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

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

Hypothesis:

The hypotheses were that the assessment and subgroup classification is clinically feasible, and that targeted treatment designed according to the characteristics of three subgroups of PFP patients would show clinical benefits over and above a multimodal intervention.

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.[2,3,6,8,14,15,20,21,25,26,32,33,45] 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, as it has been reported that 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 made a priority by previous International Patellofemoral Pain Research Retreats.[4,10,12,48] 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. The idea of clinically subgrouping PFP patients and delivering targeted treatments

has been strongly recommended for future investigations from consensus based recommendations regarding treatment for patellofemoral pain from the International Patellofemoral Pain Research Retreats .[4,12,48] Selfe et al. [39] provide an overview of previously published PFP subgroups and the methods used to derive subgroups in PFP and identified that patients with PFP exhibit different anthropometric and biomechanical characteristics and do not form a homogeneous group. Moreover, the most evidence based method for deriving subgroups found 3 subgroups in the PFP population, which were characterised as "strong", "weak and tight" and "weak and pronated foot".[38] This progress allows for a new targeted treatment approach for PFP to be explored. However, being able to classify patients into subgroups has limited clinical importance without further evidence of the efficacy of targeted interventions applied according to the characteristics of these subgroups. Therefore, 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 as described by Selfe et al.[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.[7,38,44] 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[42,50], Quadriceps length[49], Gastrocnemius length[49], 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.[20,21,32,45] 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 week, 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[43,44] which have been shown to offer improvements in movement control in patients with PFP (Selfe et al. 2011), reductions in patellofemoral reaction forces (Sinclair et al. 2016) and have been shown to reduce pain at 6 and 12 months during a PFP rehabilitation program (Uboldi et al., 2018). 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 at rest and during activity was the primary outcome measure of this study measured using the Visual Analog Scale (VAS) [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 (Selfe 2017. Chapter 4: Red Flags and Rare pathologies in 1. Selfe J, Janssen J, Callaghan M (2017). Patellofemoral Pain an evidence based Clinical Guide. Nova Science). 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 (p = ??). Consequently, non-parametric tests were indicated. 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).

Perceived Recovery Scale (PRS), and pain intensity at rest and during activity (VAS) 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 pain perception 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

176 “strong” group only gastrocnemius length was significantly different between pre- and post-
177 targeted treatment (p=0.03). Results for outcome measures are shown in Table 7.
178
179 **DISCUSSION [Au: Do not repeat results here.]**
180 This study explored the clinical outcome of multimodal followed by targeted intervention for
181 three specific subgroups of PFP patients. Findings suggest that 36% of PFP patients did
182 respond to multimodal treatment, which is lower than that reported by Brown et al.[2] (46%). .
183 The results of our study suggest that the TIPPs subgroups and the algorithm used to classify
184 PFP patients as "strong", "weak and tight", "weak and pronated foot" [38] is valid and
185 clinically implementable. The findings from this study were in agreement with Drew et al.[13]
186 who also reported differential response patterns in outcomes at 12 months in their subgroups.
187 This suggests that targeted interventions based on subgroups, provides an important
188 development in the treatment strategy for patients with PFP.[4,48]
189 When subgroups were examined separately, the distribution of patients was very similar to
190 that found by Selfe et al.[38] however there were slight differences in number of patients
191 classified as “weak and pronated foot” and “strong” The reasons for this are unclear but may
192 suggest different care seeking or life style, eating and exercise behaviours.
193 The “strong” subgroup demonstrated a poor response to multimodal treatment but a
194 significant improvement was observed after targeted treatment. This finding is consistent with
195 Greuel et al.[18] and Gallina et al.[17] who both reported results confirming that motor control of
196 the quadriceps is problematic in some PFP patients. One explanation for this is improved
197 neuromuscular control in patients classified as “strong”. Since these patients already
198 demonstrated relatively high quadriceps muscle torque, targeted intervention was delivered
199 focusing on progressive development of motor control on unstable surfaces instead of
200 conventional muscle strength exercises. Given that quadriceps strength did not change as a

result of the targeted intervention, these progressive balance exercises and the use of patellar bracing have been shown to improve motor control and stability (Selfe et al., 2011). In addition, bracing has been linked to the reduction of patellofemoral forces during activities of daily living and sporting tasks (Sinclair et al, 2016) and improvements within rehabilitation protocols (Uboldi et al., 2018). 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 entirely unexpected 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% development 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

226 the foot orthoses on the knee as the patients showed no improvement in strength after targeted
227 treatment. Moreover, optimum correction is very difficult to determine during the intervention
228 of foot orthoses. It has been reported that special single physiotherapy interventions or
229 combining interventions for patellar taping, mobilisation or manual therapy have beneficial
230 effects on pain related functional symptoms in PFP.[11,30,34] However, the therapeutic effects of
231 these applications remain limited because PFP patients exhibit a wide variety of structural
232 features and biopsychosocial differences. It was confirmed with the present study that the
233 biomechanical and anthropometric characteristics of patients were not similar. Foot
234 pronation, for example, was noticeably high in some patients, while some had neutral foot
235 alignment. Similarly, quadriceps muscle strength, which is indicated as a predisposing factor
236 or a most common symptom in previous studies[8,51] has been measured as high in some
237 patients with the remainder having considerable muscle weakness. Therefore, specific
238 applications such as foot orthoses, knee braces, tape, and even exercises may not be required
239 by every patient. Recently, Selfe et al.[38] and Drew et al.[13] demonstrated that PFP patients
240 could be classified into subgroups in multicentre studies. However, corresponding targeted
241 treatment packages have yet to be developed. The outcome of the present study indicates that
242 PFP patients who did not respond to standard multimodal rehabilitation and who were then
243 treated with targeted intervention designed specifically according to these three subgroups
244 showed improvement in the majority of symptoms related to pain, knee function and quality
245 of life.
246 The functional hop test is often used in clinics to measure functional capability.[47] Considering
247 that there was no increase in quadriceps muscle strength in the “weak and pronated foot”, and
248 “strong” subgroups, an improvement in the hop test scores was not expected. Possible
249 reasons why the hop test score did not improve despite the increase in muscle strength in the
250 “weak and tight” group can be attributed to the inconsistent hop test performance in PFP

patients. This confirms previous work that reported single legged hop testing was not a suitable alternative for strength measurements as the correlation between quadriceps strength measurement using dynamometry and distance achieved during a hop test was found to be poor.[46]

Due to the methodological design of this study, patients had received 6 weeks of multimodal treatment before 6 weeks of targeted treatment with no intervening washout period. This must be accepted as a limitation since the possible 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

The findings of the study confirm that both the TIPPs assessment and subgroup classification algorithm are clinically feasible. These findings confirm the findings of others[13,18,27,38,41] that patients with PFP are not a homogeneous group, and have biomechanical and structural differences. The results provide proof of concept that targeted interventions based on a hypothesis driven subgrouping approach confer a significant clinical benefit over and above a multimodal intervention for PFP patients.

REFERENCES

1. Bremander AB, Dahl LL, Roos EM. Validity and reliability of functional performance tests in menisectomised patients with or without knee osteoarthritis. Scand J Med Sci Sports. 2007;17:120-127.
2. Brown J. Physiotherapists knowledge of patellofemoral pain syndrome. Br J Ther Rehabil. 2000;7:346–353.

3. Callaghan MJ, Selfe J. Has the prevalence of patellofemoral pain in the general population in the United Kingdom been properly evaluated? Phys Ther Sport. 2007;8:37-43.
4. Callaghan, M., Collins, N., Sheehan F. Patellofemoral pain: proximal, distal, and local factors. 2nd International Research Retreat. JOSPT. 2012;42:A1-A20.
5. Collins N, Crossley K, Darnell R, et al. Foot orthoses and physiotherapy in the treatment of patellofemoral pain syndrome: randomised clinical trial. BMJ. 2008;337:1735.
6. Collins NJ, Barton CJ, van Middelkoop M, et al. Consensus statement on exercise therapy and physical interventions (orthoses, taping and manual therapy) to treat patellofemoral pain: recommendations from the 5th International Patellofemoral Pain Research Retreat, Gold Coast, Australia, Br J Sports Med. 2018.
7. Cook C, Hegedus E, Hawkins R, et al. Diagnostic accuracy and association to disability of clinical test findings associated with patellofemoral pain syndrome. Physiother Can. 2010;62(1):17-24.
8. Cowan SM, Bennell KL, Hodges PW, et al. Delayed onset of electromyographic activity of vastus lateralis compared to vastus medialis obliquus in subjects with patellofemoral pain syndrome. Arch Phys Med Rehabil. 2000;82:83–89.
9. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons with patellofemoral pain: which are reliable and valid? Arch Phys Med Rehabil. 2004;85:815-822.
10. Crossley KM, van Middelkoop M, Callaghan MJ, et al. Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester. Part 1: Terminology, definitions, clinical examination, natural history,

299 patellofemoral osteoarthritis and patient-reported outcome measures. Br J Sports Med.
300 2016;50:839-843.
301 **11.** Crossley KM, van Middelkoop M, Callaghan MJ, et al. Patellofemoral pain consensus
302 statement from the 4th International Patellofemoral Pain Research Retreat,
303 Manchester. Part 2: recommended physical interventions (exercise, taping, bracing,
304 foot orthoses and combined interventions). Br J Sports Med. 2016;50:844-852.
305 12. Davis I, Powers C. Patellofemoral pain syndrome: proximal, distal, and local factors.
306 An International Retreat. JOSPT. 2010;40:A1-48.
307 13. Drew BT. Stratification of patellofemoral pain using clinical, biomechanical and
308 imaging features [doctoral dissertation]. University of Leeds; 2018.
309 14. Dvir Z, Halperin N, Shklar A, et aI. Concentric and eccentric torque variations of the
310 quadriceps femoris in patello-femoral pain syndrome. Clin Biomech. 1990;5:68–72.
311 15. Dvir Z, Halperin N, Shklar A, et al. Quadriceps function and patellofemoral pain
312 syndrome. Part I: pain provocation during concentric and eccentric isokinetic activity.
313 Isok Exerc Sci. 1991;1:26–30.
314 16. Eng JJ, Pierrynowski MR. The effect of soft foot orthotics on three-dimensional
315 lower-limb kinematics during walking and running. Phys Ther. 1994;74:836-44.
316 17. Gallina A, Hunt MA, Hodges PW, et al. Vastus lateralis motor unit firing rate is higher
317 in women with patellofemoral pain. Arch Phys Med Rehabil. 2018;99:907-13.
318 18. Greuel H, Herrington L, Liu A, et al. How does pain influence arthrogenic muscle
319 inhibition and quadriceps torque in individuals with patellofemoral pain. 5th
320 International Patellofemoral Research Retreat. Gold Coast Queensland, Australia
321 2017.
322 19. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: visual analog scale
323 for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire

(mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). Arthritis Care Res. 2011;63(11):240-252.

20. Heintjes EM, Berger M, Bierma-Zeinstra SMA, et al. Exercise therapy for patellofemoral pain syndrome. Cochrane Database Syst Rev. 2003;4.
21. Heintjes EM, Berger M, Bierma-Zeinstra SMA, et al. Pharmacotherapy for patellofemoral pain syndrome. Cochrane Database Syst Rev. 2004;3.
22. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of life research. 2011;20(10):1727-1736.
23. Hinman, RS, Bowles KA, Payne C, et al. Effect of length on laterally-wedged insoles in knee osteoarthritis. Arthritis Care Res. 2008;59:144-147.
24. Hossain M, Alexander P, Burls A, et al. Foot orthoses for patellofemoral pain in adults. Cochrane Database Syst Rev. 2011;1.
25. Janssen J. Concepts of patellofemoral pain. In: Selfe J, Janssen J, Callaghan M, eds. Patellofemoral Pain an Evidence Based Clinical Guide. Nova Science; 2017:3-13.
26. Jensen R, Hystad T, Baerheim A. Knee function and pain related to psychological variables in patients with long-term patellofemoral pain syndrome. J Orthop Sports Phys Ther. 2005;35:594–600.
27. Keays SL, Mason M, Newcombe PA. Individualized physiotherapy in the treatment of patellofemoral pain. Physiother Res Int. 2015;20:22-36.
28. Koc R, Erdemoglu AK. Validity and reliability of the Turkish self-administered leeds assessment of neuropathic symptoms and signs (S-LANSS) questionnaire. Pain Med. 2010;11:1107-1114.

29. Lake DA, Wofford NH. Effect of therapeutic modalities on patients with patellofemoral pain syndrome: a systematic review. Sports health, 2011;3(2):182-189.
30. Logan CA, Bhashyam AR, Tisosky AJ, Haber DB, Jorgensen A, Roy A, Provencher MT. Systematic review of the effect of taping techniques on patellofemoral pain syndrome. Sports health. 2017;9(5):456-461.
31. Maffiuletti NA. Assessment of hip and knee muscle function in orthopaedic practice and research. J Bone Joint Surg Am. 2010;92(1):220.
32. Martimbianco AC, Torloni MR, Andriolo BNG, et al. Neuromuscular electrical stimulation (NMES) for patellofemoral pain syndrome. Cochrane Database Syst Rev. 2017;9.
33. Nordin M, Frankel V. Basic biomechanics of the musculoskeletal system. London: Lippincott Williams & Wilkins; 1989:176–202.
34. Page, P. (2011). Effectiveness of elastic resistance in rehabilitation of patients with patellofemoral pain syndrome: what is the evidence?. Sports Health, 3(2), 190-194.
35. Rathleff MS, Roos EM, Olesen JL, et al. Lower mechanical pressure pain thresholds in female adolescents with patellofemoral pain syndrome. JOSPT. 2013;3(6):414-421.
36. Redmond AC, Crane YZ, Menz HB. Normative values for the foot posture index. J Foot Ankle Res. 2008;1(1):6.
37. Selfe J, Callaghan M, Witvrouw E, et al. Targeted interventions for patellofemoral pain syndrome (TIPPS): classification of clinical subgroups. BMJ open. 2013;3(9): e003795.
38. Selfe J, Janssen J, Callaghan M, et al. Are there three main subgroups within the patellofemoral pain population? A detailed characterisation study of 127 patients to help develop targeted intervention (TIPPs). Br J Sports Med. 2016; 50(14):873-880.

372 39. Selfe J, Janssen J, Drew B, et al. Anterior knee pain subgroups: the first step towards a
373 personalized treatment. Ann Joint. 2018;3(32).
374 40. Selfe J. Exercises supervised by physiotherapists improve pain and function in patients
375 with patellofemoral pain. J Physiother. 2010;56(1):61.
376 41. Selhorst M, Rice W, Degenhart T, et al. Evaluation of a treatment algorithm for
377 patients with patellofemoral pain syndrome: a pilot study. Int J Sports Phys
378 Ther. 2015;10:178.
379 42. Skalley TC, Terry GC, Teitge RA. The quantitative measurement of normal passive
380 medial and lateral patellar motion limits. Am J Sports Med. 1993;21(5):728-732.
381 43. Smith TO, Drew BT, Meek TH, et al. Knee orthoses for treating patellofemoral pain
382 syndrome. Cochrane Database Syst Rev. 2013(5).
383 44. Syme G, Rowe P, Martin D, et al. Disability in patients with chronic patellofemoral
384 pain syndrome: a randomised controlled trial of VMO selective training versus general
385 quadriceps training. Man Ther. 2009;14:252-263.
386 45. Van der Heijden RA, Lankhorst NE, van Linschoten R, et al. Exercise for treating
387 patellofemoral pain syndrome. Cochrane Database Syst Rev. 2015;6.
388 46. Weng P, Janssen J, Selfe J, et al. Validity of two clinical knee strength assessments
389 compared to the reference standard. International Journal of Physiotherapy and
390 Research. 2015;11:1264-1270.
391 47. Wilk KE, Romaniello WT, Soscia SM, et al. The relationship between subjective knee
392 scores, isokinetic testing, and functional testing in the ACL-reconstructed knee.
393 JOSPT. 1994;20:60-73.
394 48. Witvrouw E, Crossley K, Davis I, et al. 3rd International Patellofemoral Research
395 Retreat, Vancouver, Canada. Br J Sports Med. 2014;48:411-414.

396 49. Witvrouw E, Lysens R, Bellemans J, et al. Intrinsic risk factors fror the development
397 of anterior knee pain in an athletic population: atwo year prospective study. Am J
398 Sports Med. 2000;28(4):480-489.
399 50. Witvrouw E, Werner S, Mikkelsen C, et al. Clinical classification of patellofemoral
400 pain syndrome: guidelines for non-operative treatment. Knee Surg Sports Traumatol
401 Arthrosc. 2005;13(2):122-130.
402 51. Yosmaoglu HB, Kaya D, Guney H, et al. Is there a relationship between tracking
403 ability, joint position sense, and functional level in patellofemoral pain syndrome?
404 Knee Surg Sports Traumatol Arthrosc. 2013;21:2564-2571.

405
406
407

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*

476 Table 6. Differences in subgroups before and after targeted treatment (n=40)
477

		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***

478 *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*