Targeted Treatment Protocol in Patellofemoral Pain (TIPPs): Does Treatment Designed According to Subgroups Improve Clinical Outcomes in Patients Unresponsive to Multimodal Treatment?

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Background: Targeted intervention for subgroups is a promising approach for the management of patellofemoral pain.

Hypothesis: Treatment designed according to subgroups improves clinical outcomes in patients unresponsive to multimodal treatment.

Study Design: A prospective crossover intervention.

Level of Evidence: Level III

Methods: PFP patients (n=61, mean age: 27±9 years) were enrolled. PFP patients received standard multimodal treatment three times a week for 6 weeks. Patients not responding to multimodal treatment were then classified into one of 3 subgroups "strong", "weak and tight" and "weak and pronated foot" using six simple clinical tests. They subsequently were administered a further 6 weeks of targeted intervention designed according to subgroup characteristics. Visual Analog Scale (VAS), Perception of Recovery Scale (PRS), EQ-5D-5L, and S-LANSS were used to assess pain, knee function and quality of life before and after the interventions.

Results: 36% of the patients (21 patients) demonstrated recovery following multimodal treatment. However, over 70% (29 patients) of these non-responders demonstrated recovery after targeted treatment. The VAS, PRS, S-LANSS, and EQ-5D-5L scores improved significantly after targeted intervention compared to after multimodal treatment ($p<0.001$). The

VAS score at rest was significantly lower in the weak and pronated foot, and weak and tight subgroups ($p=0.011$, $p=0.008$) respectively. Post-treatment pain intensity on activity was significantly lower in the "strong" subgroup ($p=0.006$).

Conclusion: Targeted treatment designed according to subgroup characteristics improves clinical outcomes in patients unresponsive to multimodal treatment.

Clinical Relevance: Targeted intervention could be easily implemented following six simple clinical assessment tests to subgroup patients into one of three subgroups (strong, weak and tight, weak and pronated foot). Targeted interventions applied according to the characteristics of these subgroups have more beneficial treatment effects than a current multimodal treatment program.

Key words: Rehabilitation, knee injuries, patella, treatment outcome, pain perception

INTRODUCTION

Patellofemoral pain (PFP) is a chronic musculoskeletal problem that causes persistent anterior knee pain.[2,3,6,8,14,15,20,21,25,26,32,33,49] Despite its widespread use in clinics, it is difficult to suggest that the current multimodal treatment approach leads to successful outcomes in the majority of patients with PFP, only 46% of patients' knees were pain free at discharge.[2] This indicates that over half of PFP patients do not respond to treatment and may continue their lives with chronic anterior knee pain.

Identification of the factors leading to these low treatment success rates has consistently been a priority of previous International Patellofemoral Pain Research Retreats.[4,10,12,52] The most important factor affecting the success of treatment that has emerged is that patients have a variety of musculoskeletal and biomechanical differences. The current multimodal treatment, therefore, may not affect the heterogeneous PFP patient population with the same efficiency.

Clinically subgrouping PFP patients and delivering targeted treatments has been strongly recommended for future investigations of patellofemoral pain treatment from the International Patellofemoral Pain Research Retreats.[4,12,52] An overview of previously published PFP subgroups and the methods used to derive subgroups in PFP identified patients with PFP.[39] They exhibit different anthropometric and biomechanical characteristics and do not form a homogeneous group. There are 3 subgroups in the PFP population: “strong”, “weak and tight” and “weak and pronated foot”.[38] The purpose of this study was to assess the clinical outcomes of targeted treatments designed according to the characteristics of the three subgroups of PFP patients.[38] The hypotheses were that the assessment and subgroup classification is clinically feasible, and that targeted treatments designed according to the characteristics of the three subgroups of PFP patients would show clinical benefits over and above a multimodal intervention.

METHOD

Design

A prospective crossover intervention study design was used (Figure 1).

Participants

Patients aged between 18 and 40 attending a physiotherapy outpatient clinic at a University Hospital with a clinical diagnosis of patellofemoral pain were approached for eligibility in this study. Eligibility criteria were based on previously defined PFP criteria.[7,38,47] Subjects were excluded if they had any of the following: previous knee surgery, clinical evidence of ligamentous instability and/or internal derangement, a history of patellar subluxation or dislocation, joint effusion, true knee joint locking and/or giving way, bursitis, patellar or iliotibial tract tendinopathy, Osgood Schlatter’s disease, Sinding-Larsen Johansson Syndrome, muscle tears or symptomatic knee plicae, serious co-morbidity which would preclude or affect compliance with the assessment, or were pregnant.

Subgroup Classification Method

Quadriceps and Hip Abductor muscle strength [31], Patellar glide test[44,54], Quadriceps length[53], Gastrocnemius length[53], and Foot posture index[36] assessments were performed to classify all consenting patients into one of three subgroups (strong, weak and tight, weak and pronated foot) using the algorithm derived from the work by Selfe et al.[38]

Intervention

Multimodal Treatment

The multimodal treatment program was designed based on the usual exercise and modalities used in local clinics.[20,21,32,49] All patients received standard, supervised, 60 min multimodal treatment three times a week for 6 weeks. Table 1 shows the details of the multimodal rehabilitation program.

Targeted Treatment

Patients who did not respond to multimodal treatment were assigned to one of the treatment groups "strong", "weak and tight", and "weak and pronated foot". They then followed a further 6 weeks, 45 min targeted intervention program administered three times a week. The targeted treatment program was designed according to the key deficits identified in each patient by the subgrouping clinical assessment tests. The patients in the "strong" subgroup had no muscle strength deficit therefore, the intervention program for this subgroup was targeted at improving neuromuscular control and coordination ability using proprioceptive exercises such as progressive balance exercises, and knee braces[46,47] which have been shown to offer improvements in movement control in patients with PFP,[41] reductions in patellofemoral reaction forces[44] and have been shown to reduce pain at 6 and 12 months during a PFP rehabilitation program.[48] In the "weak and tight" subgroup, the exercise program consisted of

Closed Kinetic Chain (CKC) muscle strengthening and stretching, and weight management advice, as a larger body mass index was identified as a potentially relevant clinical feature in this subgroup.[38] In the “weak and pronated foot” subgroup, muscle weakness and abnormal foot alignment were identified as the key factors. Therefore, the intervention program included CKC strengthening exercises and foot orthoses.[5,24] Table 2 shows the details of each of the specific targeted intervention programs.

Outcome measures

Pain during activity measured using the Visual Analog Scale (VAS) was the primary outcome measure of this study [19]. Activity was specified by patients.

The Perception of Recovery Scale was measured using a 7-point Likert scale ranging from “completely recovered” to “worse than ever”. Patients were classified as “recovered” if they rated themselves as “completely recovered” or “strongly recovered”. Patients rating themselves in one of the other five categories from “slightly recovered” to “worse than ever" were categorised as “not recovered”.[35]

The EQ-5D-5L was used as a self-reported generic measure of health and quality of life. Patients rated their overall health on the day of the interview on a 0–100 hash-marked, vertical visual analogue scale (EQ-5D-5L-VAS). A higher EQ-5D-5L-VAS score indicating better health status.[22]

Neuropathic Pain was measured using The Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire. The S-LANSS comprises a 5-item questionnaire regarding pain symptoms and two items for clinical signs involving self-administered sensory tests for the presence of allodynia and decreased sensation to pinprick. This was used to discriminate the small number of patients who may have neuropathic knee pain from those with nociceptive pain.[42] The possible scores range from 0 to 24, with a score of 12 or greater considered to be suggestive of neuropathic pain.[28] Finally, a single leg hop test was used to determine functional performance.[1] Distance was measured from toe to heel and the mean score of three repetitions was recorded.

Data analysis

A sample size calculation was performed based on the minimal detectable change on the pain VAS. Data from a previous study indicates that the VAS scores in patients with PFP was 4.3 ± 1 cm,[9] with 30% of the maximum score of the VAS-pain considered to be the detectable change, the sample size for each treatment subgroup was determined to be 8 patients to achieve a 90% power at the 0.05 level of significance. Data were not normally distributed when analysed with the Kolmogorov–Smirnov test Consequently, non-parametric tests were indicated. Therefore the "Wilcoxon signed rank test" was used to compare pre and post treatment outcomes with an alpha value of 0.05. In addition, the mean of rank scores, standard errors and Z scores were reported, along with descriptive statistics to describe the general features of the subjects. All statistical analysis was conducted using SPSS 21.0.

RESULTS

Of the 128 patients who were screened, 95 were included in the present study. Of these 61 patients completed the multimodal treatment (Figure 1) (Table 3). Twenty-one patients (36%) demonstrated recovery following multimodal treatment (Phase I) and were discharged. 40 Patients (64%) not responding to multimodal treatment were administered a further 6 weeks of targeted intervention designed according to subgroup characteristics (phase 2). Twenty-nine (72.5%) patients demonstrated recovery following targeted intervention (phase II) and 11 (27.5%) patients did not respond to either of the treatment approaches (Table 4).

Pain intensity (VAS) at rest and during activity, and Perceived Recovery Scale (PRS), were significantly improved after targeted intervention ($p<0.001$) (Table 5). S-LANSS, EQ-5D-5L and EQ5D-5L-VAS scores were significantly improved following targeted intervention compared to pre-targeted treatment scores ($p = 0.001$, $p<0.001$, $p = 0.02$), respectively (Table 5).

Within the three subgroups, the findings showed that PRS score was significantly improved after targeted treatment compared to pre-targeted treatment levels in the “strong”, “weak and tight”, and “weak and pronated foot” subgroups ($p= 0.005$, $p= 0.001$, $p= 0.004$) respectively. VAS pain intensity at rest was also significantly lower after targeted intervention in the “weak and pronated foot” and “weak and tight” subgroups ($p=0.011$, $p= 0.008$) respectively, however within the “strong” subgroup, no change was seen between pre-treatment and post treatment ($p = 0.245$) (Table 6). However, pain intensity during activity was significantly lower after treatment in the “strong” ($p=0.006$), the “weak and pronated foot” and “weak and tight” subgroups; although these reductions were not statistically significant ($p=0.059$, $p= 0.06$) respectively (Table 6).

Other measures including quadriceps length test, S-LANSS, EQ5D-5L, and EQ5D-VAS were significantly improved in the “weak and tight” subgroup. S-LANSS, EQ5D-5L, and patellar mobility were significantly improved in the “weak and pronated foot” subgroup. In the “strong” group only gastrocnemius length was significantly different between pre- and post-targeted treatment ($p=0.03$). Results for outcome measures are shown in Table 7.

DISCUSSION

The results of our study suggest that the TIPPs subgroups and the algorithm used to classify PFP patients as "strong", "weak and tight", "weak and pronated foot" [38] is valid and clinically implementable. The findings from this study were in agreement with previous work[13] that reported differential response patterns in outcomes at 12 months in their subgroups. This suggests that targeted interventions based on subgroups, provides an important development in the treatment strategy for patients with PFP.[4,52]

The “strong” subgroup demonstrated a poor response to multimodal treatment but a a significant improvement after targeted treatment was observed. This finding is consistent with Greuel et al.[18] and Gallina et al.[17] who both reported results confirming that motor control of the quadriceps is problematic in some PFP patients. One explanation for this is improved neuromuscular control in patients classified as “strong”. Since these patients already demonstrated relatively high quadriceps muscle torque, targeted intervention was delivered focusing on progressive development of motor control on unstable surfaces instead of conventional muscle strength exercises. Given that quadriceps strength did not change as a result of the targeted intervention, these progressive balance exercises and patellar bracing has improved motor control and stability.[41] In addition, bracing may reduce patellofemoral forces during activities of daily living and sporting tasks[44] and improvements within rehabilitation protocols.[48] This was reflected in the improvement in the other pain related parameters, However, since the average pre-treatment VAS pain level at rest in this subgroup was already low a decrease from 1.8 to 0.7 has minimal clinical relevance.

Clinically the “weak and tight” subgroup appeared to be the most responsive group to treatment overall with a relatively even split of 52% responding to multimodal treatment and all of the remaining patients responding to targeted intervention. This finding was not surprising as multimodal treatment routinely includes strengthening and stretching exercises. However, closer analysis of the outcomes in the "weak and tight" subgroup suggest that although patients’ perception of recovery improved, the VAS activity pain intensity was not significantly decreased after targeted treatment in this subgroup. Considering muscle weakness is the main issue in this subgroup, the probable cause of this unexpected finding is persistent inability to compensate patellofemoral loads especially during relatively high level activities of daily life such as ascending/descending stairs even after the targeted treatment. Targeted intervention consisting of functional strengthening may still be insufficient for high level activities of daily living which demand considerable muscular activity, although it caused approximately a 30% increase in muscle torque and a significant improvement in perception of recovery in this subgroup.

Findings from the “weak and pronated foot” subgroup suggest that targeted treatment including, foot orthoses and pain free strengthening exercises was also successful in terms of perception of recovery and VAS pain on rest. Although the same improvement was not observed in VAS pain during activity. One explanation for this could be the indirect effect of the foot orthoses on the knee as the patients showed no improvement in strength after targeted treatment. Moreover, optimum correction is very difficult to determine during the intervention of foot orthoses. Special single physiotherapy interventions or combining interventions for patellar taping, mobilisation or manual therapy may have beneficial effects on pain related functional symptoms in PFP.[11,30,34] However, the therapeutic effects of these applications remain limited because PFP patients exhibit a wide variety of structural features and biopsychosocial differences. The biomechanical and anthropometric characteristics of patients were not similar. Foot pronation, for example, was noticeably high in some patients, while some had neutral foot alignment. Similarly, quadriceps muscle strength, which is a predisposing factor or a most common symptom in previous studies[8,54] has been high in some patients with the remainder having considerable muscle weakness. Therefore, specific applications such as foot orthoses, knee braces, tape, and even exercises may not be required by every patient.

The functional hop test is often used in clinics to measure functional capability.[51] Considering that there was no increase in quadriceps muscle strength in the “weak and pronated foot”, and “strong” subgroups, an improvement in the hop test scores was not expected.

Due to the methodological design of this study, patients received 6 weeks of multimodal treatment before 6 weeks of targeted treatment with no intervening washout period. This is a study limitation since the cumulative effects of the previous treatment (multimodal) were ignored. Therefore, the observed difference in some parameters could be the result of regression to the mean.

CONCLUSION

Both the TIPPs assessment and subgroup classification algorithm are clinically feasible that those with PFP are not a homogeneous group, and have biomechanical and structural differences.

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Table 1. Multimodal Treatment Program

MODALITY	APPLICATION TYPE
Thermotherapy	Cold packs /20 min
Transcutaneous Electrical Neural Stimulation (TENS)	Conventional mode-20 min 50-100Hz, 20-60 pulse/sec
Therapeutic Ultrasound (US)	1 Watt/cm² - 5 min/ around knee joint
Hamstring/tensor fascia lata/ iliotibial band stretching	30sn/5 rep
Isometric quadriceps strengthening	10 rep x 3 set
Isometric hip adductor strengthening	10 rep x 3 set
OKC knee extension exercise	3 sets of patients' 8-10 RM, in painless ROM
OKC Hip adductor exercise	side lying/ 3 sets of patients' 8-10 RM
Home based exercise program*	

RM: Repetition Maximum, rep: repetition, ROM: Range of motion, OKC: Open kinetic chain
***Home based exercise program included the same applications except TENS, NMES, US*

Table 2. Targeted treatment program

STRONG SUBGROUP	
Progressive balance/proprioception exercises	Standing on one leg on wobble board 3 sets of 1 min exercise each leg 1-3 sets per session depending on pain Progression*: Eyes closed, bouncing ball against wall, bouncing ball against wall on an unstable surface
Patellar bracing**	Patient was asked to put on knee brace during ADL
Activity modification	Activity reduction to fit within envelope of function locally determined and negotiated with individual patient
WEAK AND TIGHT SUBGROUP	
CKC strengthening exercises	Plie/lunge/single limb squat Pain free ROM 10 reps per set/ 1-3 sets depending on pain
Gastrocnemius and Quadriceps Stretching exercises	30 seconds static stretch x 3 reps x 1 per day
Weight management strategies	Locally determined and negotiated with individual patient
WEAK AND PRONATED FOOT SUBGROUP	
CKC strengthening exercises	Plie/lunge/single limb squat Pain free ROM 10 reps per set/ 1-3 sets depending on pain
Foot orthoses	Custom made insole supporting medial longitudinal arch of foot***
Activity modification	Improve activity levels locally determined and negotiated with individual patient

ADL: Activity of Daily Life CKC: Closed Kinetic Chain
**Progression timing in balance exercise was decided by clinician based on patient pain free achievement*
*** Off the shelf knee support with patellar pad was used (Orthocare© material: 5mm neoprene /SBR /nylon jersey/pk). Brace size was selected by clinician according to patient comfort and patellar coherence (S/M/L/XL sizes were used)*
**** Custom Made Insoles are tailored individually based on static and dynamic examination of load distribution on foot. using CAT-CAM free step V.1.3.30*

Table 3 Demographic data of patients who participated in the study

PATIENTS (N=61)	MEAN	SD
AGE (YEAR)	27	9
HEIGHT (CM)	170	8
WEIGHT (KG)	65	13
TIME SINCE SYMPTOMS STARTED (MO)	24	28
BMI (KG/M2)	22.5	3

Table 4. Perception of recovery after treatments

	PHASE 1 MULTIMODAL TREATMENT (N=61)				PHASE 2 TARGETED TREATMENT (N=40)			
PRS	Overall % (n)	Weak and Tight % (n)	Weak and Pronated % (n)	Strong % (n)	Overall % (n)	Weak and Tight % (n)	Weak and Pronated % (n)	Strong % (n)
FULLY IMPROVED	11 (7)	16 (4)	-	9 (2)	7.5 (3)	8 (1)	-	11(2)
GREAT IMPROVEMENT	23 (14)	36 (9)	29 (4)	9 (2)	65 (26)	92 (11)	80 (8)	39 (7)
SOME IMPROVEMENT	48 (29)	36 (9)	57 (8)	55(12)	17.5 (7)	-	20 (2)	28 (5)
NO CHANGE	16 (10)	12 (3)	14 (2)	18 (4)	10 (4)	-	-	22 (4)
A LITTLE WORSE	4 (3)	-	-	9 (2)	0 (0)	-	-	-

Table 5. Outcome measures differences in targeted treatment

	Before Targeted Treatment		After Targeted Treatment			
Outcome Measures (n=40)	Median	Min-Max	Median	Min-Max	Z	p
Perception of recovery	3	3 - 5	2	1 - 4	-5,034	**<0.001***
VAS activity (cm)	4.4	0.1 - 8.8	1.8	0 - 7.5	-4.075	**<0.001***
VAS rest (cm)	1.7	0 - 7.4	0.5	0 - 7.0	-3.599	**<0.001***
S-LANSS	5	0 - 16	0	0 - 24	-3.449	**0.001***
EQ5D-5L	7	5 - 10	6	5 - 11	-3.704	**<0.001***
EQ5D-VAS	80	30 - 95	85	50 - 100	-2.322	**0.020***
Quadriceps muscle strength (Nm/kg)	1,1	0,5- 2,1	1,2	0,6 – 2,3	-3.644	**<0.001***
Hip abductor muscle strength (Nm/kg)	1,3	0.7 – 2,6	1,3	0,6 – 1,9	-1.456	0.145
Patellar mobility test (mm)	12	7 - 25	11	2 - 18	-2.062	**0.039***
Foot posture index	6	0 - 11	6	0 - 12	-0.372	0.710
Quadriceps length (^{0})	142.7	115 - 156	145.2	128 - 155	-2.150	0.032
Gastrocnemius length (^{0})	19.6	8 - 40	20.5	12.3 - 40	-1.358	0.174
Jump (cm)	90.2	30 - 180	91	38 - 179	-1.472	0.141

**p<0.05, VAS: Visual Analog Scale, S-LANSS: The Leeds Assessment of Neuropathic Symptoms and Signs, EQ5DL: European Quality 5 Dimension, °: degree*

Table 6. Differences in subgroups before and after targeted treatment (n=40)

		BEFORE TREATMENT		**AFTER TREATMENT**		**Z**	**P**
		Median	Min-Max	Median	Min-Max		
VAS IN ACTIVITY	Weak and Pronated (n=10)	5.3	0.5 – 8.8	2.7	0.2 – 6.6	-1.886	0.059
	Weak and Tight Group (n=12)	3.7	0.4 – 7.7	3	0 – 6.5	-1.883	0.060
	Strong Group (n=18)	5.0	0.1- 8.2	2.0	0 – 7.5	-2.741	**0.006***
VAS AT REST	Weak and Pronated (n=10)	3.9	0 – 7.1	0.8	0 – 3.4	-2.547	**0.011***
	Weak and Tight Group (n=12)	1.0	0- 3.5	0.68	0 – 1.6	-2.667	**0.008***
	Strong Group (n=18)	1.8	0 – 7.4	0.7	0 – 7	-1.161	0.245
PRS	Weak and Pronated (n=10)	3	3-4	2	2-3	-2.887	**0.004***
	Weak and Tight Group (n=12)	3	3-4	2	1-2	-3.213	**0.001***
	Strong Group (n=18)	3	3-5	2.5	1-4	-2.830	**0.005***

*p<0.05, *VAS: Visual Analog Scale, PRS: Perception of Recovery Scale*

Table 7. Outcome measures in subgroups before and after targeted treatment

	Weak and Tight subgroup (n=12)				Weak and Pronated subgroup (n=10)				Strong subgroup (n=18)			
	Before Median (Min-Max)	After Median (Min-Max)	Z	p	Before Median (Min-Max)	After Median (Min-Max)	Z	p	Before Median (Min-Max)	After Median (Min-Max)	Z	p
S-LANSS	5 (0- 11)	0 (0 – 6)	-2.716	**0.007***	6 (0-11)	0 (0 – 10)	-2.410	**0.016***	5 (0- 169)	1.5 (0 – 24)	-0.947	0.344
EQ5D-5L	7.5 (5-10)	6 (5– 9)	-2.556	**0.011***	9 (6- 9)	6 (5– 11)	-2.203	**0.028***	6 (5-10)	6 (5– 10)	-1.613	0.107
EQ5D-VAS	80 (50- 90)	90 (50-95)	-2.034	**0.042***	80 (50- 90)	80 (50-100)	-1.027	0.305	82.5 (30- 95)	82.5 (55-100)	-1.444	0.149
Quadriceps muscle strength (Nm/kg)	0.84 (0.5-.1.3)	1.05 (0.6 – 1.4)	-3.061	**0.002***	1.06 (0,6-2.1)	1.3 (0.7 – 1.6)	-1.887	0.059	1.2 (0.9 – 1.6)	1.2 (0.9 – 2.2)	-0,893	0.372
Hip abductor muscle strength (Nm/kg)	0.9 (0.7 – 1.4)	1.1 (0.6 –1.6)	-1,844	0.065	1.1 (0.7– 1.6)	1.2 (0.9– 1.6)	-0.593	0.553	1.4 (0.9– 2.6)	1.5 (1 –1.9)	-0.259	0.796
Patellar mobility test (mm)	10 (7- 15)	10 (8- 15)	-0.103	0,918	15 (11- 22)	12 (2- 18)	-2.325	**0.020***	12 (8- 25)	11 (7- 17)	-0.803	0,422
Foot posture index	5 (0-9)	5.5 (2-10)	-1.725	0.084	7.5 (4-11)	7.5 (2-12)	-0.679	0.497	5 (0-11)	6 (0-12)	-0.178	0.859
Quadriceps length (^{0})	137 (115 – 149)	140 (128 -152)	-2.134	**0.033***	140 (118 – 152)	146 (130 -155)	-1.481	0.139	147 (117 – 155)	148 (128 -155)	-0.071	0.943
Gastrocnemius length (^{0})	18.2 (10-26)	17.4 (12.6-27)	-1.295	0.195	21.3 (10-40)	17.3 (12.6-34)	-1.244	0.214	19.6 (8-27)	21.5 (12.3-40)	-2.120	**0.034***
Jump test (cm)	79.1 (30-115)	81 (38-115)	-1.718	0.286	85.4 (40-149)	84.2 (65-154)	-1.718	0.086	104.5 (49.3-180.6)	107.2 (57.3-179.3)	-0.305	0.760

**p<0.05, VAS: Visual Analog Scale, LANSS: The Leeds Assessment of Neuropathic Symptoms and Signs, EQ5DL: European Quality 5 Dimension, °: degree*