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

4

5 Hayri Baran Yosmaoğlu, Emel Sonmezer, Manolya Ozkoslu, Ezgi Sahin, Senay Çerezci, Jim
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7

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

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

12 **Study Design:** A prospective crossover intervention.

13 **Level of Evidence:** Level III

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

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

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

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

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

36
37 **Key words:** Rehabilitation, knee injuries, patella, treatment outcome, pain perception
38

39 INTRODUCTION

40 Patellofemoral pain (PFP) is a chronic musculoskeletal problem that causes persistent anterior
41 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
42 that the current multimodal treatment approach leads to successful outcomes in the majority of
43 patients with PFP, only 46% of patients’ knees were pain free at discharge.² This indicates that
44 over half of PFP patients do not respond to treatment and may continue their lives with chronic
45 anterior knee pain.

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

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

63 **METHOD**

64 **Design**

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

66 **Participants**

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

76

77 **Subgroup Classification Method**

78 Quadriceps and Hip Abductor muscle strength³¹, Patellar glide test^{44,54}, Quadriceps length⁵³,
79 Gastrocnemius length⁵³, and Foot posture index³⁶ assessments were performed to classify all
80 consenting patients into one of three subgroups (strong, weak and tight, weak and pronated
81 foot) using the algorithm derived from the work by Selfe et al.³⁸

82

83 **Intervention**

84 **Multimodal Treatment**

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

89 **Targeted Treatment**

90 Patients who did not respond to multimodal treatment were assigned to one of the treatment
91 groups “strong”, “weak and tight”, and “weak and pronated foot”. They then followed a further
92 6 weeks, 45 min targeted intervention program administered three times a week. The targeted
93 treatment program was designed according to the key deficits identified in each patient by the
94 subgrouping clinical assessment tests. The patients in the “strong” subgroup had no muscle
95 strength deficit therefore, the intervention program for this subgroup was targeted at improving
96 neuromuscular control and coordination ability using proprioceptive exercises such as
97 progressive balance exercises, and knee braces^{46,47} which have been shown to offer
98 improvements in movement control in patients with PFP,⁴¹ reductions in patellofemoral
99 reaction forces⁴⁴ and have been shown to reduce pain at 6 and 12 months during a PFP
100 rehabilitation program.⁴⁸ In the “weak and tight” subgroup, the exercise program consisted of

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

107 **Outcome measures**

108 Pain during activity measured using the Visual Analog Scale (VAS) was the primary outcome
109 measure of this study¹⁹. Activity was specified by patients.

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

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

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

126 was used to determine functional performance.¹ Distance was measured from toe to heel and
127 the mean score of three repetitions was recorded.

128 **Data analysis**

129 A sample size calculation was performed based on the minimal detectable change on the pain
130 VAS. Data from a previous study indicates that the VAS scores in patients with PFP was $4.3 \pm$
131 1 cm ,⁹ with 30% of the maximum score of the VAS-pain considered to be the detectable change,
132 the sample size for each treatment subgroup was determined to be 8 patients to achieve a 90%
133 power at the 0.05 level of significance. Data were not normally distributed when analysed with
134 the Kolmogorov–Smirnov test Consequently, non-parametric tests were indicated. Therefore
135 the “Wilcoxon signed rank test” was used to compare pre and post treatment outcomes with an
136 alpha value of 0.05. In addition, the mean of rank scores, standard errors and Z scores were
137 reported, along with descriptive statistics to describe the general features of the subjects. All
138 statistical analysis was conducted using SPSS 21.0.

139

140 **RESULTS**

141 Of the 128 patients who were screened, 95 were included in the present study. Of these 61
142 patients completed the multimodal treatment (Figure 1) (Table 3). Twenty-one patients (36%)
143 demonstrated recovery following multimodal treatment (Phase I) and were discharged. 40
144 Patients (64%) not responding to multimodal treatment were administered a further 6 weeks of
145 targeted intervention designed according to subgroup characteristics (phase 2). Twenty-nine
146 (72.5%) patients demonstrated recovery following targeted intervention (phase II) and 11
147 (27.5%) patients did not respond to either of the treatment approaches (Table 4).

148 Pain intensity (VAS) at rest and during activity, and Perceived Recovery Scale (PRS), were
149 significantly improved after targeted intervention ($p < 0.001$) (Table 5). S-LANSS, EQ-5D-5L
150 and EQ5D-5L-VAS scores were significantly improved following targeted intervention

151 compared to pre-targeted treatment scores ($p = 0.001$, $p < 0.001$, $p = 0.02$), respectively (Table
152 5).

153 Within the three subgroups, the findings showed that PRS score was significantly improved
154 after targeted treatment compared to pre-targeted treatment levels in the “strong”, “weak and
155 tight”, and “weak and pronated foot” subgroups ($p = 0.005$, $p = 0.001$, $p = 0.004$) respectively.

156 VAS pain intensity at rest was also significantly lower after targeted intervention in the “weak
157 and pronated foot” and “weak and tight” subgroups ($p = 0.011$, $p = 0.008$) respectively, however
158 within the “strong” subgroup, no change was seen between pre-treatment and post treatment (p
159 $= 0.245$) (Table 6). However, pain intensity during activity was significantly lower after
160 treatment in the “strong” ($p = 0.006$), the “weak and pronated foot” and “weak and tight”
161 subgroups; although these reductions were not statistically significant ($p = 0.059$, $p = 0.06$)
162 respectively (Table 6).

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

168

169 **DISCUSSION**

170 The results of our study suggest that the TIPPs subgroups and the algorithm used to classify
171 PFP patients as “strong”, “weak and tight”, “weak and pronated foot”³⁸ is valid and clinically
172 implementable. The findings from this study were in agreement with previous work¹³ that
173 reported differential response patterns in outcomes at 12 months in their subgroups. This
174 suggests that targeted interventions based on subgroups, provides an important development in
175 the treatment strategy for patients with PFP.^{4,52}

176 The “strong” subgroup demonstrated a poor response to multimodal treatment but a a
177 significant improvement after targeted treatment was observed. This finding is consistent with
178 Greuel et al.¹⁸ and Gallina et al.¹⁷ who both reported results confirming that motor control of
179 the quadriceps is problematic in some PFP patients. One explanation for this is improved
180 neuromuscular control in patients classified as “strong”. Since these patients already
181 demonstrated relatively high quadriceps muscle torque, targeted intervention was delivered
182 focusing on progressive development of motor control on unstable surfaces instead of
183 conventional muscle strength exercises. Given that quadriceps strength did not change as a
184 result of the targeted intervention, these progressive balance exercises and patellar bracing has
185 improved motor control and stability.⁴¹ In addition, bracing may reduce patellofemoral forces
186 during activities of daily living and sporting tasks⁴⁴ and improvements within rehabilitation
187 protocols.⁴⁸ This was reflected in the improvement⁴⁸ in the other pain related parameters,
188 However, since the average pre-treatment VAS pain level at rest in this subgroup was already
189 low a decrease from 1.8 to 0.7 has minimal clinical relevance.

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

201 living which demand considerable muscular activity, although it caused approximately a 30%
202 increase in muscle torque and a significant improvement in perception of recovery in this
203 subgroup.

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

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

223 Due to the methodological design of this study, patients received 6 weeks of multimodal
224 treatment before 6 weeks of targeted treatment with no intervening washout period. This is a
225 study limitation since the cumulative effects of the previous treatment (multimodal) were

226 ignored. Therefore, the observed difference in some parameters could be the result of regression
227 to the mean.

228 **CONCLUSION**

229 Both the TIPP's assessment and subgroup classification algorithm are clinically feasible that
230 those with PFP are not a homogeneous group, and have biomechanical and structural
231 differences.

232

233 **REFERENCES**

234

- 235 1. Bremander AB, Dahl LL, Roos EM. Validity and reliability of functional performance
236 tests in menisectomised patients with or without knee osteoarthritis. *Scand J Med Sci*
237 *Sports*. 2007;17:120-127.
- 238 2. Brown J. Physiotherapists knowledge of patellofemoral pain syndrome. *Br J Ther*
239 *Rehabil*. 2000;7:346–353.
- 240 3. Callaghan MJ, Selfe J. Has the prevalence of patellofemoral pain in the general
241 population in the United Kingdom been properly evaluated? *Phys Ther Sport*.
242 2007;8:37-43.
- 243 4. Callaghan, M., Collins, N., Sheehan F. Patellofemoral pain: proximal, distal, and local
244 factors. 2nd International Research Retreat. *JOSPT*. 2012;42:A1-A20.
- 245 5. Collins N, Crossley K, Darnell R, et al. Foot orthoses and physiotherapy in the treatment
246 of patellofemoral pain syndrome: randomised clinical trial. *BMJ*. 2008;337:1735.
- 247 6. Collins NJ, Barton CJ, van Middelkoop M, et al. Consensus statement on exercise
248 therapy and physical interventions (orthoses, taping and manual therapy) to treat
249 patellofemoral pain: recommendations from the 5th International Patellofemoral Pain
250 Research Retreat, Gold Coast, Australia, *Br J Sports Med*. 2018.

- 251 7. Cook C, Hegedus E, Hawkins R, et al. Diagnostic accuracy and association to disability
252 of clinical test findings associated with patellofemoral pain syndrome. *Physiother Can.*
253 2010;62(1):17-24.
- 254 8. Cowan SM, Bennell KL, Hodges PW, et al. Delayed onset of electromyographic activity
255 of vastus lateralis compared to vastus medialis obliquus in subjects with patellofemoral
256 pain syndrome. *Arch Phys Med Rehabil.* 2000;82:83–89.
- 257 9. Crossley KM, Bennell KL, Cowan SM, et al. Analysis of outcome measures for persons
258 with patellofemoral pain: which are reliable and valid? *Arch Phys Med Rehabil.*
259 2004;85:815-822.
- 260 10. Crossley KM, van Middelkoop M, Callaghan MJ, et al. Patellofemoral pain consensus
261 statement from the 4th International Patellofemoral Pain Research Retreat, Manchester.
262 Part 1: Terminology, definitions, clinical examination, natural history, patellofemoral
263 osteoarthritis and patient-reported outcome measures. *Br J Sports Med.* 2016;50:839-
264 843.
- 265 **11.** Crossley KM, van Middelkoop M, Callaghan MJ, et al. Patellofemoral pain consensus
266 statement from the 4th International Patellofemoral Pain Research Retreat, Manchester.
267 Part 2: recommended physical interventions (exercise, taping, bracing, foot orthoses and
268 combined interventions). *Br J Sports Med.* 2016;50:844-852.
- 269 12. Davis I, Powers C. Patellofemoral pain syndrome: proximal, distal, and local factors.
270 An International Retreat. *JOSPT.* 2010;40:A1-48.
- 271 13. Drew BT. Stratification of patellofemoral pain using clinical, biomechanical and
272 imaging features [doctoral dissertation]. University of Leeds; 2018.
- 273 14. Dvir Z, Halperin N, Shklar A, et al. Concentric and eccentric torque variations of the
274 quadriceps femoris in patello-femoral pain syndrome. *Clin Biomech.* 1990;5:68–72.

- 275 15. Dvir Z, Halperin N, Shklar A, et al. Quadriceps function and patellofemoral pain
276 syndrome. Part I: pain provocation during concentric and eccentric isokinetic activity.
277 *Isok Exerc Sci.* 1991;1:26–30.
- 278 16. Eng JJ, Pierrynowski MR. The effect of soft foot orthotics on three-dimensional lower-
279 limb kinematics during walking and running. *Phys Ther.* 1994;74:836-44.
- 280 17. Gallina A, Hunt MA, Hodges PW, et al. Vastus lateralis motor unit firing rate is higher
281 in women with patellofemoral pain. *Arch Phys Med Rehabil.* 2018;99:907-13.
- 282 18. Greuel H, Herrington L, Liu A, et al. How does pain influence arthrogenic muscle
283 inhibition and quadriceps torque in individuals with patellofemoral pain. 5th
284 International Patellofemoral Research Retreat. Gold Coast Queensland, Australia 2017.
- 285 19. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: visual analog scale
286 for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire
287 (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs),
288 short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant
289 osteoarthritis pain (icoap). *Arthritis Care Res.* 2011;63(11):240-252.
- 290 20. Heintjes EM, Berger M, Bierma-Zeinstra SMA, et al. Exercise therapy for
291 patellofemoral pain syndrome. *Cochrane Database Syst Rev.* 2003;4.
- 292 21. Heintjes EM, Berger M, Bierma-Zeinstra SMA, et al. Pharmacotherapy for
293 patellofemoral pain syndrome. *Cochrane Database Syst Rev.* 2004;3.
- 294 22. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new
295 five-level version of EQ-5D (EQ-5D-5L). *Quality of life research.* 2011;20(10):1727-
296 1736.
- 297 23. Hinman, RS, Bowles KA, Payne C, et al. Effect of length on laterally-wedged insoles
298 in knee osteoarthritis. *Arthritis Care Res.* 2008;59:144-147.

- 299 24. Hossain M, Alexander P, Burls A, et al. Foot orthoses for patellofemoral pain in adults.
300 Cochrane Database Syst Rev. 2011;1.
- 301 25. Janssen J. Concepts of patellofemoral pain. In: Selfe J, Janssen J, Callaghan M, eds.
302 Patellofemoral Pain an Evidence Based Clinical Guide. Nova Science; 2017:3-13.
- 303 26. Jensen R, Hystad T, Baerheim A. Knee function and pain related to psychological
304 variables in patients with long-term patellofemoral pain syndrome. *J Orthop Sports Phys*
305 *Ther.* 2005;35:594–600.
- 306 27. Keays SL, Mason M, Newcombe PA. Individualized physiotherapy in the treatment of
307 patellofemoral pain. *Physiother Res Int.* 2015;20:22-36.
- 308 28. Koc R, Erdemoglu AK. Validity and reliability of the Turkish self-administered leeds
309 assessment of neuropathic symptoms and signs (S-LANSS) questionnaire. *Pain Med.*
310 2010;11:1107-1114.
- 311 29. Lake DA, Wofford NH. Effect of therapeutic modalities on patients with patellofemoral
312 pain syndrome: a systematic review. *Sports health*, 2011;3(2):182-189.
- 313 30. Logan CA, Bhashyam AR, Tisosky AJ, Haber DB, Jorgensen A, Roy A, Provencher
314 MT. Systematic review of the effect of taping techniques on patellofemoral pain
315 syndrome. *Sports health.* 2017;9(5):456-461.
- 316 31. Maffiuletti NA. Assessment of hip and knee muscle function in orthopaedic practice
317 and research. *J Bone Joint Surg Am.* 2010;92(1):220.
- 318 32. Martimbianco AC, Torloni MR, Andriolo BNG, et al. Neuromuscular electrical
319 stimulation (NMES) for patellofemoral pain syndrome. *Cochrane Database Syst Rev.*
320 2017;9.
- 321 33. Nordin M, Frankel V. Basic biomechanics of the musculoskeletal system. London:
322 Lippincott Williams & Wilkins; 1989:176–202.

- 323 34. Page, P. (2011). Effectiveness of elastic resistance in rehabilitation of patients with
324 patellofemoral pain syndrome: what is the evidence?. *Sports Health*, 3(2), 190-194.
- 325 35. Rathleff MS, Roos EM, Olesen JL, et al. Lower mechanical pressure pain thresholds in
326 female adolescents with patellofemoral pain syndrome. *JOSPT*. 2013;3(6):414-421.
- 327 36. Redmond AC, Crane YZ, Menz HB. Normative values for the foot posture index. *J Foot*
328 *Ankle Res*. 2008;1(1):6.
- 329 37. Selfe J, Callaghan M, Witvrouw E, et al. Targeted interventions for patellofemoral pain
330 syndrome (TIPPS): classification of clinical subgroups. *BMJ open*. 2013;3(9): e003795.
- 331 38. Selfe J, Janssen J, Callaghan M, et al. Are there three main subgroups within the
332 patellofemoral pain population? A detailed characterisation study of 127 patients to help
333 develop targeted intervention (TIPPs). *Br J Sports Med*. 2016; 50(14):873-880.
- 334 39. Selfe J, Janssen J, Drew B, et al. Anterior knee pain subgroups: the first step towards a
335 personalized treatment. *Ann Joint*. 2018;3(32).
- 336 40. Selfe J. Exercises supervised by physiotherapists improve pain and function in patients
337 with patellofemoral pain. *J Physiother*. 2010;56(1):61.
- 338 41. Selfe et al. 2011. A clinical study of the biomechanics of step descent using different
339 treatment modalities for patellofemoral pain. *Gait & posture*. 2011;34(1): 92-96.
- 340 42. Selfe 2017. Chapter 4: Red Flags and Rare pathologies in 1. Selfe J, Janssen J,
341 Callaghan M (2017). *Patellofemoral Pain an evidence based Clinical Guide*. Nova
342 Science
343 Science
- 344
345
- 346 43. Selhorst M, Rice W, Degenhart T, et al. Evaluation of a treatment algorithm for patients
347 with patellofemoral pain syndrome: a pilot study. *Int J Sports Phys Ther*. 2015;10:178.
- 348 44. Sinclair JK., Selfe J, Taylor PJ, Shore HF, Richards JD. Influence of a knee brace
349 intervention on perceived pain and patellofemoral loading in recreational athletes. *Clin*
350 *Biomech* 2016; 37: 7-12.

- 351 45. Skalley TC, Terry GC, Teitge RA. The quantitative measurement of normal passive
352 medial and lateral patellar motion limits. *Am J Sports Med.* 1993;21(5):728-732.
- 353 46. Smith TO, Drew BT, Meek TH, et al. Knee orthoses for treating patellofemoral pain
354 syndrome. *Cochrane Database Syst Rev.* 2013(5).
- 355 47. Syme G, Rowe P, Martin D, et al. Disability in patients with chronic patellofemoral pain
356 syndrome: a randomised controlled trial of VMO selective training versus general
357 quadriceps training. *Man Ther.* 2009;14:252-263.
- 358 48. Uboldi FM, Ferrua P, Tradati D, Zedde P, Richards J, Manunta A, Berruto M. Use of
359 an elastomeric knee brace in patellofemoral pain syndrome: short-term
360 results. *Joints.* 2018;6(02):85-89.
- 361 49. Van der Heijden RA, Lankhorst NE, van Linschoten R, et al. Exercise for treating
362 patellofemoral pain syndrome. *Cochrane Database Syst Rev.* 2015;6.
- 363 50. Weng P, Janssen J, Selfe J, et al. Validity of two clinical knee strength assessments
364 compared to the reference standard. *International Journal of Physiotherapy and
365 Research.* 2015;11:1264-1270.
- 366 51. Wilk KE, Romaniello WT, Soscia SM, et al. The relationship between subjective knee
367 scores, isokinetic testing, and functional testing in the ACL-reconstructed knee. *JOSPT.*
368 1994;20:60-73.
- 369 52. Witvrouw E, Crossley K, Davis I, et al. 3rd International Patellofemoral Research
370 Retreat, Vancouver, Canada. *Br J Sports Med.* 2014;48:411-414.
- 371 53. Witvrouw E, Lysens R, Bellemans J, et al. Intrinsic risk factors for the development of
372 anterior knee pain in an athletic population: a two year prospective study. *Am J Sports
373 Med.* 2000;28(4):480-489.

- 374 54. Witvrouw E, Werner S, Mikkelsen C, et al. Clinical classification of patellofemoral pain
375 syndrome: guidelines for non-operative treatment. *Knee Surg Sports Traumatol*
376 *Arthrosc.* 2005;13(2):122-130.
- 377 55. Yosmaoglu HB, Kaya D, Guney H, et al. Is there a relationship between tracking ability,
378 joint position sense, and functional level in patellofemoral pain syndrome? *Knee Surg*
379 *Sports Traumatol Arthrosc.* 2013;21:2564-2571.

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383 Table 1. Multimodal Treatment Program

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| 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/cm ² - 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* | |

386 *RM: Repetition Maximum, rep: repetition, ROM: Range of motion, OKC: Open kinetic chain*

387 **Home based exercise program included the same applications except TENS, NMES, US*

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390 Table 2. Targeted treatment program

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| | |
|----------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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 |

392 *ADL: Activity of Daily Life CKC: Closed Kinetic Chain*

393 **Progression timing in balance exercise was decided by clinician based on patient pain free achievement*

394 *** Off the shelf knee support with patellar pad was used (Orthocare© material: 5mm neoprene /SBR /nylon jersey/pk). Brace*

395 *size was selected by clinician according to patient comfort and patellar coherence (S/M/L/XL sizes were used)*

396 **** Custom Made Insoles are tailored individually based on static and dynamic examination of load distribution on foot.*

397 *using CAT-CAM free step V.1.3.30*

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402 Table 3 Demographic data of patients who participated in the study

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| 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 |

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406 Table 4. Perception of recovery after treatments

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| PRS | PHASE 1 MULTIMODAL TREATMENT (N=61) | | | | PHASE 2 TARGETED TREATMENT (N=40) | | | |
|------------------------------|----------------------------------------------------|-------------------------------------|----------------------------------------|-------------------------|--------------------------------------------------|-------------------------------------|----------------------------------------|-------------------------|
| | 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) | - | - | - |

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433 Table 5. Outcome measures differences in targeted treatment
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| Outcome Measures (n=40) | Before Targeted Treatment | | After Targeted Treatment | | Z | p |
|--------------------------------------|---------------------------|-----------|--------------------------|-----------|--------|---------|
| | Median | Min-Max | Median | Min-Max | | |
| 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 (°) | 142.7 | 115 - 156 | 145.2 | 128 - 155 | -2.150 | 0.032 |
| Gastrocnemius length (°) | 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 |

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

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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* |

453 *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 (°) | 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 (°) | 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

