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Non-operative treatment of unicompartmental osteoarthritis of the knee: a prospective randomized trial with two different braces—ankle–foot orthosis versus knee unloader brace

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Abstract

Background The use of an unloader brace is a non-surgical treatment option for patients with medial osteoarthritis (OA). However, many patients do not adhere to brace treatment, because of skin irritation due to the pads at the level of the joint space and bad fit. A new concept to unload the medial compartment of the knee is a foot ankle brace with a lever arm pressing the thigh in valgus. The aim of this prospective randomized trial was to examine the outcomes of patients with medial OA after treatment with a conventional knee unloader brace (Unloader One®) and the new foot ankle orthosis (Agilium FreeStep®).

Methods For this multicenter trial, 160 patients (> 35 years) with medial OA were randomly allocated to treatment with a conventional knee unloader brace (Unloader One®) or treatment with the new knee OA ankle brace (Agilium FreeStep®). The primary outcome measure was pain (numerical analog scale) at baseline (T0), 8 weeks (T1), and 6 months (T2). Secondary outcome measures were knee function (Knee Injury and Osteoarthritis Outcome Score, KOOS), side effects, additional interventions, and compliance.

Results In both groups, walking pain improved between T0 and T1 and also between T0 and T2 without a significant group difference. For pain at sports, both groups showed a significant improvement between T0 and T2 without a significant group difference. The KOOS subscales symptoms, pain, activity, sport, and quality of life increased significantly in both treatment groups without any significant group differences at T 0, T1, and T2. There was also no significant group difference in additional interventions and weekly or daily brace use. In the Agilium FreeStep® group (23.5%), significantly less patients reported bruises in contrast to the Unloader One® group (66.7%).

Discussion The results of this clinical trial show that the foot ankle brace is as effective as a conventional knee unloader brace for the treatment of medial knee OA with regard to clinical outcome. The rate of side effects such as bruises was significantly lower in the Agilium FreeStep® group.

Trial registration DRKS00009215, 13.8.2015.

Keywords Knee pain · Varus malalignment · Varus deformity · Biomechanics · Non-surgical OA interventions · Biomechanical interventions

Background

Medial osteoarthritis (OA) is a frequent cause of knee pain predominantly affecting patients who have a varus deformity [27]. The initial treatment of OA is non-operative and consists of patient education, weight reduction, physical therapy, and medication [13].

Knee joint loading is a key factor for the development of pain and the progression of OA [1, 9, 15]. In the frontal

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plane, the ground reaction force passes medial to the knee during walking [9, 23]. This creates an adduction moment loading the medial compartment almost 2.5 times more than that on the lateral compartment [9, 23]. The knee adduction moment is considered to be the primary factor for dynamic load distribution in the knee joint and therefore also for progression of medial knee OA [9]. For this reason, the reduction of the knee adduction moment seems to be an important factor in the treatment of medial knee OA [5]. The high tibial osteotomy is a surgical solution to correct varus deformity to reduce the knee adduction moment. Non-surgical interventions are knee braces which may alter the alignment of the lower extremity [2, 3, 6, 7, 11, 16, 19–21]. These so-called unloader braces apply an external valgus moment to the knee to shift loads away from the degenerative medial compartment [16, 19]. The external valgus moment acts via condylar pads or straps while opposing counterforces which arise from the supports proximal and distal to the knee joint (Fig. 1a). A systematic review of biomechanical studies has confirmed this concept [18]. This review has shown that medial unloader braces reduce the external adduction moment of the knee significantly [18].

Randomized controlled trials (RCT) have shown that knee bracing results in improved knee function compared with no brace in patients with OA and varus malalignment [3, 16]. However, well-known side effects of brace treatment are skin irritations caused by the condylar pads or straps with the consequence that the patients do not adhere to treatment [28, 29].

Insoles with a lateral wedge do not cause any skin irritation, but their biomechanical effect to reduce the knee adduction moment is limited [18]. However, a biomechanical study has shown that an additional stabilization of the ankle can significantly improve the effectiveness of lateral wedged insoles [25]. In this study, the sole application of a laterally wedged insole had no biomechanical effect [25]. The additional application of an orthosis, which stabilized the upper ankle, led however to a significant reduction of the external knee adduction moment [25]. Thus, it was shown that the stability in the upper ankle is a factor which supports the effect of laterally wedged insoles. This study led to the development of an ankle orthosis, which is used to correct the leg axis (Fig. 1b) [14]. This ankle foot orthosis (Agilium FreeStep®, Otto Bock, Duderstadt, Germany) consists of a non-flexible insole which is connected to a lever with a pad that applies a valgus force to the shank. The hypothetical mechanism of the foot ankle orthosis is that the medially directed pressure to the lower leg reduces the varus angle of the knee joint and shifts the vector of the ground reaction force from medial to lateral. In this way, the knee adduction moment can be reduced. In addition, a limitation of ankle eversion should affect a pathological tibia rotation [14]. The rate of skin irritations should be reduced due to the lack of condylar pads.

Fig. 1 **a** Unloader One® (Össur, Reykjavik, Iceland), **b** Agilium FreeStep® (Otto Bock, Duderstadt, Germany)

A recent biomechanical study has shown that this new brace concept is effective in reducing the knee external adduction moment in comparison to the treatment with insoles alone [8]. A recently published clinical case series has shown that an OA ankle brace can improve pain and knee function in patients with unicompartmental OA [14]. However, controlled clinical trials on the effect of knee OA ankle braces are still lacking.

Because of this lack of evidence, we performed a prospective randomized clinical trial to compare the knee OA ankle brace (Agilium FreeStep®) with a conventional knee unloader brace (Unloader One®). This clinical trial targets patients older than 35 years of age presenting with symptoms of medial OA and varus malalignement.

Based on the results of the previous studies [8, 14], we hypothesized that the passive realignment provided by the ankle foot orthosis decreases pain and improves knee function. Since the ankle foot orthosis has no pads at the level of the knee, we expected that the rate of skin irritations will be lower in this treatment group or move to the contact area of the ankle brace.

Methods/design

Study design

This study was a randomized clinical trial examining the short-term effectiveness of a knee OA ankle brace (Agilium FreeStep®, Otto Bock, Duderstadt, Germany) in comparison to a conventional knee unloader brace (Unloader One®, Össur, Reykjavik, Iceland) (Fig. 1). The study design was

based on the protocol of another intervention study for the treatment of medial OA with an unloader brace [29].

This study design was approved by the medical ethics committee of the medical faculty of the Charité—Universitätsmedizin Berlin (EA 1/069/15, 26.3.2015). All patients provided written informed consent.

The study protocol was registered with the *Deutsches Register Klinischer Studien* ("German Clinical Trials Register") as DRKS-ID number DRKS00009215. The WHO universal trial number (UTN) is U1111-1173-1492. Figure 2 shows a flowchart of the study design.

The sponsor of the clinical trial was Otto Bock HealthCare Germany GmbH.

Study centers

This study was a multicenter clinical trial. The principal investigator was Prof. Dr. med. Wolf Petersen, Martin Luther Krankenhaus, Berlin, Germany. Patients were recruited from the following hospitals and orthopedic practices:

1. Klinik für Orthopädie und Unfallchirurgie, Martin Luther Krankenhaus, Berlin, Germany: 18 patients.
2. Krankenhaus Lahnhöhe, Zentr. für konserv. Orthopädie, Am Kurpark 1, 56112 Lahnstein: 11 patients.
3. Asklepios Harzklinik Fritz-König-Stift, Ilsenburger Straße 95, 38667 Bad Harzburg: 16 patients.
4. Donau Universität Krems, Dr. Karl Dorrek Straße 30 A-3500 Krems: 8 patients.
5. Arcus Sportklinik, Rastatter Straße 17, 75179 Pforzheim: 20 patients
6. Orthopädische Klinik der MHH, Anna-von-Borries-Straße 1-7, 30625 Hannover Kleefel: 18 patients.
7. Orthopädisch Chirurgisches Centrum Tübingen, Wilhelmstr. 134 72074 Tübingen: 8 patients.

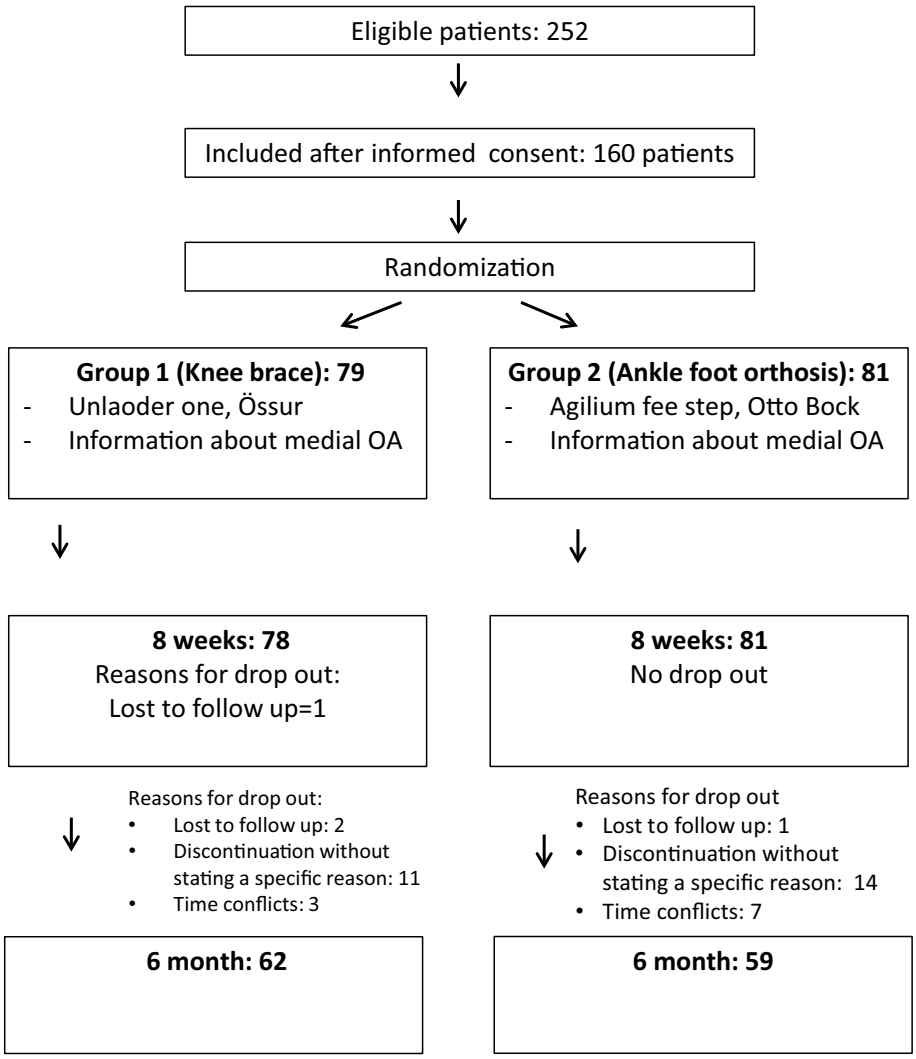

Fig. 2 Flowchart showing the study design

8. Fisiotherapia Albasini and Müller, Viale Giuseppe Motta 15, CH-6500 Bellinzona: 16 patients
9. St. Vinzenz Hospital, Dinslaken, Dr. Otto-Seidel Str. 31, 46535 Dinslaken: 8 patiensts.
10. Gemeinschaftspraxis Rosenthal and Schubert, Viktoriastr. 66-70, 44787 Bochum: 3 patients.
11. Gelenk und Wirbelsäulenzentrum, Kieler Str. 1, 12163 Berlin: 22 patients
12. Orthopaedicum Northeim-Göttingen, Sturmbäume 3, D-37154 Northeim: 15 patients.

The clinical outcome parameters were collected and analyzed at the principal study center (Klinik für Orthopädie und Unfallchirurgie, Martin Luther Krankenhaus, Berlin, Germany).

Patient selection

Adults aged 35 years and older suffering from medial OA with a desire for a non-operative treatment qualified for inclusion in the present study.

Medial OA was defined as pain located at the medial joint space in combination with radiological signs of OA (grade 1 or higher). The radiological signs of OA were assessed on whole leg X-rays using the classification stated by Kellgren and Lawrence [10] (grade 0–IV). The recruitment period took place from September 2015 to October 2016.

Exclusion criteria

Exclusion criteria included the following: (1) no knowledge of the German language, (2) pain which was not caused by medial OA, (3) lateral OA grade I and more, (4) no varus malalignement.

Varus malalignment was assessed on whole leg X-rays using the hip knee ankle angle (HKA) which is the angle between a line from the middle of the hip to the notch and a second line from the middle of the ankle to the intercondylar eminence or clinically using the caliper method [4]. A positive value indicated a varus malalignement. Patients with an HKA angle of 0 or less were excluded. No condylar distance and a malleolar distance of more than 2 cm were considered as neutral axis or valgus.

Informed consent

Patients who qualifed as study participants on the basis of inclusion and exclusion criteria were informed about the study. This information included written general information on medial OA and a written description of the present study. These instructions included information about the purpose of the study and potential risks. All participants had to sign an informed-consent form.

Sample size calculation

In an intervention study by van Raaij et al. [29], the difference in pain between the intervention and control groups was 15% (1.5 points on VAS). This difference was statistically significant (power 0.8, alpha 0.05). The present study however had a non-inferiority design. With an irrelevant difference of 10 for pain on a numerical analog scale (NAS), a pooled standard deviation of 2.25, and a potential dropout rate of about 10%, approximately 154 patients had to be enrolled in this study (power 0.80, alpha 0.05). For this sample size calculation, a one-sided test (two sample *t* test) for non-inferiority was presupposed.

Intervention

The two treatment groups in this trial underwent the following interventions:

Group 1: patients received written information about medial OA and a conventional unloader brace (Unloader One®, Össur, Reykavik, Iceland) (Fig. 1a).

Group 2: patients received written information about medial OA and a knee OA ankle brace (Agilium FreeStep®, Otto Bock, Duderstadt, Germany) (Fig. 1b).

The braces were adapted to the patient by an orthopedic technician at the study center, and its function explained to the patient. Study participants also received appropriate patient information about the braces provided by the manufacturers. They were instructed to use the orthosis for at least 6 h a day.

Co-interventions

During the course of the study, the following co-interventions were allowed: application of ice, ointment dressings, weight reduction, accupuncture, intraarticular injection of hyaluronic acid or corticoids, bandages, crutches or cane, consumption of oral analgesics (nonsteroidal anti-inflammatory drugs or paracetamol), and physiotherapy. Patients were asked to report on co-interventions after 8 weeks and 6 months.

Randomization

After patients were recruited and informed consent had been obtained, the patients were randomized to the two treatment groups. All study centers received the randomization documents in a sealed envelope. After opening the envelope, the group to which each patient was assigned would be seen. Patients were allocated to either group 1 or group 2.

Baseline examination

The following data were collected during the baseline examination: date, patient age, sex, contact information, affected side (left or right knee), symptoms, localization of pain, current treatment, medical history, clinical examination findings including range of motion, stability tests (Lachman, pivot shift, and posterior drawer tests), meniscus signs, intraarticular effusion, soft tissue swelling, and leg alignment.

At baseline, all primary and secondary outcome parameters were also assessed.

Data processing

Patient name and contact information, along with the results of the baseline examination, were transmitted to the evaluation center (Martin Luther Hospital, Berlin). The assessor was blinded for treatment. After evaluation, the data were processed anonymously.

Outcome parameters

Primary outcome measure was subjective assessments of pain at rest, with walking, and sports activity, reported on a numerical scale (0–100) [3] at baseline, 8 weeks, and 6 months. This outcome parameter was used for the sample size calculation.

Secondary outcome measures were the German version of the Knee Injury and Osteoarthritis Outcome Score (KOOS) [22]; self-reporting of skin irritations; review of compliance and review of additional interventions. All these measurements were evaluated via questionnaire at baseline, 8 weeks, and 6 months. Additional interventions were recorded by the patient over the course of the study.

All patients were instructed that skin irritations can occur at sites where the pads of the brace press against the skin. In this case, the patients should take a photo of the skin irritation and contact the study center.

For the assessment of compliance, the patients required to complete a wear diary. The study participants were asked by a questionaire how often they used the brace per week (answer options: every day, >5 days/week, >3 days/week, 1–3 days/week, 0 days/week) and how many hours they used the brace daily (answer options: ≥ 6 h, <6 h). Additional interventions ware assessed with a questionnaire with check boxes for all allowed additional interventions such as application of ice, ointment dressings, weight reduction, accupuncture, intraarticular injection of hyaluronic acid or corticoids, bandages, crutches or cane, consumption of oral analgesics (nonsteroidal anti-inflammatory drugs or paracetamol), and physiotherapy. Patients were instructed to note also additional interventions which were not presented on the questionaire.

Statistical analyses

Statistical analysis was performed by Ulrike von Hehn (Medistat, Kiel, Germany) with IBM SPSS Statistics 24 (SPSS, Inc., IBM Company, Chicago, IL).

Between-group differences in clinical outcomes were analyzed on the basis of intention to treat. Logistic regression techniques were used for dichotomous outcome parameters. Continuous outcomes were analyzed with linear regression techniques.

The Chi-square test was used to check for a dependency or a difference. Fisher's exact test was used as an alternative. If an ordinal scale was used, the Chi-square test was used for a linear trend to use this in addition to the frequency distribution.

Pain measured on the numerical analog scale and the KOOS subscales (symptoms, pain, activity, sports and quality of life) were described as quantitative parameters describing the mean and standard deviation, minimum and maximum, as well as the quartiles, including the median, and the Kolmogorov–Smirnov test was used for testing for normal distribution. In case of significant deviations from a normal distribution, the two treatment groups were compared with the *U* test according to Mann and Whitney with regard to the scores at the three time points as well as to the absolute and percent changes. To check whether there was a significant change in the course of time between each of the two sampling times, the Wilcoxon non-parametric test was used for pair differences.

A one-sided equivalence test was used to prove the non-inferiority of the Agilium FreeStep® in comparison to the Unloader One® orthosis. A one-sided equivalence test corresponds to a one-sided test for difference with inverse hypothesis formulation. Because of the non-normal distributed NAS values, the non-parametric Mann–Whitney *U* test was used at this point. In the null hypothesis, it is examined whether the median difference achieved in the Agilium FreeStep® patient group is significantly greater than that of the Unloader One® patient group plus 10 points (equivalence range), which is to be rejected, in favor of the alternative hypothesis that the difference in the Agilium FreeStep® group is smaller than the difference in the equivalence between the Unloader One® group.

For pain measured with the NAS, 95% Moses confidence intervals were calculated using the Hodges–Lehmann valuer for the difference Unloader One vs. Agillium FreeStep.

Results

Recruitment, inclusion, and follow-up

Figure 2 shows a flowchart with recruitment, inclusion, and follow up. The dropout rate and the reasons for dropout of the different groups did not differ considerably (Fig. 2).

Table 1 shows the patient characteristics. For sex, OA grade, side, age, and BMI, there was no significant difference between the two treatment groups (*t* test for independent samples, *U* test, Chi-square test, and Chi-square test on linear trend, $p \leq 0.05$). The descriptive statistics showed a homogeneous distribution in the two treatment groups.

Primary outcome measure: pain

Pain was assessed for rest, walking, and sports on a numerical analog scale (NAS).

The effects of both orthosis on pain at rest were minimal. In group I, a small but significant improvement in pain at rest was detected only in the comparison between T0 and T2 (Wilcoxon test for pair differences, $p = 0.026$). There was no significant group difference (*U* test, $p \geq 0.05$) in the direct comparison of the groups at the individual points in time and also in the absolute and percentage change between the two points in time (Fig. 3a).

Figure 3b shows the results of walking pain. In both groups, walking pain improved between T0 and T1 (Wilcoxon test for pair differences, $p < 0.001$) and also between T0 and T2 ($p = 0.004/p < 0.001$). There was no significant change between T1 and T2 in both groups ($p \leq 0.05$). Significant group differences were not detectable either at the three time points—T0, T1 and T2—or in the absolute or percent change between the two time points (*U* test, $p \geq 0.05$). In the walking pain scale, the non-inferiority of the Agilium FreeStep® orthosis could be demonstrated both in the difference T1 − T0 and in the difference T2 − T0. For pain at sports, both groups showed a significant improvement between T0 and T2 ($p = 0.017$ Unloader One® and $p = 0.011$ Agilium FreeStep®) (Fig. 3c). In the Agilium FreeStep® group, a significant improvement (Wilcoxon test for pair differences, $p = 0.001$) was also found between T0 and T1, which was not detectable in the group of patients treated with an Unloader One® orthosis ($p = 0.162$). There was no significant difference between the time points T1 and T2 in either group ($p \geq 0.05$). A significant difference between the treatment groups was also not detectable in the achieved absolute or percent changes between two time points (*U* test, $p \geq 0.05$). For pain at sports, a significant non-inferiority of the Agilium FreeStep® orthosis was shown in the difference between T0 and T1 ($p < 0.001$) and in the difference between T0 and T2 ($p = 0.095$).

Table 2 shows the 95% Moses confidence intervals (Hodges–Lehmann valuer for the difference Unloader One vs. Agillium FreeStep) for pain at rest, walking pain, and pain at sports.

Secondary outcome measures

KOOS subscales

Figure 4 shows the results of the five KOOS subscales. The KOOS subscales symptoms, pain, activity, sport, and quality of life increased in both treatment groups over all the follow-up time points. In particular the pain score and the quality of life score improved. For pain, an improvement of 8.3 points was achieved in the Unloader One® group in comparison to an improvement of 11.1 points in the Agilium FreeStep® group. Quality of life improved twice as much in the Agilium FreeStep® group (median score increase of 12.5 points) in comparison to the Unloader One® group (median score

Table 1 Patient characteristics

	Group		Total
	I: Unloader One®	II: Agilium FreeStep®	
Sex, *N* (%)			
W	29 (36.7%)	42 (51.9%)	71 (44.4%)
M	50 (63.3%)	39 (48.1%)	89 (55.6%)
Side, *N* (%)			
Left	35 (46.1%)	33 (41.3%)	68 (43.6%)
Right	40 (52.6%)	47 (58.8%)	87 (55.8%)
Bilateral	1 (1.3%)	0 (0.0%)	1 (0.6%)
OA grade, *N* (%)			
Grade I	11 (13.9%)	10 (12.3%)	21 (13.1%)
Grade II	37 (46.8%)	37 (45.7%)	74 (46.3%)
Grade III	24 (30.4%)	29 (35.8%)	53 (33.1%)
Grade IV	7 (8.92%)	5 (6.2%)	12 (7.5%)
Total number of patients (%)	79 (100.0%)	81 (100.0%)	160 (100.0%)
Age (years), mean ± SD	57.3 ± 9.7	57.2 ± 10.5	57.3 ± 10.1
BMI (kg/m^2), mean ± SD	29.0 ± 4.7	28.2 ± 5.6	28.6 ± 5.2

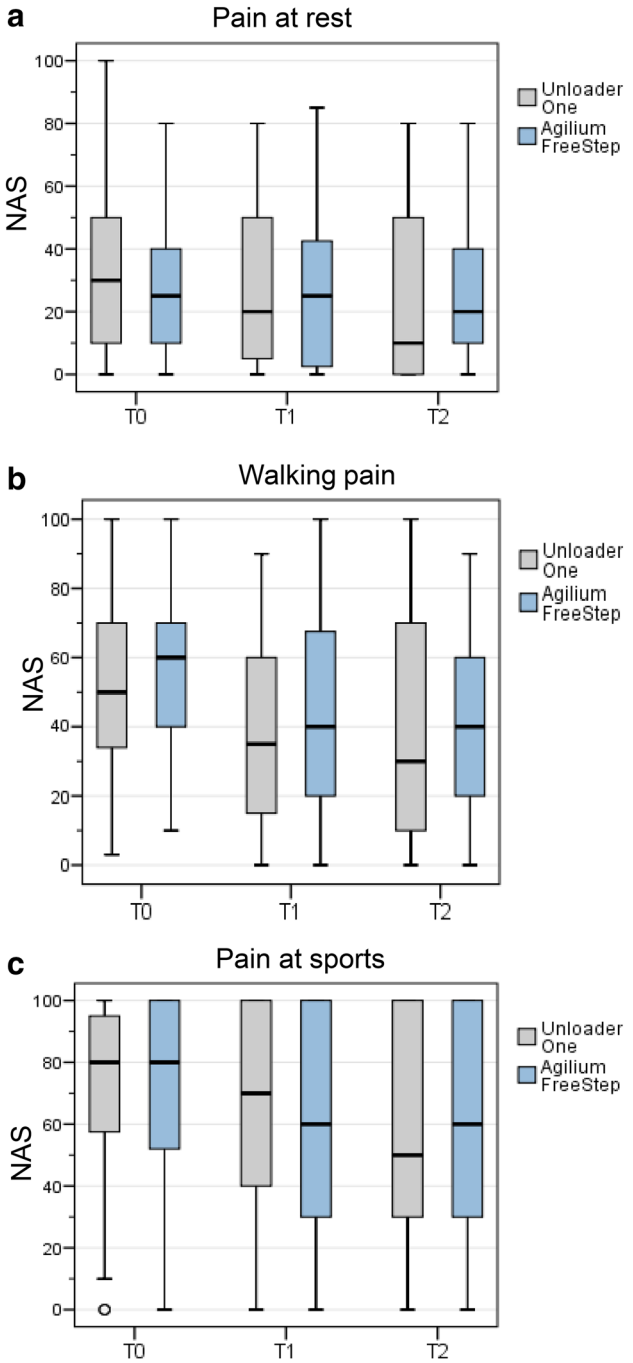

Fig. 3 Pain assessment on a numerical analog scale (NAS)

Table 2 Ninety-five percent Moses confidence intervals (Hodges–Lehmann valuer for the difference Unloader one vs. Agillium FreeStep) for pain at rest, walking pain, and pain at sports

	T0	T1	T2
Pain at rest	− 10.0, 0.0	− 10.0, 10.0	0.0, 10.0
Pain on walking	0.0, 10.0	− 10.0, 10.0	0.0, 20.0
Pain with sports	0.0, 10.0	− 15.0, 0.0	0.0, 20.0

increase of 6.25 points). However the statistical analysis did not reveal any significant group differences at T0, T1, and T2.

There was no significant group difference for the KOOS subscale activity at T0, T1, and T2 (U test, $p \geq 0.05$). Both groups showed a significant improvement in the temporal course between T 0 and T1 (Wilcoxon-test, $p < 0.001$) and between T0 und T2 ($p < 0.001$). Between time points T1 and T2, a significant improvement was only observed in the Unloader One® group ($p = 0.044$). There was also an increase in the subscale sports. However, only the Unloader One® group showed a significant improvement between T1 and T2 as well as between T0 and T2 ($p = 0.021$ and $p = 0.042$). No significant group difference was observed for the subscale sports in T0, T1, or T2 in terms of absolute or percent differences (U test, $p \geq 0.05$).

Additional interventions

The study participants used several additional interventions during the course of the study (Tables 2, 3). Pain medication and physiotherapy were the most frequently prescribed therapies. Other supplementary treatments included lymphatic drainage, fitness sport, rehabilitation sports, osteopathy, massage, and shoe orthotics. At each follow-up examinations (T0, T1, and T2), there were no significant differences between the two groups (Tables 3, 4). Only the number of patients who used additional bandages after 6 months was significantly higher in the Agilium FreeStep® group than in the Unloader One® group (Fisher's exact test, $p = 0.001$).

Compliance

At 8 weeks follow-up and at the 6 months follow-up, there was no significant group difference in weekly (days per week) or daily (hours per day, < 6 h or > 6 h) brace use (8 months: Chi square-test on linear trend, $p = 0.170$; 6 months: Chi square-test on linear trend, $p = 0.252$) (Table 5).

Adverse effects

The only adverse effects reported during the course of the study were bruises under the pads of the orthosis. In the Agilium FreeStep® group only 23.5% of the patients reported bruises in contrast to 66.7% in the Unloader One® group. This difference was statistically significant (Chi-square test, $p < 0.001$).

Discussion

The results of this prospective randomized trial support our hypothesis. There was no remarkable difference in the clinical outcome between the two orthosis tested. The rate of skin

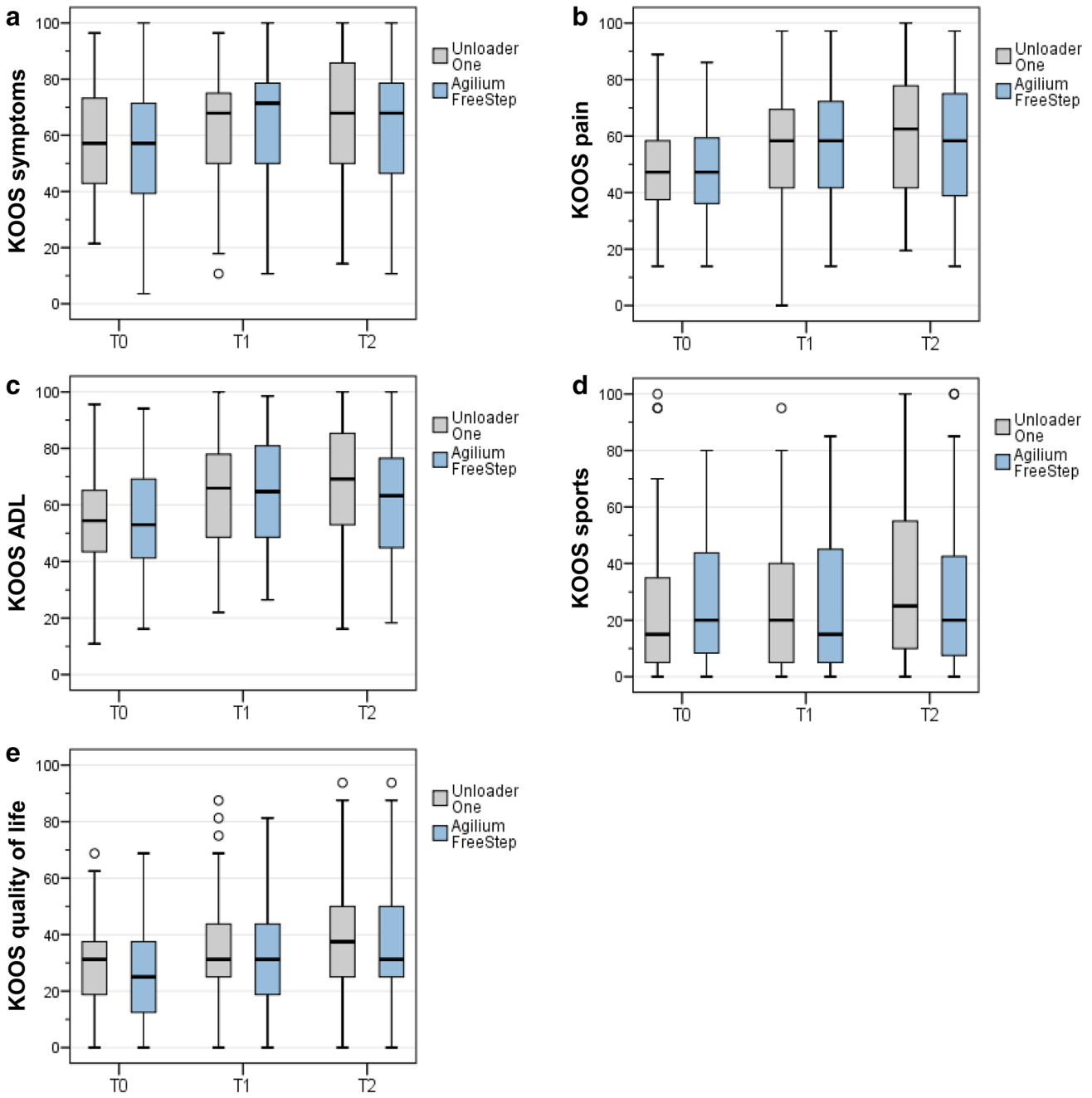

Fig. 4 Knee function measured with the five different KOOS subscales

irritations, however, was significantly lower in the group treated with the OA ankle brace compared to the group treated with the knee unloader brace.

The clinical outcome with regard to pain reduction and improvement of function was expected because the biomechanical and clinical effects of interventions such as unloader braces, which are recommended by the Osteoarthritis Research Society International guidelines for the treatment of knee OA, are well documented [2, 3, 6–8, 11, 16, 19, 20, 24]. A systematic review has shown that knee unloader braces have the potential to reduce the knee adduction moment [18]. A recent meta-analysis of controlled clinical trials has shown that that valgus bracing improves pain and knee function [16]. When compared to a control group that did not use an orthosis, the effect size was moderate for both factors, pain and function [16]. Briggs et al. conducted a prospective cohort study to evaluate the clinical effect of the Unloader One® brace [2]. In this study, patients had significant improvement in quality of life measured with the SF-12 and there was

Table 3 Additional interventions after 8 weeks

Additional interventions T1 (8 weeks)	Group		Statistic *p*
	Unloader One®	Agilium FreeStep®	
Cooling	13 (16.7%)	16 (20.0%)	0.588[a]
Topical NSAIDs	14 (17.9%)	19 (23.8%)	0.370[a]
Weight reduction	2 (2.6%)	4 (5.0%)	0.682[b]
Acupuncture	3 (3.8%)	5 (6.3%)	0.720[b]
Intraarticular hyaluronic acide injection	3 (3.8%)	4 (5.0%)	> 0.999[b]
Intraarticular cortisone injection	4 (5.1%)	3 (3.8%)	0.718[b]
Bandage	5 (6.4%)	12 (15.0%)	0.081[a]
Cane or crutches	4 (5.1%)	4 (5.0%)	> 0.999[b]
Oral NSAIDs	28 (35.9%)	35 (43.8%)	0.314[a]
Physiotherapy	27 (34.6%)	25 (31.3%)	0.653[a]
Manual therapy	7 (9.0%)	11 (13.8%)	0.345[a]
Physical therapy	9 (11.5%)	10 (12.5%)	0.853[a]
Other	18 (20.8%)	17 (21.3%)	0.942[a]
Total	77 (100.0%)	80 (100.0%)	

[a]Chi-quadrat test

[b]Fisher's exact test

Table 4 Additional interventions after 6 months

Additional interventions T2 (6 months)	Group		Statistic *p*
	Unloader One®	Agilium FreeStep®	
Cooling	12 (20.0%)	12 (20.7%)	0.926[a]
Topical NSAIDs	14 (23.3%)	9 (15.5%)	0.284[a]
Weight reduction	3 (5.0%)	1 (1.7%)	0.619[b]
Acupuncture	2 (3.3%)	2 (3.4%)	> 0.999[b]
Intraarticular hyaluronic acid injection	2 (3.3%)	4 (6.9%)	0.435[b]
Intraarticular cortisone injection	0 (0.0%)	3 (5.2%)	0.116[b]
Bandage	0 (0.0%)	9 (15.5%)	0.001[b]
Cane or crutches	4 (6.7%)	2 (3.4%)	0.680[b]
Orale NSAIDs	20 (33.3%)	27 (46.6%)	0.143[a]
Physiotherapy	14 (23.3%)	22 (37.9%)	0.085[a]
Manual therapy	4 (6.7%)	10 (17.2%)	0.076[a]
Physical therapy	6 (10.0%)	6 (10.3%)	0.951[a]
Other	12 (20.0%)	11 (17.2%)	0.700[a]
Total	77 (100.0%)	80 (100.0%)	

[a]Chi square-test

[b] Fisher's exact test

significant improvement in pain, stiffness, and function measured with the WOMAC [2].

In contrast to the number of studies on knee unloader braces, the number of studies evaluating the biomechanical and clinical effects of a foot ankle orthosis for the treatment of medial OA is limited. One recent biomechanical study has shown that the foot ankle orthosis is effective at reducing the knee abduction moment [8]. A clinical case series has shown that this orthosis is effective at significantly reducing pain and stiffness as well as improving physical function of patients with mild to moderate unicompartmental OA of the knee [14].

Several studies have shown that skin irritations are a frequent cause for discontinuing therapy with conventional knee unloader braces [3, 28, 29]. The present study confirms the high rate of skin irritations for the knee brace group. As expected, in patients treated with the ankle foot orthosis the rate of skin irritations was significantly lower. A possible reason for the high rate of skin irritation in the knee brace group is seen in the pressure of the brace pads on the lateral

Table 5 Brace use per week and per day after 8 weeks and 6 months

	8 weeks		6 months	
	Unloader One®	Agilium FreeStep®	Unloader One®	Agilium FreeStep®
Use of the orthesis per week				
Every day	37 (47.44%)	50 (61.73%)	24 (39.3%)	31 (52.5%)
> 5 days/week	17 (21.79%)	11 (13.58%)	14 (23%)	10 (16.9%)
> 3 days/week	19 (24.36%)	15 (18.52%)	17 (27.9%)	13 (22%)
1–3 days/week	4 (5.13%)	5 (6.17%)	6 (9.8%)	5 (8.5%)
Never	1 (1.28%)	0 (0%)	0 (0%)	0 (0%)
Daily brace use (h)				
< 6	36 (46.2%)	34 (42.5%)	32 (55.2%)	31 (52.5%)
> 6	42 (53.8%)	46 (57.5%)	26 (44.8%)	28 (47.5%)

Use of the orthesis per week: no significant group difference in 8 weeks (Chi-square test on linear trend, $p = 0.170$) or 6 months (Chi-square test on linear trend, $p = 0.252$). Daily brace use: no significant group difference in 8 weeks (Chi square-test, $p = 0.644$) and 6 months (Chi square-test, $p = 0.775$)

femoral condyle [18, 28, 29]. The lower rate of skin irritations in the foot ankle brace group could be an explanation for the trend toward more frequent brace use per week after 8 weeks (61.73% vs. 47.44%) and after 6 months (52.5% vs. 39.3%).

The high rate of skin irritations which has been observed with the use of knee unloader braces could be a reason why for most patients valgus bracing is not a long term therapy. A study of Wilson et al. [30] has shown that after 2.7 years only 41% of patients were still using the unloader brace. Thirty-five percent had discontinued brace use, and 24% had undergone knee replacement. After 11.2 years, 58.6% of patients had undergone arthroplasty and none of the patients was still wearing the brace [30]. Due to the lower rate of side effects such as skin irritations, the acceptance of the ankle foot orthosis over the course of time could be better than that of a knee orthosis. However, further research is needed to evaluate if the use of the ankle foot orthosis can improve the long term outcome of brace treatment for unicompartmental knee OA.

The exact mechanism of action of knee unloader braces is unknown. Some authors have been able to demonstrate biomechanical effects of brace application [6, 7, 11, 18]; others have demonstrated improved stability, muscular function, proprioception or effects on brain activity [20, 21]. Possibly, the stabilizing effect of a knee orthosis reduces the necessary muscular strength-and thus the stress on the joint. It is known that instability is a typical symptom of osteoarthritis but also a causative factor for knee OA progression [12, 20, 21, 26]. As a consequence of instability, increased muscle activity results with co-contractions of the antagonistic muscle groups [20, 21]. Due to these co-contractions, the joint is stabilized, but on the other hand the joint is also increasingly loaded. The stabilizing effect of an ankle foot orthosis is probably less pronounced because it does not act directly on the knee. Unfortunately, the sample size of this clinical trial is too small to perform a subgroup analysis to find out if OA patients with symptoms of instability profit more from a knee brace than patients without instability.

The present study has some limitations. One limitation of the present study design is that the kind of interventions does not allow blinding of patients. However, due to the multicenter design the assessor was not the caregiver and not the one who informed the patient about the aims of the study. Therefore, it was possible to blind the assessor for the treatment groups. Another limitation could be the lack of a true control group without any treatment or placebo. Since the results of previous controlled clinical trials have shown have proven that valgus bracing improves pain and knee function in patients with medial OA a knee brace was chosen as treatment for the control group. Lack of generalizability is a major problem for randomized clinical trials. Normally only a small percentage of the patients (participation rate) can be enrolled due to the strict enrollment criteria and due to the risk to receive a placebo treatment [17]. Therefore, the participation rate of some randomized controlled trials is less than 15% [17]. RCT enrollment scenarios can be far from the "real world" and thus often difficult to translate into a daily orthopedic practice environment [17]. In the present study, however, the participation rate was high in comparison to other RCT. One hundred and sixty patients out of 252 eligible patients could be included in the present study. An explanation for the high participation rate could be that the patients in the control group received active treatment and not placebo.

In conclusion, the present prospective randomized clinical trial shows that an ankle foot orthosis is as effective as a conventional knee brace for the improvement of pain and function in patients with unicompartmental osteoarthritis.

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