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Gait retraining using real-time feedback in patients with medial knee osteoarthritis: Feasibility and effects of a six-week gait training program

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ABSTRACT

Background: The knee adduction moment (KAM) is often elevated in medial knee osteoarthritis (KOA). The aim of this study was to evaluate effects on KAM and patient-reported outcomes of a six-week gait training program.

Methods: Twenty-one patients (61 ± 6 years) with KOA participated in a six-week biofeedback training program to encourage increased toe-in (all patients) and increased step-width (five patients). Patients received real-time visual feedback while walking on an instrumented treadmill. We analysed the effect of the gait modification(s) on peak KAM in week six and three and six months post-training. We also evaluated the effect on pain and functional ability.

Results: Of 21 patients starting the program, 16 completed it with high attendance (15 and 16 respectively) at the three and six month follow-ups. First peak KAM was significantly reduced by up to 14.0% in week six with non-significant reductions of 8.2% and 5.5% at the follow-ups. Functional ability (assessed using the WOMAC questionnaire) improved significantly after the training (eight point reduction, $p = 0.04$ in week six and nine point reduction, $p = 0.04$ at six-month follow-up). There was also a trend towards reduction in WOMAC pain ($p = 0.06$) at follow-up.

Conclusions: Biofeedback training to encourage gait modifications is feasible and leads to short-term benefits. However, at follow-up, reductions in KAM were less pronounced in some participants suggesting that to influence progression of KOA in the longer term, a permanent regime to reinforce the effects of the training program is needed.
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1. Introduction

Osteoarthritis is the most common cause of chronic disability in older adults (>55 years), particularly in the developed world [1, 2] with knee osteoarthritis (KOA) among the most common types of osteoarthritis [3, 4]. The symptoms of KOA include knee pain, stiffness and reduced functional mobility. As a result of the ageing population and increasing levels of obesity [5, 6], the prevalence of KOA is expected to increase dramatically [7, 8]. One of the biomechanical factors that is commonly linked to

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KOA is the knee adduction moment (KAM) which is the moment applied to the knee in the frontal plane. Increased KAM in people with KOA in the medial compartment of the knee is associated with increased progression of knee osteoarthritis [9, 10]. Given the increasing prevalence of KOA [11], there is a real need to develop interventions that can slow the disease progression. One of the suggested options is by reducing the KAM [9, 10]. KAM can be reduced through a variety of methods including surgical interventions such as high tibial osteotomy (HTO) [12], and non-surgical interventions such as assistive devices including unloading braces [13, 14], lateral wedged insoles (LWIs) [15, 16] or walking poles [17]. KAM reduction is highest in the case of HTO, between 31 and 58% [18–21], but this has risks associated with the surgery [22]. Reduction of KAM with unloader braces is lower, between 10 and 13% [13, 14] and with LWIs it is between nine and 12% [15, 16]. However, compliance with such devices is generally low [23–26] due to skin irritation, swelling or inconvenience of use [23]. The change in KAM with walking poles is variable, between 33.1% decrease and 5.9% increase [17, 27].

Taken together this evidence reinforces the need for a non-surgical intervention which reduces KAM without the need to use an assistive device. In recent years there has been a focus on the use of gait modifications to reduce the KAM. Gait modifications that can reduce the KAM include walking more slowly [28], walking with increased trunk lean [29, 30], increased medial thrust of the knee [30, 31], increased step width [32–34] or modified foot progression angle [35–38]. Changes in foot progression angle (FPA), walking with toe-in or toe-out gait, are most commonly investigated. Generally speaking toe-in gait reduces the first peak KAM through lateralising the centre of pressure in early stance and moving the knees to a more medial position [36, 37] and toe-out gait reduces the second peak KAM through lateralising the centre of pressure in late stance [35, 36]. Reduction of both peaks simultaneously has also been achieved in healthy individuals during stair ascent using a combination of toe-in gait and wider steps [32]; however this has not been replicated in people with medial KOA. Although several studies have shown that gait modifications can indeed reduce the KAM (first or second peak) in the short term (i.e. within a single session) [29–34, 36, 37], to date only two studies have evaluated the effect of gait modifications on the KAM over multiple sessions in people with KOA [35, 38]. This lack of multiple-session training studies is a serious limitation in the transferability of such gait interventions to the clinic. Furthermore, long term follow-up measurements to evaluate long-term effects have been limited to one-month post training [38]. Given that KOA is a chronic disease, evaluation of the long-term effects of new treatments/interventions, especially those that show promising results in the short term, is essential [39].

The aims of this study therefore were to 1) evaluate the feasibility and 2) evaluate the short and long term effects of a six-week gait re-training program with personalised gait modifications in patients with radiographic medial KOA. We hypothesised that the gait training program for teaching the modification to reduce the KAM would be feasible (with a completion rate of over 75% and no serious adverse events) and that of those completing the training program, compliance would be high (≥5 out of six training sessions attended). In terms of the effects of the program we hypothesised that a) the first peak of KAM would be reduced after six weeks being trained to walk with a modified gait pattern with reductions maintained at the three and six month follow-ups and b) that patients completing the program would report reduced pain and improved function after the program and that change would also be maintained at three and six month follow-up assessments with the changes greater or equal to the minimal clinically important difference (MCID) of between 16 and 18% [26, 40].

2. Material and methods

2.1. Participants

Twenty-one patients (15F, 6M) with medial KOA (mKOA) were enrolled in this study; demographics presented in Table 1. Patients were recruited from an in-house Vrije Universiteit medical centre (VUmc) database of KOA patients from a previous study [41]. Ethical approval for this study was granted by the Medical Ethics Committee of the VUmc, Amsterdam, Netherlands in September 2015. All patients provided written consent for their participation in the study, prior to the obtaining of any research data. Inclusion criteria for this study were Kellgren & Lawrence (KL) grades 1 to 4, aged between 50 and 75 and ability to walk unaided for at least 30 min. Furthermore, we included people who were able to reduce the first peak KAM by a minimum of 10% in an earlier study where we investigated how people with mKOA responded to different types of feedback during a single session [41]. A 10 percent change was regarded to be a meaningful change based on previous literature [35, 38]. In addition we excluded patients where the knee flexion moment (KFM) increased by >20% in our previous study [41], since KFM increases also contribute to increases in internal joint forces [42, 43]. Furthermore, all patients were assessed for inclusion by a physiotherapist (ME) who evaluated their clinical suitability for the training program, based on sagittal and frontal plane videos of the patients during

Table 1
Patient demographics.

	Mean (standard deviation)
Age	61.3 (5.73)
Gender	15F 6M
Height	1.72 (0.08)
Weight	75.9 (11.0)
BMI	25.4 (2.6)
KL grade	I 14, II 2, III 4, IV 1

walking with toe-in gait and wider step gait (data from previous study [41]). Specifically the videos were assessed to check for compensatory strategies used concurrently with the gait modifications which may lead to pain in other joints.

2.2. Training sessions and measurement of gait

Patients attended the Virtual Reality lab at the VUmc once per week for six weeks for gait training using the Gait Real-time analysis interactive laboratory (GRAIL) system, incorporating an instrumented treadmill, 10 Vicon cameras for motion capture, three video cameras, two ForceLink force-plates, and a 180-degree surround screen. Reflective markers were applied over bony landmarks (first, second and fifth metatarsal head, calcaneus (rear aspect), medial and lateral malleoli, tibial tuberosity, head of the fibula, medial and lateral epicondyles, anterior and posterior superior iliac spine, navel, xyphoid process, jugular notch, 7th cervical vertebrae and 10th thoracic vertebrae), with additional tracking markers as required. The calibrated anatomical systems technique (CAST) method of calculating joint kinematics based on Capozzo et al. [44] was used to calculate the kinematics from the position of the tracking markers and anatomical landmarks. We marked key anatomical landmarks with a ultraviolet (UV) pen, still visible after one week but not at the follow-up measurements, to improve marker placement repeatability. We also marked the positions on the shoes; critical markers for calculation of the FPA. The FPA was defined as the angle of the foot in the horizontal plane relative to the direction of walking. UV marker positions on the shoes were still visible at the follow-up measurements. For each measurement session, markers were placed by the same researcher, who was experienced in marker placement with the CAST marker model.

After preparation, patients walked on the treadmill for three minutes at comfortable walking speed, determined during their first visit to the lab [41]. Each training session consisted of five gait trials: Natural walking was recorded for 150 s (>100 individual gait cycles). This was followed by three training blocks with real-time feedback on the FPA with a personalised target angle (increased toe-in). Each session ended with a retention trial, where patients received no feedback and were asked to maintain the modified gait pattern.

The target FPA was based on the individual patient's performance during a prior study [41], using regression analysis to calculate the required angle to reduce first peak KAM by 10%. A 10 percent reduction was chosen based on previous studies which have shown that a 10% reduction in KAM is possible using gait modifications [35, 38] and additionally was chosen to limit the increase in KFM. Higher KFM is known to be associated with knee joint contact forces [42] and therefore it is important to limit increases in the KFM while maximising the reduction in KAM. The mean standard deviation (SD) target angle across the group was 3.0(2.5)° with a range from −3° (external) to eight degrees internal. The mean change in the FPA was 7.3 (4.5)°. Five (of 21) patients were trained to walk with a combination of toe-in gait and wider steps (target step width between 15 and 20 cm), considered to be more effective for them based on our previous results [41]. Patients received visual feedback on their

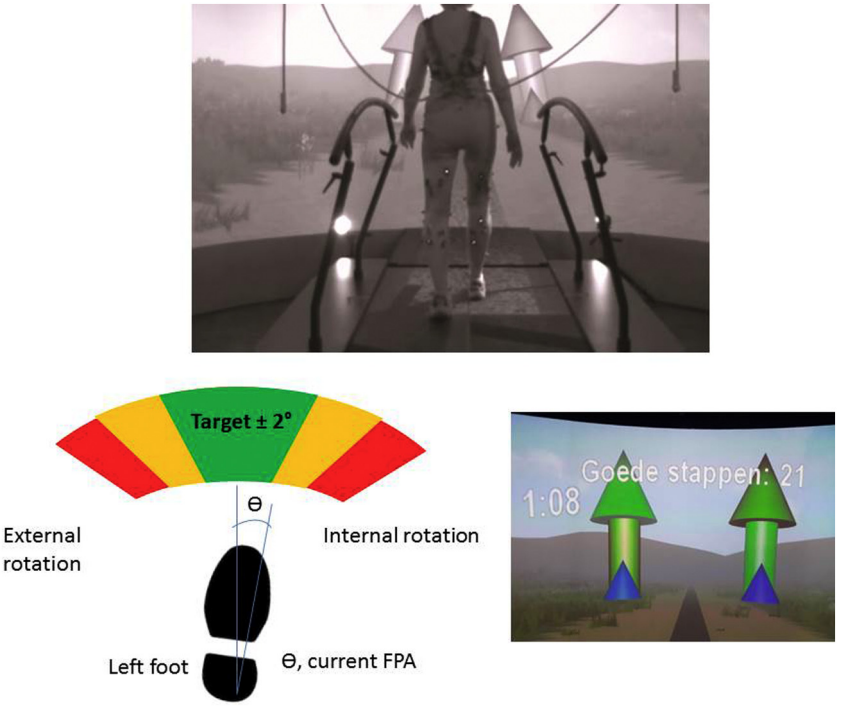

Figure 1. The training process. From top left, the patient walks on the instrumented treadmill at fixed pace walking speed. Markers affixed to the patient are used to calculate the FPA in real-time. The current FPA is compared to the target angle and feedback is provided to the patient via the big screen. The smaller blue arrows represent the current position of the feet, with the larger arrows representing the target angle The difference between the actual and target angle is given by the colour of the large arrows green is ≤2° either side of the target (on-target), orange is ≥2° and ≤5° either side of the target and red is >5° either side of the target). The aim is to turn both arrows green by aligning both feet with the target arrows.

FPA on the screen in front of the treadmill (Figure 1). Patients trained with both step width and toe-in modifications also received feedback on their step width, separately or in combination with the FPA, but modification of the FPA was the primary focus.

Training time increased from nine minutes by three minutes each week, while relative feedback time decreased from 100% in the first three weeks to 25% in the final week, in accordance with a faded feedback protocol, used in previous gait retraining studies [35, 38, 45] and considered to promote motor learning and reduce reliance on feedback [46, 47]. Following the training blocks, we collected an additional trial condition where patients received no feedback and were asked to maintain the modified gait pattern (retention condition).

During the follow-up assessments at three and six months patients did not receive any gait training. We recorded the patient's natural walking at the same speed as used during the training sessions to evaluate the longer-term retention of the modifications.

2.3. Gait data analysis

We post-processed the gait data using BodyMech (www.bodymech.nl/), an in-house MATLAB-based[1] biomechanics software, to calculate the external joint moments and angles for the more affected knee (defined using the KL score or symptomatically in the case of equal KL scores) for all complete cycles within each trial condition (>60 cycles). For consistency with previous studies [38, 41] we expressed the joint moments in the tibial coordinate segment, since the choice of reference frame can affect the magnitude of the KAM during modified gait [48]. From each time-normalised cycle we extracted first peak KAM (hypothesised to be reduced with toe-in gait), peak KFM, KAM impulse, FPA and step width. We analysed two conditions in week one and week six specifically i) **natural walking condition** and ii) **retention condition**. At three and six-month follow-up measurements we analysed only the **natural walking** condition.

2.4. Patient reported outcome measures

At the start and end of the program and at the follow-up measurements, we collected patient reported outcome measures including pain, functional ability, and knee stiffness using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire [49] and knee confidence on a five-point numeric rating scale (NRS). Patients also completed a weekly walking diary and a questionnaire about their experiences with the modified gait pattern. Knee pain was recorded during gait and at rest weekly on a scale of 0 to 10 where 0 represents no pain and 10 represents extreme pain [50].

2.5. Functional measures

In week one, week six and at the follow-up measurements, we assessed the patient's functional ability using the timed 10 m walk test and the 15 m timed up and go (TUG) test [51]. Patients were instructed to complete the tests as quickly as possible and for the TUG test to try not to use their hands when getting up from the chair [52].

2.6. Statistical analyses

Prior to statistical analysis, all outcome measures were checked for normality with the Shapiro–Wilk and Kolmogorov–Smirnov tests as well as inspection of the QQ plots. To evaluate the short-term effects of the program on the first peak KAM, KAM impulse, peak KFM, FPA and step width we used a two-way repeated measures analysis of variance, with two-time points (week one and week six) and two conditions (natural walking and retention). To evaluate longer term effects, we used repeated measures analysis of variance with three-time points (week one, three months and six months) considering only the natural walking condition. Post-hoc pairwise comparisons were corrected using the Bonferroni correction.

Similarly, when assessing the effect of the program on patient reported outcome measures and functional tests, we considered first the short-term effects and then the longer-term effects. Due to non-normal distribution, we used the Wilcoxon signed rank test to assess short-term effects and the Friedman test to assess longer-term effects. For post-hoc pairwise comparisons we used the Wilcoxon-signed rank test, corrected for multiple testing. Statistical significance was set to $\alpha = 0.05$. All analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 22.0 (SPSS, Chicago, IL, USA).

3. Results

3.1. Recruitment, adherence and side effects

Of the 40 participants who participated in our previous study in this area of research [41], 30 were invited to participate in the training program. Of these 30, 21 started and 16 completed the program, see Figure 2 for an overview of the recruitment and inclusion process. No significant differences were found between the demographics of the group completing the training program and those who dropped out. Reasons for dropping out are presented in Figure 2. Adherence to the program was high with 16

[1] MATLAB Release 2012b, The MathWorks, Inc., Natick, Massachusetts, United States.

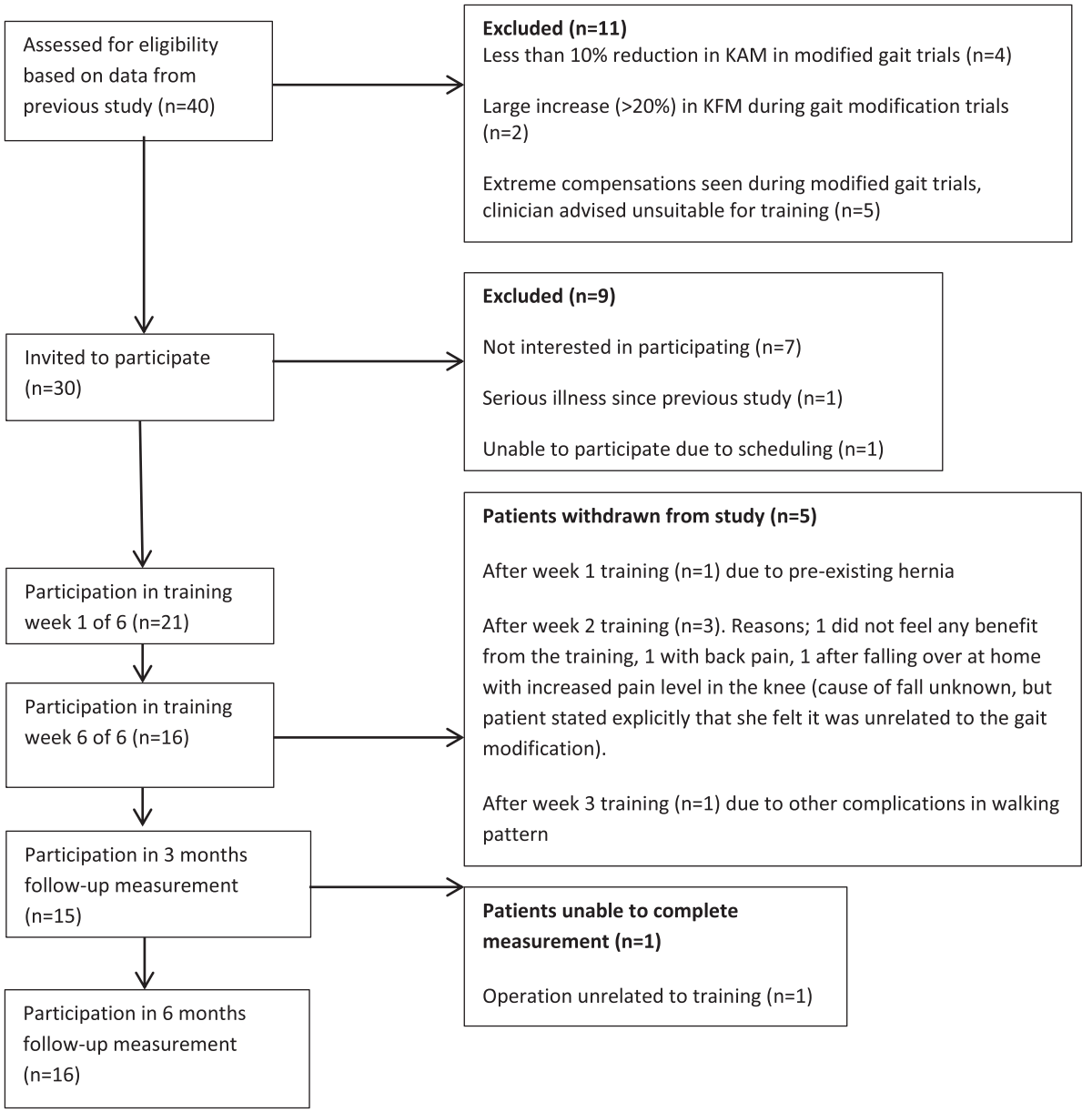

Figure 2. Flow chart showing participant recruitment and inclusion.

participants completing all training sessions (Table 2). Attendance to the follow-up measurements was also high, 15/16 attending at three months and 16/16 attending at six months of follow-up (Table 2).

The most commonly self-reported side effects during the training program were muscle soreness, and hip or back pain. All side effects reduced during the course of the training program (Table 2). No serious adverse events were reported during or after the training program.

3.2. Kinetics and kinematics

Between week one and week six, first peak KAM reduced by 10% or greater in 11/16 patients with a mean difference of −0.22 (95% confidence interval (CI): −0.44, −0.00) %BW * Ht ($p = 0.049$) across the two conditions (natural walking and retention), Table 3. Between conditions, the mean difference was −0.29 (−0.47, −0.11) %BW * Ht ($p = 0.003$). Compared to natural walking in week one, in week six first peak KAM was reduced by 6.9%, moreover during retention (after training with the feedback) the reduction was 14.0%. While significant effects of both time-point and condition on the first peak were observed (Table 3), there was no significant interaction between time and condition ($p = 0.492$).

Table 2
Adherence to the program, reported side effects and serious adverse events.

	Time point	Adherence	Side effects						Serious adverse events
		Number of patients attending (%)	Number of patients (%)[a]					Total number of side effects[b]	Number of patients (%)[a]
			Muscle soreness	Hip pain	Back pain	Other	Total		
Training program	Week 1	21 (100.0)	4 (19.0)	2 (9.5)	3 (14.3)	4 (19.0) Ankle pain, n = 1 Achilles pain, n = 1 Calf pain, n = 1 Foot pain, n = 1	9 (42.9)	13	0 (0.0)
	Week 2	20 (95.2)	1 (5.0)	2 (10.0)	3 (15.0)	2 (10.0) Shoulder pain, n = 1 Achilles pain, n = 1	7 (33.3)	8	0 (0.0)
	Week 3	17 (80.9)	2 (11.76)	1 (5.9)	2 (11.76)	1 (5.9) Foot pain, n = 1 (5.9)	4 (23.5)	6	0 (0.0)
	Week 4	16 (76.2)	2 (12.5)	2 (12.5)	1 (6.3)	1 (6.3) Achilles pain, n = 1	6 (37.5)	6	0 (0.0)
	Week 5	16 (76.2)	1 (6.3)	1 (6.3)	1 (6.3)	1 (6.3) Calf pain, n = 1	4 (25.0)	4	0 (0.0)
	Week 6	16 (76.2)	1 (6.3)	1 (6.3)	1 (6.3)	1 (6.3) Foot pain, n = 1 (6.3)	3 (18.8)	4	0 (0.0)
Follow-up measurements	Month 3	15 (71.4)	1 (6.7)	0	0	0	1 (6.7)	1	0 (0.0)
	Month 6	16 (76.2)	1 (6.3)	1 (6.3)	0	0	2 (12.6)	2	0 (0.0)

[a] Percentage of patients attending the session at a given time point.
[b] Note some patients reported more than one side effect so the total number of side effects is not equal to the number of patients reporting side effects.

KAM impulse was reduced over both time and condition although the changes were not statistically significant, Table 3. No statistically significant changes in peak KFM were noted with a mean difference of 0.11 (−0.37, 0.16) %BW * Ht ($p = 0.391$) between natural walking and retention conditions and a mean difference of 0.11 (−0.26, 0.47) %BW * Ht * sec ($p = 0.532$) between week one and week six. Furthermore no significant interaction effect was observed ($p = 0.663$).

As anticipated the FPA was more internally rotated in week six than in week one with a mean difference of 2.1 (0.2, 3.9)°, $p = 0.028$. A larger change in FPA was observed between conditions, mean difference: 4.8 (3.5, 6.1)°, $p < 0.001$.

Regarding step width, a significant interaction between time and condition was found ($p = 0.048$) with a significant increase in step width between week one and week six in the natural walking condition of 2.4 (3.7, 1.2) cm, $p = 0.001$ but not in the retention condition (change in step width 1.2 (−2.3, 2.6) cm, $p = 0.094$). At both time points a significant increase in the step width was observed between conditions, during week one, mean difference of 3.7 (2.4, 5.0) cm, $p < 0.001$ and during week six, mean difference of 2.5 (1.4, 3.6) cm, ($p < 0.001$).

At three and six-month follow-up small reductions in first peak KAM were observed, particularly at the three month follow-up (cf. with week six), Table 4. However, the changes were not statistically significant, with mean differences compared to week one of −0.31 (−0.71, 0.10) %BW * Ht ($p = 0.179$) at the three month follow-up and −0.21 (−0.51, 0.10) %BW * Ht ($p = 0.263$) at

Table 3
Short-term effects of the training program: group mean (SD) values for biomechanical parameters at week one and week six during natural walking and retention conditions.

	Week 1 (n = 16)		Week 6 (n = 16)		Comparison of time points (week six–week one)		Comparison of effects (retention–natural walking)		Interaction effect
	Natural walking	Retention	Natural walking	Retention	Mean difference (CI)[a]	p[a]	Mean difference (CI)[a]	p[a]	p time * condition
First peak KAM (%BW * Ht)	3.65 (0.83)	3.31 (0.88)	3.37 (0.79)	3.14 (0.89)	**−0.22 (−0.44, −0.00)**	**0.049**	**−0.29 (−0.47, −0.11)**	**0.003**	0.492
KAM impulse (%BW * Ht * sec)	1.17 (0.33)	1.14 (0.37)	1.15 (0.35)	1.09 (0.38)	−0.03 (−0.14, 0.07)	0.534	−0.05 (−0.10, 0.01)	0.084	0.649
Peak KFM (%BW * Ht)	2.09 (0.85)	1.92 (0.85)	2.14 (0.86)	2.09 (0.91)	0.11 (−0.26, 0.47)	0.532	−0.11 (−0.37, 0.16)	0.391	0.663
Foot progression angle[b] (°)	−4.4 (4.4)	1.2 (3.6)	−1.6 (2.8)	2.5 (2.3)	**2.1 (0.3, 3.9)**	**0.028**	**4.8 (3.5, 6.1)**	**<0.001**	0.061
Step width (cm)	11.8 (3.0)	15.5 (2.9)	14.2 (2.1)	16.7 (2.8)	**Natural walking: 2.4 (1.1, 3.7)**	**0.001**	**Week 1: 3.7 (2.4, 5.0)**	**<0.001**	**0.048**
					Retention: 1.2 (−2.3, 2.6)	0.094	**Week 6: 2.5 (1.4, 3.6)**	**<0.001**	

Data in bold represent statistically significant differences.
[a] After Bonferroni correction for multiple testing (CI = confidence interval).
[b] Positive foot progression defined as internally rotated and negative as externally rotated.

the six month follow-up, equivalent to mean reductions of 8.2% and 5.5% respectively. Similarly, no statistically significant reductions in the KAM impulse were observed. Peak KFM was not significantly increased between week one and month six but showed a trend towards an increase. Foot progression was significantly more internally rotated at the six month follow-up measurements compared to week one with a mean difference of 2.9 (0.5, 5.2)° ($p = 0.017$). The step width was increased in both follow-up measurements compared to week one (mean difference in month three of 3.0 (1.5, 4.6) cm, $p < 0.001$ and mean difference in month six of 2.3 (0.0, 4.3) cm, $p = 0.024$), Table 4.

3.3. Patient reported outcome measures and functional tests

Between weeks one and six, all divisions of the WOMAC questionnaire reduced (Table 5), being only statistically significant for the function sub-score (reduction in median of eight points, $p = 0.038$). Pain at rest and during gait on the NRS scale, as well as self-perceived knee confidence also reduced but changes were not statistically significant. Finally, small non-significant reductions (<1 s) in the TUG test and 10 m walk test were observed (Table 5).

At the follow-up measurements all WOMAC subscales were reduced compared to week one, with the changes reaching statistical significance for the total score and function score (Table 6). Post-hoc testing revealed significant differences between the function and total WOMAC scores in week one and month six ($p = 0.041$ and $p = 0.010$ respectively). Pain during gait on the NRS scale was reduced at the follow-up measurements ($p = 0.025$) but post-hoc testing did not reveal any significant differences between time-points after the Bonferroni correction for multiple testing. The longer-term changes in self-perceived knee confidence and the functional tests were similar to the short-term changes and were small and non-significant (Table 6).

4. Discussion

In this study we investigated the feasibility and effects of a six-week gait retraining program to reduce the knee adduction moment in patients with medial KOA. To the best of our knowledge this is the first study to assess effects on the KAM after more than one month. We hypothesised that the program would be feasible with a completion rate of over 75%. Sixteen out of 21 (76.2%) patients completed the program, with 15/21 (71.4%) attending the follow-up measurement at three months and 16/21 (76.2%) the six-month follow-up. High adherence and relatively low drop-out suggest that the intervention is feasible for use in medial KOA patients. Furthermore, no serious adverse events were reported and the number of reported side effects reduced as the program progressed.

The main outcome of this study was change in the first peak of the KAM. After completing the gait retraining program with gait modifications personalised to the individual, first peak KAM was reduced in 11/16 patients, with a mean reduction across all 16 patients of 6.9% during normal walking. There were no statistically significant differences in the changes in KAM in participants who were trained with toe-in gait modification only versus toe-in gait combined with wider steps, corroborating the finding that personalisation of the gait modification to the individual is important [31, 53]. At the three and six-month follow-up measurements we observed small but non-significant reductions. While not reaching the target KAM reduction, the achieved reduction might still lead to clinically important changes over a longer period of time. KAM impulse decreased across all time-points but did not meet statistical significance. However, unlike in other studies using toe-in gait modifications [36, 54], where reductions in first peak KAM were accompanied by increases in second peak KAM, post-hoc testing showed no increase in second peak KAM in our study across the four time points ($p = 0.185$).

At the first peak, the short-term effect in our study was lower than that reported previously by Shull et al. [38] after a six-week gait training program (16.1%). This is likely due to the smaller change in foot progression (mean of 2.0°) in our study during natural walking compared 7.0° in their study [38]. When asked to concentrate on their gait pattern, patients in our study were able to walk with a larger change in FPA (4.8°), which consequently further reduced the KAM (14%), more in line with the results of Shull et al. [38]. However, significant heterogeneity between the two studies exists in terms of patient characteristics and training methods. Patients in

Table 4
Longer term effects of the training program: group mean (SD) values for biomechanical parameters at week one and at the three and six month follow-up measurements during natural walking condition.

	Week 1 (n = 15)	Month 3 (n = 15)	Month 6 (n = 15)	p	Post-hoc comparison with week 1	
					Mean difference (CI)[a]	p[a]
First peak KAM (%BW * Ht)	3.64 (0.86)	3.34 (0.76)	3.44 (0.84)	0.101	Month 3: −0.31 (−0.71, 0.10)	0.179
					Month 6: −0.21 (−0.51, 0.10)	0.263
KAM impulse (%BW * Ht * sec)	1.16 (0.34)	1.03 (0.33)	1.12 (0.42)	0.101	Month 3: −0.13 (−0.28, 0.03)	0.122
					Month 6: −0.04 (−0.18, 0.09)	1.000
Peak KFM (%BW * Ht)	1.98 (0.84)	1.99 (0.78)	2.18 (0.81)	0.079	Month 3: 0.02 (−0.22, 0.26)	1.000
					Month 6: 0.20 (−0.09, 0.50)	0.244
Foot progression angle[b] (°)	−4.9 (4.0)	−2.4 (3.2)	−2.0 (3.5)	**0.005**	Month 3: 2.5 (−0.1, 5.0)	0.060
					Month 6: 2.9 (0.5, 5.2)	**0.017**
Step width (cm)	12.0 (2.9)	15.0 (2.7)	14.3 (3.4)	<**0.001**	**Month 3: 3.0 (1.5, 4.6)**	<**0.001**
					Month 6: 2.3 (0.0, 4.3)	**0.024**

Data in bold represent statistically significant differences.
[a] After Bonferroni correction for multiple testing (CI = confidence interval).
[b] Positive foot progression defined as internally rotated and negative as externally rotated.

Table 5
Short-term effects of the training program: group median inter-quartile range (IQR) values for self-reported data and physical functioning tests.

	Week 1 (n = 16)	Week 6 (n = 16)	p
WOMAC pain (maximum 36)	10.5 (9)	7 (6)	0.242
WOMAC function (maximum 68)	14.5 (16)	6.5 (10)	**0.038**
WOMAC stiffness (maximum 8)	3 (3)	2.5 (3)	0.905
WOMAC total (maximum 112)	25 (21)	16 (17)	0.120
Knee confidence (scale from 1 to 4)	3 (1)	2 (1)	0.257
NRS pain in knee during rest (scale from 0 to 10)	2 (3)	0.5 (2)	0.126
NRS pain during walking (scale from 0 to 10)	1.5 (2)	1 (2)	0.107
Timed up and go (TUG) test (s)	8.76 (1.46)	8.39 (2.17)	0.569
10 m walk test (s)	5.94 (1.12)	5.28 (1.02)	0.313

Data in bold represent statistically significant differences.

[38] generally had higher KL scores than in our study, so we may speculate that the effect size of the gait modifications increases with KOA severity. Due to the sample size in our study, sub-group analysis to investigate this relationship was not possible.

During natural walking, the seven percent reduction in first peak KAM as a result of the gait retraining program was lower than that reported in knee braces (10–13%) [13, 14], lateral wedges (nine to 12%) [15, 16] and walking poles (six to 33%) [27]. However, during the retention trial, the change in KAM was similar to that achieved using assistive devices (14%).

Follow-up measurements showed non-statistically significant changes in the peak KAM and KAM impulse. Shull et al. [38] reported a significant reduction at one month follow-up, however the data shows a small regression of peak KAM towards the baseline value at this time. Although our results suggest a wash-out of the effect, it might also be a result of limited power. When asked to concentrate on their gait pattern, larger changes in KAM were observed, which implies that the gait modification is not fully automated and hence cognitive effort is required to walk in a way that significantly reduces the KAM. However, we argue that in the long term, even a small reduction (of less than our 10% target) in KAM may be clinically important, due to the cumulative reduction in KAM over many thousands of steps, since both magnitude and frequency of loading are associated with knee pain in KOA [55].

In this study we make the assumption that reducing KAM leads to reduced joint loading in the medial compartment. However, the effects of gait modifications on the joint contact forces are not well understood and show conflicting results from musculoskeletal modelling or instrumented prostheses in the literature [27, 56–58]. Moreover, to assess the effects of gait modifications on the cartilage, more complex finite element analyses using personalised knee models [59] are required.

Post-hoc correlation of the change in (delta Δ) KAM vs. ΔFPA revealed a positive relationship between the two measures on a group level ($r = 0.41$, $R^2 = 0.17$). Including Δ step width in the model improved the relationship to $r = 0.53$, $R^2 = 0.29$. Although stronger than the relationship reported by Hunt and Takacs [35] after a 10 week training program ($r = -0.15$, $R^2 = 0.05$), the correlations were nonetheless lower than may be anticipated. This can be explained by the fact that the relationship between the ΔFPA and ΔKAM is specific to the individual [53]. Therefore, we cannot extrapolate our data to predict changes in KAM in future studies.

Over the training program, all sub-scales of the WOMAC questionnaire decreased, with a statically significant reduction in the WOMAC function score. At follow-up, similar changes were shown, with significant reductions in WOMAC function and total score between week one and the six-month follow-up and a trend towards reduced pain. We hypothesised that changes in self-reported pain and function across the program would be greater than or equal to the MCID of 16–18% [26, 40]. Eight patients (50%) patients reported a change in the total WOMAC score >MCID (mean difference of 47.6%). Although statistical significance was only reached on one sub-scale, all changes were in the same direction. Group level changes in pain and function in our study were lower than other studies [35] [38] which may be due to differences in baseline characteristics of the patients, patients in our study tended to have low self-reported pain and high function at the start of the study.

Table 6
Longer term effects of the training program: group median (IQR) values for self-reported data and physical functioning tests.

	Week 1 (n = 15)	3 month follow-up (n = 15)	6 month follow-up (n = 15)	p	Post hoc testing[a]
WOMAC pain (maximum 36)	10 (9)	6 (7)	6 (8)	0.055	n/a
WOMAC function (maximum 68)	15 (16)	8 (8)	6 (6)	**0.036**	Week 1 > 6 month follow-up p = 0.041
WOMAC stiffness (maximum 8)	3 (3)	2 (1)	2 (1)	0.122	n/a
WOMAC total (maximum 112)	25 (22)	16 (19)	15 (7)	**0.012**	Week 1 > 6 month follow-up p = 0.010
Knee confidence (scale from 1 to 4)	3 (1)	2 (1.25)	2 (0.25)	0.058	n/a
NRS pain in knee at rest (scale from 0 to 10)	2 (3)	1 (2)	1 (2)	0.101	n/a
NRS pain during walking (scale from 0 to 10)	2 (2)	1 (1)	0 (1)	**0.010**	No significant differences after adjustment for multiple testing
Timed up and go (TUG) test (s)	8.77 (1.67)	8.44 (1.99)	8.09 (1.55)	0.332	n/a
10 m walk test (s)	5.93 (1.19)	5.33 (1.18)	5.25 (1.08)	0.344	n/a

n/a not applicable.
Data in bold represent statistically significant differences.
[a] After Bonferroni correction for multiple testing.

To summarise, we found that patients were able to modify their gait pattern to reduce the knee adduction moment in the short-term. However, this effect was not maintained on a group level in the longer term, which makes it difficult to conclude whether this type of training can truly contribute to a decline in the rate of progression of medial KOA. Given this, there is a real and urgent need to develop methods which can enable a sustained change in peak KAM over time. To achieve such sustained change, a device that can be used in activities of daily living, for example foot-worn sensors [60] that provide (continuous) feedback via a mobile application, may be required.

4.1. Limitations

We aimed to recruit 30 persons to give sufficient power and take into account drop-outs. However, as seen in Figure 2, we did not achieve this aim. In addition to low power, this study was limited by a non-homogenous population, both in terms of general demographics and those directly related to the KOA (i.e. KL score and baseline pain). The small sample size and heterogeneous population mean that our results may not be generalizable to the wider medial KOA community. Furthermore, we selected patients who had already participated in our previous study, who had already shown that they could perform the gait modification in the immediate-term (within-session). Pre-selection of suitable patients may be a necessary preliminary step for such a program. However it may also limit the external validity of our results.

While we tried to reduce as much as possible errors associated with repeated measurements of gait parameters, we must acknowledge that there are factors that can contribute to measurement error in the KAM (such as marker placement errors and errors in the location of the force plates relative to the motion capture origin). Eliminating these errors altogether is likely only possible using fluoroscopy based motion capture instead of traditional motion capture [61]. However, this is unlikely to be feasible in such a training study due to the repeated radiation doses, albeit small doses.

Assessments for this study were undertaken in a tightly controlled lab environment, on a fixed pace level treadmill, in order to control for confounders such as speed. This means it is difficult to extrapolate the findings of our study to the real environment. Future studies that can measure KAM and FPA and provide feedback outside of a laboratory environment are urgently needed. Current developments such as electronic skins [62] and sensors for estimating KAM without the need for optical tracking and a force plate [63] might enable such personalised feedback.

Finally, based on the measurement of the KAM and KFM (external joint moments), we are unable to conclude whether walking with gait modifications is effective in reducing the stresses in the knee joint cartilage, or in delaying the progression of KOA in the long term. To assess this, an RCT with long-term follow-up (minimum two years) and detailed musculoskeletal modelling and finite element analysis of the knee cartilage, such as that used by Halonen et al. [64] is likely needed.

5. Conclusions

After six weeks of gait training patients with medial knee OA were able to reduce the first peak KAM, particularly when concentrating on their gait pattern. At the three and six month follow-up measurements, the effect was less pronounced in some patients. Significant improvements in functional ability together with a trend towards improvements in pain were observed across the four-time points. Future studies in this area are strongly encouraged to extend the training program or to provide a method of home training or smart personalised feedback to maintain the effects over a longer term and to allow the modified gait pattern to become “second nature”.

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Contributions

1) Conception and design of the study — RR, JvdN, JH, MvdE, MB
2) Obtaining of funding — JH
3) Collection and assembly of data — RR, MB
4) Analysis and interpretation of the data — RR, JvdN, JH
5) Provision of study patients — MvdE
6) Statistical expertise — MvdE
7) Drafting the article — RR, JvdN
8) Critical revision of the article — RR, JvdN, MvdE, JH, MB
9) Final approval of the article — RR, MvdE, MB, JvdN, JH
10) Full integrity of the work as a whole from inception to finished article — RR, JvdN, (r.richards@vumc.nl, j.vandennoort@vumc.nl)

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Competing interests

RR — no financial or personal conflicts of interest.
JvdN — no financial or personal conflicts of interest.
MB — no financial or personal conflicts of interest.
MvdE — no financial or personal conflicts of interest.
JH — no financial or personal conflicts of interest.

Ethics

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Ethical approval for this study was granted by the Medical Ethics Committee of the VU Medical Centrum, Amsterdam, Netherlands in September 2015.

All patients provided written consent for their participation in the study, prior to the obtaining of any research data.

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