, which relate to the before mentioned compensatory movements. Previous studies investigating kinematic effects of AFOs in the first months after stroke only compared walking with and without AFO immediately after AFO-provision. Positive effects of AFOs on ankle kinematics^{74,75} and walking speed⁷⁴⁻⁷⁶ and no effects on sagittal knee or hip kinematics⁷⁴⁻⁷⁶ were found. Effects of AFOs on frontal pelvis and hip kinematics (i.e. pelvis obliquity and hip abduction) are unknown since these outcomes were not included. However, including these frontal plane measurements to study effects of AFOs early after stroke is relevant, since compensatory movements like circumduction, pelvis obliquity and hip flexion are reported to achieve foot-clearance in case of insufficient dorsiflexion.⁷⁰⁻⁷²

Besides the previously mentioned early mobilization,⁷⁶ another possible beneficial effect of early AFO-provision might be a decrease in the development of compensatory movements in proximal joints, when foot-drop is limited by AFO-use early after stroke. We recently reported the short-term results of a study focusing on the timing of AFO-provision. Kinematics effects of AFO-provision, including frontal pelvis and hip kinematics were assessed.⁸² Positive effects of walking with AFOs on ankle dorsiflexion, but no effects of AFOs on the pelvis and hip were found. A possible explanation for not finding effects might be that compensatory movements at these joint-levels were not developed yet. Subjects were

early after stroke and measured within one session. Results of the follow-up measurements to study the effects of timing of AFO-provision over a longer period have not yet been reported.

Therefore, the primary aim of the current paper was to compare the effects of AFO-provision at two different points in time (early versus delayed) on frontal pelvis and hip, and sagittal hip and knee kinematics in patients with sub-acute stroke. Effects were assessed after 26 weeks. We hypothesized that early AFO-provision was beneficial compared to delayed provision with respect to the development of compensatory movements. In the frontal plane, we expected less pelvic obliquity (ipsilateral frontal plane elevation of the pelvis) and less abduction of the ipsilateral limb during swing in the early group compared to the delayed group. In the sagittal plane, we expected less excessive hip and knee flexion during swing.

In a previous publication on the effects of early and delayed AFO-provision on functional outcome measures,⁸³ we found significantly different patterns of recovery during the 26-weeks follow-up period between both groups. Therefore, we also wanted to study whether the patterns of recovery over time in terms of kinematics differed between early and delayed provision. Since walking speed is known to influence gait kinematics,⁸⁴ we included walking speed in our study. Our secondary aim was to study whether possible changes in kinematics or walking speed during the 26-weeks follow-up period differed between both groups. In analogy with our previous findings on functional outcomes,⁸³ we hypothesized that if any differences appeared between both groups during the 26-weeks follow-up, they appeared at an early point in time (first eight weeks) for the early group, compared to the delayed group, since the early group was provided with an AFO from the start of the study.

METHODS

We conducted a single center, randomized, controlled, parallel group study. The study was approved by the Medical Ethical Committee Twente, registered in “the Netherlands Trial Register”, number NTR1930 and followed the CONSORT-guidelines.⁷⁷ All subjects provided written informed consent.

Subjects

We recruited subjects from the Roessingh, Center for Rehabilitation in Enschede, the Netherlands. Inclusion criteria were: 1) unilateral ischemic or hemorrhagic stroke leading to hemiparesis (single and first-ever stroke or history of previous stroke with full physical recovery); 2) minimal 18 years; 3) maximal six weeks post-stroke; 4) receiving in-patient rehabilitation care at inclusion; 5) able to follow simple verbal instructions; 6) indication for AFO-use (i.e. abnormal initial floor contact and/or problems with toe-clearance in swing and/or impaired ability to take bodyweight through the paretic lower limb in stance) determined by

the treating rehabilitation physician and physiotherapist. Subjects suffering from severe comprehensive aphasia, neglect or cardiac, pulmonary or orthopedic disorders that could interfere with gait were excluded.

Randomization

An independent person allocated participants to one of two intervention-groups using stratified block-randomization: 1) AFO-provision at inclusion, study week 1 (early group); or 2) AFO-provision eight weeks later, in study week 9 (delayed group). Stratification was based on the Functional Ambulation Categories (FAC)⁴¹: walking with (FAC 0-2) and without (FAC 3-5) physical support of another person at inclusion were used as stratification-categories before randomization.

AFO-provision

Subjects were provided with one of three commonly used types of off-the-shelf, non-articulated, posterior leaf design, polyethylene or polypropylene AFOs: flexible, semi-rigid or rigid (Basko Healthcare, Zaandam, the Netherlands). AFO-fitting was performed by a licensed orthotist. AFO-type was chosen according to a custom developed protocol.⁶⁵ After AFO-provision, subjects were instructed to use the AFO throughout the day, including during their stay at the ward, during therapies and when subjects went home. After AFO-provision, special attention was paid to possible pressure marks by the rehabilitation physician. Besides the AFO-intervention, all subjects received usual care from experienced physiotherapists according to the Dutch guidelines for physiotherapy after stroke.⁶⁷

Procedures

3D gait-analysis was performed four times in both groups: in week 1, 9, 17 and 26 of the study (T1, T2, T3 and T4, respectively). T1 and T2 correspond with the point in time at which the AFO was provided in both groups. The eight weeks between T1 and T2 were also incorporated between T2 and T3, T4 was planned as follow-up measurement after 26 weeks, since most improvements after stroke are observed within the first six months after stroke.⁸⁵ The measurements required that subjects were able to walk without physical support of another person ($FAC \geq 3$) and had sufficient endurance to complete the measurement. If this was not the case, the measurement was postponed until these requirements were met. All measurements were performed with and without AFO in randomized order. The delayed group did not use AFOs at T1 and were therefore measured without AFO only at T1.

Data collection and processing

At inclusion, basic demographic data were recorded. Whether the AFO was actually used in the period before the measurement was assessed during every gait analysis-measurement. Motion data were collected at 100 Hz in a gait-laboratory, using a six-camera Vicon MX13+ motion-analysis system (Vicon, Oxford, UK). Reflective 25-millimeter markers were placed

on the skin and shoes according to the modified Helen-Hayes marker set. Two additional markers were placed on each shoe at metatarsal I and V to assess in/eversion movements. Subjects walked on a level walkway over a distance of eight meters at self-selected walking speed, wearing their own shoes. Markers were not removed between measurements with and without AFO. Assistive devices (such as cane or quad stick) were permitted.

Data-processing was performed using the lower-body Plug-In-Gait model from Vicon and custom in-house software, developed in Matlab (MathWorks, Natick, Massachusetts). Initial contact and foot-off were determined manually. Marker trajectories were time-normalised to stride duration and averaged, with 0% representing initial contact and 100% representing the next initial contact of the same foot. Eight to ten representative strides were used for further analysis.

Outcome measures

The effects of AFOs on compensatory movements in proximal joints can only be assessed under the assumption that the AFO sufficiently corrects the ankle. We previously reported that AFOs properly corrected drop-foot on the short-term.⁸² To confirm effects in the long-term, ankle kinematics were included in the current study as well.

Pelvic obliquity, hip ab/adduction and hip and knee flexion/extension at week 26 were defined as primary outcome measures. Frontal plane pelvic obliquity and hip ab/adduction both contribute to the circumduction-movement. Together with hip and knee flexion/extension (both sagittal plane), these movements are responsible for the main compensatory movements to improve foot-clearance after stroke in case of drop-foot and therefore could be affected by AFO-provision.

Walking speed was assessed by calculating the mean speed of the anterior superior iliac spine-markers along the axis of progression.

For all angles, minimal and maximal values in swing, and values at initial contact and foot-off were calculated. Only results of the affected side are presented in this paper.

Statistical analysis

SPSS version 19 (IBM SPSS Statistics, Chicago, USA) was used for data-analysis. Normality was checked visually and using the Shapiro-Wilk test. Assuming interdependence among joints, the level of significance for analysing kinematics related to the primary and secondary aim were corrected for multiple testing at similar phases of gait using the Holm-Bonferroni correction. For other analyses (like baseline demographics, walking speed) the level of significance was set at $p < 0.05$. A power-calculation could not be performed since data of previous studies measuring timing effects of AFO-provision was not available.

Basic demographic data of both groups at inclusion were compared using independent samples *t*-test/Mann-Whitney *U* test for continuous and chi-squares test/Fisher exact test for categorical variables, as appropriate. Kinematics at T1 without AFO were compared to detect possible baseline differences between both groups. For this, independent samples

t-test or Mann-Whitney *U* test were used, as appropriate.

To confirm whether the AFO properly corrected drop-foot, a within-group analysis comparing ankle dorsi/plantarflexion data with and without AFO at T4 was performed for both groups. Paired samples *t*-test or Wilcoxon signed-rank tests were used, as appropriate.

To study our primary aim, the effects after 26 weeks were compared using between-group analysis of data at T4. Independent samples *t*-tests or Mann-Whitney *U* tests were used, as appropriate.

To study our secondary aim, whether changes in kinematics or walking speed during the 26-weeks follow-up period differed between both groups, a mixed-model repeated measures analysis was performed to compare group-by-time interactions.

The primary analysis only included data after 26 weeks (T4). This analysis was performed both without and with AFO. The secondary analysis included data of all four measurements (T1, T2, T3 and T4). Since data of four measurements was only available without AFO (the delayed group did not use an AFO at T1 yet), the mixed-model repeated measures analysis was only performed for data without AFO.

RESULTS

Baseline

Figure 5.1 details the participant-flow through the study. In total 33 subjects (16 early, 17 delayed) were included in the study. Of these, 26 subjects (15 early, 11 delayed) were included in the analysis. Six subjects (one early, five delayed) did not complete the study (drop-out after T1 or T2). They were not included in the analysis since their data was insufficient to answer the research questions (missing T4). One additional subject (delayed) is missing since performing a 3D gait-analysis was not possible (measurements were too tiring). Of the 26 included subjects, five (one early, four delayed) were not able to perform T1, as they were not able to walk without physical support of another person and/or had insufficient endurance to complete T1. Data of one subject in the early group is missing at T3 because no lab-space was available.

Table 5.1 shows the subject characteristics. No statistically significant differences at inclusion were found between both groups. Most subjects were provided with a flexible type of AFO (see Table 5.1). Of them, one subject (early group) changed from a flexible to a semi-rigid AFO in the period after T1, as rehabilitation physicians judged that the flexible AFO did not provide enough support anymore. All subjects used their AFO daily at the time of the gait-analysis at T1, T2, T3 and T4, except for three subjects (two early, one delayed) at T4. These three subjects used their AFO regularly (during some days of the week), but not daily (every day) at T4. However, they were measured both with and without AFO at T4.

Baseline comparison of kinematics and walking speed at T1 without AFO between the early (*n*=14) and delayed (*n*=7) group revealed no significant differences.

Figure 5.1: CONSORT Flowchart.
The figure shows the participant flow through the study.

Table 5.1: Subject characteristics.

	Total (n=26)	Early (n=15)	Delayed (n=11)
Sex (male/female) ^a	17/9	10/5	7/4
Age (years) ^b	56.4 (9.8)	57.0 (9.9)	55.6 (10.1)
Height (cm) ^c	174.0 (169.8-179.0)	174.0 (169.0-179.0)	171.0 (170.0-178.0)
Weight (kg) ^b	81.1 (12.5)	84.4 (11.4)	76.5 (12.8)
Time since stroke at inclusion (days) ^b	30.4 (6.3)	29.1 (6.5)	32.2 (6.0)
Affected body side (left/right) ^a	16/10	8/7	8/3
Type of stroke (ischemic/hemorrhagic) ^a	22/4	14/1	8/3
Type of AFO (flexible/semi-rigid/rigid) ^a	23/0/3	13/0/2	10/0/1
Sensation* Tactile (normal/impaired/absent) ^a	21/2/3	12/1/2	9/1/1
Proprioception (normal/impaired/absent) ^a	21/4/1	12/2/1	9/2/0
Mini-Mental State Examination ^c	27.0 (24.8-28.0)	27.0 (25.0-28.0)	28.0 (24.0-28.0)
Motricity Index, lower limb ^c	39.5 (10.5-42.0)	37.0 (18.0-42.0)	42.0 (0.0-42.0)
Time since stroke at gait analysis (days)	T1 ^b 51.6 (15.3) (n=21)	51.3 (16.1) (n=14)	52.1 (14.9) (n=7)
	T2 ^b 90.8 (7.4) (n=26)	90.1 (6.5) (n=15)	91.8 (8.7) (n=11)
	T3 ^b 146.0 (6.5) (n=25)	146.8 (7.4) (n=14)	145.1 (5.5) (n=11)
	T4 ^c 209.7 (7.0) (n=26)	209.4 (7.4) (n=15)	210.1 (6.6) (n=11)

Mean (SD) or median (interquartile range) are presented. ^aFisher exact test (2-tailed); ^bindependent samples *t*-test;

^cMann-Whitney *U* test with median (IQR); * tested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part. Gait analysis were planned in week 1 (T1), 9 (T2), 17 (T3), and 26 (T4) of the study, but measurements were postponed in case subjects were not able to walk without physical support of another person and/or had insufficient endurance to complete a gait analysis measurement. The time since stroke (days) at which gait analysis was performed was reported.

Ankle dorsi/plantaflexion

Ankle dorsi/plantarflexion angles without and with AFO are presented in Table 5.2 and 5.3, respectively. In general, the ankle showed plantarflexion angles without AFO, whereas with AFO dorsiflexion angles were found. Within-group analysis comparing walking with and without AFO at T4 showed significant effects of AFO-provision for both the early and delayed group (*p* between ≤ 0.001 and $p=0.048$), confirming proper correction of drop-foot by the AFO at T4.

Table 5.2: Mean (SE) scores without AFO for the early (T1-T4) and delayed (T1-T4) group; the between group-differences at T4.

	Early Mean SE				Delayed Mean SE				Independent samples <i>t</i> -test	
	T1 (n=14)	T2 (n=15)	T3 (n=14)	T4 (n=15)	T1 (n=7)	T2 (n=11)	T3 (n=11)	T4 (n=11)	Δ T4 Early group- Delayed group (95% CI)	p-value
Without AFO										
Kinematics (°)										
Pelvis										
Obliquity at foot-off	1.4 (0.8)	3.0 (0.8)	2.7 (1.0)	1.7 (0.9)	2.5 (1.1)	3.4 (0.9)	3.2 (1.2)	2.8 (1.0)	-1.0 (-3.8;1.7)	0.448
Min. obliquity during swing	20.7 (0.8)	1.9 (0.7)	1.7 (0.9)	0.7 (0.8)	2.3 (1.1)	3.1 (0.8)	2.0 (1.0)	2.1 (1.0)	-1.4 (-4.0;1.2)	0.280
Max. obliquity during swing	4.0 (0.7)	5.6 (0.9)	5.4 (1.1)	4.6 (1.0)	5.0 (1.0)	6.2 (1.0)	5.8 (1.3)	5.1 (1.2)	-0.5 (-3.7;2.7)	0.770
Obliquity at initial contact	1.6 (0.7)	2.8 (0.8)	2.4 (0.9)	1.4 (0.8)	3.3 (1.0)	4.0 (0.9)	2.9 (1.0)	2.3 (1.0)	-0.8 (-3.5;1.8)	0.523
Hip										
Adduction at foot-off	-2.5 (0.7)	-1.7 (1.0)	-2.0 (1.2)	-2.9 (1.1)	-3.1 (0.9)	-3.0 (1.2)	-3.6 (1.4)	-4.8 (1.3)	1.9 (-1.7;5.4)	0.292
Min. adduction during swing	-3.6 (0.7)	-2.9 (0.9)	-3.9 (1.2)	-4.7 (1.0)	-3.8 (0.9)	-4.2 (1.1)	-4.9 (1.3)	-6.5 (1.1)	1.8 (-1.3;4.9)	0.239
Max. adduction during swing	0.7 (0.6)	1.6 (0.8)	1.2 (1.0)	-0.3 (1.0)	-0.2 (0.9)	0.1 (1.0)	-1.3 (1.1)	-2.7 (1.2)	2.4 (-0.8;5.6)	0.128
Adduction at initial contact	-0.2 (0.7)	0.9 (0.8)	0.6 (1.0)	-1.5 (1.0)	-1.5 (1.0)	-0.8 (1.0)	-2.9 (1.1)	-4.0 (1.2)	2.5 (-0.7;5.7)	0.119
Knee										
Flexion at foot-off	16.0 (2.5)	10.0 (2.4)	10.5 (2.3)	8.4 (2.7)	11.8 (3.2)	10.0 (2.8)	9.9 (2.7)	6.8 (3.1)	1.6 (-6.9;10.0)	0.703
Min. flexion during swing	15.8 (2.5)	9.6 (2.5)	9.6 (2.4)	7.8 (2.7)	11.7 (3.2)	9.8 (2.9)	9.6 (2.8)	6.8 (3.1)	1.0 (-7.5;9.6)	0.807
Max. flexion during swing	30.7 (2.5)	28.9 (2.6)	27.6 (2.5)	27.2 (2.3)	26.4 (3.0)	26.3 (3.0)	26.4 (2.9)	24.0 (2.7)	3.2 (-4.1;10.5)	0.372
Flexion at initial contact	28.0 (2.5)	26.9 (2.5)	25.7 (2.3)	25.6 (2.2)	22.1 (3.1)	22.0 (2.9)	22.8 (2.7)	21.0 (2.6)	4.6 (-2.4;11.6)	0.188
Knee										
Flexion at foot-off	35.5 (3.3)	38.1 (2.9)	37.2 (3.5)	37.1 (3.4)	34.7 (4.0)	37.2 (3.4)	36.7 (4.1)	38.2 (4.0)	-1.1 (-11.9;9.8)	0.843
Min. flexion during swing	13.9 (1.5)	13.9 (1.9)	12.4 (1.9)	14.0 (1.8)	18.1 (2.1)	18.9 (2.2)	17.6 (2.1)	15.6 (2.1)	-1.6 (-8.1;4.9)	0.604
Max. flexion during swing	39.0 (3.4)	43.0 (3.3)	41.1 (3.8)	41.1 (4.1)	35.9 (4.1)	39.0 (3.9)	38.7 (4.4)	40.9 (4.8)	-3.3 (-8.2;1.6)	0.938 ^a
Flexion at initial contact	15.4 (1.4)	16.3 (1.8)	14.4 (1.7)	15.4 (1.5)	19.6 (1.9)	20.0 (2.1)	20.2 (1.9)	18.7 (1.8)	-3.3 (-8.2;1.6)	0.175

^aMann-Whitney *U* test. Table continues on the next page.

Table 5.2: Mean (SE) scores without AFO for the early (T1-T4) group; the between group-differences at T4 (*continued*).

Early Mean SE					Delayed Mean SE				Independent samples <i>t</i> -test					
Without AFO					T1 (n=14)	T2 (n=15)	T3 (n=14)	T4 (n=15)	T1 (n=7)	T2 (n=11)	T3 (n=11)	T4 (n=11)	ΔT4 Early- Delayed (95% CI)	p-value
Kinematics (°)														
Ankle														
Dorsiflexion at foot-off					-2.6 (2.3)	-3.0 (2.3)	-2.1 (2.4)	-0.1 (2.3)	-0.3 (3.0)	1.6 (2.7)	-0.2 (2.7)	-3.0 (2.7)	2.9 (-5.5;11.3)	0.485
Min. dorsiflexion during swing					-9.2 (2.4)	-10.7 (2.4)	-8.3 (2.4)	-7.7 (2.4)	-6.0 (3.0)	-4.8 (2.8)	-6.2 (2.8)	-8.0 (2.8)	0.3 (-8.9;9.6)	0.937
Max. dorsiflexion during swing					0.8 (2.0)	1.3 (1.8)	1.9 (2.0)	4.0 (2.3)	1.9 (2.5)	2.9 (2.1)	1.5 (2.3)	0.4 (2.7)	3.6 (-4.6;11.9)	0.362
Dorsiflexion at initial contact					-6.1 (2.1)	-6.2 (1.9)	-4.6 (2.0)	-3.4 (2.4)	-4.3 (2.6)	-3.3 (2.3)	-3.9 (2.3)	-4.4 (2.8)	1.0 (-6.5;8.4)	0.793
Inversion at foot-off					6.9 (1.5)	6.1 (1.4)	4.8 (1.8)	6.0 (1.5)	7.0 (1.9)	8.3 (1.7)	8.7 (2.1)	7.6 (1.7)	-1.7 (-3.0;6.3)	0.465
Min. inversion during swing					11.1 (1.5)	10.5 (1.1)	9.1 (1.6)	9.7 (1.5)	11.6 (1.9)	13.2 (1.3)	14.2 (1.8)	13.2 (1.8)	-3.6 (-1.2;8.4)	0.138
Max. inversion during swing					5.1 (1.2)	3.5 (1.2)	3.0 (1.7)	3.7 (1.5)	6.0 (1.6)	7.7 (1.3)	7.8 (2.0)	6.1 (1.7)	-2.5 (-2.1;7.1)	0.280
Inversion at initial contact					5.8 (1.5)	5.1 (1.2)	4.8 (1.6)	4.5 (1.6)	7.5 (1.9)	9.3 (1.4)	9.9 (1.8)	8.4 (1.8)	-3.9 (-1.1;8.9)	0.121
Walking speed (m/s) ^a														
					0.36 (0.05)	0.53 (0.07)	0.57 (0.07)	0.60 (0.08)	0.35 (0.07)	0.39 (0.08)	0.51 (0.08)	0.57 (0.09)	0.03 (-0.21;0.26)	0.823

^asignificant group*measurement interaction effect ($p=0.034$).

Table 5.3: Mean (SE) scores without AFO for the early (T1-T4) and delayed (T2-T4) group; the between group-differences at T4.

	Early Mean SE				Delayed Mean SE				Independent samples t-test	
	T1 (n=14)	T2 (n=15)	T3 (n=14)	T4 (n=15)	T1 (n=7)	T2 (n=11)	T3 (n=11)	T4 (n=11)	Δ T4 Early group- Delayed group (95% CI)	p-value
Kinematics (°)										
Pelvis										
Obliquity at foot-off	1.3 (1.4)	2.1 (0.7)	2.5 (0.9)	1.2 (0.8)		3.0 (0.8)	2.8 (1.1)	1.9 (0.9)	-0.6 (-3.1;1.8)	0.586
Min. obliquity during swing	0.5 (0.9)	1.1 (0.6)	1.1 (0.8)	-0.1 (0.7)		2.6 (0.7)	2.0 (1.0)	1.4 (0.8)	-1.5 (-3.6;0.7)	0.179
Max. obliquity during swing	3.7 (0.7)	5.0 (0.8)	5.1 (1.0)	4.1 (0.8)		5.5 (0.9)	5.5 (1.1)	4.6 (1.0)	-0.6 (-3.3;2.1)	0.666
Obliquity at initial contact	1.4 (0.7)	2.2 (0.7)	2.1 (0.9)	0.8 (0.8)		3.9 (0.8)	2.9 (1.0)	2.2 (0.9)	-1.4 (-3.8;1.0)	0.241
Hip										
Adduction at foot-off	-2.6 (0.6)	-1.7 (1.0)	-1.7 (1.1)	-3.0 (1.1)		-3.1 (1.2)	-3.7 (1.3)	-4.7 (1.3)	1.7 (-1.8;5.2)	0.318
Min. adduction during swing	-3.7 (0.7)	-3.1 (0.9)	-3.7 (1.0)	-4.8 (0.9)		-4.2 (1.1)	-4.7 (1.2)	-6.1 (1.1)	1.3 (-1.7;4.3)	0.392
Max. adduction during swing	1.1 (0.5)	1.5 (0.8)	1.7 (1.0)	0.3 (1.0)		-0.1 (0.9)	-1.1 (1.1)	-2.1 (1.2)	2.4 (-0.8;5.6)	0.135
Adduction at initial contact	-0.4 (0.7)	0.1 (0.8)	0.3 (0.9)	-1.9 (0.9)		-1.0 (0.9)	-2.4 (1.1)	-3.3 (1.1)	1.4 (-1.5;4.3)	0.155
Flexion at foot-off	15.8 (2.5)	9.7 (2.5)	9.4 (2.2)	8.0 (2.4)		10.3 (2.9)	8.2 (2.6)	5.1 (2.8)	2.9 (-4.8;10.6)	0.440
Min. flexion during swing	15.1 (2.5)	8.8 (2.5)	8.8 (2.2)	7.6 (2.4)		10.3 (2.9)	7.9 (2.6)	4.9 (2.8)	2.7 (-5.0;10.4)	0.477
Max. flexion during swing	31.1 (2.6)	29.3 (2.5)	28.7 (2.4)	28.3 (2.2)		26.4 (2.9)	26.5 (2.8)	24.7 (2.6)	3.7 (-3.3;10.6)	0.285
Flexion at initial contact	29.7 (2.4)	28.4 (2.5)	27.3 (2.3)	27.3 (2.0)		23.7 (2.9)	24.2 (2.7)	22.7 (2.4)	4.7 (-1.9;11.2)	0.155
Knee										
Flexion at foot-off	34.7 (3.0)	36.5 (3.2)	36.8 (3.3)	37.0 (3.5)		38.7 (3.7)	38.3 (3.9)	38.1 (4.1)	-1.1 (-12.1;10.0)	0.845
Min. flexion during swing	14.9 (1.6)	14.7 (1.6)	13.4 (1.6)	14.8 (1.6)		21.4 (1.9)	19.2 (1.9)	16.8 (1.9)	-2.0 (-7.6;3.5)	0.460
Max. flexion during swing	37.6 (3.2)	40.9 (3.7)	41.1 (3.8)	40.9 (4.1)		39.7 (4.3)	40.8 (4.4)	41.0 (4.8)	-0.1 (-13.2;13.0)	0.987
Flexion at initial contact	16.4 (1.7)	16.3 (1.6)	15.3 (1.7)	16.6 (1.6)		22.8 (1.9)	21.1 (1.9)	19.3 (1.9)	-2.7 (-7.9;2.5)	0.302

Note: data with AFO in the delayed group at T1 is not available since these subjects were not provided with an AFO yet. Table continues on the next page.

Table 5.3: Mean (SE) scores without AFO for the early (T1-T4) and delayed (T2-T4) group; the between group-differences at T4 (*continued*).

	Early Mean SE				Delayed Mean SE				Independent samples t-test	
	T1 (n=14)	T2 (n=15)	T3 (n=14)	T4 (n=15)	T1 (n=7)	T2 (n=11)	T3 (n=11)	T4 (n=11)	ΔT4 Early group- Delayed group (95% CI)	p-value
Kinematics (°)										
Ankle										
Dorsiflexion at foot-off	4.4 (0.9)	3.2 (1.1)	2.7 (1.1)	3.4 (1.5)		5.2 (1.3)	3.8 (1.3)	3.8 (1.8)	-0.4 (-5.2;4.4)	0.878
Min. dorsiflexion during swing	1.3 (1.0)	-0.5 (1.0)	-0.4 (1.0)	0.3 (1.4)		2.5 (1.1)	0.7 (1.2)	1.0 (1.7)	-0.7 (-5.7;4.3)	0.769
Max. dorsiflexion during swing	5.6 (1.1)	5.2 (1.1)	5.0 (1.2)	6.1 (1.7)		6.2 (1.3)	5.3 (1.4)	5.6 (1.9)	0.5 (-4.8;5.8)	0.850
Dorsiflexion at initial contact	1.6 (1.2)	0.7 (1.1)	0.6 (1.3)	1.7 (1.6)		2.2 (1.3)	0.9 (1.5)	1.3 (1.9)	0.4 (-4.7;5.4)	0.874
Inversion at foot-off	4.0 (1.0)	3.8 (0.9)	2.8 (1.0)	2.0 (0.9)		5.7 (1.0)	4.5 (1.2)	3.6 (1.0)	-1.6 (-1.1;4.4)	0.239
Min. inversion during swing	5.9 (1.0)	6.1 (0.8)	5.2 (0.9)	4.3 (0.9)		7.9 (0.9)	7.4 (1.0)	6.4 (1.1)	-2.1 (-0.9;5.1)	0.161
Max. inversion during swing	3.0 (0.9)	2.9 (0.8)	1.7 (0.9)	1.0 (0.8)		5.0 (1.0)	3.6 (1.0)	2.4 (0.9)	-1.4 (-1.1;3.8)	0.256
Inversion at initial contact	3.9 (1.0)	4.3 (0.7)	3.5 (0.7)	2.1 (0.9)		6.1 (0.8)	4.7 (0.8)	4.0 (1.1)	-1.8 (-1.1;4.8)	0.213
Walking speed (m/s)	0.37 (0.04)	0.56 (0.07)	0.59 (0.07)	0.64 (0.08)		0.40 (0.08)	0.58 (0.08)	0.63 (0.09)	0.01 (-0.23;0.25)	0.932

Note: data with AFO in the delayed group at T1 is not available since these subjects were not provided with an AFO yet.

Figure 5.2a: Mean kinematics (°) of the affected pelvis and hip in the frontal, and the hip and knee in the sagittal plane, without AFO, as % of the gait cycle. The early group (left) and delayed group (right) are depicted. Results of measurements at week 1 (T1), 9 (T2), 17 (T3) and 26 (T4) are shown. The vertical lines represent foot-off. For reference, kinematic values (mean +/- SD) and foot-off (dashed vertical line) of nine healthy elderly (mean age 60.9 (SD3.4) years) are depicted in grey. Subjects walked at comfortable walking speed in our own lab.

Figure 5.2b: Mean kinematics (°) of the affected pelvis and hip in the frontal, and the hip and knee in the sagittal plane, with AFO, as % of the gait cycle. The early group (left) and delayed group (right) are depicted. Results of measurements at week 1 (T1), 9 (T2), 17 (T3) and 26 (T4) are shown. The vertical lines represent foot-off. For reference, kinematic values (mean $\pm$ SD) and foot-off (dashed vertical line) of nine healthy elderly (mean age 60.9 (SD3.4) years) are depicted in grey. Subjects walked at comfortable walking speed in our own lab.

Effect after 26 weeks

Table 5.2 (without AFO) and Table 5.3 (with AFO) show pelvis, hip, and knee kinematics and walking speed of the early and delayed group at T1, 2, 3 and 4. Figure 5.2a and b show the frontal pelvis and hip, and sagittal hip and knee movement during the gait cycle, respectively without and with AFO.

The lowest p -value should be ≤ 0.008 (α of 0.05 / 6 joint-levels) in order to be statistically significant after Holm-Bonferroni correction. After 26 weeks (T4), between-group analysis showed no statistically significant differences between both groups for any of the joint angles. This was found for walking without (Table 5.2) and with AFO (Table 5.3).

No differences in walking speed were found between both groups at T4, both without (Table 5.2) and with AFO (Table 5.3).

Changes during the 26-weeks follow-up

Mixed-model repeated measures analysis showed that changes in kinematics during the 26-weeks follow-up did not differ between both groups for any of the joint-levels during walking without AFO (Table 5.2).

Significant differences in changes in walking speed during the 26-weeks follow-up were found between both groups ($p=0.034$), see Table 5.2. Both groups showed the greatest increase in walking speed during the first period of eight weeks in which they used their AFO (i.e. from T1-T2 (early) and from T2-T3 (delayed)). In these periods, walking speed without AFO increased from 0.36 to 0.53 m/s and from 0.39 to 0.51 m/s, respectively.

DISCUSSION

Our primary aim was to compare the effects of AFO-provision at two different points in time (early or delayed) on frontal pelvis and hip, and sagittal hip and knee kinematics in patients with sub-acute stroke. We performed a between-group comparison, comparing the effects of early and delayed AFO-provision at 26 weeks. Secondly, we studied whether changes in kinematics and walking speed during the 26-weeks follow-up period differed between both groups.

After 26 weeks, we expected less upward pelvic obliquity and abduction in the frontal plane, and less hip and knee flexion in the sagittal plane in the early group. However, no significant differences between both groups were found, in both the without and with AFO-condition. This means that, against our expectations, early corrections of drop-foot in the distal part of the lower limb with an AFO did not influence movements in the proximal joints (i.e. pelvis, hip and knee) at 26 weeks.

In agreement with previous studies,^{72,86} our study population showed pelvic upward obliquity (pelvic elevation) in swing, combined with hip abduction, both without and with AFO. The most striking deviation comparing our results with healthy individuals is found in

pelvic obliquity, as normally a pelvic drop is present during swing,^{86,87} see Figure 5.2. Furthermore, hip abduction in swing was somewhat less than normal, which can be explained by the upward pelvic obliquity we found. This combination of pelvic upward obliquity and hip abduction is previously reported.⁸⁶ These findings indicate that although both groups did not differ in pelvic obliquity and hip abduction angles, deviations from normal gait were present. In the sagittal plane, we expected less excessive hip and knee flexion in the early group due to early AFO-provision. We found maximal hip and knee flexion angles in swing around 25°-30° and 35°-40° (Table 5.2 and 5.3), respectively. For hip flexion this is within, and for knee flexion this is below the values for healthy subjects,⁸⁷ see Figure 5.2. This indicates that excessive hip and knee flexion were not present as compensatory movement patterns in our population.

Secondarily, we studied whether possible changes in kinematics or walking speed during the 26-weeks follow-up period differed between the early and delayed group. Subjects were measured four times in a period of 26 weeks to assess changes over time. In analogy with previous findings on functional outcomes in the same subjects, we expected that in case differences during the 26-weeks follow-up period would appear between groups, they would appear in the beginning (first eight weeks) of the study.⁸³ However, we did not find any significant different changes in kinematics during the 26-weeks follow-up between both groups without AFO. We already reported that different timing of AFO-provision had no short-term effects.⁸² Together with our current findings, we must conclude that AFO-provision at different points in time does not affect the development of compensatory movements in the short-term, as well as in the long-term. In contrast to the kinematics, we did find significant differences in changes in walking speed during the 26-weeks follow-up comparing both groups ($p=0.034$) without AFO. The changes correspond to the first eight weeks after AFO-provision (+0.17 m/s from T1-T2 (early) and +0.12 m/s from T2-T3 (delayed)). Post-hoc within-group analysis showed that the increase in walking speed in the first eight weeks after AFO-provision was statistically significant ($p \leq 0.041$ for all analysis) in both groups, with and without AFO. According to Perera et al.⁵² these increases can be considered clinically relevant significant.

The results of our study contain valuable information for clinicians in relation to the discussion whether to provide an individual subject with an AFO earlier or later after stroke. If the goal of AFO-provision is to improve drop-foot in order to prevent development of compensatory movement patterns around pelvis and hip, we did not find any evidence that early AFO-use is beneficial, since no differences were found with the delayed group, who started using their AFOs eight weeks later. The upward pelvic obliquity combined with hip abduction found in our subjects can help to swing the affected leg forward. Because these kinematic patterns were present in both groups right from the start, one can discuss whether these frontal pelvis and hip movements are actually compensatory movement patterns. Compensatory movements suggest that these movements can be voluntarily controlled, which apparently, they cannot. As an alternative, these frontal plane movements may be an integral

part of the gait pattern after stroke, as was also mentioned by Kerrigan et al.⁸⁶ suggesting these movements as intrinsic abnormalities directly associated with upper motor neuron injury. Future research on this topic is needed, including the contribution of the unaffected leg to the gait pattern after stroke, and the effects of timing of AFO-provision on muscle activation patterns to study whether or not AFO-provision affects muscle activation patterns in the long-term.

Although early AFO-provision may not be beneficial with respect to kinematics of the pelvis, knee and hip, other, for patients and clinicians relevant outcome measures may benefit from early AFO-provision. Direct effects of AFOs on ankle kinematics were found in the current study, changing the ankle from plantarflexion into dorsiflexion (i.e. improve drop-foot) during swing. Drop-foot is reported to contribute to high fall-risk,²¹ and by improving drop-foot AFOs may reduce fall-risk.¹¹ Furthermore, we previously found beneficial functional effects of early AFO-provision.⁸³ Based on the current study, the achievements on functional gains do not seem to be related to kinematics. This raises the question how these functional improvements after stroke are achieved. Again, the contribution of the unaffected limb may play an important role and should be included in future research.

To the best of our knowledge, this is the first study incorporating longitudinal 3D gait-analysis to measure effects of timing of AFO-provision. This is an important strength of the current study. Previous longitudinal studies on the effects of AFOs after stroke are lacking 3D gait-analysis,^{39,40} or 3D gait-analysis was included, but focus was on comparing AFOs with functional electrical stimulation,^{61–63,88} instead of focusing on the effects of timing of the AFO-provision itself. Another strength of our study is that we included the subjects in an early phase after stroke. Thereby, the study conditions match with the situation in which clinicians often consider AFOs.

The major study-limitation is the small sample size, probably underpowering the results. The sample size was limited further at T1 since not all subjects were able to perform this measurement. We did not include subjects that dropped-out after T1 or T2 in the original analysis. Post-hoc intention-to-treat analysis including these subjects showed that this did not affect results. Other study-limitations relate to the longitudinal study-design. We measured in a period in which large functional improvements after stroke are seen,⁸⁵ which means that it was inevitable that some measurement conditions changed during the study. Although we tried to limit variation as much as possible, changes in walking aids and shoes between measurements could have affected our results. Furthermore, it was not possible to blind subjects and assessor for AFO-use.

In conclusion, the results of our study indicate that AFO-use, both early and delayed after stroke, does not influence frontal pelvis and hip, and sagittal hip and knee movements of the affected limb after 26 weeks, despite that the AFO properly corrected drop-foot. Therefore, AFOs should be provided to improve drop-foot, but not with the intention to prevent or affect development of compensatory movement patterns around pelvis and hip after stroke.

Chapter 6

Effect of long-term use of ankle-foot orthoses on tibialis anterior muscle electromyography in patients with sub-acute stroke: A randomized controlled trial

Corien DM Nikamp
Jaap H Buurke
Leendert Schaake
Job van der Palen
Johan S Rietman
Hermie J Hermens

ABSTRACT

Objective To determine: 1) whether the use of ankle-foot orthoses (AFOs) over a period of 26 weeks affects tibialis anterior muscle activity; 2) whether the timing of provision of AFOs (early or delayed) affects results; 3) whether the provision of AFOs affects tibialis anterior-activity within a single measurement.

Design Randomized controlled trial.

Subjects Unilateral hemiparetic subjects, a maximum of six weeks post-stroke.

Methods Subjects were assigned randomly to early (at inclusion; week 1) or delayed provision of AFOs (eight weeks later; week 9). Tibialis anterior electromyography was measured with and without AFO, in study week 1, 9, 17 and 26.

Results A total of 26 subjects were analyzed. In a single measurement, use of an AFO significantly reduced the activity levels of the tibialis anterior muscle during the swing phase ($p=0.041$) compared with walking without an AFO. During the 26-week follow-up, no changes were found in tibialis anterior muscle activity in the swing phase without an AFO, both within-groups ($p=0.420$ early; $p=0.282$ delayed), and between-groups ($p=0.987$). After 26 weeks, no differences were found in tibialis anterior muscle activity between both groups in the swing phase, with ($p=0.207$) or without AFO ($p=0.310$).

Conclusions Use of AFOs post-stroke reduced tibialis anterior muscle activity in the swing phase within one measurement; however, long-term use of AFOs for 26 weeks did not affect such activity. Early or delayed provision of AFOs did not affect the findings. The results indicate that there is no need to fear negative consequences on tibialis anterior muscle activity because of long-term AFO-use (early) after stroke.

INTRODUCTION

Walking function is often impaired after stroke.⁵ Insufficient foot-clearance during the swing phase is an important alteration contributing to limited walking function post-stroke. Activity of the tibialis anterior (TA) is important for foot-clearance. In healthy subjects, the TA becomes active just before foot-off in order to lift the foot during the swing phase, peaking during early swing.⁸⁷ A second burst of activity controls pre-positioning before initial contact and controls plantarflexion during the loading response.

Ankle-foot orthoses (AFOs) are often provided post-stroke to improve foot-clearance in swing,¹⁴ although the optimal timing of provision after stroke is unclear.¹⁷ Some clinicians are reluctant to prescribe AFOs post-stroke as they fear AFOs may result in disuse of muscles, in particular the TA muscle.^{14,29,30} Several studies compared walking with and without AFOs.^{28–30,79,89} Within a single session a decrease in electromyography (EMG) of the TA muscle was found during walking with AFOs.^{28–30,79} Only one study included a follow-up period.²⁸ Geboers et al.²⁸ found immediate reduced activity of the ankle dorsiflexors of 7% in patients with peripheral paresis, calculated over the whole step cycle. Six weeks of AFO-use, however, did not change EMG activity levels. Therefore, they concluded that AFO-use is safe, even for recently paretic patients. It is unknown whether AFO-use over a longer period of time after stroke has negative effects. Furthermore, it is not known whether early or late provision of AFOs post-stroke affects muscle activity.

The aim of this study was to determine the long-term effects of AFO-use on muscle activity of the TA muscle. The primary aim was to determine whether AFO-use affects TA muscle activity over a period of 26 weeks within subjects provided with AFOs early or delayed after stroke. Secondly, between-group differences in TA muscle activity were measured for early and delayed provision of AFOs. Thirdly, whether provision of AFOs affects TA muscle activity within a single measurement session was determined when walking with and without AFOs.

In agreement with previous literature, it was hypothesized that AFO-use decreases TA muscle activity during the swing phase, comparing walking with and without AFOs within a measurement. However, it was also hypothesized that TA muscle activity over time would not be affected by AFO-use, and it was not expected that timing of AFO-provision would influence the results.

METHODS

Study design

Study data were collected as part of a single center, randomized controlled, parallel group study, which aimed to study the effects of different timing of provision of AFOs. The study was approved by the Medical Ethical Committee Twente, registered in “the Netherlands Trial

Register", number NTR1930 and followed the CONSORT guidelines.⁷⁷ All subject provided written informed consent.

Subjects

Subjects were recruited by the main researcher between December 2009 and March 2014, follow-up continued until 2015. Stroke subjects were recruited from the Roessingh Centre for Rehabilitation in Enschede, The Netherlands. Inclusion criteria were: 1) unilateral ischemic or hemorrhagic stroke leading to hemiparesis (single and first-ever stroke or history of previous stroke with full physical recovery); 2) minimum 18 years; 3) maximum six weeks post-stroke; 4) receiving in-patient rehabilitation care at inclusion; 5) able to follow simple verbal instructions; 6) indication for AFO-use (i.e. abnormal initial floor contact and/or problems with foot-clearance in swing and/or impaired ability to take bodyweight through the paretic lower limb in stance) determined by the treating rehabilitation physician and physiotherapist. Exclusion criteria were: subjects with severe comprehensive aphasia, neglect or cardiac, pulmonary or orthopedic disorders that could interfere with gait.

Randomization

An independent person allocated participants to one of the two intervention groups using stratified block-randomization: 1) AFO-provision at inclusion, in study week 1 (early group); or 2) AFO-provision eight weeks later, in study week 9 (delayed group). Randomization was performed with sealed envelopes in blocks of four with a ratio of 1:1. Stratification was based on the Functional Ambulation Categories (FAC).⁴¹ Walking with (FAC 0-2) and without (FAC 3-5) physical support from another person at inclusion were used as stratification categories before randomization.

Provision of AFOs

Subjects were provided with one of three commonly used types of off-the-shelf, non-articulated, posterior leaf design, polyethylene or polypropylene AFOs; flexible, semi-rigid or rigid (Basko Healthcare, Zaandam, the Netherlands). The type of AFO was chosen in week 1 (early group) or week 9 (delayed group). AFO-fitting was performed by a licensed orthotist. AFO-type was chosen according to a custom developed protocol.⁶⁵ Besides the AFO-intervention, all subjects received usual care from experienced physiotherapists according to the Dutch guidelines for physiotherapy after stroke.^{42,67}

Procedures

Measurements were performed four times in both groups and were planned in week 1 (T1), 9 (T2), 17 (T3) and 26 (T4) of the study. T1 and T2 correspond with the point in time at which the AFO was provided in both groups. The eight weeks between T1 and T2 were also incorporated between T2 and T3, T4 was planned as follow-up measurement after 26 weeks. The measurements required that subjects were able to walk without physical support from

another person ($FAC \geq 3$) and had sufficient endurance to complete a measurement. If this was not the case, the measurement was postponed until these requirements were met. Measurements were performed with and without AFO in randomized order. Subjects in the delayed group did not use an AFO at T1 and were therefore measured at T1 without AFO only.

Data collection and processing

At inclusion, basic demographic data were recorded. Actual AFO-use was assessed for every measurement. Measurements were performed in a gait laboratory. Muscle activation pattern of the TA muscle was assessed using surface EMG (sEMG), using a wireless 16-channel Biotel 99 EMG-amplifier (Glonner, Munich, Germany) with a cut-off frequency of 600 Hz/-3 dB and a first order 17 Hz high-pass filter. Arbo sg93 electrodes (Covidien, Mansfield, MA, USA) were used and electrode-placement and skin preparation were according to the SENIAM protocol.⁹⁰ Subjects walked on a level walkway over a distance of eight meters at self-selected walking speed, wearing their own shoes. sEMG electrodes were not removed between measurements with and without AFO. Assistive devices (such as cane or quad stick) were allowed and subjects were allowed to rest between the trials if necessary.

Raw sEMG-signals were digitized at 1,000 Hz sampling rate with 16-bits resolution and stored on a VICON MX13+ motion-analysis system (Vicon, Oxford, UK). Simultaneously with the sEMG-recordings, 3D gait-analysis was recorded, using a six-camera Vicon MX13+ motion-analysis system for capturing marker trajectories. Reflective 25-mm markers were placed directly on the skin and shoes, according to the modified Helen Hayes marker-set. Marker trajectories of the foot were used to manually determine initial contact (IC) and foot-off (FO). Marker trajectories of the left and right anterior superior iliac spine along the axis of progression were averaged and used to calculate walking speed.

Data-processing was performed using custom in-house software, developed in Matlab (MathWorks, Natick, Massachusetts, USA). sEMG data were first band-pass filtered with cut-off frequencies 25 and 450 Hz. After processing, data were manually checked for artefacts. If artefacts were found, the specific gait cycle was removed from the analysis. Subsequently, sEMG data were rectified and smoothened using a low-pass filter with cut-off frequency of 10 Hz and split into four sub-phases of gait using foot-events (IC and FO) of both sides: (1) first double support (DS1), from IC to opposite FO; (2) single support (SS), from opposite FO to opposite IC; (3) second double support (DS2), from opposite IC to FO; (4) swing (SW), from FO to IC. Once the data were segmented into the four sub-phases, each sub-phase was time-normalized to 100%. These time-normalized sub-phases were used to calculate the area under the curve (AUC) to express the activity level per sub-phase.

Outcome measures

The primary outcome measure was TA muscle activity during swing, as the swing phase is the main sub-phase of gait in which TA activity is shown during normal walking to evoke

foot-clearance.⁸⁷ The secondary outcome measure was TA muscle activity during the other sub-phases. Outcomes were calculated for each of the four measurements T1-T4, with and without AFO. Walking speed without and with AFO was calculated, since walking speed is known to affect EMG.⁹¹

Statistical analysis

SPSS version 19 (IBM SPSS Statistics, Chicago, IL, USA) was used for data-analysis. The level of significance for all analyses was set at $p < 0.05$. No power-calculation was performed, since relevant data regarding timing of AFO-provision were not available. Because TA muscle activity per sub-phase did not show a normal distribution, logarithmic transformations were performed prior to statistical testing.

Baseline data, including TA muscle activity of both groups at T1 without AFO, were compared using independent samples *t*-test/Mann-Whitney *U* test for continuous variables and chi-squares test/Fisher-exact test for categorical variables, as appropriate.

Mixed-model repeated measures analyses were performed, both within-groups to study whether AFO-use affected TA muscle activity over a period of 26 weeks, and between-groups over time, in order to assess a group-by-time interaction. Both analyses included walking speed as a confounder. The analyses included data of all four measurement (T1, T2, T3, T4). Since data of four measurements was available only without AFO (the delayed group did not yet use an AFO at T1), the mixed-model analyses were performed for data without AFOs only.

Between-group effects after 26 weeks were studied comparing the data of both groups using the independent samples *t*-test, both for the without and with AFO condition.

The third objective was to determine whether AFO provision decreased TA muscle activity when walking with and without the AFO was compared within a single measurement session. In order to be able to compare these results with those of previous studies (mainly including subjects with chronic stroke), data of the total (early and delayed) group at T4 were included in this analysis. A paired samples *t*-test was used to compare data with and without AFO.

RESULTS

Baseline

Figure 6.1 details the participant flow through the study. Thirty-three subjects (16 early, 17 delayed) were included in the study. Of these, 26 subjects (15 early, 11 delayed) were included in the analysis. Six subjects (one early, five delayed) did not complete the study (drop-out after T1 or T2). They were not included in the analysis since their data was insufficient to answer the research questions (missing T4). One additional subject (delayed) was excluded, since it was not possible to perform the measurements (measurements were too

tiring). Of the included 26 subjects, five (one early, four delayed) were not able to perform T1, as they were not able to walk without physical support from another person and/or had insufficient endurance to complete T1. In 19 of the 21 subjects who were able to perform T1, measurements had to be postponed with 1-5 weeks, resulting in T1 being performed approximately 51 days after stroke, see Table 6.1. In general, measurements T2, T3 and T4 could be performed as planned. Data of one subject (early) is missing at T3 because no laboratory space was available.

Table 6.1 shows the subject characteristics. No statistically significant differences were found between the groups at inclusion. The type of AFO provided, and whether subjects use their AFO in daily life was registered. Most subjects were provided with a flexible type of AFO (Table 6.1). One subject (early) changed from a flexible to a semi-rigid AFO between T1 and T2, as rehabilitation physicians judged that the flexible AFO did not provide enough support any longer. All subjects used their AFO daily at the time of the measurements at T1, T2, T3 and T4, except for three subjects (two early, one delayed) at T4. These three subjects used their AFO during some days of the week at T4, mainly during walking outdoors for longer distances. These subjects were measured both with and without AFO at T4.

The median number of gait cycles used to calculate the average AUC per sub-phase was ≥ 9 for each measurement and group. Baseline comparison at T1 did not reveal significant differences in TA muscle activity without AFO ($n=14$ early; $n=7$ delayed), except for TA muscle activity during the second double support phase ($p=0.016$). No differences in walking speed without an AFO were found at baseline (0.37 vs 0.39 m/s for the early and delayed group, respectively, $p=0.804$).

Effects on TA muscle activity during a 26-weeks period

Table 6.2 and Figure 6.2 show the median AUC for TA muscle activity of the early and delayed group at T1, 2, 3 and 4 for the different phases in gait. The original data without logarithmic transformation are shown.

No changes in TA muscle activity were found during the 26-weeks period in SW without AFO in both groups (mixed-model repeated measures analysis within-groups $p=0.420$ and $p=0.282$ for the early and delayed group, respectively). During the other sub-phases of gait, significant changes were found only for DS1 and SS in the delayed group ($p=0.013$ and $p=0.007$, respectively).

Effects of early versus delayed provision of AFOs

After 26 weeks (T4), no differences in TA muscle activity between both groups were found in SW (independent samples t -test $p=0.310$ and $p=0.207$ for without and with AFO, respectively) or any of the other sub-phases of gait ($p \geq 0.192$ in all cases). Furthermore, mixed-model repeated measures analysis between-groups showed that changes in TA muscle activity during the 26-weeks follow-up period were not different between the early and delayed group in SW ($p=0.987$) or any of the other sub-phases of gait, see Table 6.2.

Figure 6.1: CONSORT Flowchart.
The figure shows the participant flow through the study.

Table 6.1: Subject characteristics.

		Total (n=26)	Early (n=15)	Delayed (n=11)
Sex (male/female) ^a		17/9	10/5	7/4
Age (years) ^b		56.4 (9.8)	57.0 (9.9)	55.6 (10.1)
Height (cm) ^c		174.0 (169.8-179.0)	174.0 (169.0-179.0)	171.0 (170.0-178.0)
Weight (kg) ^b		81.1 (12.5)	84.4 (11.4)	76.5 (12.8)
Time since stroke at inclusion (days) ^b		30.4 (6.3)	29.1 (6.5)	32.2 (6.0)
Affected body side (left/right) ^a		16/10	8/7	8/3
Type of stroke (ischemic/hemorrhagic) ^a		22/4	14/1	8/3
Type of AFO (flexible/semi-rigid/rigid) ^a		23/0/3	13/0/2	10/0/1
Sensation*	Tactile	21/2/3	12/1/2	9/1/1
	(normal/impaired/absent) ^a			
	Proprioception	21/4/1	12/2/1	9/2/0
		(normal/impaired/absent) ^a		
Mini-Mental State Examination ^c		27.0 (24.8-28.0)	27.0 (25.0-28.0)	28.0 (24.0-28.0)
Motricity Index ^c	total lower limb	39.5 (10.5-42.0)	37.0 (18.0-42.0)	42.0 (0.0-42.0)
	ankle	9.0 (0.0-14.0)	9.0 (0.0-14.0)	9.0 (0.0-14.0)
	knee	14.0 (6.8;14.0)	14.0 (14.0;14.0)	14.0 (0.0;14.0)
	hip	14.0 (0.0;14.0)	14.0 (9.0;14.0)	14.0 (0.0;14.0)
Time since stroke at gait analysis (days)	T1 ^b	51.6 (15.3) (n=21)	51.3 (16.1) (n=14)	52.1 (14.9) (n=7)
	T2 ^b	90.8 (7.4) (n=26)	90.1 (6.5) (n=15)	91.8 (8.7) (n=11)
	T3 ^b	146.0 (6.5) (n=25)	146.8 (7.4) (n=14)	145.1 (5.5) (n=11)
	T4 ^c	209.7 (7.0) (n=26)	209.4 (7.4) (n=15)	210.1 (6.6) (n=11)

Mean (SD) or median (interquartile range) are presented. ^a Fisher exact test (2-tailed); ^b independent samples *t*-test; ^c Mann-Whitney *U* test with median (IQR); * tested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part. Gait analysis were planned in week 1 (T1), 9 (T2), 17 (T3), and 26 (T4) of the study, but measurements were postponed in case subjects were not able to walk without physical support of another person and/or had insufficient endurance to complete a gait analysis measurement. The time since stroke (days) at which gait analysis was performed was reported.

Table 6.2: Area under the curve of the tibialis anterior muscle and walking speed for the early and delayed group (T1-T4); the mixed model repeated measures analysis within and between groups; and the independent samples t-test between the early and delayed group at T4.

Median AUC of the tibialis anterior (IQR)					Median AUC of the tibialis anterior (IQR)					Mixed model repeated measures analysis*		Independent samples t-test†
Early					Delayed					Within groups		
AUC (μV)	T1 (n=14)	T2 (n=15)	T3 (n=14)	T4 (n=15)	T1 (n=7)	T2 (n=11)	T3 (n=11)	T4 (n=11)	Early, p-value	Delayed, p-value	p-value	T4, p-value
Without AFO												
SW	21 (11;63)	24 (7;62)	22 (8;63)	33 (9;81)	43 (26;67)	40 (17;90)	45 (25;98)	40 (16;121)	0.420	0.282	0.987	0.310
DS1	12 (5;58)	20 (4;61)	17 (7;67)	23 (12;64)	23 (7;59)	31 (8;49)	45 (22;68)	21 (8;105)	0.922	0.013	0.119	0.975
SS	5 (3;21)	8 (3;12)	8 (4;19)	12 (6;20)	9 (5;34)	8 (6;32)	22 (9;47)	11 (5;42)	0.531	0.007	0.117	0.760
DS2	13 (3;24)	14 (3;43)	20 (4;64)	22 (6;52)	29 (22;50)	31 (10;46)	39 (20;63)	36 (14;48)	0.404	0.248	0.912	0.225
With AFO												
SW	14 (4;64)	24 (2;53)	15 (4;64)	18 (6; 91)	-	37 (16;89)	43 (16;85)	40 (14; 112)			0.207	
DS1	7 (4;43)	21 (5;51)	14 (4;47)	30 (9; 82)	-	19 (8;49)	32 (9;48)	21 (9; 81)			0.921	
SS	4 (3;10)	9 (3;13)	7 (4;18)	8 (6; 21)	-	7 (5;36)	5 (6;30)	15 (6; 41)			0.445	
DS2	6 (3;25)	14 (3;36)	16 (4;47)	24 (5; 56)	-	23 (9;50)	30 (15;66)	39 (14; 63)			0.192	
Mean (SD) walking speed (m/s)												
Without AFO												
	0.37	0.53	0.56	0.60	0.40	0.39	0.51	0.58				
	(0.19)	(0.29)	(0.29)	(0.31)	(0.25)	(0.21)	(0.24)	(0.26)				
With AFO												
	0.38	0.56	0.58	0.64	-	0.40	0.58	0.63				
	(0.17)	(0.28)	(0.30)	(0.31)		(0.20)	(0.24)	(0.26)				

AFO: ankle-foot orthosis; AUC: Area Under the Curve. For Tibialis anterior, median (IQR) values are presented. * Statistical test based on logarithmic transformed data and walking speed included as confounder; * Statistical test based on logarithmic transformed data.

Figure 6.2: Boxplots of tibialis anterior area under the curve (AUC) without AFO. AUC is presented per sub-phase, for the early (left) and delayed (right) group separately. Circles and asterisks represent outliers and extreme outliers, respectively.

Effects of use of AFO within a single measurement session

TA muscle activity without and with AFO were compared at T4 for the total group ($n=26$) to study the effects of AFO-use within a measurement. AFO-use significantly lowered TA muscle activity in SW ($p=0.041$) compared with walking without an AFO. No effects were found in the other sub-phases of gait ($p=0.398$, 0.696 and 0.407 for DS1, SS and DS2, respectively).

DISCUSSION

This study shows that AFO-use after stroke decreases TA muscle activity during swing within a single measurement session, without negatively affecting TA muscle activity over 26 weeks.

The results comparing TA muscle activity with and without AFO are according with our hypothesis and in agreement with previous studies comparing the effects of AFOs in the swing-phase during a single measurement session.^{29,30,79}

Based on the results of previous studies assessing the effects of AFO-use only at a certain point in time, AFO-use was suggested to decrease activation of muscles around the ankle, thereby encouraging disuse of muscles.^{14,29,30} Consequently, AFO-use was thought to worsen the existing loss of strength and possibly delaying recovery,²⁸ resulting in permanent gait impairments and AFO dependence.³⁰ To our best knowledge, the present study

is the first to assess the long-term effects of AFO-use after stroke. No changes were found in AUC of the TA in swing during the follow-up period of 26 weeks while walking without AFO, for subjects either in the early or delayed group. Significant changes in AUC in SS were found for the delayed group. Post-hoc analysis revealed that AUC at T3 differed significantly from T1 and T2, showing higher levels at T3. We have no explanation for this increase at T3. Significant changes were also found in DS2, but post-hoc analysis did not reveal any significant differences between individual measurements. The results for the swing phase did not show any negative effects of long-term AFO-use on TA muscle activity post-stroke. This is in accordance with a study by Geboers et al., which included patients with peripheral paresis.²⁸ They found reduced activity of ankle-dorsiflexors with AFO within a single measurement session, but six weeks of AFO-use did not lead to a general lower level of EMG activity. To explain our results, studies suggest that the possible negative effects of AFOs on muscle activity in a single gait cycle might be counteracted by the fact that AFOs improve walking in general.^{28,30} An increase in amount of walking (steps taken) is suggested to offset a decrease in EMG during one single step.³⁰

Ideally, one would need a long-term longitudinal randomized controlled trial, including a control group with no AFO-use to determine whether long-term AFO-use affects TA muscle activity after stroke. However, this is not feasible for ethical reasons. Instead, groups were provided with an AFO early or delayed after stroke, which was not found to influence the results. We already reported positive effects of AFO-provision on ankle kinematics early after stroke,⁸² while no effects of early versus delayed AFO-provision on pelvis, hip and knee kinematics were found after 26 weeks.⁹² At the same time, beneficial effects of AFO-provision were found on functional levels.⁶⁵ After 26-weeks no differences with respect to balance and mobility were found between early and delayed provision, but early provision showed favorable outcomes in the first 11-13 weeks, possibly resulting in earlier independent and safe walking.⁸³ For clinical practice, this means that clinicians, together with the patient, can decide when to start AFO-treatment based on personal priorities and preferences. Early AFO-provision is expected to provide beneficial effects on a functional level in a short-term, without negatively affecting muscle activity of the TA in the long-term.

An important strength of the study is that this is the first study to measure the effects of AFOs on muscle activity of the TA in a longitudinal study-design post-stroke. Furthermore, subjects were included early (within six week) after stroke, both with independent and dependent walking ability at the start of the study. Thereby, our study conditions match with the situation in which clinicians often consider AFOs in daily clinical practice.

Study limitation

This study has some limitations. First, the sample-size was relatively small, and this was limited further at T1 since not all subjects were able to perform this measurement at that time. Secondly, the longitudinal design included four separate EMG measurements during the 26-weeks follow-up period. Changes in electrode-position may arise and could affect

results. This was limited, since a standard protocol was used to define electrode positioning.⁹⁰ Changes in measurement conditions are inevitable in a longitudinal design including subjects early after stroke. This includes changes in the use of walking aids and shoes during the follow-up period. Although we tried to limit variation as much as possible, changes in walking aids and shoes between measurements could have affected our results.⁹³ The results may also be affected by the use of different types of AFOs in our study. However, because of the small sample size, a sub-group analysis per type of AFO was not possible. Furthermore, walking speed increased during the study, which is known to affect EMG.⁹¹ Therefore, walking speed was included as confounder in the mixed-model analyses. *Post-hoc* analysis revealed that walking speed did not differ between both groups after 26 weeks. Finally, it was not possible to blind subjects and assessor for AFO-use.

Conclusion

Within a single measurement session, AFO-use lowers TA muscle activity in the swing phase when walking with AFO is compared with walking without AFO. However, long-term AFO-use for a period of 26 weeks after stroke does not affect TA muscle activity. Furthermore, early or delayed provision of AFOs does not affect the results. The results clearly indicate that there is no need to fear negative consequences on the level of muscle activity of the TA muscle because of long-term AFO-use (early) after stroke.

Chapter 7

The effect of ankle-foot orthoses on fall/near fall incidence in patients with (sub-)acute stroke: A randomized controlled

Corien DM Nikamp
Marte SH Hobbelink
Job van der Palen
Hermie J Hermens
Johan S Rietman
Jaap H Buurke

ABSTRACT

Falls are commonly reported post-stroke. Ankle-foot orthoses (AFOs) are often provided to improve safety and walking, but the effect of their use in the reduction of falls after stroke is unknown. A randomized controlled trial (RCT) on the effects of AFO-provision after stroke was performed. Effects on clinical scales, 3D-gait kinematics and muscle-activity were previously reported. This paper aims to study the effects of AFO-provision on occurrence and circumstances of falls/near falls. The RCT included unilateral hemiparetic stroke patients. AFOs were provided either early (study week 1) or delayed (study week 9). Both groups were compared in the first eight weeks of the study and diaries were used to register falls/near falls and their circumstances. Follow-up measurements were performed in week 9-52, in which both groups were provided with AFOs. Functional Ambulation Categories and Berg Balance Scale were assessed to determine walking independence and balance, respectively. Last known scores were noted in case of an incident. Thirty-three subjects were included (16 early, 17 delayed). In week 1-8, the early group, who were provided with AFOs, fell significantly more frequently compared with the delayed group, 11 versus 4 times, respectively (Incidence Rate Ratio=2.9, $p=0.039$). Out of the falls recorded in the early group, 63.6% occurred without wearing AFOs. Most of these falls occurred during transfers (36.4%) and standing (27.3%), and notably it were the subjects who did not have independent walking ability. No differences were found for near falls in week 1-8, or for falls/near falls in week 9-52. Six severe consequences (including fractures) were reported from a fall. To conclude, the subjects provided with AFOs early after stroke reported a higher number of falls, compared to the subjects that had not yet been provided with AFOs. However, in the subjects provided with AFOs, 63.6% of the falls occurred whilst without wearing the AFO. Furthermore, the majority of these incidents took place whilst subjects had no independent walking ability. This raises an interesting question of the importance of careful instructions to patients and their relatives, and the influence of potential cognitive impairments on the ability of the subjects to take on these instructions.

INTRODUCTION

Loss of postural control is a major health problem in patients after stroke.⁹⁴ Delayed muscle, kinetic and kinematic responses to external perturbations are found.¹¹ Together with reduced postural stability during quiet standing, these delayed and less coordinated responses to both self-induced and external balance perturbations are reported as risk factors for falls.¹¹ In addition, walking ability is often affected after stroke. Insufficient foot clearance because of decreased flexion of the affected lower limb increases the risk for stumbling and falls.¹¹ Furthermore, depression, hemineglect, sensory and cognitive deficits have been explored and are important fall risk factors.^{11,95} As a result of one or more of these factors, falls occur frequently.⁹⁶ Studies show that after stroke, between 14%-65% of patients fall at least once during hospitalization, and between 37%-73% fall during the first six months following discharge from hospital.⁹⁵ The high risk of falls is present in all stages of rehabilitation, but higher fall rates are found immediately after discharge from hospital or rehabilitation clinic.¹¹ The number of falls that are reported varies widely between studies, with fall incidence rates varying between 1.3-6.5 falls each person-year.¹¹ Noteworthy is that these rates are much higher than the incidence rates of ~0.65 falls each person-year which have been documented in the general population of older people.⁹⁷ Soft tissue injuries are the most common injury from a fall.^{11,95} Serious injuries such as fractures are also reported, with numbers ranging between 0.6%-8.5%¹¹ and 1%-15%.⁹⁵ In addition to the physical consequences, falls often result in fear of falling, which in turn is related to balance and gait deficits and reduced physical activity and deconditioning.¹¹ Fear of falling is found in many patients who fall (88%),⁹⁸ this concern is cited by their carers too.⁹⁹

In general, most falls after stroke are reported during the daytime,^{11,95} in the patient's own room and in the bathroom/toilet area. In acute and inpatient rehabilitation, most falls are reported during transfers. In the community, falls occur most frequently during walking (predominantly indoors).¹¹ Loss of balance, misjudgement and foot dragging during either walking, turning and sit to stand transfers were reported by fallers as the suspected causes and activities leading to falls.¹⁰⁰

Walking aids are often used to improve stability and walking following stroke.^{101,102} Ankle-foot orthoses (AFOs) are prescribed to provide mediolateral stability in stance, facilitate toe-clearance in swing and promote heel strike.¹⁴ Positive effects of AFOs on mobility, walking speed and balance are reported.^{17,65} Furthermore, beneficial effects on knee¹⁸ and ankle kinematics^{18,82,92} are found. As a result, AFO-use may positively influence the prevalence of falls. However, literature studying the effects of AFOs in relation to falls after stroke is limited. AFO-use is reported to decrease the fear of falling^{21,103} and to improve balance confidence.¹⁰⁴ Cakar et al. reported that "AFOs seem to be a good supportive choice for the fall risk reduction in chronic stroke patients".¹⁰² Several balance and fall risk tests were performed with and without AFO in their study, but actual falls were not included as an

outcome measure. Prospective intervention studies assessing effects of AFOs on falls are lacking. Three review studies on falls in patients after stroke concluded that there is limited evidence as to whether interventions for preventing falls (including studies assessing effects of AFOs) are effective and recommended further research.^{11,95,105}

This paper aims to study the effects of early AFO-provision on the occurrence and circumstances of falls and near falls in patients after stroke. The results from this current paper originate from a larger randomized controlled trial, in which specifically the effects of the timing of the provision of AFOs early or delayed after stroke (study week 1 vs week 9) were studied and several outcome levels were used. The effects of timing of providing AFOs on clinical scales,^{65,83} lower limb kinematics^{82,92} and tibialis anterior muscle electromyography¹⁰⁶ have been previously reported. In the current paper, the early group (provided with AFOs after inclusion), was compared with the delayed group (not yet provided with AFOs) for eight weeks. Furthermore, follow-up measurements were performed in which occurrence and circumstances of falls/near falls were studied from week 9 to 52. In this period, both groups were provided with AFOs.

METHODS

Study data were collected as part of a single center, randomized, controlled, parallel group study. The study was approved by the Medical Ethical Committee Twente, registered in “the Netherlands Trial Register”, number NTR1930 and followed the CONSORT-guidelines.⁷⁷ All subjects provided written informed consent.

Subjects

Subjects were recruited by the main researcher between December 2009 and March 2014, follow-up continued until 2015. We recruited subjects from the Roessingh, Center for Rehabilitation in Enschede, the Netherlands. Inclusion criteria were: 1) unilateral ischemic or hemorrhagic stroke leading to hemiparesis (single and first-ever stroke or history of previous stroke with full physical recovery); 2) indication for AFO-use (i.e. abnormal initial floor contact and/or problems with toe-clearance in swing and/or impaired ability to take body-weight through the paretic lower limb in stance) determined by the treating rehabilitation physician and physiotherapist; 3) maximal six weeks post-stroke; 4) minimal 18 years; 5) receiving in-patient rehabilitation care at inclusion; 6) able to follow simple verbal instructions. Subjects suffering from severe comprehensive aphasia, neglect or cardiac, pulmonary or orthopedic disorders that could interfere with gait were excluded.

Randomization

An independent person, not involved in the study, allocated participants to one of two intervention-groups using stratified block-randomization: 1) AFO-provision at inclusion, in

study week 1 (early group); or 2) AFO-provision eight weeks later, in study week 9 (delayed group). Randomization was performed with sealed envelopes in blocks of four with ratio 1:1. Stratification was based on the Functional Ambulation Categories (FAC).⁴¹ Walking with (FAC 0-2) and without (FAC 3-5) physical support of another person at inclusion were used as stratification categories before randomization.

AFO-provision

Subjects were provided with one of three commonly used types of off-the-shelf, non-articulated, posterior leaf design, polyethylene or polypropylene AFOs: flexible, semi-rigid or rigid (Basko Healthcare, Zaandam, the Netherlands). All orthoses were worn inside the shoe and included a proximal calf strap. AFO-fitting was performed by a licensed orthotist. The same orthotist was involved during the entire study. The type of AFO was chosen in week 1 (early group) or week 9 (delayed group) according to a custom developed protocol.⁶⁵ The effect of the prescribed AFO was verified and confirmed by the responsible physician in all subjects. After AFO-provision, subjects were instructed to use the AFO throughout the day, including during their stay at the ward, during therapies and when subjects went home. Besides the AFO-intervention, all subjects received usual care from experienced physiotherapists according to the Dutch guidelines for physiotherapy after stroke.⁶⁷ All subjects started with inpatient rehabilitation. If necessary, patients followed outpatient rehabilitation after discharge.

Falls and near falls definitions

A fall was defined as “an event that results in a person coming to rest unintentionally on the ground or other lower level, not as a result of a major intrinsic event of overwhelming hazard”.¹⁰⁷ A near fall was defined as “an occasion on which an individual felt that they were going to fall but did not actually do so”.¹⁰⁸ Falls and near falls were excluded if they were not related to gait, for example a fall with a bicycle.

Data-collection

At inclusion, basic demographic data were recorded. The number of falls/near falls during the first year after inclusion was assessed using a diary. The diary was filled in weekly during the first 17 weeks of the study. Subsequently, in week 26 the diary was filled in to cover study week 18-26, and in week 52, to cover week 27-52 of the study. A researcher or physiotherapist involved in the study, visited the subject to make sure that the diary was completed each time. In the diary, the number of falls, near falls and actual AFO-use were registered. For every reported incident, information related to the circumstances of the incident was obtained through open-ended questions to establish whether the AFO was used during the incident, the location of the incident, the activity being performed and possible injuries. This information was then further categorized: 1) AFO-use (with/without); 2) location (rehabilitation center/home-inside/outside/other); 3) activity (transfer/standing/walking); and 4)

Table 7.1: Categories used to determine fall and near fall conditions.

Main categories	AFO-condition	Location	Activity	Consequences
Sub-categories	<ul style="list-style-type: none">• With AFO• Without AFO• Unknown	<ul style="list-style-type: none">• Rehabilitation center• Home environment (inside)• Outside• Other• Unknown	<ul style="list-style-type: none">• Transfers• Standing• Walking• Unknown	<ul style="list-style-type: none">• No consequences• Fear of falling (such as becoming startled or anxious for new incidents)• Mild physical consequences (bruises or grazes)• Severe physical consequences, requiring medical care (such as fractures or cuts)• Unknown

consequences (none/fear of falling/mild physical/severe physical), see Table 7.1. “Unknown” was noted when the diary was incomplete, for example when the subject remembered the fall, but did not remember whether the AFO was used.

As part of the longitudinal study, walking independence and balance were assessed using the Functional Ambulation Categories (FAC)⁴¹ and the Berg Balance Scale (BBS),⁴⁷ respectively. FAC scores ≤ 2 indicate that a subject requires physical support, or verbal supervision (FAC 3) for functional ambulation. BBS scores below 45 points are related to increased fall-risk.⁶⁶ The FAC and BBS were assessed biweekly for the first 17 weeks, and a follow-up measurement was performed in week 26. All falls/near falls were labelled with the last known BBS and FAC score. For instance, a fall incident in week 6 was labelled with the score from week 5, an incident in week 18-25 with the score from week 17. All incidents in week 26-52 were labelled with the scores from week 26. The early group performed the tests without AFO in week 1, and in the other weeks with AFO. The delayed group performed the tests without AFO until week 9, and from week 11 with AFO.

Statistical analysis

SPSS version 19 (IBM SPSS Statistics, Chicago, IL, USA) was used for data-analysis. The level of significance for all analyses was set at $p < 0.05$. No power-calculation was performed, since relevant data regarding timing of AFO-provision were not available.

Basic demographic data of the early and delayed groups at inclusion were compared using independent samples *t*-test/Mann-Whitney *U* test for continuous variables and chi-squares test/Fisher exact test for categorical variables, as appropriate. The person-time fall/near fall incidence rate (number of falls/near falls per person week, per study group,

per period) was calculated by dividing the total number of falls or near falls, by the sum of the total amount of measurement weeks. This was calculated for the early and delayed group separately, for study week 1-8 and study week 9-52. To answer the research question, occurrence of number of falls and near falls in study week 1-8 were compared between the early (who had already been provided with AFOs) and delayed group (who had not yet been provided with AFOs). Furthermore, the occurrence of falls and near falls in study week 9-52 were compared. In this period, both groups of subjects had been provided with AFOs. Poisson regressions were chosen in case of mean-variance equality, negative binomial regressions (generalized Poisson regression) were used for over-dispersed count data (variance exceeded mean number of incidents). Because subjects reported relatively low number of incidents, fall/near fall circumstances and related FAC and BBS scores were only presented in a descriptive way. All obtained data were included in the analysis. Therefore, a participant was included in the number of patients if at least one week in the corresponding period was filled in.

RESULTS

Baseline

In total 33 subjects were included in the study, 16 in the early group and 17 in the delayed group. No statistically significant differences were found between both groups at baseline (see Table 7.2). Figure 7.1 details the participants flow through the study. Before completing the first eight weeks, in which the early group had been provided with an AFO and the delayed not yet, two subjects (one early, one delayed) dropped out. After week 8, one subject (delayed) dropped out. Of the 30 subjects (15 early, 15 delayed) that were included in the period week 9-52, three subjects (in the delayed group) dropped out. Two of them dropped out already after week 9, at the moment of AFO-provision. Of the thirteen subjects in the delayed group that had been provided with an AFO, one dropped out after week 16. In total, 27 subjects (15 early and 12 delayed) completed the study until week 52. Six weeks of diaries entries, involving four subjects (two early, two delayed), are missing due to illness or vacation.

AFO-compliance

In general, subjects reported that they used the AFO from the week of prescription, i.e. study week 1 or 9 for the early and delayed group, respectively. One subject (delayed) experienced pressure sores and did not wear the AFO for five weeks (week 10-11 and 13-15). Three participants stopped using the AFO in the period of week 18-26 (two early, one delayed). These subjects reported that they felt that they did not need the AFO anymore because their walking pattern improved. In the period of week 27-52 five subjects stopped using the AFO (one early, four delayed). Four because they felt they did not need the AFO anymore,

Figure 7.1: CONSORT Flowchart.
The figure shows the participant flow through the study.

Table 7.2: Subject characteristics at inclusion.

	Total (n=23)	Early (n=16)	Delayed (n=17)
Sex (male/female) ^a	20/13	10/6	10/7
Age (years) ^b	57.2 (9.2)	56.9 (9.6)	57.5 (9.1)
Time since stroke at inclusion (days) ^b	31.4 (6.3)	32.0 (6.2)	30.8 (6.5)
FAC-level at inclusion (0/1/2/3/4/5) ^c	0/7/14/11/1/0	0/3/7/6/0/0	0/4/7/5/1/0
Affected body side (left/right) ^a	16/17	8/8	8/9
Type of stroke (ischemic/haemorrhagic) ^c	27/6	14/2	13/4
Type of AFO* (flexible/semi-rigid/rigid/no orthosis) ^c	27/0/3/3	14/0/2/0	13/0/1/3
Sensation**			
Tactile	26/4/3	13/1/2	13/3/1
(normal/impaired/absent) ^a			
Proprioception	26/6/1	13/2/1	13/4/0
(normal/impaired/absent) ^a			
Mini-Mental State Examination ^d	27.0 (23.5-28.0)	27.0 (25.3-28.0)	27.0 (22.5-28.0)

FAC: Functional Ambulation Categories; AFO: ankle-foot orthosis. Mean (SD) or median (interquartile range) are presented. ^aPearson chi-squared test (2-tailed); ^bindependent samples *t*-test; ^cFisher exact test; ^dMann-Whitney *U* test with median (IQR); * Three subjects were not provided with an orthosis: one dropped-out before orthosis-provision (after week 4); one preferred wearing high mountain shoes instead of an orthosis and one had no longer an indication for an AFO at the moment of provision in week 9. Furthermore, two subjects (both early) changed from a flexible to a semi-rigid type during the study (in week 4 and 8, respectively) since support provided by the flexible type appeared to be insufficient. ** tested with Erasmus MC modifications to the Nottingham Sensory Assessment, lower limb part.

two of them (both delayed) preferred to use a cane instead of an AFO, and orthopedic shoes instead of an AFO were provided.

Study week 1-8

Falls and near falls

Nine out of 16 subjects in the early group (56.3%), compared to four out of 17 subjects in the delayed group (23.5%) experienced at least one fall during the first eight weeks of the study, see Table 7.3. Nine subjects in the early group reported 11 falls during this period, of which one subject reported three falls. Four subjects in the delayed group (who had not use an AFO yet) reported each one fall. Out of the 16 subjects in the early group, five (31.1%) reported a near fall, one each. Six out of 17 subjects in the delayed group (35.5%) reported in total seven near falls. Person-time fall incidence rate was 0.087 and 0.031 per person week, for the early and delayed group, respectively. For near falls the person-time incidence rate was 0.040 and 0.054, for the early and delayed group, respectively. Falls occurred significantly more in the early group compared to the delayed group, with an Incidence Rate (IR) of 0.69 for the early, and 0.24 for the delayed group (Incidence Rate Ratio (IRR)=2.92; 95%CI=1.06-8.08, $p=0.039$). No significant differences were found in near fall rates (IR 0.31 (early) and 0.41 (delayed) (IRR=0.76; 95%CI=0.28-2.07, $p=0.59$).

Fall and near fall circumstances

Despite the fact that AFOs were provided in week 1-8 in the early group, seven out of 11 falls (63.6%) and two out of five near falls (40%) in the early group occurred without wearing the AFO, see Table 7.4. Conforming to the protocol, all falls and near falls reported in the delayed group were without using an AFO. No remarkable differences were found in locations of the incidents between the early and delayed group, all falls/near falls occurred in the rehabilitation centre or inside the home. The majority of the falls occurred during transfers or standing (early 36.4% transfers, 27.3% standing; delayed 75.0% transfers). Only one fall (9.1% early; 25.0% delayed) and near fall (20.0% early; 14.3% delayed) in each group were related to walking. Most falls (72.7% early; 50.0% delayed) and near falls (100.0% early; 85.7% delayed) in week 1-8 did not have serious consequences.

Walking independence and balance levels

In week 1-8, 10 out of the 11 falls (90.9%) in the early group occurred when participants had a FAC-score ≤ 3 , see Figure 7.2. This score indicates that a subject required physical support or verbal supervision for functional ambulation. In six of these incidents, the AFO was not used. Incidents were reported during transfers ($n=4$), standing ($n=2$) and walking ($n=1$). In the delayed group two out of the four falls (both during transfers) were related to a FAC-score ≤ 3 . BBS-score was <45 in seven out of the 11 falls in the early group in week 1-8, compared to two out of the four falls in the delayed group. AFOs were not used in respectively five and two of these falls.

Study week 9-52

Falls and near falls

During week 9-52, when both groups were provided with an AFO, eight of the 15 subjects in the early group (53.3%) reported in total 12 falls (1-2 falls per person), see Table 7.3. The delayed group reported 14 falls, which were experienced by 10 of the 15 subjects (66.7%), (1-3 falls per person). Near falls were reported by eight of the 15 subjects in the early group (53.3%) and by five of the 15 subjects in the delayed group (33.3%). In total, 16 and nine near falls were reported by the early and delayed group, respectively, 1-4 near falls per person. In the early and delayed group, the person-time fall incidence rate was 0.018 and 0.026 falls per person week, respectively. The person-time incidence rate for near falls in the early and delayed group was 0.024 and 0.017, respectively. Statistical analysis did not show any significant differences between the groups with respect to falls (IR 0.80 (early) and 0.92 (delayed) (IRR=0.86; 95% CI=0.39-1.89, $p=0.702$)) and near falls (IR 1.07 (early) and 0.60 (delayed) (IRR=1.79; 95%CI=0.59-5.39, $p=0.310$)).

Table 7.3: Total number of falls and near falls in week 1-8 and 9-52.

	Week 1-8						Week 9-52					
	Falls			Near falls			Falls			Near falls		
	Early	Delayed	Early	Delayed	Early	Delayed	Early	Delayed	Early	Delayed	Early	Delayed
Number of subject	16	17	16	17	15	15*	15	15*	15	15	15	15
At start interval	15	16	15	16	15	12	15	12	15	12	15	12
Completed interval	11	4	5	7	12	14	16	14	16	9	16	9
Number of incidents reported	9 (56.3)	4 (23.5)	5 (31.3)	6 (35.3)	8 (53.3)	10 (66.7)	8 (53.3)	10 (66.7)	8 (53.3)	5 (33.3)	8 (53.3)	5 (33.3)
Number of subjects reporting incidents (%)	1.0 (0-3)	0.0 (0-1)	0.0 (0-1)	0.0 (0-2)	1.0 (0-3)	1.0 (0-3)	1.0 (0-4)	1.0 (0-4)	1.0 (0-4)	0.0 (0-4)	1.0 (0-4)	0.0 (0-4)
Median number of incidents per subject (min-max)	126	130	126	130	656	538	656	538	656	538	656	538
Total number of measurement weeks	0.087	0.031	0.040	0.054	0.018	0.026	0.018	0.026	0.024	0.017	0.024	0.017
Person-time incidence rate (number of incidents per person week, per study group, per period)												

*two subjects dropped out after week 9 and were included for only one week in this interval.

Table 7.4: AFO-conditions, locations, activities and consequences related to falls and near falls in week 1-8 and 9-52.

Week 1-8														Week 9-52																																									
Falls														Near falls														Falls														Near falls													
Number of subjects	At start interval ^a	Completed interval	Falls				Delayed				Early				Delayed				Early				Delayed				Early				Delayed																								
			Early	Delayed	NoI	%	Early	Delayed	NoI	%	Early	Delayed	NoI	%	Early	Delayed	NoI	%	Early	Delayed	NoI	%	Early	Delayed	NoI	%	Early	Delayed	NoI	%																									
Number of incidents			11	4	5	7	12	14	16	9																																													
	AFO-use	With AFO	NoI	3	27.3	n.a.	3	60.0	n.a.	3	25.0	5	35.7	11	68.8	4	44.4																																						
		Without AFO	7	63.6	4	100.0	2	40.0	7	100.0	8 ^b	66.7	9 ^c	64.3	4 ^d	25.0	3	33.3																																					
		Unknown	1	9.1	n.a.	-	-	n.a.	1	8.3	-	1	6.3	2	22.2																																								
Locations	Total		100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0																																							
	Rehab. center	6	54.5	2	50.0	4	80.0	5	71.4	2	16.7	2	14.3	1	6.3	3	33.3																																						
	Home (inside)	5	45.5	1	25.0	1	20.0	1	14.3	8	66.7	8	57.1	9	56.3	4	44.4																																						
	Outside	-	-	-	-	-	-	-	-	1	8.3	3	21.4	5	31.3	1	11.1																																						
	Other	-	-	-	-	-	-	-	-	-	-	1 ^e	7.1	-	-	1 ^e	11.1																																						
	Unknown	-	-	1	25.0	-	-	1	14.3	1	8.3	-	-	1	6.3	-	-																																						
Activities	Total		100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0																																							
	Transfers	4	36.4	3	75.0	1	20.0	3	42.9	1	8.3	2	14.3	-	-	5	55.6																																						
	Standing	3	27.3	-	-	2	40.0	2	28.6	4	33.3	5	35.7	3	18.8	1	11.1																																						
	Walking	1	9.1	1	25.0	1	20.0	1	14.3	5	41.7	6	42.9	9	56.3	3	33.3																																						
	Unknown	3	27.3	-	-	1	20.0	1	14.3	2	16.7	1	7.1	4	25.0	-	-																																						
	Total		100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0																																						

NoI, number of incidents per AFO-condition, location or activity; %, percentage of incidents per AFO-condition, location or activity; n.a., not applicable, since the delayed group was not provided with an AFO in this period. ^aA participant is included in the number of participants if at least one week of the diary is completed during the corresponding period; ^bOne of these falls was experienced by a participant who already stopped wearing the AFO; ^cTwo of these falls were experienced by one participant who already stopped wearing the AFO; ^dTwo of these near falls were experienced by two participants who already stopped wearing the AFO; ^eLocations were categorized as "other" when incidents took place at locations other than the rehabilitation center, at home (inside) or outside. In this case at the library and at work. *Table continues on the next page.*

Table 7.4: AFO-conditions, locations, activities and consequences related to falls and near falls in week 1-8 and 9-52 (*continued*).

		Week 1-8						Week 9-52					
		Falls			Near falls			Falls			Near falls		
		Early	Delayed	NoI	Early	Delayed	NoI	Early	Delayed	NoI	Early	Delayed	NoI
Number of subjects	At start interval ^a	16	17	17	16	17	17	15	15	15	15	15	15
	Completed interval	15	16	16	15	16	16	15	15	12	15	12	12
Number of incidents		11	4	5	7	12	14	16	16	9			
Consequences	None	NoI 8	% 72.7	NoI 2	% 50.0	NoI 5	% 100.0	NoI 6	% 85.7	NoI 1	% 8.3	NoI 7	% 50.0
	Fear of falling	NoI 1	% 9.1	NoI 1	% 25.0	-	-	-	-	-	-	NoI 2	% 14.3
	Mild physical	NoI 2	% 18.2	NoI 1	% 25.0	-	-	NoI 1	% 14.3	NoI 5	% 41.7	NoI 4	% 28.6
	Severe physical	NoI -	% -	NoI -	% -	-	-	-	-	NoI 5	% 41.7	NoI 1	% 7.1
	Unknown	NoI -	% -	NoI -	% -	-	-	-	-	NoI 1	% 8.3	-	-
Total		NoI 100.0	% 100.0	NoI 100.0	% 100.0	NoI 100.0	% 100.0	NoI 100.0	% 100.0	NoI 100.0	% 100.0	NoI 100.0	% 100.0

NoI, number of incidents per consequences; %, percentage of incidents per consequences.

Fall and near fall circumstances

No significant differences were established in fall and near fall circumstances between both groups in week 9-52, see Table 7.4. In this period all subjects had been provided with an AFO. However, approximately two-third of the falls occurred while the AFO was not used (66.7% early; 64.3% delayed). Near falls were mainly reported whilst using the AFO (68.8% early; 44.4% delayed). Both groups reported that most falls/near falls took place inside the home (falls 66.7% early and 57.1% delayed; near falls 56.3% early and 44.4% delayed). One (8.3%) and three (21.4%) falls in the early and delayed group, and five (31.3%) and one (11.1%) near falls were reported outside the home in week 9-52, whereas in week 1-8 no incidents were reported outside. The highest number of fall incidents in both the early and delayed group occurred whilst walking (41.7% early; 42.9% delayed), and approximately one-third of the incidences took place while standing. Near falls occurred primarily during walking (56.3%) in the early group. In the delayed group this was during transfers (55.6%). Noteworthy is that in contrast to week 1-8, a total of six falls resulted in severe injuries (five early (41.7%); one delayed (7.1%)). Three fractures were reported (two early (ankle fracture, without AFO; humerus fracture, with AFO); one delayed (hip fracture, without AFO)). Furthermore, a painful foot required an X-ray, a painful shoulder required a medical check and a cut in the face required stitches. Most near falls were reported without consequences.

Walking independence and balance levels

In week 9-52, one out of the 12 falls in the early group occurred with FAC-score ≤ 3 , see Figure 7.2. For the delayed group this was six out of the 14 falls. The majority of these falls were without AFO. BBS-score was ≥ 45 in all 12 falls in the early group, while six out of 14 were < 45 in the delayed group.

DISCUSSION

The current paper studied the effects of AFO-provision on the occurrence and circumstances of falls and near falls after stroke. We found that during the first eight weeks of the study, falls occurred significantly more often in patients who had been provided with AFOs, compared to patients who had not yet been provided with AFOs. However, it is important to note that in 63.6% of the falls in patients who had been provided with an AFO, the AFO was not worn at the time of the incident. In week 9 to 52, when all subjects had been provided with an AFO, there was no difference in the number of falls between the groups. No effects on near falls were found between the groups, both in week 1-8 and week 9-52. Although the actual number of falls were relatively low, serious injuries including fractures were reported.

To the best of our knowledge, this is the first prospective study on the effects of AFO-provision on falls early after stroke. We established that 13 subjects (nine early, four delayed) experienced at least one fall in week 1-8 of our study, which is 39.3%. In week 9-52

this was 60.0% (18 subjects in total; eight early, 10 delayed). These numbers are in accordance with previous studies on falls after stroke, reported rates of patients falling during inpatient rehabilitation from 10.5%-47.0%.¹¹ Rates of 37%-73% and 43%-70% during the first six months after discharge from hospital⁹⁵ and 1-year follow-up¹¹ are reported, respectively. We found near fall rates of 33.3% for the subjects in week 1-8 and 48.1% in week 9-52. Interestingly, our findings are less than the almost 80% previously reported by Hyndman et al.¹⁰⁰ However, they included subjects living at home for at least 3 months following the stroke and results were obtained by interviews including frequency and circumstances of falls/near falls from the past 12 months.

The current study found that falls occurred more frequently in subjects who had been provided with AFOs early after stroke. Based on these results, one may be inclined to conclude that it is not beneficial to use AFOs early after stroke. However, further analysis of this information is needed. The clinical reasoning used in the consideration for the provision of AFOs early after stroke is multifaceted and therefore it would be remiss not to examine the other aspects and potential merits. We previously reported the beneficial effects of AFOs on other outcome levels. Principally, we established that early AFO-provision tends to results in higher functional levels (i.e. higher levels of independence of walking and higher balance levels) earlier on in the rehabilitation.⁸³ This can be important in order to perform task-specific rehabilitation exercises with high repetitions early in the rehabilitation, which is known to be important for improved outcomes.⁶⁷ These beneficial effects on functional outcomes were found without negative consequences of AFO-use on muscle activity of the tibialis anterior.¹⁰⁶ In addition, decreased foot-clearance is reported as an increased risk for stumbling and falls.¹¹ AFOs are provided to improve foot-clearance in swing phase,¹⁴ under the assumption that this improves safety of walking. It is possible that the AFOs provided did not improve foot-clearance sufficiently. However, we previously reported on kinematic effects of AFOs on the gait pattern.^{82,92} These studies included the same subjects as the current study, and confirmed that the ankle was sufficiently corrected. Therefore, insufficient correction of foot-clearance during walking because of AFO-use cannot explain the higher number of falls that were reported in the first eight weeks of our study by the group that was provided with AFOs.

We suggest that the higher number of falls we established in the early group after been provided with AFOs can most likely be explained by factors related to the situations in which falls occurred and to patient characteristics, rather than to the AFO. We advise that these factors be taken into consideration when considering the benefits of using or not using AFOs early after stroke. Importantly, in seven out of 11 falls (63.6%) the AFO was not used, despite the fact that the subjects reported that they used the AFO when diaries were completed. A closer analysis of the data revealed that most falls without AFO (five out of seven) occurred in the bed- and bathroom, during activities related to getting dressed, getting out of bed during the night, toileting and showering. These are all situations which are often related to walking on bare feet, and in which it may not be possible to wear AFOs (such as showering),

Figure 7.2: Functional Ambulation Categories (FAC) and Berg Balance Scale (BBS) scores related to falls and near falls in the early and delayed group.

The position of the circle represents the BBS- or FAC-score at the time of the incident. The colour of the circle represents whether the AFO was used at the time of the incident. The numbers around the circles represent the activities performed during the incident. The vertical grey lines represent study week 9 (before week 9 the delayed group had not use an AFO), the horizontal grey lines indicate FAC-scores of 3 and BBS-scores of 45.

or at least would be very inconvenient to use an AFO (for example transfer out of bed at night). As a results, falls without AFO happen, even when AFOs are used as they should be. Secondly, the majority of the falls (90.9%) in week 1-8 were reported while the related level of walking was a FAC-score 3 or lower, in combination with lower levels of balance (often <45 on BBS), see Figure 7.2. This implies that at least verbal supervision or stand-by help without physical contact from another person should have been provided to these subjects at the time of the fall. Nyberg et al. previously reported that in 58% of the falls after stroke at a stroke rehabilitation unit, patients acted against instructions by the rehabilitation team (such as transferring or walking without recommended supervision or aids used).¹⁰⁹ Ignoring instructions by patients, or unclear instructions by clinicians, could very likely explain the high number of falls related to low FAC-levels in our population. In addition, we previously reported trends of higher levels of independence of walking and higher balance levels earlier on in the rehabilitation.⁸³ As a result, the early group is hypothetically also more likely to fall, as they are more active earlier on in the rehabilitation. Attention deficits (as part of cognitive deficits) are common after stroke and are correlated to falls.^{110,111} Although this was not part of our study and therefore speculative, the higher activity-levels earlier on in the rehabilitation, in combination with possible attention deficits often present early after stroke, are probably important aspects to take into consideration in the case AFOs are provided early after stroke. Perhaps some patients are physically able to perform mobility-tasks independently due to early AFO-provision, but their cognitive function may not yet be sufficient. Based on our results, we would like to emphasize the importance of careful instructions from clinicians and nursing staff to patients and their relatives, and to emphasize the potential risks of performing activities without the proper assistance, especially in situations in which an AFO is not worn.

Another important finding in our study is that, although AFOs are often provided to improve safety during walking, the majority of fall incidents between week 1-8 occurred during transfers and standing. This is in accordance with previous literature on falls after stroke.¹⁰⁹ The main mechanisms to prevent falls in these situations, are thought to be accurate balance reactions (including the ability to use arms and hands to grasp for example a (wheel)chair) and AFOs are not likely to contribute to this. This finding highlights the importance, as previously mentioned, of careful instructions. In daily clinical practice, the decision on whether patients are able to ambulate independently is often made based on walking ability while wearing an AFO. Based on our results, we would like to emphasize the importance of targeting safe transfers and standing during therapy, even when subjects have already reached independent walking levels. Furthermore, practicing daily life activities on bare feet should be taken into consideration. Again, careful instructions by clinicians and nursing staff to patients and their family are important in these activities. This includes the effects and differences of performing activities with or without AFO, taking the cognitive level of the patient into consideration. All these factors may be subject of future research aiming to reduce fall incidence after stroke.

An important strength of our study is that we prospectively included the provision of AFOs in relation to falls after stroke. To the best of our knowledge, this is the first time. Previous studies on falls after stroke did not include the effects of AFO-use.^{11,95,105} Only one study on the effects of AFOs included outcome measures related to falls.¹⁰² However, actual falls were not included as outcome measure in this study. We prospectively assessed falls and near falls on a weekly basis during the first 17 weeks of the study, thereby limiting recall bias as much as possible in this period.

A major study-limitation is the small sample size. Within this limited sample size, the actual number of falls and near falls reported were relatively low. Therefore, no statistical analysis could be performed in relation to the falls/near fall circumstances and related FAC- and BBS-scores. The power was sufficient for falls in study week 1-8, significant results were found. Outcomes for near falls in week 1-8, and falls and near falls in week 9-52 were found non-significant. Post-hoc power analysis with the reported hazard ratios (IRR 0.76, IRR 0.86 and IRR 1.79, respectively) resulted in a power of 8% for near falls in week 1-8, and 16% and 14% for falls and near falls in week 9-52, respectively, confirming that the sample size was not sufficient for these outcome parameters. We included participants in our analysis in case at least one week was completed in the diary in a particular period. Two subjects (both delayed) dropped-out after week 9 of the study. Thus they only contributed one week of data to the period of week 9-52. Post-hoc analysis without these two subjects showed that conclusions with respect to IRR for falls and near falls in week 9-52 did not change. Despite the short recall period of one week during a large part of the study, there were some situations in which the subjects could not remember the exact circumstances of the fall/near fall. In addition, diaries of week 26 and 52 included a large recall period, from week 18-26 and week 27-52, respectively. This may have affected the results. Furthermore, results with respect to BBS- and FAC-scores in relation to falls in week 26-52 must be interpreted with caution, as incidents reported in this period were labelled with BBS- and FAC-scores from week 26. BBS and FAC were not recorded after week 26. Therefore, potential changes in BBS and FAC after week 26 were not registered. In addition, some subjects in our study stopped using the AFO because they felt it was no longer required. This was documented previously as an important reason to stop using AFOs.¹¹² However, falls and near falls reported by these subjects after stopping using their AFO were included in our analysis, which may have affected our results. Finally, it was not possible to blind subjects and assessor for AFO-use.

Conclusions

This study showed that falls occurred significantly more often in patients who had been provided with AFOs early after stroke, compared to subjects who had not yet been provided with AFOs. However, it is important to notice that in the subjects who had been provided with AFOs, 63.6% of the falls in the first eight weeks of the study occurred without wearing the AFO. The majority of these incidents took place during standing and transfers, whilst subjects had no independent walking ability and had low levels of balance. Beneficial effects

of early AFO-provision on clinical scales and ankle-kinematics were reported previously. The current study highlights the importance of careful instructions by clinicians and nursing staff to patients and their relatives concerning AFO-use early after stroke, and which activities can, and maybe even more importantly, cannot be performed independently. Whether the AFO is used or not in these activities, is of considerable importance when instructing patients.

Chapter 8

General discussion

This thesis aims to increase the understanding of the effects of providing ankle-foot orthoses (AFOs) early after stroke. To achieve our aim a randomized controlled trial was conducted in which subjects were provided with an AFO in week one of the study (early group) and were compared with subjects provided with an AFO eight weeks later, in week 9 of the study (delayed group). We used a wide range of outcome measures. The individual chapters addressed the short-term (chapter 2) and long-term (chapter 3) effects on functional clinical scales. In addition, short- and long-term effects on gait kinematics were described in chapter 4 and 5, respectively. Chapter 6 described the effects of timing of AFO-provision on muscle activity of the tibialis anterior and chapter 7 on the occurrence and circumstances of (near) falls. This general discussion combines the individual chapters. The results and conclusions drawn from the individual chapters will be summarized first. Subsequently, results and conclusions for the individual chapters will be discussed in relation to each other and in relation to previous work on the use of AFOs after stroke, and rehabilitation after stroke in general. Strengths and limitations of this thesis will be discussed, as well as implications for clinical practice and future studies.

Conclusions from individual chapters

We found positive effects of AFO-provision on clinical scales measuring balance, walking and activities of daily living related to walking (such as turning, walking stairs). The effects were measured two weeks after provision of the AFO in stroke subjects that had not used an AFO before. These positive effects were present both when AFOs were provided early (in week 1) and delayed (in week 9 of the study). We subsequently compared the positive effects of AFO-provision between the early and delayed group, and we corrected for differences in baseline values at the two time points of AFO-provision. We then found that early provision of AFOs after stroke resulted in increased levels of improvement on several clinical scales. This suggests that providing AFOs early after stroke might be beneficial. This was confirmed when we studied the effects of early or delayed provision of AFOs over six months. No differences in functional outcomes were found between both groups after 26 weeks. However, the results suggest that early provision results in better outcomes in the first 11-13 weeks of the study. We found clinically relevant but statistically non-significant differences from 4-10 weeks in reaching independent walking levels and reaching higher balance levels thus favoring early provision.

In addition to the effects on functional outcomes, we studied the effects of different timing of AFO-provision on gait kinematics and the muscle activation pattern of the tibialis anterior muscle. Ankle dorsiflexion angles significantly improved directly after AFO-provision, changing the ankle from a plantarflexion into a dorsiflexion angle at initial contact, foot-off and during swing. These results were obtained regardless of AFO-provision early or delayed after stroke. In general, knee, hip and pelvis angles did not change directly after AFO-provision. In analogy with the functional outcome measures, we also measured the effects on gait kinematics over a period of 26 weeks. Again, we found that the AFO ac-

curately corrected drop-foot. After 26 weeks, no differences in kinematics in any of the joint angles were found between the two groups. This was the case for both the condition with or without AFO. Furthermore, changes in the kinematics during the 26-weeks follow-up period did not differ between both groups. These kinematic results indicate that early or delayed AFO-use after stroke did not influence pelvis, hip and knee movements after 26 weeks. AFOs improved drop-foot, but did not influence movement patterns around pelvis and hip. Muscle activation patterns of the tibialis anterior muscle were measured during gait analysis. Results showed that AFO-use reduced muscle activity during swing within a measurement session, compared to walking without AFO. However, 26 weeks use of an AFO did not affect tibialis anterior muscle activity during walking without AFO. Again, early or delayed AFO-provision did not affect the results. These results indicate that there is no need to fear negative consequences on tibialis anterior-activity because of long-term AFO-use (early) after stroke.

In addition to effects on functional outcome measures, gait kinematics and muscle activation patterns, the effects on the occurrence and circumstances of (near) falls were studied. We found that subjects in the early group, who had already been provided with AFOs, fell significantly more often in the first eight weeks of the study, compared to the delayed group, who had not yet been provided with AFOs. The majority of these falls occurred however, without wearing the AFO. Falls mainly occurred during transfers and standing, during activities related to getting in/out bed, toileting and showering. The majority of the subjects had not yet reached an independent ambulation level at the time of the fall. This highlights the need for careful instructions.

Effect of AFOs on gait kinematics

Insufficient foot-clearance is often a problem in gait pattern after stroke. Circumduction,^{9,71} pelvic hiking,^{9,71,72} hip hiking⁸⁶ and increased hip flexion⁷⁰ are reported to overcome this problem, depending on the patient's specific impairments and residual function. These terms relate to (a combination of) movements of the pelvis and hip in the frontal, sagittal and/or transverse plane and are often referred to as compensatory movements. Despite the fact that this term is often used to describe gait pattern after stroke, clear descriptions or definitions of these gait patterns are lacking.⁸⁶ Within this thesis, we studied the effects of AFOs on compensatory movements at the pelvis (up/downward obliquity) and hip (ab/adduction) in the frontal plane, and at the hip (flexion/extension) and knee (flexion/extension) in the sagittal plane. In chapter 4 and 5 we found that AFOs positively affected the ankle angle in correcting drop-foot. This is in accordance with previous research, that studied the effects of AFOs on ankle kinematics in mainly chronic stroke subjects already using an AFO¹⁸ and demonstrated that the AFO worked in the way it was intended to. We hypothesized that early AFO-provision, and thereby early correction of drop-foot, would be beneficial and reduce the development of compensatory movements around the pelvis and hip. Compensatory movements were present in our population, specifically pelvic up-

ward obliquity (elevation), combined with hip abduction. These results comply with previous literature.^{72,86} However, against our expectations, frontal and sagittal movement around the pelvic, hip and knee were not affected by early AFO-use and did not differ between the early and delayed group. In addition, no significant changes in kinematics during the 26-weeks follow-up period were found. Therefore early corrections of drop-foot in the distal part of the lower limb did not affect movements in the proximal joints. For clinicians this means that (early) AFO-provision is beneficial to correct drop-foot, but that it does not affect or prevent the development of compensatory movements around the pelvis and hip.

Chapter 5 discussed whether the movements around pelvis and hip actually are compensatory movements, since they were present in both groups immediately following -stroke. "Compensatory" would suggest that these movements are voluntarily, or at least can be influenced by improving the underlying problem responsible for the compensatory movements. Improving drop-foot did not affect pelvis and hip kinematics. This would suggest that the movements around pelvis and hip are either fixed, as an integral part of the affected gait pattern (early) after stroke as was also suggested by Kerrigan et al.,⁸⁶ or compensate for other gait impairments besides drop-foot, such as inadequate push-off and decreased knee flexion during swing. Decreased knee flexion during swing is among the most common gait disturbances in hemiplegic gait¹¹³ and was also present in our study population. Stiff knee gait, characterized by reduced peak knee flexion during swing,¹¹⁴ is a characteristic pattern of this disturbance.¹¹³ Overactivity of the rectus femoris and inadequate push-off are often mentioned as causes of stiff knee gait.^{113,114} Inadequate push-off is associated with muscle weakness of the calf muscles^{69,115} and calf muscle paresis is found as one of the primary impairments related to decreased gait performance after stroke.⁶⁹ Inadequate push-off and as a result limited knee flexion during swing, may evoke compensational movements of the pelvis and hip to achieve adequate foot-clearance. Provision of a conventional AFO does not improve push-off. Actually, in subjects with some residual calf muscle function, an AFO often limits possible push-off in stance phase, as most AFOs prevent the ankle joint moving from neutral position to plantarflexion direction during the third rocker.¹¹⁶

We found that kinematics over time did not change over a period of 26 weeks. At the same time, the overall impression (including the impression of the treating therapists), was that subjects improved their walking pattern over time. We believe spatiotemporal changes probably play an important role and may explain at least part of this mismatch. We found that walking speed improved over time. For example, in the early group from 0.36 m/s without AFO during the first measurement (T1), to 0.60 m/s during the last measurement (T4). During the 26-weeks period, the largest changes in walking speed were found in the first eight weeks after AFO-provision (T1-T2 for the early group, from 0.36 to 0.53 m/s; and T2-T3 for the delayed group, from 0.39 to 0.51 m/s). These changes were statistically significant and clinically relevant.⁵² Walking speed can increase by increasing step length and/or cadence. Post-hoc analysis of the spatiotemporal data showed that in the early group walking

speed was mainly increased by increasing cadence (from 55.9 (5.8) steps/min at T1 to 75.5 (5.7) steps/min at T4), rather than increasing step length (0.41 (0.02) m at T1, 0.47 (0.02) m at T4). The same results were found for the delayed group. Besides walking speed, the use of walking aids was observed to improve in the study population, often from a 4-point cane towards a cane or no walking aids at all. In addition, balance (simultaneously measured within the study using the Berg Balance Scale) improved within these subjects. The increase in walking speed by increasing cadence, together with improvements in balance and the use of walking aids, reflects an overall picture of improved walking. The results of this thesis indicate that these improvements can be achieved without changes in joint angles of the affected lower limb.

Effect of AFOs on muscle activity

Literature reports about clinicians who are reluctant to prescribe AFOs, as AFOs are suggested to result in muscle disuse.^{14,19,29,30} These thoughts are primarily based on research studying electromyography (EMG) of the tibialis anterior (TA) muscle, comparing walking with and without AFO within a single session. In these studies, AFOs were found to decrease EMG of the TA.^{28-30,79} These results were confirmed in this thesis, as in chapter 6 we found that AFO-use significantly lowered TA activity in swing compared to walking without AFO within a single measurement session. However, long-term studies investigating AFO-use after stroke are lacking. These long-term studies are needed to actually confirm or reject the fear of clinicians with respect to muscle disuse because of AFO-use. The only trial including EMG with a follow-up period studying effects of AFO-use was performed in patients with peripheral paresis.²⁸ Six weeks of AFO-use did not change EMG-activity levels and it was concluded that AFO-use was safe, even in acute stroke patients. To study whether this would also account for stroke patients, we included follow-up measurements including EMG in our gait analysis measurements. We did not find changes in TA muscle activity in swing during the 26-weeks period. This is in accordance with a lack of changes in gait kinematics of the affected lower limb. These results were obtained whilst walking without AFO and were found both in the group provided with AFOs early and delayed after stroke. Our results demonstrated that clinicians do not need to fear negative consequences of long-term AFO-use with respect to TA muscle-activity (early) after stroke. Previous literature studying longitudinal changes in EMG after stroke is scarce. Studies did report on the temporal patterns of surface EMG post-stroke including multiple muscles in a longitudinal design.^{117,118} Temporal EMG-patterns did not change significantly over time, although significant improvements in functional recovery were found. Although we studied the magnitude of the EMG-signal instead of temporal factors, results of these previous studies are in line with our findings.

Improvement after stroke

As was previously mentioned, we found no changes in kinematics and TA muscle activity over a period of 26 weeks after stroke, whilst at the same time subjects showed improvements on a functional level. This provokes further discussion about how recovery after stroke is achieved. As recently agreed in the stroke recovery and rehabilitation roundtable taskforce,¹¹⁹ behavioral restitution and compensation need to be distinguished in this discussion. Behavioral restitution is defined as return towards more normal patterns of motor control with the impaired effector (for instance the impaired ankle), and reflects the process towards “true recovery”.^{119,120} Neural repair is required for true recovery. Evaluation at this level includes EMG activation and co-activation patterns and movement kinematics.^{120,121} Compensation is described as a patient’s ability to accomplish a goal through substitution with a new approach, rather than using normal pre-stroke behavior.¹¹⁹ This includes the use of intact muscles and joints in the affected limb, or the unaffected limb to accomplish the goal. Previous studies have already suggested that functional improvements after stroke may be more related to compensatory strategies in the unaffected leg and biomechanical changes than by restitution of muscle coordination patterns in the affected leg.^{117,118} The results from this current thesis also indicate to similar findings. Improvements on clinical scales were recorded over time as discussed in Chapter 3. However, these scales do not differentiate behavioral restitution from compensation. During the experiments described in this thesis, EMG and kinematic outcome measures were obtained simultaneously. These outcome measures, together with kinetic measures, are currently defined as the best way to differentiate behavioral restitution from compensation. Kinematics of the affected leg, together with affected tibialis anterior EMGs did not change over time, while subjects functionally improved. It would suggest that compensation appears to be an important factor in stroke rehabilitation and highlights the need for further research such as the contribution of the trunk and the unaffected lower limb in the rehabilitation after stroke.

AFO and walking speed

Walking speed is a primary parameter when studying gait in patients with stroke¹²² and recommended as a suitable variable for quantifying deficits and changes during rehabilitation after stroke.¹²³ Furthermore, walking speed could potentially be used for differentiating between household and community levels of ambulation.⁵⁴ Not surprisingly, walking speed is one of the most frequently reported outcome measures in studies on the effects of AFOs after stroke.¹⁷ Mainly positive effects of AFOs on walking speed are reported,^{17,23} whilst no effects on walking speed were also found.⁷⁴ Within this thesis, a few remarkable aspects concerning the effects of AFOs on walking speed are noticed.

First of all, our reported improvements of AFOs on walking speed (+0.23m/s comparing walking without (week 1) and with (week 3) AFO, chapter 2) for the early group are greater compared to previously reported results in chronic stroke subjects already using an AFO (+0.06 m/s (95% CI 0.03-0.08)).¹⁷ These considerable improvements were not found in our

delayed group. Thus, the notable improvement in walking speed cannot be explained by the measurements of early stroke onset and the two week time interval between the measurements. We propose that the differences between our results and results from previous literature can be explained by the fact that in our study AFOs were provided to subjects not used to walk with AFOs, whereas in previous studies mainly subjects already using an AFO were included. In these studies the effect of removing the AFO was assessed. This is relevant information for clinicians considering AFO-provision in stroke rehabilitation. It would suggest that the positive effects of AFOs reported in the literature may actually underestimate the effect of AFOs on walking speed, when they are provided to subjects that do not have experience in walking with AFOs. Since walking speed is related to different levels of ambulation,⁵⁴ the actual effect of AFOs may also affect these ambulation levels.

Another remarkable aspect concerning walking speed is that the effect of AFOs on walking speed within this thesis appears to depend on the way the outcome variable was measured. In chapter 2 and 3 walking speed was assessed using the 10m walking test⁴⁶ and positive effects of AFOs were found. However, no effects of AFOs on walking speed were found during 3D gait analysis (chapter 4 and 5), when walking speed was assessed by calculating the main speed of reflective markers of the anterior superior iliac spine along the axis of progression. It is our clinical observation that walking speed is lower during 3D gait analysis, which is performed in a specialized gait laboratory using equipment like 3D markers and EMG, compared to measuring walking speed over 10m whilst wearing just normal clothes. This observation was confirmed with a post-hoc test including data of 15 subjects performing the 10m walking test (chapter 2) in the same period as they were measured using 3D gait analysis (chapter 4). Results showed that walking speed without AFO during 3D gait analysis was 0.07 m/s slower than during 10m walking test without AFO.

The aforementioned aspects of walking speed show that it is important to pay attention to the way walking speed is measured and to which comparisons are made (providing or removing an AFO), when interpreting the effects of AFOs in relation to walking speed.

AFO and falls

So far, in the above-discussed chapters of this thesis no negative effects of early AFO provision after stroke were found. This would support the thoughts that in order to reach a higher functional level earlier in the rehabilitation, without negatively affecting lower limb kinematics or muscle activity patterns of the tibialis anterior on the affected side, early provision of an AFO is beneficial. An important aspect to take into consideration in reaching higher functional is the effect of AFOs on falls. Foot dragging (limited foot clearance in swing) is reported as suspected cause of falls.¹⁰⁰ AFOs are thought to be beneficial in preventing or limiting falls after stroke, as they are often prescribed to improve drop-foot. Despite that AFOs improved drop-foot (as shown in chapter 4 and 5), chapter 7 showed that falls occurred more often in the group of subjects provided with AFOs early after stroke, when results were compared in the first 8 weeks of the study. In this period the delayed

group was not yet provided with AFOs. Following AFO-provision to the delayed group in week 9 of the study, no differences in fall rates were found between both groups in the period of week 9-52.

With these results in mind, together with the potential serious consequences of falls, one may be inclined to reconsider the early provision of AFOs after stroke. After all, both groups reached similar functional levels after 26 weeks, with no differences in lower limb gait kinematics or tibialis anterior muscle activity, but with less risk of falls in the first period after stroke. However, a closer look into the results of chapter 7 shows that the relationship between early AFO-provision and falls needs further discussion, before considering rejecting early AFO-provision after stroke as the preferred treatment after stroke. Falls occurred more often in the group already provided with an AFO, compared to the delayed group which was not using an AFO. But a more in depth analysis of these falls revealed some interesting outcomes. First of all, 63.6% of the falls in the early group occurred without wearing the AFO, despite that AFOs were provided. Most of these falls without AFO occurred during activities related to getting dressed, getting out of bed during the night, toileting and showering and occurred in the bed- and bathroom. During many of these situations it may not be possible, or at least it would be very inconvenient to use an AFO. This may explain the high percentage of falls without AFO, whilst AFOs were provided. Furthermore, the majority of the falls occurred during transfers or standing and the subjects did not have an independent walking ability at the time of the incident. Taking these findings into consideration, one could suggest that these incidents could have been prevented, when verbal supervision or stand-by help without physical contact from another person was provided to these subjects with reduced walking ability. Patients ignoring instructions was previously reported in 58% of the falls at a stroke rehabilitation unit.¹⁰⁹ This could also explain the high number of falls related to the limited walking ability levels in our population. In addition, it appears important that there is provision of clear instructions on how and when to use AFOs after stroke.

The effect of AFO-use on the level of independent ambulation, is also important. In chapter 3 we found trends that the subjects in the early group reached independent levels of walking with higher levels of balance earlier in the rehabilitation when using the AFO. "When using the AFO" should be emphasized! It may be the case that due to early AFO-provision, subjects are physically able to perform mobility related activities more independently earlier on in the rehabilitation. It is important to note that patients after stroke may also suffer from varying degrees of cognitive impairments. These impairments may influence the ability to judge whether activities that can be performed safe and independently with AFO, can also be performed safe and independently without an AFO.

Although it was not a topic for this thesis, the aforementioned results highlight the importance of careful instructions to patients and their relatives concerning AFO-use, and which activities can, and maybe even more importantly, cannot be performed independently. Whether the AFO is used or not in these activities, is of considerable importance

when instructing patients. Practicing bare feet walking during rehabilitation also seems to be important. Both for the patient, to experience which difficulties can be expected, as well as for the therapist to establish the patient's functional level and help in goal setting. In daily clinical practice, decisions on whether patients are able to ambulate independently are often based on the walking ability while using an AFO. Practicing bare-foot walking would enable therapists to correctly instruct patients during activities like getting dressed or showering, or to discuss with patients that these activities cannot be performed independently without AFO (yet) in their particular phase of rehabilitation.

The cognitive level of the patient is important in these specific training sessions and instructions. Although it was not studied within this thesis, the cognitive levels appear to be important in the decision as to whether to provide AFOs early after stroke. Based on this thesis, early AFO-provision is expected to result in higher functional levels earlier on in the rehabilitation, whilst no changes in kinematics and EMG are expected. In the early provision of AFOs correct instructions and training related to activities that can be performed with the use of an AFO and specifying those activities that should not be performed without an AFO are expected to reduce the risk of falls. In case there are doubts as to whether the patient has the cognitive ability to follow these instructions, AFOs can be provided later in the rehabilitation phase without negatively affecting functional outcomes in the long-term. However, less functional improvements are to be expected in the short-term. The risk of falls from the patient ignoring instructions and performing activities independently without AFO is expected to be lower. After 26 weeks no differences on a functional level, or effects with respect to gait kinematics (compensatory movements) are expected because of delayed AFO-provision.

Strengths and limitations

One of the strengths of this thesis is that we studied a population after stroke, the results of which are relevant to daily clinical practice and can therefore be applied to practice. In contrast to most of the existing literature, we studied the effects of AFO-provision by including subjects within the first weeks following stroke. We also included subjects that were not yet able to walk independently. One of the challenges of studying subjects early after stroke, is that the progress of time itself also explains part of the observed improvements.⁵⁵ In our study, the delayed group can serve as a control group during the first eight weeks of the study, as they had comparable stroke onset time and measurements compared to the early group, but had not yet started with AFO-intervention. Another strength of our population in relation to clinical practice, is that our subjects had not use AFOs previously. Therefore we could study the effect of the actual AFO-provision. Which is in contrast to most previous studies, that included subjects already accustomed to wearing AFOs, often for many years. By including a subject population that closely matches the population entering a rehabilitation center after stroke, we expect that the results of our study are valid and valuable for use in clinical practice.

Another strength of our study is that we measured the effects of AFO-provision over a longer period of time than in previous studies and used a wide variety of outcome measures. Functional outcome measures and gait analysis were measured over a period of 26 weeks, whilst (near) fall incidents were measured over a period of 52 weeks. It was noted that including frequent measurements with long-term follow-up appeared to be important, in particular for the functional tests. Potential beneficial effects of early AFO-provision were found to be present in the first 11-13 weeks of the study, while after 26 weeks no differences were found. We would have possibly drawn different conclusions if we would have chosen to measure for only a period of for example three months (which is already quite long for many AFO-studies), or if we would have chosen to measure less frequently. This conjecture is supported by a review stating that benefits of treatments early after stroke “could go undetected if the primary outcome is ≥ 3 months after stroke, by which the control group may have caught up”.²² Increasing multiple clinical assessments during and after treatment enables “treatment effects on the rate of recovery to be detected even in the absence of an effect on final outcome”. The latter is exactly the case for outcomes on the functional tests in our study.

Another strength of this thesis is that we used a wide variety of outcome measures, including effects on the levels of “body functions and structures” and “activities” from the International Classification of Functioning, Disability and Health framework of the World Health Organization.³² Including these various outcome measures resulted in a quite intensive measurement protocol. It enabled us to measure the effects on a functional level and on falls, levels that are directly relevant to patients themselves. By including kinematics and EMG in our outcome measures, we included levels that are relevant for clinicians. For example, for therapist considering early AFO provision, in order to positively affect compensation patterns around the hip and pelvis (for which early AFO-provision was not found to be beneficial), or therapists considering delayed provision in order to prevent disuse of the tibialis anterior muscle (for which early AFO-provision was not found to have any negative effects). Furthermore, by including kinematics and EMG in combination with functional tests, we hope to increase our understanding on how these functional levels are accomplished. Therefore, our results are believed to be relevant in the discussion on the role of behavioral restitution and compensation in the recovery after stroke.

The aforementioned strengths of our study are supported in a publication by Stinear et al.²² They state that RCTs that enroll and randomize patients to begin the intervention within 30 days after stroke have several potential benefits, like studying effects of treatments in a period in which they may interact with and benefit the spontaneous recovery process. Furthermore, translation into clinical practice is easier if treatments are tested in a time and place of their intended application. In addition, these studies are more relevant for clinical guidelines. As previously mentioned, guidelines currently lack information about the timing of providing AFOs after stroke.²⁴⁻²⁷ With this thesis, we expect to have made a substantial contribution to this topic.

One of the major limitations of this thesis is the limited sample size. This affected the statistical power of our study. The sample size was further limited since some subjects dropped out during the study or were not able to perform all measurements at the beginning of the study, which required independent walking levels of Functional Ambulation Categories ≥ 3 . Within our study, we limited the number of different types of AFOs to three for practical reasons. This is rather low compared to the large variety of AFOs that are available. However, the three included types are commonly used in daily practice of rehabilitation after stroke in the Netherlands. Since protocols to determine which type of AFO a patient needs were unavailable, we developed our own protocol to decide which AFO was provided to an individual subject. The three types of AFOs included varied in stiffness. A sub-group analysis per type of AFO was not possible because of the small sample size. Furthermore, it turned out that out of the three available types of AFOs, the most flexible one was provided most. A limitation of our study is that we did not actually assess or quantify the stiffness or neutral angle of the different types of AFOs, although previous research showed that mechanical AFO characteristics can be reliably measured.¹²⁴ Besides the stiffness around the ankle joint, the stiffness around the metatarsal-phalangeal region of the AFO and the combination of the AFO with the shoes are important, as well as in relation to the effects on walking.¹²⁴ These aspects have not been studied within the current thesis, but are interesting to further improve the effects of AFOs after stroke and to provide the appropriate AFO to the patient.

We chose to include a wide variety of outcome measures in a longitudinal study design to assess effects of AFO-provision. We considered this as a strength of our study, but it also introduced limitations. Primarily, we were not able to measure all the outcome measures for the same follow-up period. The diary including fall registration was repeated from 26 to 52 weeks, but the other outcome measures were not. Secondly, since large functional improvements are seen after stroke,⁸⁵ it was inevitable that some measurement conditions changed during the study. For example, changes in walking aids or shoes could have affected our results, we tried to limit variation as much as possible. Another limitation is that it was not possible to blind subjects and assessors for early or delayed AFO-provision, which is a potential risk of bias.

Implications for clinical practice

Within this thesis, we studied the effects of AFO-provision after stroke on a functional level, on kinematics of the affected leg, on EMG of the affected tibialis anterior muscle and on (near) falls. Early and delayed AFO-provision were compared. Based on the results of this thesis, we conclude that clinicians, together with the patient, can decide what they value most in when making the decision on when to commence with AFO-provision. Early AFO-provision is expected to result in higher functional levels earlier in the rehabilitation. This is valuable information as it may increase the ability to perform task-specific rehabilitation exercises earlier in the rehabilitation. This may be beneficial for the length of in-clinic stay.

Despite potential functional gains in the first period of rehabilitation, early AFO-provision does not lead to higher functional levels after 26 weeks, compared to delayed provision. Therefore the long-term, effects of early or delayed provision are equal with respect to functional levels.

Early or delayed AFO-provision did not affect muscle activity of the tibialis anterior. In this thesis, we found no reason to be concerned about muscle disuse of the tibialis anterior because of early AFO-provision. Therefore, in our opinion fear of disuse concerning the tibialis anterior is not a justifiable reason to delay AFO-use in the rehabilitation after stroke.

With respect to gait kinematics, AFOs were found to improve drop-foot, regardless of the timing of AFO-provision after stroke. Furthermore, early or delayed AFO-provision did not influence pelvis, hip and knee kinematics in the long-term. Therefore, AFOs should be provided to correct the drop-foot post-stroke. Results from this thesis, however, suggest that there is no reason to assume that early AFO-provision will influence the development of compensatory movements around the pelvis and hip in the rehabilitation after stroke.

One should be aware of the fact that we found higher numbers of falls in the case that subjects were provided with AFOs earlier after stroke. Since the majority of these falls occurred without wearing the AFO, special attention needs to be made to the specific instructions given regarding AFO-use. This should include the difference between performing activities with or without wearing the AFO, and therefore, which activities can, and cannot be performed independently with or without wearing the AFO. It is anticipated that the cognitive level of the patient plays an important role in whether or not these instructions regarding AFO-use can be followed. Since delayed AFO-provision does not negatively affect results in the long-term, one might also consider later AFO-provision in cases where there are doubts as to whether the patient is cognitively able to ambulate with AFOs independently early in the rehabilitation.

Implications for future studies

Within this thesis and general discussion, several implications for future studies are proposed. First of all, there is data non-analyzed that was gathered during this randomized controlled trial that needs further study. Besides the tibialis anterior, other muscles of the affected limb were measured during 3D gait analysis. Of these muscles, the gastrocnemius is especially interesting as calf muscle paresis is related to inadequate push off.^{69,115} Most AFOs limit push-off. It would therefore be interesting to study whether early AFO-provision affects gastrocnemius muscle activity. Besides effects related to muscle paresis, the gastrocnemius muscle is also interesting in relation to overactivity or spasticity, and the effects of AFO-use on this. Furthermore, data analysis of the unaffected leg could contribute to our understanding of the role of the unaffected side in the recovery after stroke.

The results of this thesis are based on a rather small population. Future research including larger populations are desirable from a scientific point of view. Within this thesis, only ankle kinematics were found to be affected by AFO-provision. Other outcomes on the

level of “body functions” of the ICF, like EMG or other joint angles did not change, despite that higher functional levels were found. The control and associated internal forces of the affected and unaffected leg and trunk might offer more and new insights on this topic. For this thesis, measurements were performed in a laboratory setting. Previously, van Meulen et al.^{125,126} showed that ambulatory techniques including instrumented shoes containing 3D force and torque sensors, and activity monitors, can be used to quantify daily-life walking performance and walking balance without being restricted to the lab. Further development of these techniques would enable measurements of subjects in the early phase after stroke in the clinic and the home situation. This could increase our knowledge on walking during activities of daily life, and on the actual performance of patients during rehabilitation and in their home environment. In contrast with the current evaluation methods such as clinical tests and gait analysis, which assess the capacities of the patient.

Another aspect of considering possible beneficial effects of early AFO-provision is from a cost-effective perspective. AFOs are mentioned in relation to saving costs in terms of length of stay in clinics.²⁶ New studies on timing of AFO-provision could focus on whether reductions in length of in-clinic stays can be accomplished with early AFO-provision, and to what extent extra costs related to possible falls would negatively influence cost-effectiveness of early AFO-provision.

Conclusions

Summarizing the results of this thesis for clinical practice, we found that clinicians, together with the patient, can decide what they value most in their decision on when to start with AFOs. AFOs were found to improve drop-foot regardless of the timing of AFO-provision after stroke. Early AFO-use is expected to result in higher functional levels earlier on in the rehabilitation. Despite potential gains in the first period of rehabilitation, early AFO-provision does not lead to higher functional levels after 26 weeks, compared to delayed provision. In addition, early or delayed AFO-provision did not influence pelvis, hip and knee kinematics on the short- or long-term. Therefore, AFOs should be provided to correct drop-foot. Results from this thesis show no reason to assume that early AFO-provision influences the development of compensatory movements around the pelvis and hip in the rehabilitation following stroke. AFO-use reduced muscle activity of the tibialis anterior in swing compared to walking without AFO, when the effects were measured within one measurement session. However, no negative effects after 26-weeks were found. Therefore, based on the results of our study, fear of disuse concerning the tibialis anterior does not seem to be a justified reason to delay AFO-use in the rehabilitation after stroke. One should be aware that higher numbers of falls were found in case AFOs are provided early after stroke. Special attention to careful instructions to patients and their relatives should be provided, since the majority of the falls occurred without wearing the AFO and whilst subjects had no independent walking ability.

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SUMMARY

In stroke, the blood circulation in the brain is affected, being either ischemic or hemorrhagic. Depending on the location of the lesion, the effects can widely vary. Initial walking function is limited in approximately two-third of the patients. A “drop-foot”, the inability to dorsiflex the foot, with or without excessive inversion is estimated to be present in 20-30% of the people after stroke. Together with decreased knee and hip flexion, drop-foot causes foot-clearance problems during swing phase and also affects initial contact at the start of the stance phase. Insufficient foot-clearance is associated with high risks for stumbling and falling.

Ankle-foot orthoses (AFOs) are commonly used to correct drop-foot after stroke, as they can provide mediolateral stability in stance, facilitate toe-clearance in swing phase and promote heel strike. Positive effects of AFOs after stroke are reported on mobility and balance, ankle kinematics, walking speed, self-confidence and fear of falling. However, most of the studies reporting on AFOs after stroke included chronic patients, already provided with AFOs in daily life and able to walk independently, with or without AFO. Most studies assessed the immediate or short-term effects of AFOs. As a result, long-term studies on the effects of AFOs including more severely affected subjects, and studies including subjects early after stroke are lacking. In addition, an important question like the effect of timing of providing AFOs after stroke remains unanswered in the literature.

As presented in **Chapter 1**, the general aim of this thesis was to increase the understanding of the effects of providing AFOs early after stroke. Therefore, the EVOLUTIONS-project was conducted, a randomized controlled trial in which the effects of AFO-provision on two different time points in the rehabilitation after stroke were studied. Subjects were included within six weeks after stroke and randomized for AFO-provision at inclusion of the study (in week 1) or eight weeks later (in week 9). The subjects were provided with one of three commonly used types of off-the-shelf, non-articulated AFOs with variability in stiffness. Subjects randomized for delayed provision did not use an AFO in the first eight weeks of the study. Subjects were studied up to 17 weeks with (bi)weekly intervals. Follow-up measurements up to 26 and 52 weeks were included.

In **Chapter 2**, the effects of actual AFO-provision on functional outcomes related to balance, walking and activities of daily life are presented. Positive effects were found both when AFOs were provided early or delayed. When the positive effects of AFO-provision were compared between both groups, and corrected for differences in baseline values at the two time points of AFO-provision, we found that early provision resulted in increased levels of improvement on several clinical scales, compared to delayed provision. This suggested that providing AFOs early after stroke might be beneficial. These results were confirmed in **Chapter 3**, where the effects of early or delayed AFO-provision on a functional level were studied over six months. After 26 weeks no differences in functional outcomes were

found between both groups. However, the results suggest that early provision results in better outcomes in the first 11-13 weeks of the study. Clinically relevant, but statistically non-significant differences of 4-10 weeks were found in reaching independent walking levels and reaching higher balance levels thus favoring early provision.

In addition to functional outcomes, gait kinematics were studied. In **Chapter 4** we measured the short-term effects of AFO-provision using 3D gait-analysis in one single session. Ankle dorsiflexion significantly improved directly after AFO-provision, changing the ankle from a plantarflexion into a dorsiflexion angle at initial contact, foot-off and during swing. These results were obtained regardless of AFO-provision early or delayed after stroke. In general, knee, hip and pelvis angles did not change directly after AFO-provision. The long-term kinematic effects of early versus delayed AFO-provision are included in **Chapter 5**. We studied whether early AFO-provision decreased the development of compensatory movements in proximal joints, when foot-drop is limited by AFO-use early after stroke. 3D gait-analysis performed in week 1, 9, 17 and 26 of the study were included. Again, we found that the AFO accurately corrected drop-foot. After 26 weeks, no differences in kinematics in any of the joint angles were found between the two groups. This was the case for both the condition with or without AFO. Furthermore, changes in kinematics during the 26-weeks follow-up period did not differ between both groups. These kinematic results indicate that early or delayed AFO-use after stroke did not influence pelvis, hip and knee movements after 26 weeks. AFOs improved drop-foot, but did not influence movement patterns around pelvis and hip.

Previous literature suggested that AFO-use might increase muscle weakness, and thereby could impede recovery. Therefore, **Chapter 6** addresses the effects of AFO-provision on muscle activity of the tibialis anterior. Results showed that AFO-use reduced muscle activity during swing within a measurement session, compared to walking without AFO. However, 26 weeks use of an AFO did not affect tibialis anterior muscle activity during walking without AFO. Again, early or delayed AFO-provision did not affect the results. These results indicate that there is no need to fear negative consequences on tibialis anterior activity because of long-term AFO-use (early) after stroke.

In addition to effects on functional outcome measures, gait kinematics and muscle activation patterns, the effects on the occurrence and circumstances of (near) falls were studied. In **Chapter 7** diaries were used to register the number of falls/near falls, and in case of an incident, the location, performed activity, possible injuries and whether the AFO was used. We found that subjects in the early group, who had already been provided with AFOs, fell significantly more often in the first eight weeks of the study, compared to the delayed group who had not yet been provided with AFOs. No differences were found for near falls in this period, or for falls/near falls in week 9-52, in which both groups had been provided with AFOs. The majority of the falls in the early group in week 1-8 occurred without wearing the AFO. Falls mainly occurred during transfers and standing, during activities related to getting in/out bed, toileting and showering. The majority of the subjects had not yet reached an

independent ambulation level at the time of the fall (Functional Ambulation Categories ≤ 3) and had low balance levels (Berg Balance Scale < 45). This highlights the need for careful instructions from clinicians and nursing staff to patients and their relatives, and to emphasize the potential risks of performing activities without the proper assistance, especially in situations without wearing the AFO and without independent walking ability.

Finally, in **Chapter 8** the main findings of this thesis are discussed, together with strengths and limitations of this research. In addition, implications for clinical practice and future studies are presented. Summarizing, the results of the current thesis show that clinicians, together with the patient, can decide what they value most in when making the decision on when to commence with AFO-provision. AFOs were found to improve drop-foot regardless of the timing of AFO-provision after stroke. Early AFO-use is expected to result in higher functional levels earlier in the rehabilitation. Despite potential functional gains in the first period of rehabilitation, early AFO-provision does not lead to higher functional levels after 26 weeks, compared to delayed provision. In addition, early or delayed AFO-provision did not influence pelvis, hip and knee kinematics on the short- or long-term. Therefore, AFOs should be provided to correct the drop-foot, but there is no reason to assume that early AFO-provision will influence the development of compensatory movements around the pelvis and hip in the rehabilitation after stroke. AFO-use reduced muscle activity of the tibialis anterior in swing compared to walking without AFO, when effects were measured within one measurement session. However, no negative effects over 26-weeks were found. Therefore, based on the results of our study, fear of disuse concerning the tibialis anterior does not seem to be a justifiable reason to delay AFO-use in the rehabilitation after stroke. One should be aware that higher numbers of falls were found in case that subjects were provided with AFOs early after stroke. Special attention needs to be made to the specific instructions given regarding AFO-use, since the majority of the falls occurred without wearing the AFO and while subjects were not allowed to ambulate independently.

SAMENVATTING

Bij een beroerte of Cerebro Vasculair Accident (CVA) is de bloedcirculatie in de hersenen aangedaan, door een vernauwing of verstopping (ischemie) of door een bloeding. De effecten kunnen sterk variëren en zijn afhankelijk van de locatie van het letsel. Loopvaardigheid is in eerste instantie verminderd bij ongeveer twee-derde van de patiënten. Bij een sleepvoet is er sprake van onvoldoende dorsaalflexie van de voet, al dan niet gecombineerd met overmatige inversie van de voet. Een sleepvoet komt volgens schattingen bij ongeveer 20-30% van de mensen voor na een beroerte. Samen met verminderde knie- en heupflexie veroorzaakt een sleepvoet problemen met de voet clearance tijdens de zwaai fase en heeft het ook invloed op het eerste voetcontact met de grond tijdens de start van de standfase. Onvoldoende voet clearance wordt ook geassocieerd met hogere risico's op struikelen en vallen.

Enkel-voet orthesen (EVO's) worden algemeen gebruikt om een sleepvoet na een beroerte te corrigeren. EVO's kunnen mediolaterale stabiliteit in stand geven, faciliteren dat de tenen loskomen van de grond tijdens de zwaai fase en een haklanding bevorderen. Positieve effecten van EVO's worden gerapporteerd op het gebied van mobiliteit en balans, enkel kinematica, loopsnelheid, zelfvertrouwen en angst om te vallen. Echter, de meeste studies hebben daarbij chronische patiënten geïnccludeerd die in het dagelijks leven al een EVO gebruikten en in staat waren zelfstandig te lopen, met of zonder een EVO. De meeste studies evalueerden de directe of korte-termijn effecten van EVO's. Als gevolg daarvan missen lange-termijn studies naar de effecten van EVO's waarbij ook ernstiger aangedane patiënten worden geïnccludeerd, en studies die patiënten vroeg na een beroerte includeren. Daarnaast blijft een belangrijke vraag zoals het effect van de timing van het aanbieden van een EVO in de revalidatie na een beroerte onbeantwoord in de literatuur.

Zoals gepresenteerd in **hoofdstuk 1**, was het algemene doel van dit proefschrift om het begrip van de effecten van het verstrekken van EVO's vroeg na een beroerte te vergroten. Daarom werd het EVOLUTIONS-project uitgevoerd, een gerandomiseerde gecontroleerde studie (RCT) waarin de effecten van EVO-verstrekking op twee verschillende tijdstippen in de revalidatie na een beroerte werden bestudeerd. De proefpersonen werden binnen zes weken na een beroerte geïnccludeerd en gerandomiseerd voor EVO-verstrekking bij inclusie in de studie (in week 1) of acht weken later (in week 9). De proefpersonen werden voorzien van één van drie veel gebruikte soorten kant-en-klare EVO's, zonder scharnier en met variabiliteit in stijfheid. Proefpersonen die gerandomiseerd waren voor latere verstrekking gebruikten in de eerste acht weken van het onderzoek geen EVO. De proefpersonen werden tot 17 weken bestudeerd met (twee-)wekelijkse intervallen. Na 26 en 52 weken vonden vervolgmetingen plaats.

In **hoofdstuk 2** worden de effecten van de daadwerkelijke EVO-verstrekking op functionele uitkomstmaten met betrekking tot balans, lopen en activiteiten van het dagelijks leven

besproken. Positieve effecten werden zowel bij vroege als latere EVO-verstrekking gevonden. Wanneer de positieve effecten van EVO-verstrekking tussen beide groepen werden vergeleken en werden gecorrigeerd voor de verschillen in waarden op het moment dat de EVO's werden verstrekt, vonden we dat vroege verstrekking resulteerde in grotere verbeteringen op verschillende klinische schalen, in vergelijking met latere verstrekking. Dit suggereerde dat vroegtijdige verstrekking van EVO's na een beroerte mogelijk gunstig is. Deze resultaten werden bevestigd in **hoofdstuk 3**, waar de effecten van vroege en latere EVO-verstrekking op een functioneel niveau gedurende zes maanden bestudeerd werden. Na 26 weken werden geen verschillen in functionele uitkomsten tussen beide groepen gevonden. Echter, de resultaten suggereren dat vroege verstrekking betere resultaten oplevert in de eerste 11-13 weken van het onderzoek. Klinisch relevante, maar statistisch niet-significante verschillen van 4-10 weken werden gevonden bij het bereiken van zelfstandige loopniveaus en het bereiken van hogere balansniveaus, ten gunste van vroege verstrekking.

Naast functionele uitkomstmaten werd kinematica tijdens lopen bestudeerd. In **hoofdstuk 4** hebben we de korte-termijneffecten van EVO-verstrekking gemeten met behulp van 3D gangbeeldanalyse in één enkele sessie. De enkel-dorsaalflexie verbeterde significant direct na EVO-verstrekking, waarbij de enkel van plantairflexie in een dorsaalflexie-hoek veranderde bij het eerste voetcontact met de grond, het verlaten van de grond en tijdens de zwaai. Deze resultaten werden verkregen ongeacht of de EVO vroeg of later na een beroerte werd verstrekt. Over het algemeen veranderden de knie-, heup- en bekkenhoeken niet direct na EVO-verstrekking. De lange-termijn effecten op het gebied van kinematica van vroege versus latere EVO-verstrekking worden besproken in **hoofdstuk 5**. We onderzochten of vroege EVO-verstrekking de ontwikkeling van compensatoire bewegingen in proximale gewrichten verminderde, wanneer een sleepvoet wordt gecorrigeerd door EVO-verstrekking vroeg na een beroerte. 3D gangbeeldanalyses uitgevoerd in week 1, 9, 17 en 26 van de studie werden geïnccludeerd. We vonden wederom dat de EVO de sleepvoet voldoende corrigeerde. Na 26 weken werd in geen enkele gewrichtshoek een verschil tussen de twee groepen gevonden. Dit was het geval voor zowel de conditie met als zonder EVO. Bovendien waren de veranderingen in de kinematica tijdens de follow-up periode van 26 weken niet verschillend tussen beide groepen. Deze kinematische resultaten geven aan dat vroeg of later EVO-gebruik na een beroerte de bekken-, heup- en kniebewegingen na 26 weken niet beïnvloedde. EVO's verbeterden de sleepvoet, maar had geen invloed op bewegingspatronen rond het bekken en de heup.

Eerdere literatuur suggereerde dat EVO-gebruik spierzwakte zou kunnen vergroten en daardoor het herstel zou kunnen belemmeren. Daarom gaat **hoofdstuk 6** in op de effecten van EVO-verstrekking op de spieractiviteit van de tibialis anterior. De resultaten toonden aan dat EVO-gebruik de spieractiviteit verminderde tijdens de zwaai binnen een meetsessie, in vergelijking met lopen zonder EVO. Echter, 26 weken gebruik van een EVO had geen invloed op de spieractiviteit van de tibialis anterior tijdens het lopen zonder AFO. Wederom had vroege of latere EVO-verstrekking geen invloed op de resultaten. Deze resultaten geven aan

dat er geen reden is om bang te zijn voor negatieve gevolgen op de activiteit van de tibialis anterior vanwege langdurig EVO-gebruik (vroeg) na een beroerte.

In aanvulling op effecten op functionele uitkomstmaten en kinematica en spieractiviteitspatronen tijdens lopen, werden de effecten op het aantal (bijna) valincidenten en de omstandigheden ervan bestudeerd. In **hoofdstuk 7** werden dagboeken gebruikt om het aantal vallen/bijna-vallen te registreren, en in geval van een incident, de locatie, uitgevoerde activiteit, mogelijke verwondingen en of de EVO werd gebruikt. We vonden dat proefpersonen in de vroege groep, die al voorzien waren van een EVO, significant vaker vielen in de eerste acht weken van de studie, in vergelijking met de latere groep die nog niet was voorzien van EVO's. Er werden geen verschillen gevonden voor bijna-vallen in deze periode, of voor vallen/bijna-vallen in week 9-52, waarin beide groepen waren voorzien van EVO's. De meerderheid van de vallen in de vroege groep in week 1-8 vond plaats zonder de EVO te dragen. Valincidenten deden zich vooral voor tijdens transfers en staan, tijdens activiteiten met betrekking tot in- en uit bed stappen, toiletbezoek en douchen. De meerderheid van de proefpersonen had op het moment van de val nog geen onafhankelijk loopniveau bereikt (Functional Ambulation Categories ≤ 3) en had lage balansniveaus (Berg Balance Scale < 45). Dit benadrukt de noodzaak van zorgvuldige instructies van klinici en verplegend personeel aan patiënten en hun familieleden, en benadrukt de potentiële risico's van het uitvoeren van activiteiten zonder de juiste hulp, vooral in situaties waarin de EVO niet gedragen wordt en er geen zelfstandig loopniveau aanwezig is.

Tot slot worden in **hoofdstuk 8** de belangrijkste bevindingen van dit proefschrift besproken, samen met de sterke punten en beperkingen van dit onderzoek. Daarnaast worden implicaties voor de klinische praktijk en toekomstige studies gepresenteerd. Samenvattend laten de resultaten van dit proefschrift zien dat klinici, samen met de patiënt, kunnen beslissen wat zij het belangrijkste vinden bij het nemen van de beslissing wanneer zij moeten beginnen met EVO-verstrekking. EVO's bleken de sleepvoet te verbeteren ongeacht de timing van EVO-verstrekking na een beroerte. Vroeg EVO-gebruik zal naar verwachting resulteren in hogere functionele niveaus eerder in de revalidatie. Ondanks mogelijke functionele winst in de eerste revalidatieperiode, leidt vroeg EVO-verstrekking na 26 weken niet tot hogere functionele niveaus, vergeleken met latere verstrekking. Bovendien had vroege of latere EVO-verstrekking geen invloed op bekken-, heup- en kniekinematica op de korte of lange termijn. Daarom kunnen EVO's verstrekt worden om de sleepvoet te corrigeren, maar er is geen reden om aan te nemen dat vroege EVO-verstrekking de ontwikkeling van compensatoire bewegingen rond het bekken en de heup in de revalidatie na een beroerte zal beïnvloeden. EVO-gebruik verminderde de spieractiviteit van de tibialis anterior tijdens de zwaafase in vergelijking met lopen zonder EVO, wanneer de effecten binnen één meetsessie werden gemeten. Er werden echter geen negatieve effecten gevonden gedurende 26 weken gebruik. Gebaseerd op de resultaten van onze studie lijkt angst voor disuse ten aanzien van de tibialis anterior daarom geen gegronde reden te zijn om EVO-gebruik in de revalidatie na een beroerte uit te stellen. Men moet zich ervan bewust zijn dat een hoger aantal vallen

werd gevonden in het geval dat proefpersonen al vroeg na een beroerte werden voorzien van een EVO. Daarbij moet speciale aandacht worden besteed aan de specifieke instructies die worden gegeven met betrekking tot het gebruik van EVO's, aangezien de meerderheid van de valincidenten plaatsvond zonder de EVO te dragen en terwijl proefpersonen niet zelfstandig mochten lopen.

DANKWOORD

HET IS AF! Ja echt, het is af. Na bijna 10 jaar kan ik eindelijk dit antwoord geven op de vraag die me al talloze keren is gesteld. Ik ben trots op het resultaat en heel blij dat ik eindelijk bij dit gedeelte van mijn proefschrift ben aanbeland. Een promotietraject doe je nooit alleen, heel cliché maar helemaal waar. In al die jaren zijn er ontzettend veel mensen op één of andere manier betrokken geweest bij mijn onderzoek die ik graag wil bedanken. Ik had het graag kort willen houden, maar vrees dat me dat niet gaat lukken. Al is het maar omdat een aantal personen een eigen pagina in mijn dankwoord verdienen en er nu eindelijk eens geen woordenlimiet is.

Allereerst wil ik mijn promotoren bedanken. Alles ging bij mijn promotietraject al anders dan anders ("iets" meer tijd dan gemiddeld, heen en terug wisselen van vakgroepen) dus dan past een "anders dan anders" begeleidingstraject er ook wel bij. Ik had namelijk 3 promotoren, ook al staan er maar 2 in dit proefschrift vermeld. Jaap, Hans en Hermie, dank jullie wel voor al die jaren begeleiding bij het EVOLUTIONS-project en de feedback om m'n proefschrift te maken tot wat het nu is geworden.

Jaap, mijn dankwoord begint natuurlijk bij jou. Jij gaf me de kans na m'n afstuderen bij RRD aan de slag te gaan. Een kans die ik met beide handen heb aangegrepen, ook al waren er soms wat creatieve contract-constructies voor nodig. Na een aantal kleinere onderzoeksprojecten kwam je in 2009(!) met het idee en de vraag aan mij om te gaan promoveren. In lijn van mijn afstudeeropdracht hebben we vervolgens samen het onderzoek zoals het in dit proefschrift uiteindelijk opschreven is vanaf de grond toe opgezet. Hoe bijzonder het is dat je je eigen promotiestudie vanaf de basis zelf op kan zetten, realiseerde ik me toen niet, nu des te meer. Als iemand me toen verteld had dat we er zolang mee bezig zouden zijn, weet ik niet of ik er destijds wel aan begonnen was, maar terugkijkend had ik het niet willen missen. Ook al hebben we elkaar de afgelopen jaren meerdere malen de vraag gesteld "wie dit onderzoek ook al weer bedacht had...?" Jouw relaxte, nuchtere en positieve kijk waren meer dan eens precies wat ik nodig had als ik het gevoel had te verdrinken in m'n eigen onderzoek en de hoeveelheid data die we in de loop van de jaren verzameld hadden. Je ongelooflijk grote kennis op het gebied van CVA-revalidatie zijn onmisbaar geweest voor de totstandkoming van de verschillende artikelen en dit proefschrift. Altijd ging ik weer met nieuwe energie weg uit onze werkoverleggen. Je hebt daarbij het vermogen om "de mens achter de onderzoeker" nooit uit het oog te verliezen. Mede daardoor was het mogelijk de afgelopen jaren onderzoek te combineren met de nodige veranderingen in mijn thuissituatie. Ook aan de verschillende buitenlandse reizen voor congressen en projecten bewaar ik goed herinneringen (mijn eerste congres in een all-inclusive resort in Turkije (jouw droge reactie "dit is geen gemiddelde congreslocatie hoor"), het Londense nachtleven, Kaap de

Goede Hoop, de route vinden met een huurauto in Genua (is dat nou voor de 3e keer ons hotel?) en het gat in de heg in Dublin). Dat mijn promotietraject de nodige jaren heeft geduurd heeft wel een bijkomend voordeel gehad. Toen ik bij RRD startte werkte je nog als fysio op het Roessingh. Bij mijn verdediging ben je hoogleraar! Dank je wel voor al die jaren samenwerking en ik kijk uit naar wat er nog gaat komen.

Hans, ook jij bent vanaf de start bij mijn promotie betrokken geweest. Jouw inbreng en scherpe blik vanuit de dagelijkse praktijk als revalidatiearts waren heel waardevol in de vele discussies die we de afgelopen jaren hebben gehad. Ook je feedback op artikelen en het proefschrift waren (nadat ik je handschrift ontcijferd had) vaak aanleiding een stuk toch weer anders in te steken. Dank daarvoor. Met je humor en hilarische opmerkingen wist je altijd weer een sfeer te creëren waarin we serieus, maar ook met een hoop lol van gedachten konden wisselen. Ik hoop dat onze onderzoeken elkaar in de toekomst blijven kruisen. In ieder geval staat er nog een mooie trip naar Japan gepland!

Hermie, jij staat niet als promotor in dit proefschrift vermeld, maar ik beschouw je wel als zodanig. Vanaf het begin was jij bij mijn "RRD-carrière" betrokken als promotor. Ik heb veel respect voor je beslissing om een stap terug te doen in die officiële rol. Dank je wel voor al onze overlegmomenten en je rol in mijn promotietraject. Als niet-clinicus stond mijn promotieonderwerp wellicht wat verder van je af vergeleken met de e-health onderzoeken waar je je de afgelopen jaren met name mee bezig hebt gehouden. Maar jouw helikopterview en ongekende kennis als wandelende EMG-encyclopedie waren voor mij heel waardevol en belangrijk. Dank je wel voor alles.

Ik wil ook alle leden van de promotiecommissie bedanken voor hun kostbare tijd om mijn proefschrift te beoordelen en in de oppositie plaats te nemen.

Een onderzoek op het gebied van revalidatie na een CVA kan natuurlijk niet plaatsvinden zonder proefpersonen. Ik wil daarom alle proefpersonen en hun families van harte bedanken voor hun bijdrage aan mijn onderzoek. Het was en is heel bijzonder dat jullie mij letterlijk en figuurlijk mee lieten lopen in een periode waarin jullie leven en dat van jullie families volledig op z'n kop stond. Ik heb groot respect voor de manier waarop jullie alle veranderingen een plaats probeerden te geven en knokten om de draad van het leven weer op te pakken en het beste ervan probeerden te maken. Door de vele metingen zagen we elkaar gedurende een aantal maanden (meer dan) wekelijks. Dat ik een stukje van het revalidatieproces van zo dichtbij mee mocht maken vind ik heel bijzonder. Dank jullie wel daarvoor.

Deze studie en dit proefschrift zijn wat mij betreft het levende bewijs dat de verschillende Roessingh-onderdelen goed en intensief samen kunnen werken. Allereerst een groot dank-

jewel aan alle fysiotherapeuten van afdeling 2 en 3 van het Roessingh. Vele jaren was ik vaak dagelijks “aan de overkant” te vinden. Zonder jullie hulp bij de inclusie van proefpersonen en jullie creativiteit om waar nodig te schuiven met planningen was het nooit gelukt alle metingen tot een goed einde te brengen. Een speciaal dankjewel aan Martijn, Milou, Jolande en Jacintha, die in de loop van de jaren direct betrokken zijn geweest bij het uitvoeren van de klinische testen. Frank en Stienie, jullie hulp maakte het elke keer weer mogelijk patiënten, proefpersonen en therapeuten op te sporen, hoe ver ze ook in het Roessingh-gebouw verstopt zaten.

Ook wil ik alle revalidatieartsen en arts-assistenten van afdeling 2 en 3 hartelijk bedanken voor hun medewerking aan mijn onderzoek. Zonder direct en snel contact is het niet mogelijk in de vroege fase na CVA nieuwe proefpersonen te includeren.

Het was af en toe een hele puzzel alle metingen in te plannen in de revalidatieschema's van de proefpersonen. Ik wil daarom iedereen van de afdeling planning van het Roessingh bedanken voor het wekelijks wegplannen van al die metingen.

Als “2e Roessingh-onderdeel” was Roessingh Revalidatie Techniek heel belangrijk voor mijn studie. Dank je wel JohnJohn, Jeroen en het RRT-secretariaat voor het steeds weer op korte termijn inplannen en aanmeten van alle enkel-voet orthesen. Ook als er nog wat last-minute aanpassingen nodig waren kon ik altijd bij jullie terecht, dank daarvoor. Daarbij wil ik Basko bedanken voor het beschikbaar stellen van de EVO's.

De aanleiding van mijn promotiestudie kwam vanuit de klinische praktijk. Ik hoop dat mijn proefschrift bijdraagt deze dagelijkse praktijk met wetenschappelijke bewijzen te onderbouwen. Ik kijk er dan ook erg naar uit de komende periode verder met RCR en RRT samen te werken om de resultaten van dit proefschrift te implementeren!

Dan ben ik nu aangekomen bij mijn (oud) RRD-collega's. Ik wil iedereen die de afgelopen jaren bij RRD gewerkt heeft en daarbij heeft bijgedragen aan de prettige en laagdrempelige werksfeer bij RRD, en de gezellige praatjes bij de koffieautomaat, de vele borrels, clusteruitjes en reizen hartelijk bedanken. Een aantal mensen in het bijzonder. Jos, Leendert, Wendy, Wiebe en Wil, dankjewel bij al jullie hulp in het fixen van alle technische en computerproblemen (“dat mag niet mogen kunnen”) die ik in de loop van de jaren op kamer 15 veroorzaakt heb en de oplossingen die jullie daar steeds weer voor vonden. Leendert, een speciaal woord van dank voor al je hulp bij de vele metingen met Vicon en EMG, en alle bijbehorende analyses. Als duizendpoot bij RRD was je ook in mijn onderzoek een onmisbare schakel met betrekking tot alle gangbeeldmetingen en analyses. Inger, Gerda en Joke: zonder jullie was het nooit gelukt alle agenda's op elkaar af te stemmen voor werkoverleggen. Job en Marjolein, dank jullie wel voor al jullie hulp en advies bij alle statische analyses (en dat waren er nogal wat) die voorbij gekomen zijn in de afgelopen jaren. Heel fijn hoe jullie in normale-mensen-taal voor mij ingewikkelde statistiek uit kunnen leggen. Job, bedankt voor je bijdrages als co-auteur aan mijn artikelen. In tijden van woorden-limiet beperkingen wist je feilloos hele paragrafen van een delete-functie te voorzien, top! Marc, dankjewel voor je

betrokkenheid in de beginfase van mijn studie en onze huidige samenwerking bij de gang-beeldcursussen. Manon, Sharon, Dionne, Marte, Dianne, Wietse en Dorien en Vera, hartelijk bedankt voor jullie bijdrage als (master)studenten aan mijn promotieproject. I would like to thank all my colleagues from the Interaction-project and the XoSoft-project for their collaboration on the European projects, which I worked on besides my PhD-project. Thank you Elizabeth, for your help on improving this thesis.

Anke, Gerdienke, Brigitte, Jasper, Stephanie, Simone, Hester en Miriam, als buurvrouwen en -man naast en tegenover kamer 15 stond en staat jullie kamerdeur altijd open voor de broodnodige koppen thee en de inhoudelijke hulp. Minstens zo belangrijk zijn de vele minder serieuze gesprekken die van levensbelang zijn in tijden van Vicon-klik-moeheid, data-analyse frustraties en review-commentaar-verwerk-documenten. Dank jullie wel!

Martin, onze promotietrajecten (en vooral de lengte daarvan) hebben heel wat overeenkomsten, waarbij we allebei de laatste jaren parttime aan onze studies werkten. “En Corrie, heb je nog wat te zeuren?” is de standaard-quote waarbij je kamer 15 (en kamer 15 bij jou omgekeerd) met een bezoekje komt verblijden. De keren dat ik zo ongeveer onder de tafel van het lachen heb gelegen om je anekdotes en schuine grappen zijn ontelbaar. Dankjewel voor al deze zeurmomenten, je humor en onze geweldige tripjes naar Trondheim, Vancouver en Kaapstad. Hopelijk volgen er nog meer en ik hou 2-2-2022 in mijn agenda gereserveerd!

Erik, Marieke en Thijs, hierbij start de speciale pagina (of althans een deel daarvan) voor jullie in mijn dankwoord. Dank jullie wel voor (oud-)collega zijn, maar vooral het “mooi mens zijn” en onze bijzondere vriendschap. Wat hebben we er in de periode dat we met z’n vieren bij RRD werkten wat afgelachen. Regelmatig barstte er op 1 van de kamers een lachsalvo los, welke al snel gevolgd werd door de andere kamers als er weer eens een grap op de app werd geslingerd. Het kwam het werktempo misschien niet altijd ten goede, maar de gezelligheid bij RRD des te meer. Vele borrels en etentjes hebben we al gehad, ik hoop dat er nog velen, inclusief weekendjes weg (Thessaloniki beviel prima) volgen! Thijs, bedankt voor je altijd attente verwijzingen naar bananen en je rol als pas gepromoveerde vraagbaak. Erik en Marieke, jullie zijn en waren mijn roomies van kamer 15. Samen hebben we de afgelopen jaren lief en leed gedeeld. Dank jullie wel voor al die jaren hulp bij van alles en nog wat, zowel werkinhoudelijk als privé. Dank jullie wel dat jullie (samen met Martin) als “happy-helpers” hebben gefungeerd bij de talloze gangbeeldmetingen. De kroon op het “happy-helper-schap” is toch wel dat jullie mijn paranimfen willen zijn! Marieke, samen hebben we beheer regelmatig tot wanhoop gedreven met onze computerproblemen. “Danger, blond” staat nog steeds geheel terecht als waarschuwing bij m’n kantoordeur, en “JPLMO” komt nog meer dan me lief is voorbij. . . Erik, dankjewel voor alles, en dat is teveel om te proberen hier op te schrijven, je weet wat ik bedoel. Zonder jouw hulp was dit proefschrift letterlijk niet tot stand gekomen. Dankjewel voor je al je programmeer-skills, die op vele manieren

van grote waarde zijn geweest. De afgelopen jaren deelden wij kamer 15, onderzoeksprojecten, reizen, goede gesprekken en een hoop lol. Ik hoop dat er van dat alles nog veel volgt.

Een promotie-traject zonder de broodnodige afleiding en ontspanning is niet mogelijk. Mariëtte en Loes, sinds ons 1^e jaar studiejaar in Nijmegen kennen wij elkaar en weten jullie als geen ander hoe het werkt in het onderzoeks-wereldje. Heel fijn dat we met enige regelmaat een date hebben in de (buurt van de) driehoek Enschede-Den Bosch-Heeten om weer bij te kletsen. . . Judith, vanaf het vwo gingen we beiden naar Nijmegen, om vervolgens via Boston en Enschede weer bij elkaar in de buurt te komen wonen. Dank je wel voor de vele borrels en etentjes die we al gehad hebben en hopelijk nog volgen. Mariëtte, dank voor de vele uurtjes ontspanning door te borrelen, samen wat te eten of te shoppen. Heel wat telefoontjes zijn er al geweest, en die zullen ongetwijfeld ook nog volgen. Lieve Heren 1/mix-teamgenootjes, dank voor jullie interesse de afgelopen jaren in mijn werk, en de nodige uurtjes afleiding door samen lekker een balletje te slaan. Lieve Tuffels-vriendjes en vriendinnetjes, bedankt voor alle afleiding van mijn werk!

Tot slot mijn lieve (schoon)familie. Pap, mam, Menno en Elleke, Harry, Mariet, Lisette en Casper. Dank jullie wel voor jullie steun en oprechte interesse in mijn onderzoek, ook al was het soms misschien wat vaag waar ik nou precies mee bezig was. Zonder jullie hulp had dit proefschrift nog 10 jaar extra op zich laten wachten. Dank jullie wel voor de vele oppas-uurtjes die jullie verzorgd hebben als er weer eens een buitenlandse trip gepland stond, of omdat de agenda's thuis weer eens asynchroon liepen. Het moet nogal gek gaan, of jullie weten wel een oplossing voor mijn soms logistieke chaos te vinden. Ik kan altijd met een gerust gevoel thuis achter me laten, omdat ik weet dat alles goed geregeld is. Pap en mam, bedankt dat jullie me altijd in alles hebben gesteund en voor jullie vertrouwen.

En dan als laatste mijn echte thuisfront. Lieve Niek, jij bent mijn basis is alles. Zonder jouw onvoorwaardelijke steun was een combinatie van promotie en gezin niet mogelijk geweest. Jij wist altijd precies wat nodig was om me te motiveren of af te remmen, of alles even lekker te relativiseren, het is tenslotte maar onderzoek. Hvj. Len en Ise, mijn lieve schatten. Jullie zijn een mooi eigenwijs stel bij elkaar en mijn grote trots. "Moet je nou alweer typen?" is een vraag die jullie de afgelopen tijd veel te vaak hebben moeten stellen. Het boekje is nu echt af (ja echt echt) dus ik stop met typen. Het feestje komt eraan!

ABOUT THE AUTHOR

Corien Nikamp-Simons was born on May 14th 1984 in Heeten, the Netherlands. In 2002, she obtained her high school diploma from Carmel College Salland in Raalte, after which she started studying Biomedical Sciences at the Radboud University in Nijmegen. In 2005, she obtained her Bachelor's degree, followed by a Master's degree in Human Movement Sciences in 2007. Corien completed her Master's thesis on the effects of ankle-foot orthoses on static and dynamic balance in patients after stroke at Roessingh Research and Development (RRD), under the supervision of Jaap Buurke. After her graduation in 2007, she continued to work for RRD and contributed to several research projects, including a continuation of her master's project and a training study with the robotic gait trainer LOPES. In 2009, she started her PhD-project at Roessingh Research and Development and the University of Twente. Her PhD-project focussed on the effects of providing ankle-foot orthoses in the rehabilitation after stroke. The results of this research are presented in this thesis.

Besides her PhD-project, Corien was involved in two European projects in which a monitoring system to measure daily-life activities for patients after stroke using instrumented clothing was tested (FP7 INTERACTION, 2011-2015) and a soft lower-limb exoskeleton to assist people with mobility problems was developed (H2020 XoSoft, 2016-2019). In addition, she is involved in the gait analysis courses organized by RRD. Currently, Corien is working on several projects as a researcher at RRD. One of her projects involves the implementation of the results of her thesis into the clinical practice of the Roessingh, Centre for Rehabilitation.

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ISBN 978-90-365-4747-5