Optimizing ankle foot orthosis stiffness in calf muscle weakness

Waterval, N.F.J.

Link to publication

Creative Commons License (see https://creativecommons.org/use-remix/cc-licenses):
Other

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: https://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
GENERAL DISCUSSION
GENERAL DISCUSSION

In people with neuromuscular disorders, non-spastic calf muscle weakness largely affects the gait pattern, and causes walking problems, like diminished speed, increased walking energy cost, pain and imbalance [1-3], often leading to limitations in activities of daily living [4]. In usual orthotic care, persons with non-spastic calf muscle weakness are commonly provided with an AFO to improve gait and reduce walking problems. In case of spring-like dorsal leaf AFOs, besides restricting ankle dorsiflexion, the AFO can support the push-off by storing energy in the stance phase and releasing this energy during push-off, which, in turn, may reduce walking energy cost [5]. The effect of this mechanism though depends largely on the AFO’s ankle stiffness. A very flexible AFO will not restrain the ankle dorsiflexion, as it offers not enough bending resistance, and has a limited energy storing capacity. Contrary, a very stiff AFO has a high resistance to bending thereby reducing the ankle dorsiflexion and normalizing the knee angle but limits the ankle range of motion too much to store energy effectively. Simulations and experimental results in healthy individuals have indicated that somewhere in between these extremes an optimal stiffness for the reduction in walking energy cost exist [5, 6]. Yet, the effects of AFO ankle stiffness on gait biomechanics and walking energy cost in persons with non-spastic calf muscle weakness have not been previously studied. Therefore, the aim of this thesis was to expand the knowledge on how AFO ankle stiffness affects gait in persons with non-spastic calf muscle weakness and secondly, if optimization of the AFO ankle stiffness reduces walking energy cost and improves gait biomechanics, in order to optimize orthotic care. In this final chapter the main findings and methodological considerations are critically discussed, and clinical implications and future research directions are addressed.

MAIN FINDINGS

Gait compensations in response to non-spastic calf muscle weakness

In persons with push-off deficits due to calf muscle weakness, the upward acceleration during pre-swing is reduced, which results in more energy dissipation at contralateral heel-strike [7, 8]. As positive work needs to balance negative work at a steady walking speed, the increased energy losses induce the need for compensatory lower limb joint work. Insight into these compensatory gait strategies will enhance the understanding of pathological gait, which may be useful for clinical decision making and orthosis design. In chapter 2, it was demonstrated that at a fixed normalized walking speed, persons with unilateral calf muscle weakness compensate for the increased energy losses by redistributing positive mechanical work towards more proximal and contralateral joints,
as has been previously reported in simulation studies [9, 10], elderly [11], and patients with stroke [12] and multiple sclerosis [13]. In our sample of persons with calf muscle weakness, two different compensatory strategies were identified, namely 1) increased positive work in the hip of the affected leg or 2) increased positive work in the hip and knee of the unaffected leg. More severely weakened individuals used both strategies, which is in correspondence with recent experiments in elderly showing a relation between change in ankle work and compensatory hip work [14] and studies showing a relation between severity of weakness and walking speed in persons with Charcot-Marie-Tooth disease and polio [15, 16].

At self-selected comfortable speed, persons with calf muscle weakness did not demonstrate increased energy losses and, consequently, no compensatory mechanical work at the proximal lower limb joints was necessary. This indicates that persons with calf muscle weakness prefer to compensate by walking at a slower speed instead of generating less efficient compensatory joint work [8], probably to minimize increases in walking energy cost [17, 18]. However, a relation between compensatory joint work and walking energy cost could not be demonstrated, which was also found in other clinical populations [19] and healthy individuals [20]. Mechanical work does not directly reflect muscle work and metabolism [21], and likely measures of muscle activation are necessary to explain the relation between gait compensations and walking energy cost.

**Usual orthotic care in calf muscle weakness**

To improve gait and reduce walking energy cost, persons with calf muscle weakness are commonly provided with an AFO. As currently no general accepted AFO prescription guideline exist, it was expected to observe a wide variety of AFOs in usual orthotic care, with substantial variation in effectivity due to differences in mechanical properties. In the cross-sectional study in **chapter 3**, the mechanical properties of AFOs provided in usual care, as well as their effects on gait and the relation between mechanical properties and effectivity were evaluated. The studied population used various AFO types, consisting of dorsal AFOs, ventral AFOs, dorsiflexion-stop AFOs and high shaft-reinforced orthopedic shoes that differed substantially in weight, ankle stiffness and footplate stiffness. The effect of the AFOs was related to the AFOs’ ankle stiffness and varied from almost no effect to substantial reductions in walking energy cost (range: +0.01 to -1.84 J/kg/m) and ankle dorsiflexion angle.

Although the AFOs reduced the maximal ankle dorsiflexion in the majority of participants, a substantial percentage used AFOs with suboptimal stiffness properties to normalize ankle and knee biomechanics. Mostly, AFOs with stiffness values below 1 Nm/degree were used, which corresponds with AFOs designed to correct a drop-foot caused by
dorsiflexion weakness [22-26]. Such a low stiffness is sufficient to prevent ankle plantar flexion and keep the foot in a neutral position during swing [23]. However as shown in **chapter 3**, AFOs with a low stiffness, mainly prefabricated dorsal AFOs and custom made high orthopedic shoes, were insufficient to normalize the ankle dorsiflexion angle during the stance phase (Chapter 3 & 5). Normally, the calf muscles contract during stance to control the forward rotation of the tibia, which allows the ground reaction force to move forward along the foot in front of the ankle. In case of calf muscle weakness, the AFO should take over this function, by restraining dorsiflexion, in order to normalize the ankle dorsiflexion angle and knee moment, which apparently requires a more substantial stiffness [27, 28]. Additionally, the fact that higher AFO stiffness’s in the established range between 0.2 and 2.5 Nm/degree related with larger reductions in walking energy cost indicates that persons with calf muscle weakness benefit more from higher AFO stiffness levels.

Chapter 3 also showed that, in line with previous studies in polio survivors and individuals with Charcot-Marie-Tooth [29, 30], AFOs provided in usual care lacked an effect on ankle push-off power. This lack of effect limits the AFO’s effectiveness, as a reduced push-off power is the main reason of the diminished walking speed, increased walking energy cost [7, 8] and compensation strategies causing overuse symptoms [31, 32] in persons with calf muscle weakness. Therefore, the provision of AFOs that support ankle push-off power are assumed to improve orthotic care.

**Effect of AFO ankle stiffness**
To support ankle push-off power, spring-like AFOs can be provided as their energy storing and releasing capacity results in higher ankle powers compared to conventional orthoses [5, 33, 34]. However, the effect of these AFOs on gait depends highly on the AFO ankle stiffness [5, 6], which was shown in simulations and experiments in healthy subjects, but not yet in persons with non-spastic calf muscle weakness. Therefore, **chapters 4 and 5** evaluated the effects of varying the AFO ankle stiffness on gait biomechanics, walking energy cost and speed in this population.

Results with regard to gait biomechanics were as expected: an increase of 1 Nm/degree in stiffness reduced the maximal ankle dorsiflexion angle by 1 degree but also negatively affected the generation of ankle power, while only minimal effects on the knee angle and knee moment were found. This is in agreement with previous studies evaluating a wide range of stiffness values in healthy individuals [6] and stroke patients [35], but in contrast with previous studies in persons with lower limb salvage in which a 20% variation in stiffness levels showed no clinically relevant changes in gait biomechanics [36, 37]. However, as shown in chapter 3, the variation in stiffness levels of AFOs provided in usual
care appeared much larger (range: 0.2 Nm/degree to more than 2.5 Nm/degree) and showed to be related with gait outcomes. Taken into account the results of chapters 4 and 5, it can be assumed that the differences in effects between the various AFO designs found in chapter 3 are indeed, partly, the result of differences in AFO stiffness.

With regard to walking energy cost, no effect of stiffness variation on group level was found (Chapter 5), while on the individual level the most and least efficient stiffness differed up to 10.7%, indicating that no ‘one-stiffness-fits-all’ existed. This is in contrast with previous small studies evaluating the effect of varying AFO stiffness in healthy subjects and neurological patients [6, 38]. The main difference with the study in neurological patients was that their studied population was more homogeneous with regard to severity of calf muscle weakness and had mild spasticity. This homogeneity in impairments could well explain the finding of an optimal stiffness on group level [5]. In addition, in the study on neurological patients, the AFO had a substantially more rigid footplate compared to the AFOs used for the studies described in this thesis (0.2 versus 2.24 Nm/degree). A more rigid footplate allows the ground reaction force to move more anterior of the ankle in late stance independent of the AFO ankle stiffness and, consequently, is likely to influence the effect of ankle stiffness on gait [39]. Other studies support the finding that personalization of orthotic properties is necessary to achieve a maximal reduction in energy cost. In cerebral palsy children, the AFO with the largest reduction in walking energy cost differed between flexible, stiff and rigid AFOs[26]. In healthy individuals, the importance of individualization of orthotic properties was indicated using a spring-like hip orthosis [40] and active ankle orthosis [41], providing further evidence that individualization is required to maximally reduce the walking energy cost.

Contrary to the substantial reduction in walking energy cost (-10.7%), walking speed only increased by 4.7% with stiffness-optimization. Improvements in ankle power are suggested to have a relatively larger effect on walking energy cost than on speed. In healthy individuals a 0.6 W/kg increase in ankle power increased speed by 5.9%, while reducing the walking energy cost by 13.2% [42]. The improvements found with AFO stiffness variation in chapter 5 are in line with this study as ankle power differed up to 0.4 W/kg.

**Individually optimizing the AFO ankle stiffness**

Chapters 4 and 5 clearly showed that one single AFO stiffness does not fit all persons with non-spastic calf muscle weakness, indicating the importance of individually optimizing the AFO ankle stiffness for maximally reducing walking energy cost. However, whether an individually stiffness-optimized AFO is also beneficial in reducing walking energy cost compared to regular AFOs provided in usual care had never been studied. Therefore, the PROOF-AFO trial (chapter 6) was conducted, in which AFO users with non-spastic calf
muscle weakness were provided an individually stiffness-optimized spring-like AFO. AFO stiffness was optimized primarily based on walking energy cost and secondarily on speed and gait biomechanics. After optimization, participants used the stiffness-optimized AFO in daily life for 3-months. The primary outcome, walking energy cost, and secondary outcomes, e.g. gait biomechanics and perceived fatigue, were assessed at baseline when using the regular AFO provided in usual care and after using the stiffness-optimized AFO for 3 months.

In chapter 7, the results of the PROOF-AFO trial are presented. Stiffness-optimized AFOs reduced the walking energy cost by an additional 9.2% compared to AFOs provided in usual care, which corresponds to a 60% increase in effect (from -0.70 J/kg/m to -1.12 J/kg/m compared to shoes only). This is a larger effect than that found in children with cerebral palsy, where AFO stiffness-optimization reduced the energy cost by 9% compared to shoes only [43]. Contrary to the hypothesis, the reduction in walking energy cost was not the result of an increased ankle power in all participants. Only in individuals walking with a low ankle power when using their regular AFO, increments in ankle power of more than 0.2 W/kg were achieved with the stiffness-optimized AFO, which, at least partly, might explain the reduction in walking energy cost in these individuals [44]. However, in case the regular AFO was more flexible and individuals had a substantial remaining ankle power, the stiffer optimized AFO reduced the ankle push-off power, which is in agreement with chapter 5. Stiffer AFOs reduce the strain on the calf muscles and stretch of the Achilles-tendon [45], resulting in a lower passive power generation [46]. Apparently, this disadvantage is larger than the push-off support by the energy storing and releasing capacity of the stiffness-optimized AFO. In these persons, walking energy cost probably reduced by an improved external knee-extension moment, which, in children with cerebral palsy also appeared to be associated with walking energy cost reduction when wearing solid or dorsal leaf AFOs compared to barefoot walking [47]. Taken together, the optimal stiffness is a trade-off between rigidity to normalize the ankle and knee kinematics and enough flexibility to be able to generate ankle power.

In bilaterally affected persons larger reductions in walking energy cost (-12%) were achieved, which was accompanied by a 9% increase in walking speed. That the AFOs showed larger effects in bilaterally affected persons compared to unilateral affected patients, may be caused by the remaining push-off asymmetry in unilateral affected persons. In healthy subjects, push-off symmetry is important to achieve maximal reductions in energy cost [48].

The favorable effects of stiffness-optimized AFOs on walking energy cost were demonstrated in a laboratory setting on level ground, but also transferred well to daily life. Namely, the reduction in walking energy cost was accompanied by a reduction in
perceived fatigue, which is related with energy cost, as shown in persons with mild multiple sclerosis [49]. Besides these positive effects, the stiffness-optimized AFOs also induced limitations during daily life activities in some persons such as walking stairs or driving a car. However, apparently participants regarded these limitations less important than the improvements in gait as the majority of participants (60%) favored the stiffness-optimized AFO above the regular AFO, which demonstrates the relevance of stiffness-optimization for usual-care.

Methodological considerations

Study design
To evaluate the effect of AFO ankle stiffness variation and stiffness optimization on gait, a prospective uncontrolled intervention study design was used. This allowed us to compare the effect of multiple AFO stiffness conditions in the same person, without potential meaningful differences in patient characteristics like severity of weakness. However, this study design may have resulted in biased results in two ways. First, the optimized AFO was compared with an AFO provided before study enrollment in usual care, which could have been suboptimal at the start of the study due to disease progression or wear of the AFO. Secondly, it may have imposed a selection bias if mainly patients dissatisfied with their usual care AFO were included. However, there is no indication that the usual care AFOs were insufficient as the effects reported in chapter 3 were larger than generally reported in the literature [15, 29].

Study population
To enlarge generalizability, multiple neuromuscular disorders causing non-spastic calf muscle weakness were included. In most studies evaluating the effect of AFOs, only persons with a specific diagnosis were included although the mechanical aim and effectivity of the AFO are not diagnosis specific, but depend on the nature and severity of the impairment(s). In total, eleven different diagnoses were included, most commonly polio and Charcot-Marie-Tooth disease. These are the most prevalent neuromuscular disorders causing non-spastic calf muscle weakness [50-52]. Due to the heterogeneity in neuromuscular disease and impairments, the demonstrated effect-sizes might not represent the expected results in all persons with non-spastic calf muscle weakness. The expected effect of the AFO likely depends on factors like the presence of uni- or bilateral calf muscle weakness, sensory deficits and/or mild proximal weakness [53]. In bilaterally affected persons, a larger effect of stiffness-optimization on walking energy cost and speed is expected as shown in chapter 7. Sensory deficits negatively affect gait irrespective of muscle weakness, and the increased sensory sensations of the orthosis might increase its effect. In persons with mild quadriceps, smaller effects of the dorsal leaf AFO might be expected as it enforces an external knee flexion moment in early stance which may
induce balance problems [27]. This was found in two drop-out cases of chapter 7 who were unable to walk with the intervention AFO while they were able to walk with their own ventral AFO.

**Outcome measures**

Walking energy cost was selected as the primary outcome to objectively determine the effect of stiffness-optimized AFOs on walking performance, as it takes into account both walking speed and metabolic cost, while it also relates to fatigue, a major complaint of persons with calf muscle weakness [49]. It was deemed necessary to first firmly demonstrate possible beneficial effects of stiffness-optimization on objective measures of gait, which justifies the selection of walking energy cost as primary measure. In addition, the minimal detectable change of walking energy cost (9.4%) is relatively low compared to, for example, perceived fatigue for which a minimal detectable change of 20% has been reported [54]. However, by powering the trial for walking energy cost, no firm conclusion about perceived improvements in daily life can be drawn, although secondary outcomes indicate the existence of these improvements.

Walking energy cost was measured at comfortable speed, instead of at fixed speed, to be able to determine the effect of the (stiffness-optimized) AFO on walking speed, which is regarded an important clinical measure. However, changes in comfortable speed influence walking energy cost [55]. Consequently, it is likely that energy cost is reduced by both an improved gait efficiency as well as an increase in walking speed. As also gait biomechanics depend on walking speed (chapter 2), it is challenging to relate the gait biomechanics to changes in energy cost. To resolve these uncertainties walking energy cost and gait biomechanics should have been measured at both a self-selected and fixed speed, although this was regarded to demanding for the included population.

**Design of the intervention AFO**

To modify and optimize the AFO ankle stiffness in chapter 5 and 7, a modular AFO consisting of off-the-shell carbon dorsal leaf springs and a custom-made calf casing and footplate was used. The major advantage of this modular AFO system was that it enabled constant footplate stiffness, and AFO length, weight, fitting and alignment across stiffness conditions, ensuring that the results truly reflect the effect of ankle stiffness modification. However, the modular AFO design also had some disadvantages. The shape and neutral angle of the dorsal leafs could not be personalized, which limited the fitting and comfort around the heel. In addition, the necessary modularity limited the number of stiffness levels that could be tested, as more flexible dorsal leafs were smaller and could not be incorporated in the modular design. Consequently, the most flexible AFO stiffness tested was already stiffer than the highest stiffness of the AFOs provided in usual-care
as presented in chapter 3. As such, the effect of AFO ankle stiffness variation was tested in a higher stiffness range. Nevertheless, it is highly likely that the optimal stiffness was included in the tested range as in the large majority of participants a medium stiffness turned out to be optimal, indicating that a range extension towards more flexible stiffness levels would not have led to a different optimization outcome.

**Optimization protocol**
The optimization was primarily based on walking performance outcomes (walking energy cost & speed), and secondarily on an appreciation of ankle and knee biomechanics by three experts. Although considering both factors for the optimization requires more time-consuming measurements, it is regarded necessary. Inclusion of gait biomechanics in the optimization algorithm appeared essential as in 90% of the subjects it was not possible to differentiate the optimal AFO solely based on walking energy cost and speed as differences between stiffness levels were within the measurement error. Determination of the optimal AFO solely on gait biomechanics is not ideal either, as normal-like gait may not result in the best functional outcome, indicated by the unclear relation between gait biomechanics with walking energy cost [19, 32, 29].

The individual preference was not taken into account when optimizing the AFO stiffness. It is likely that persons would prefer a stiffness close to their AFO provided in usual care, based on their previous experience. Therefore, inclusion of individual preference in the optimization algorithm might introduce a bias towards selecting a stiffness close to the patient’s own AFO, which was suboptimal in most participants (chapter 3).

**Clinical implications**
The results of this thesis showed the importance of evaluating the effects of AFO ankle stiffness on gait, and individualizing the AFO ankle stiffness in people with neuromuscular disorders exhibiting non-spastic calf muscle weakness in order to improve orthotic care. Although, AFOs currently provided in usual care reduce walking energy cost by 13.3%, an additional 9.2% reduction was achieved by individually optimizing the AFO ankle stiffness. These individually optimized AFOs led to improvements in patient reported outcomes such as perceived fatigue and physical functioning. Therefore, to maximize the functional benefit of AFOs for the individual patient, implementation of AFO stiffness–optimization procedures in clinical practice is recommended, especially in persons reporting fatigue and increased walking effort.

In chapter 2, it was shown that persons with calf muscle weakness increased mechanical work at the knee and hip joints when they walked at a fixed, higher than comfortable, speed. This increase in mechanical work may explain complaints of muscle fatigue and
pain around these joints [31]. To identify the individuals at risk for overuse symptoms, gait compensations should be assessed when physical examination reveals calf muscle weakness. To identify the used gait compensations, a 3D-gait analysis at a fixed, higher than comfortable, speed should be performed. At such a speed, persons are unable to compensate by lowering their speed and, consequently, need to use their compensation strategy. To reduce the compensations, treatment should focus on ankle push-off support as this has been shown to result in reduced hip compensations and a higher walking speed as demonstrated in elderly [14]. In persons with calf muscle weakness such support can be provided by spring-like dorsal leaf AFOs [5]. Results in chapters 4, 5&7 of this thesis show that spring-like AFOs indeed reduce walking energy cost in persons with neuromuscular disorders when the stiffness is appropriate. Data of chapter 3, 4&5 show that the stiffness of these AFOs should be individualized and at least be 2 Nm/degree when provided in case of non-spastic calf muscle weakness.

Chapters 4, 5&7 demonstrated that the effect on walking energy cost of stiffness-optimization appeared to depend on the improvements in ankle power and external knee moment. To gain information about the potential effect of stiffness-optimization and inform patients about potential benefits, it is advised to assess the baseline gait biomechanics and walking energy cost. In persons walking with low ankle power, a continuous external knee flexion moment and/or showing bilateral muscle weakness, stiffness optimization showed to improve treatment outcomes largely beyond usual-care. However, also in other subsets of patient’s stiffness-optimization should be considered, as due to the low sample size the possible positive effects could not be demonstrated.

Implications for optimizing AFO stiffness
The process of providing and optimizing the AFO should follow a general rule: ‘providing the most flexible AFO that normalizes gait biomechanics and shows a substantial effect on walking energy cost’. Normalization of gait biomechanics is necessary to reduce compensations and walking energy cost, while providing the most flexible AFO limits the constraints induced by the AFO in daily activities. The five persons provided with a stiff optimal AFO (K4 and K5), whom were heavy (80+ kg) and walked slowly (slower than 1 m/s), reported disadvantages with activities of daily living such as walking uphill and walking stairs (chapter 7). Given the small sample of patients in which a stiff AFO was optimal and the disadvantages these patients experienced when using their AFO, for clinical practice an optimization with three stiffness levels between 2.5 and 5 Nm/degree seems appropriate. It should be noted that the lowest stiffness (2.8 Nm/degree) is already substantially stiffer compared to AFOs provided in usual care as described in chapter 3. Furthermore, to manage patient expectations, the disadvantages of the AFO in relation to the patient goals need to be addressed before optimization. Although it is challenging to
incorporate such goals within the optimization, a modular AFO design allows a test period to experience the constraints in daily living and adaptation of the stiffness if necessary, which may lead to better AFO adherence [56].

**Future research directions**
Although this thesis expanded the knowledge on how AFO ankle stiffness affects gait in persons with non-spastic calf muscle weakness, future research should build further on the results in order to optimize orthotic care.

**Gait compensations**
Chapter 2 demonstrated that persons with calf muscle weakness have an increased mechanical workload on the knee and hip joints that may explain pain and osteoarthritis, which are common secondary problems in persons with muscle weakness [57, 58]. Future research should evaluate this relation, and study whether joint loading is increased, which requires the measurement of muscle activation. Furthermore, results of later chapters indicate that AFOs increase compensations for forward propulsion. When using an AFO, persons with calf muscle weakness substantially increase their walking speed compared to shoes only but, meanwhile, the AFO does not increase ankle power. Consequently, to maintain the higher walking speed, more positive hip work for forward propulsion is necessary. Future clinical work should aim to reduce these compensations, which may reduce the walking energy cost further [40]. However, more research in patient groups about how orthotic assistance leads to reductions in energy cost is necessary, which requires the assessment of muscle activations to model the effects of the AFO on the muscular level [21, 46].

**Improvements in activities of daily living**
In current care, the effect of AFOs is commonly assessed on level ground, while in daily life more challenging environments are usually encountered. Consequently, the stiffness-optimized AFO might induce negative effects on activities of daily living, such as standing still, walking stairs, uphill walking or walking on uneven terrain as reported by some persons in chapter 7. Future research should focus on reducing these limitations in daily life. To accomplish this, it is necessary to quantify how AFOs with different properties function during various activities, for example using uneven ground treadmills [59]. Furthermore, more insights about the limitations encountered when using an AFO should be gained using qualitative measures such as interviews and focus-groups. Specific training with the orthosis in these circumstances may reduce the limitations by learning new control strategies. Healthy individuals need specific training to converge to optimal gait with an orthosis [60, 61], but whether such training is necessary in patient’s populations is unknown. In addition, limitations in daily activities may be reduced by innovations in
orthotic design. For example, orthoses with a clutch allowing free non-sagittal motion and free plantarflexion movement under non-weight bearing circumstances, may be beneficial for driving a car [62]. For walking stairs or walking uphill, design innovations should focus on adjustment of the ankle angle restriction based on the specific task.

**AFO stiffness optimization protocol**

While AFO stiffness optimization appeared relevant, the optimization procedure should be made more feasible for implementation in usual care by a shorter, faster and more manageable protocol. First, the protocol can be made faster by validating optimization of the AFO stiffness on self-paced treadmills, such as the GRAIL (Gait Real-time Analysis Interactive Lab, Motek, Amsterdam), as this would allow for simultaneous measurement of gait biomechanics and walking energy cost. Time on the treadmill for each stiffness-condition can be reduced further by using instantaneous cost mapping, which allows for the determination of the walking energy cost within 2-minutes although it is uncertain whether this holds in patient populations [63]. Using a treadmill, this is also ample time to collect gait biomechanics and may reduce optimization time from multiple hours to 30 minutes.

To reduce the time of manually changing the AFO stiffness, AFOs of which the stiffness can be instantaneously altered using emulators can be used. Such devices allow for human-in-the-loop optimizations, which can improve precision of the optimal stiffness by exploring and optimizing the effect of a unlimited range of AFO ankle stiffness’s in a limited time-frame [41]. However, currently such methods have only been used to optimize orthotic assistance in healthy individuals [41, 64]. Furthermore, human-in-the-loop optimizations allow for the optimization of multiple properties simultaneously. Previous small studies have indicated that footplate stiffness and alignment have an effect on gait biomechanics and possibly also on walking energy cost [39, 65-67]. Optimization of these parameters simultaneous with ankle stiffness would improve AFO related outcomes, which is not possible by manually changing the properties as this would be time-consuming and outcomes may be counterintuitive due to interaction effects.

**Prediction of the optimal AFO properties**

To achieve the provision of optimized-AFOs on a much broader scale, future research should aim to predict optimal AFO properties as this would eliminate the need for extensive personalized procedures in expensive laboratories. In recent years, simulations have demonstrated potential in predicting gait in various circumstances [68, 69] and predicting pathological gait, but extensive validations against patient data are necessary [70]. A first step towards predicting the optimal stiffness is the determination of how individual factors like severity of (calf) muscle weakness, weight and speed, influence the
optimal stiffness, footplate stiffness and their possible interaction. In addition, simulations can provide insights into the effect of various designs of assistive devices, without the need of trial-and-error [71]. This may help designing new AFOs and fit the most suitable and effective orthosis to each individual.

**Conclusion**

In conclusion, this thesis demonstrated that AFOs currently provided in usual-care to persons with non-spastic calf muscle weakness often have a too low ankle stiffness, leading to suboptimal treatment outcomes. Individually optimizing the AFO ankle stiffness improves treatment outcomes, such as walking energy cost, but also perceived fatigue and perceived physical functioning. Therefore, to improve orthotic care, implementation of stiffness-optimization in usual care is warranted. Future research should focus on improving optimization methods and prediction of the optimal AFO stiffness, in order to individually tune multiple AFO properties and further improve the effect of AFOs for calf muscle weakness in persons with neuromuscular disorders.
REFERENCES


