Effects of a Targeted Exercise Program on Inter-Leg Asymmetries in Patients with Patellofemoral Pain

Denisa Manojlović 1, Martin Zorko 2, Darjan Spudić 3 and Nejc Šarabon 1,4,*

1 Department of Physical Therapy, Faculty of Health Sciences, University of Primorska, Polje 42, 6310 Izola, Slovenia; denisa.manojlovic@fvz.upr.si
2 Clinical Institute of Occupational, Traffic and Sports Medicine, University Medical Centre Ljubljana, Zaloška Costa 7, 1000 Ljubljana, Slovenia; martin.zorko@akclj.si
3 Department of Kinesiology, Faculty of Sport, University of Ljubljana, Gortanova Ulica 22, 1000 Ljubljana, Slovenia; darjan.spudic@fsp.uni-lj.si
4 Laboratory for Motor Control and Motor Behavior, Science to Practice, Ltd., S2P, Tehnološki Park 19, 1000 Ljubljana, Slovenia
* Correspondence: nejc.sarabon@fvz.upr.si; Tel.: +386-5-662-6466

Abstract: Patellofemoral pain (PFP) is often associated with impaired muscle strength, flexibility, and stability. It has been suggested that inter-leg asymmetries have an important role in increasing the risk of musculoskeletal injuries, including PFP. Thus, the aim of this study was to identify significant asymmetries and determine the effects of a symmetry targeted exercise program in patients with PFP. Eighteen patients aged 13 to 54 years (24.17 ± 12.52 years) with PFP participated in this study. Strength, flexibility and stability outcomes of the trunk, hip, knee and ankle muscles were assessed. A single-group pretest–posttest design was used to assess changes in inter-leg and agonist–antagonist asymmetries resulting from the 8-week period of the supervised exercise program. Results indicated a significant improvement in inter-leg symmetry regarding bilateral stance in a semi-squat position (p = 0.020, d = 0.61, df = 17) and ankle plantarflexion (p = 0.003, d = 0.32, df = 17) and ankle dorsiflexion strength (p < 0.001, d = 0.46, df = 17). In addition, the ratio of ankle dorsiflexion/plantarflexion (p = 0.036, d = 1.14, df = 17) and hip extension/flexion (p = 0.031, d = 0.94, df = 16) changed significantly during the intervention period. To our knowledge, this was the first study to evaluate inter-leg asymmetries resulting from a period of a supervised exercise program. The results indicate that an exercise program focusing on individual asymmetries may influence specific deficits and contribute to better rehabilitation outcomes.

Keywords: patellofemoral pain; asymmetry; strength; stability; flexibility

1. Introduction

Patellofemoral pain (PFP) is a widespread, non-traumatic knee condition, described as pain around or behind the patella, aggravated by activities excessively loading the patellofemoral joint (PFJ) [1]. Along with pain during jogging, squatting, stair climbing/descending or prolonged sitting with the knees flexed more than 90°, patients with PFP often experience crepitus [2], decreased coordination [3] and strength impairments [4]. Biomechanical asymmetries have been associated with unilateral pain in knee osteoarthritis [5] and may contribute to an increased risk of injury [6]. However, the extent of muscle strength, flexibility, and knee loading asymmetries during standing, walking or running in patients with PFP remains to be clearly determined.

To date, few studies have examined specific asymmetries present in patients with PFP, with conflicting results. A significant asymmetry in the activation of the gluteus medius muscle of the affected and the non-affected side, as measured by ultrasound, has been reported to be associated with pain levels in patients with PFP [7]. In addition, it has been demonstrated that women with PFP have up to 20% asymmetry in posterolateral hip
muscle strength between the affected and the non-affected side [8]. On the other hand, female runners in early stages of PFP do not demonstrate significant associations between asymmetry in hip abduction strength and levels of perceived pain [9]. While these studies provided valuable information about the manifestations of PFP at different stages, they focused mainly on hip muscle strength, neglecting potential asymmetries of trunk, knee and ankle muscle strength in patients with PFP [7–9]. Additionally, these studies focused mainly on females, while it has been previously suggested that males and females have different kinematic profiles leading to PFP [10]. The importance of gender differences in kinematic profiles and exercise interventions have been previously highlighted for knee disorders such as anterior cruciate ligament injury, emphasizing its value in the overall knee rehabilitation process [11–13]. Accordingly, differences between males and females may further influence inter-leg asymmetries present in patients with PFP. Although a vast body of literature focus their interest on improving absolute strength and flexibility in patients with PFP, there is arising evidence that individual asymmetries may play an important role in the effectiveness of PFP rehabilitation [14]. Inter-leg asymmetry levels may, through excessive loading of the affected leg, lead to increased stress on the PFJ [15]. Therefore, it is essential to determine predominant muscle strength, flexibility and stability asymmetries, as these findings may be valuable contributions to the design of effective exercise programs in patients with PFP.

In addition to inter-leg imbalances, Baldon et al. [14] suggest that asymmetries between agonists and antagonists may have an important role in the development and manifestation of PFP. Accordingly, it has been suggested that impaired agonist/antagonist strength ratios may affect lower limb stability during weight bearing tasks [15]. Magalhães et al. [8] reported a 23% higher hip adduction/abduction, and 8% higher anteromedial/posterolateral isometric strength ratio in patients with PFP compared to pain-free controls. Although these findings encourage clinicians to consider the hip muscle strength ratios in the treatment of PFP, there is insufficient evidence to conclude with certainty whether a targeted exercise program affects these asymmetries and contributes to the management of PFP.

A large body of evidence indicates that clinicians could influence the strength, flexibility, and stability deficits in patients with PFP through a targeted exercise program [16–19]. A recent study reported that, although 34% of patients responded to a general multimodal exercise program, over 70% of patients recovered after targeted treatment based on their individual deficits [20]. It is therefore essential to design and evaluate exercise programs based on individual asymmetries found in patients with PFP. It has been suggested that asymmetry levels may contribute to impaired performance during functional activities as well as increase stress on the PFJ [15]. However, we found no studies that examined the relationship between individually tailored exercise programs and their influence on asymmetries and perceived pain in patients with PFP.

Therefore, the aim of our study was to identify relevant stability, flexibility and strength asymmetries between (a) the affected and the non-affected side and (b) the agonistic and the antagonistic musculature in patients with PFP. In addition, we aimed to investigate the change occurring during a supervised exercise program on the asymmetry values, as well as its correlation with the levels of PFP. We hypothesized that patients with PFP exhibit significant inter-leg and agonist–antagonist asymmetries, that may further influence the effectiveness of rehabilitation. Finally, we hypothesized that an exercise program tailored to address individual asymmetries would be effective in reducing the abovementioned asymmetries and perceived PFP.

2. Materials and Methods
2.1. Participants

This study included 18 patients (five male and 13 female) with PFP aged 13 to 54 years (Table 1). The majority of patients (88.8%) exercised regularly at least once a week (4.06 ± 2.44 times per week) with a minimum duration of 30 min (92.8 ± 24.6 min). Patients present at the sports clinic were screened for PFP by a sports medicine physician. The inclusion
criteria were a) pain $\geq 3$ on the Visual Analogue Scale (VAS) lasting more than 3 months before the participation in the study and present during two or more of the following activities: running, squatting, jumping, prolonged sitting with knees flexed above 90°, stair descending/climbing, or isometric contraction of the quadriceps muscle, and b) a positive sign on the manual compression or patellar tilt test [21]. Exclusion criteria were as follows: pre/infrapatellar bursitis, previous hip or knee surgery, meniscal or other intra-articular injuries, patellar tendinopathy, involvement of the cruciate or collateral ligaments, patellar apprehensions, knee joint effusions, and Sinding–Larsen–Johansson or Osgood–Schlatter syndromes [22,23]. All eligible adult patients signed an informed consent form before participating in the study, while for underage patients, the form was signed by a parent or guardian. This study was approved by the Slovenian National Ethics Committee (approval number: 0120-99/2018/5) and was conducted in accordance with the Helsinki Declaration.

Table 1. Patients’ basic characteristics.

|                | Females | Males  | All    |
|----------------|---------|--------|--------|
| N              | 13      | 5      | 18     |
| Age (years)    | 19.11 ± 8.42 | 37.43 ± 12.31 | 24.17 ± 12.52 |
| Body height (cm) | 167.52 ± 7.07 | 181.04 ± 11.38 | 171.22 ± 10.24 |
| Body mass (kg) | 57.94 ± 6.67  | 84.21 ± 19.71  | 65.22 ± 16.42  |
| Body mass index | 20.63 ± 1.74  | 25.58 ± 4.77   | 22.41 ± 3.56   |

2.2. Study Design, Tasks and Measurement Procedure

A single-group pretest–posttest design was used to evaluate differences in inter-leg and agonist–antagonist asymmetries after the implementation of a targeted exercise program in patients with PFP. Following each measurement, patients were asked to rate their current PFP level on the VAS ranging from 0 to 10.

2.2.1. Stability Measurements

Loading symmetry (%) was assessed in the standing, semi-squat and full-squat positions. Patients were asked to stand hip-wide, with both feet flat on bilateral force platforms (9260AA, Kistler, Winterthur, Switzerland). All measurements were performed barefoot, with hands on hips, eyes open and directed on a stable point in front of them. Body sway was evaluated in a barefoot one-legged stance with hands on hips. Patients were asked to stand as still as possible for 30 s before repeating the measurement on the other leg. Participants performed three repetitions, with a 30 s rest period in between [24].

2.2.2. Strength Measurements

Custom-built dynamometers (S2P Ltd., Science to practice, Ljubljana, Slovenia) were used to assess maximal voluntary isometric contractions (MVIC) of trunk, hip, knee and ankle muscles. Trunk strength was assessed standing hip-wide with both feet flat on the dynamometer platform. The patient’s pelvis was secured with a provided strap and they were asked to cross their arms on their chest to avoid potential compensatory movements. Patients were then instructed to push as hard as possible against the dynamometer’s sensor, which was positioned at shoulder height. To assess hip muscle strength, patients were positioned in the prone (internal/external rotation and extension), or supine (flexion, abduction, and adduction) position on the non-slip platform of the dynamometer. A custom-made fixation belt was placed over the patients’ pelvis to provide stabilization and prevent compensating movements during the measurement. Finally, the strength of the knee and ankle muscles were assessed in a sitting position with the adjacent segments fixed (Figure 1). All strength measurements were performed three times, with a 30 s rest period in between [24]. Patients were required to hold each isometric contraction for approximately 5 s. The best of the three consecutive measurements was used for further analysis [25]. During each trial, loud and clear instructions were given to stimulate the patients as much as possible.
Symmetry 2021, 13, x FOR PEER REVIEW 4 of 11

made fixation belt was placed over the patients’ pelvis to provide stabilization and pre-


dators were consistent throughout the study, performing the same task on each


e of motion (RoM) of the trunk, hip, knee and ankle was assessed by three investigators. 



\[ \text{Asymmetries were calculated for each outcome measurement.} \]



\[ \text{A single measurement was performed, based on previous recommendations by Norkin and White (2016) [28], who report comparable reliability of one RoM measurement and the mean of multiple measurements. Patients were required to lie down still in the supine position while one investigator marked anatomical orientational landmarks of the hip, knee, and ankle joints.} \]

2.2.3. Flexibility Measurements

Flexibility was measured with a plastic goniometer with 1° accuracy/interval and 360° scale, and with a digital inclinometer with 0.01° accuracy/interval (Baseline Digital Inclinometer, Fabrication Enterprises, White Plains, NY, USA). The intra- and inter-rater reliability of both measurement tools were previously reported as excellent [26,27]. Passive range of motion (RoM) of the trunk, hip, knee and ankle was assessed by three investigators. Investigators were consistent throughout the study, performing the same task on each patient. One investigator was responsible for performing the movement, the second assisted as needed and read the measurement, while the third investigator recorded the results on a separate sheet for each patient. No test or warm-up trials were allowed prior to flexibility assessment. A single measurement was performed, based on previous recommendations by Norkin and White (2016) [28], who report comparable reliability of one RoM measurement and the mean of multiple measurements. Patients were required to lie down still in the supine position while one investigator marked anatomical orientational landmarks of the hip, knee, and ankle joints.

2.3. Data Processing and Statistical Analysis

Strength, flexibility, and stability measurements were collected in MS Excel prepared worksheets (Version 2019, Microsoft, Redmond, WA, USA). A frequency of 1000 Hz was used to collect muscle strength data and filtered with a low-pass Butterworth filter (20 Hz cut-off frequency, 2nd order). The maximum value reached during a 1 s interval of a single repetition was referred to as the maximum torque. Prior to further analysis, all strength data were normalized to patient body mass (Nm/kg). The data were then adjusted to reflect the “affected” and the “non-affected” leg for each patient. In the case of bilateral PFP, the leg defined by the patient as the more painful, was designated as “affected”. Asymmetries were calculated for each outcome measure, with a threshold of 10% indicating increased asymmetry in stability and strength [29–31] and a cut-off point of 15% indicating clinically relevant asymmetry in flexibility measures [32,33]. Statistical analysis was performed in SPSS software (version 26.0, SPSS INC., Chicago, IL, USA). The Shapiro-Wilk test was used to assess the normal distribution of the data. Differences between pre-test and post-test values were calculated using the Student’s t-test for paired samples. The Cohen’s d was used to determine the effect size with d ≤ 0.01 considered to be very small, d ≥ 0.20 small, d ≥ 0.50 medium and d ≥ 0.80 large [34]. Finally, Spearman’s correlation was used to calculate the correlation between the stability, flexibility and strength measures pre-post changes with the changes in the VAS during various testing positions (no association (0.0–0.1), poor to fair association (0.1–0.4), moderate associa-

![Figure 1](image-url) Isometric strength measurements of the (a) knee and (b) hip muscles.
tion (0.4–0.6), strong association (0.6–0.8) and very strong associations (>0.8) [35]). The significance level $\alpha$ was set at $p < 0.05$ for all statistical analysis.

2.4. Intervention Procedure

After the initial assessment, patients were enrolled in an 8-week exercise program. Sessions were conducted under the supervision of an experienced kinesiologist three times per week for 60 min per session. Resistance exercises were tailored to target specific deficits previously demonstrated in PFP patients [1]. The exercise program consisted of strength, flexibility and stability exercises targeting individual asymmetries of each patient–following progressive overload principle. Strength exercises consisted of squats and lunges up to 45° of knee flexion, side plank, plank, deadlifts, and standing calf raises [36]. Stability exercises consisted of single leg balance on an unstable surface with the knee slightly flexed [21]. Additionally, patients were asked to include trunk rotations and ball throwing without losing their balance. Finally, flexibility exercises consisted of a 30 s static stretching of individually detected flexibility deficits. Each flexibility exercise was performed three times before proceeding to the next [21,37]. In addition, each patient received a customized home exercise program based on their individual most prominent asymmetries, with instructions to perform these exercises in the days between supervised sessions. Patients provided their written feedback on the changes in PFP and potential symptoms at the beginning of each week (Supplementary File 1).

3. Results

3.1. Inter-Leg Asymmetry and Agonist–Antagonist Ratios

The mean values, inter-leg asymmetry indexes and asymmetry changes during the intervention period for all outcome measures are presented in Appendix A Table A1. Although all stability measures showed a positive change during the intervention period in weight distribution symmetry, the change reached statistical significance only in the semi-squat position ($p = 0.020$, $d = 0.61$, df = 17). The results indicate a significant improvement during the intervention period in inter-leg symmetry, both in terms of ankle plantarflexion ($p = 0.003$, $d = 0.32$, df = 17) and dorsiflexion strength ($p < 0.001$, $d = 0.46$, df = 17). Furthermore, there was a significant improvement in symmetry of hip flexion strength ($p = 0.049$, $d = 0.10$, df = 16) and ankle dorsiflexion flexibility ($p = 0.025$, $d = 0.83$, df = 17). Although there were no significant asymmetries in knee flexion or extension strength, the Nordic hamstrings showed an overall improvement in muscle strength during the intervention period, as well as an increase in inter-leg symmetry ($p = 0.010$, $d = 0.28$, df = 16). Regarding the gender differences in symmetry levels, only trunk lateral flexion strength showed significant differences between males and females ($p = 0.046$, $d = 0.34$, df = 16). In terms of agonist–antagonist intra-leg ratios, the asymmetry indexes changed significantly during the intervention period in the case of ankle dorsiflexion/plantarflexion ($p = 0.036$, $d = 1.14$, df = 17) and hip extension/flexion ($p = 0.031$, $d = 0.94$, df = 16) (Table 2).

Table 2. Pre- and post-test asymmetry indexes for agonist/antagonist strength ratios of the affected leg.

|                      | Pre-Test Asymmetry Index (%) | Post-Test Asymmetry Index (%) | Cohen’s $d$ | Degrees of Freedom | $p$-Value |
|----------------------|------------------------------|------------------------------|-------------|--------------------|-----------|
| Knee Ext/Flex (%)    | 45.30 ± 12.11               | 47.18 ± 11.39               | 0.16        | 16                 | 0.941     |
| Ankle PlantFlex/DorsiFlex (%) | 45.87 ± 23.11    | 67.92 ± 10.03               | 1.24        | 17                 | 0.036 *   |
| Trunk Ext/Flex (%)   | 29.53 ± 15.10              | 28.03 ± 17.74               | 0.09        | 16                 | 0.836     |
| Hip Abd/Add (%)      | 5.74 ± 9.86                 | 9.86 ± 9.30                 | 0.43        | 16                 | 0.472     |
| Hip ExtRot/IntRot (%)| 16.63 ± 13.05               | 19.91 ± 13.06               | 0.25        | 16                 | 0.106     |
| Hip Ext/Flex (%)     | 17.70 ± 14.73               | 6.15 ± 9.37                 | 0.94        | 16                 | 0.031 *   |

* Statistically significant difference.
3.2. Correlation with VAS

There was a strong correlation between PFP reduction and the changes in the knee extension/flexion strength ratio during the isometric knee extension and flexion strength testing ($r = 0.610, p = 0.009$). Additionally, a strong correlation was found between the reduction in PFP during the stability testing and the improvements in weight distribution in a semi-squat position ($r = 0.621, p = 0.008$) and ankle plantarflexion flexibility ($r = 0.760, p < 0.001$). A moderate correlation between PFP changes during the stability testing was found for body sway ($r = 0.485, p = 0.049$), trunk lateral flexion strength ($r = 0.596, p = 0.012$), hip extension strength ($r = 0.512, p = 0.036$), and hip external rotation flexibility ($r = 0.515, p = 0.035$).

4. Discussion

There were two main aims to this study. First, our purpose was to identify prominent stability, strength and flexibility asymmetries between the “affected” and the “non-affected” leg, as well as to determine the strength ratios between agonist/antagonist in patients with PFP. Second, we aimed to investigate the influence of a targeted exercise program on the change in asymmetry and its correlation with PFP levels during various testing positions. To the best of our knowledge, this was the first study to investigate the extent of asymmetries, their changes during a targeted exercise program and their correlations with perceived pain in patients with PFP.

We found that patients with PFP did not exhibit stability or weight distribution asymmetries based on the usual >10% asymmetry threshold. However, it was noticeable that the asymmetry indexes increased when transitioning from a standing (3.77%), through a semi-squat (4.70%), to a squat position (4.85%). It has been previously suggested that ankle dorsiflexion RoM restriction may lead to increased loading asymmetries during a bilateral squat [38,39]. Accordingly, the patients in our study demonstrated significant ankle dorsiflexion RoM asymmetry (50.01%) before participating in the exercise program. Although this inter-leg asymmetry persisted throughout the program, a significant improvement with a large effect size was observed in ankle dorsiflexion RoM (21.61%), followed by a more symmetrical weight distribution in the standing (3.05%), semi-squat (3.48%) and squat positions (3.95%). In addition, we found a strong correlation between improvements in PFP levels on a VAS scale and a more symmetrical weight distribution in the semi-squat position. These results are consistent with previous studies indicating that patients with PFP experience greater asymmetries during the single-leg squat [40] and functional activities such as ascending or descending stairs [41]. However, the causal relationship between improvements in asymmetry levels and the perceived PFP level is still to be clearly determined. Furthermore, we found a strong correlation between PFP reduction and changes in knee extension/flexion strength ratio during isometric knee muscle testing. Considering the overall improvement in knee extension and flexion strength during the intervention period, it is likely that the reduction of PFP levels is due to improvements in muscle strength. However, further studies are needed to clarify the causal relation between PFP reduction and improvements in muscle strength. Several studies have confirmed that exercise programs can lead to significant improvements in PFP through kinematic improvements [42–44], but to our knowledge, no study to date has tailored their exercise program to address individual asymmetries to affect PFP. Nevertheless, asymmetry levels are arising as an important factor in musculoskeletal injury prevention and rehabilitation [45], and various authors discussed its importance in patients with PFP [46,47]. It was suggested that strength and flexibility asymmetries may cause excessive loading of the PFJ during functional activities and eventually lead to greater PFP levels. Therefore, it is important to address individual asymmetries as a mean of prevention and rehabilitation of PFP. Furthermore, we found significant gender differences in terms of trunk lateral flexion strength, which suggest that additional attention is warranted in the design and implementation of rehabilitation programs including both males and females. These results are in accordance with previous studies highlighting differing risk factors between genders.
for the development of PFP [10] and may help further address individual asymmetries to achieve better rehabilitation results. It is important to note that given the lack of a control group, spontaneous recovery is possible. Therefore, we cannot conclude with certainty whether the observed changes were due to participation in the exercise program. However, all included patients experienced PFP for a long period of time, making the changes during the intervention period less likely to be due to spontaneous recovery.

There are a large number of studies investigating the influence and effects of hip muscles on PFP [21,38,48,49], with evidence confirming positive effects of hip strengthening exercises on PFP. However, most of these studies focused their interest on strength deficits that are present in patients with PFP compared to healthy individuals, rather than on inter-leg asymmetries present in patients with PFP alone. The present study found no statistically significant hip strength asymmetries or flexibility asymmetries in patients with PFP. Although these results are surprising, they are consistent with recent studies [9], that found no asymmetry in hip abduction strength in patients with early PFP. One explanation could possibly be found in the late recruitment of the hip abductors, which may lead the dysfunction to manifest in late muscle activation rather than in muscle strength [7,50]. However, changes found during the intervention period show that strength values for all hip outcome measures increased, indicating an overall improvement in proximal strength.

We found significant improvements in symmetry during the Nordic hamstring and hip flexion assessment, as well as an improvement in the extension/flexion ratio of the hip.

It has been previously suggested that foot posture impairments may be a risk factor for the development of various lower limb injuries, including PFP. Recently, a 20–30% higher medial foot loading was reported in patients with PFP [51], which may be associated with increased stress on the PFJ [1]. In the present study, we found considerable levels of inter-leg asymmetry in terms of ankle plantarflexion (11.17%) and dorsiflexion (14.73%) strength in patients with PFP. However, during the intervention period, significant improvements in inter-leg symmetry, along with a very large effect size regarding the improvement in the agonist/antagonist strength ratio between the ankle muscles were observed. These findings are consistent with previous literature supporting the implementation of ankle and foot exercises in PFP rehabilitation protocols in terms of increased ankle strength and reduced levels of PFP [52]. In addition, we found a strong correlation between ankle plantarflexion flexibility and PFP during stability testing, which may indicate an improvement in foot-loading during bilateral stance. Overall, given the growing evidence supporting the influence of distal factors on PFP, exercise programs that address ankle and foot muscle strength in addition to knee and hip muscle groups are warranted [53].

There are a number of limitations to the present study. Firstly, a control group was not included in our study. However, all included patients experienced PFP for an extended period of time, so the observed changes during the intervention period are less likely to be due to spontaneous recovery. Furthermore, considering that PFP is predominantly a functional limitation, it might be appropriate to assess kinematic asymmetries during functional tasks such as stair climbing/descending, or jogging. However, we focused our study on strength and flexibility asymmetries based on previous findings suggesting that such deficits may be a predominant risk factor for PFP [1]. Additionally, our sample consisted of a small number of both male and female patients with no restriction on age or activity level. Although this gave us a broader insight into PFP, it may have limited specific conclusions regarding a single age group, gender or activity level. Finally, our exercise program lasted 8 weeks, with an immediate testing aimed to reveal changes during the intervention period. Considering that PFP is both a chronic and prevalent condition, future studies examining the long-term effects of a targeted exercise program on strength, flexibility and stability asymmetries are warranted.
5. Conclusions

The present study examined the predominant changes in inter-leg strength, flexibility and stability asymmetries in patients with PFP during participation in a targeted exercise program. We conclude that patients with PFP exhibit significant ankle muscles strength and flexibility asymmetries, which may influence their weight loading symmetry during bilateral stance and thus, increase the stress on the PFJ. Furthermore, a targeted exercise program that focuses on individual asymmetries may influence specific asymmetries and contribute to better rehabilitation outcomes. Therefore, identifying individual asymmetries may have an important role in designing and implementing an effective exercise program for patients with PFP.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/sym13061075/s1, Supplementary File 1: Targeted exercise program for patients with patellofemoral pain.

Author Contributions: Conceptualization, N.Š. and D.M.; methodology, N.Š., M.Z., D.S. and D.M.; validation, N.Š., M.Z., D.S. and D.M.; formal analysis, D.M.; investigation, D.M., M.Z. and D.S.; resources, N.Š.; data curation, D.M.; writing—original draft preparation, D.M.; writing—review and editing, N.Š., M.Z., D.S. and D.M.; visualization, D.M.; supervision, N.Š.; project administration, N.Š. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Slovenian National Ethics Committee (approval number: 0120-99/2018/5).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data have been published previously in papers cited in the Introduction, Methods and Discussion.

Acknowledgments: The Slovenian Research Agency provided author N.Š. with support in the form of salary through the programme ‘Kinesiology of monostructural, polystructural and conventional sports’ [P5-0147 (B)] and the project TELASI-PREVENT [L5-1845] (Body asymmetries as a risk factor in musculoskeletal injury development: studying aetiological mechanisms and designing corrective interventions for primary and tertiary preventive care). The funders did not have any additional role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Conflicts of Interest: The authors declare no conflict of interest.
Table A1. Pre- and post-test mean values, inter-leg asymmetry indexes changes during the intervention period for stability, muscle strength and flexibility asymmetries.

|                      | Pre-Test | Post-Test |            |            |            | Cohen's d | Degrees of Freedom | p-Value |
|----------------------|----------|-----------|------------|------------|------------|------------|--------------------|---------|
| **Body Sway (mm)**   | 13.59 ± 1.78 | 14.87 ± 1.62 | 0.59 ± 0.12 | 13.87 ± 1.67 | 0.54 ± 0.12 | 17 | 0.001  |
| **Weight—standing (%)** | 0.34 | 0.27 | 0.34 | 0.27 | 0.34 | 0.27  |
| **Weight—squat (%)**  | 0.82 | 0.34 | 0.82 | 0.34 | 0.82 | 0.34  |
| **Hip Flex (Nm/kg)** | 1145.29 ± 277.07 | 1121.28 ± 263.89 | 9.85 ± 0.12 | 1058.67 ± 281.75 | 8.86 ± 0.12 | 17 | 0.007  |
| **Hip ExtRot (Nm/kg)** | 0.31 | 0.27 | 0.31 | 0.27 | 0.31 | 0.27  |
| **Knee Flex (N/m/kg)** | 1.20 | 0.34 | 1.20 | 0.34 | 1.20 | 0.34  |
| **Knee Ext (N/m/kg)** | 2.21 | 0.52 | 2.21 | 0.52 | 2.21 | 0.52  |
| **Ankle PlantarFlex (N/m/kg)** | 1.68 | 0.73 | 1.68 | 0.73 | 1.68 | 0.73  |
| **Ankle Dorsiflex (N/m/kg)** | 0.82 | 0.34 | 0.82 | 0.34 | 0.82 | 0.34  |
| **Trunk LatFlex (N/m/kg)** | 0.76 | 0.17 | 0.76 | 0.17 | 0.76 | 0.17  |
| **Hipp Abs (Nm/kg)** | 0.79 | 0.16 | 0.79 | 0.16 | 0.79 | 0.16  |
| **Hipp Add (Nm/kg)** | 0.42 | 0.11 | 0.42 | 0.11 | 0.42 | 0.11  |
| **Ankle PlantarFlex (%)** | 14.73 | 16.17 | 14.73 | 16.17 | 14.73 | 16.17  |
| **Ankle Dorsiflex (%)** | 0.76 | 0.16 | 0.76 | 0.16 | 0.76 | 0.16  |
| **Trunk LatFlex (%)** | 0.76 | 0.16 | 0.76 | 0.16 | 0.76 | 0.16  |
| **Hipp Add (%)** | 0.79 | 0.16 | 0.79 | 0.16 | 0.79 | 0.16  |
| **Hipp Flex (%)** | 0.42 | 0.11 | 0.42 | 0.11 | 0.42 | 0.11  |
| **Hipp Extrot (%)** | 0.34 | 0.08 | 0.34 | 0.08 | 0.34 | 0.08  |
| **Hipp Inflex (%)** | 0.90 | 0.27 | 0.90 | 0.27 | 0.90 | 0.27  |
| **Hipp Ext (%)** | 0.42 | 0.11 | 0.42 | 0.11 | 0.42 | 0.11  |
| **Ankle PlantarFlex (%)** | 14.73 | 16.17 | 14.73 | 16.17 | 14.73 | 16.17  |
| **Ankle Dorsiflex (%)** | 0.76 | 0.16 | 0.76 | 0.16 | 0.76 | 0.16  |

*Statistically significant pre-post difference.
10. Boling, M.C.; Nguyen, A.D.; Padua, D.A.; Cameron, K.L.; Beutler, A.; Marshall, S.W. Gender-Specific Risk Factor Profiles for Patellofemoral Pain. Clin. J. Sport Med. 2021, 31, 49–56. [CrossRef]

11. Marotta, N.; Demeco, A.; de Scorpio, G.; Indino, A.; Iona, T.; Ammendolia, A. Late activation of the vastus medialis in determining the risk of anterior cruciate ligament injury in soccer players. J. Sport Rehabil. 2020, 29, 952–955. [CrossRef] [PubMed]

12. Marotta, N.; Demeco, A.; Moggio, L.; Isabella, L.; Iona, T.; Ammendolia Prof. A. Correlation between dynamic knee valgus and quadriceps activation time in female athletes. J. Phys. Educ. Sport 2020, 20, 2508–2512. [CrossRef]

13. de Sire, A.; Demeco, A.; Marotta, N.; Moggio, L.; Palumbo, A.; Iona, T.; Ammendolia, A. Anterior Cruciate Ligament Injury Prevention Exercises: Could a Neuromuscular Warm-Up Improve Muscle Pre-Activation before a Soccer Game? A Proof-of-Principle Study on Professional Football Players. Appl. Sci. 2021, 11, 4958. [CrossRef]

14. Baldon, R.D.M.; Nakagawa, T.H.; Muniz, T.B.; Amorim, C.F.; Maciel, C.D.; Serrão, F.V. Eccentric hip muscle function in females with and without patellofemoral pain syndrome. J. Athl. Train. 2009, 44, 490–496. [CrossRef] [PubMed]

15. Powers, C.M. The Influence of Altered Lower-Extremity Kinematics on Patellofemoral Joint Dysfunction: A Theoretical Perspective. J. Emerg. Phys. Sci. Ther. 2003, 33, 639–646. [CrossRef]

16. Chevidikunnan, M.F.; Saif, A.A.; Gaowgzeh, R.A.; Mamdouh, K.A. Effectiveness of core muscle strengthening for improving pain and dynamic balance among female patients with patellofemoral pain syndrome. J. Physiol. Sci. 2016, 28, 1518–1523. [CrossRef]

17. Tyler, T.F.; Nicholas, S.J.; Mullane, M.J.; McHugh, M.P. The role of hip muscle function in the treatment of patellofemoral pain syndrome. Am. J. Sports Med. 2006, 34, 630–636. [CrossRef]

18. Villafañe, J.H.; Bissolotti, L.; Touche, R.L.; Pedersini, P.; Negrini, S. Effect of muscle strengthening on perceived pain and static knee angles in young participants with perceived pain and patellofemoral pain syndrome. J. Exerc. Rehabil. 2019, 15, 454–459. [CrossRef]

19. Keays, S.L.; Mason, M.; Newcombe, P.A. Individualized physiotherapy in the treatment of patellofemoral pain. Physiother. Res. Int. 2015, 20, 22–36. [CrossRef]

20. Yosmao güçlü, H.; Sonmez, E.; Ozkoslu, M.; Sahin, E.; Çerezici, S.; Richards, J.; Selfe, J.; Janssen, J. Targeted Treatment Protocol in Patellofemoral Pain (TIPPs): Does Treatment Designed According to Subgroups Improve Clinical Outcomes in Patients Unresponsive to Multimodal Treatment? Sports Health 2019, 12, 170–180. [CrossRef]

21. Dolak, K.L.; Silkman, C.; Mckeeon, J.M.; Hosey, R.G.; Lattermann, C.; Uhl, T.L. Hip strengthening prior to functional exercises reduces pain sooner than quadriceps strengthening in females with patellofemoral pain syndrome: A randomized clinical trial. J. Orthop. Sports Phys. Ther. 2011, 41, 560–570. [CrossRef]

22. Nakagawa, T.H.; Moriya, E.T.U.; Maciel, C.D.; Serrão, F.V. Trunk, pelvis, hip, and knee kinematics, hip strength, and gluteal muscle activation during a single-leg squat in males and females with and without patellofemoral pain syndrome. J. Orthop. Sports Phys. Ther. 2012, 42, 491–501. [CrossRef] [PubMed]

23. Boling, M.C.; Bolgla, L.A.; Mattacola, C.G.; Uhl, T.L.; Hosey, R.G. Outcomes of a Weight-Bearing Rehabilitation Program for Patients Diagnosed With Patellofemoral Pain Syndrome. Arch. Phys. Med. Rehabil. 2006, 87, 1428–1435. [CrossRef]

24. Kozinc, Ž.; Smajla, D.; Sarabon, N. Relationship between hip abductor strength, rate of torque development scaling factor and medio-lateral stability in older adults. Gait Posture 2020. [CrossRef]

25. Nakagawa, T.H.; Maciel, C.D.; Serrão, F.V. Trunk biomechanics and its association with hip and knee kinematics in patients with and without patellofemoral pain. Man. Ther. 2015, 20, 189–193. [CrossRef] [PubMed]

26. Fraeulini, L.; Holzgreve, F.; Maffiuletti, N.; Marcara, S.M. A vertical jump force test for assessing bilateral strength asymmetry in athletes. J. Sports Sci. Med. 2008, 7, 267–269. [CrossRef]

27. Piriya prasarth, P.; Morris, M.E.; Winter, A.; Bialocerkowski, A.E. The reliability of knee joint position testing using electrogoniometry. BMC Musculoskelet. Disord. 2008, 9, 6. [CrossRef]

28. Norkin, C.; White, J.D. Measurement Of Joint Motion: A Guide To Goniometry. Available online: https://books.google.hr/books?hl=sl&lr=&id=TSluDQAQBAJ&oi=fnd&pg=PR1&ots=2h2Qy7BdE_&sig=LJEU65O1rtE4GiYmR2ZL1y7mwE&redir_esc=y#v=onepage&q&f=false (accessed on 27 January 2021).

29. Koczín, Ž.; Sarabon, N. Inter-limb asymmetries in volleyball players: Differences between testing approaches and association with performance. J. Sport. Med. Sci. 2020, 19, 745–752.

30. Workman, C.D.; Fetsiam, A.C.; Rudroff, T. Associations of lower limb joint asymmetry with fatigue and disability in people with multiple sclerosis. Clin. J. Sport Med. 2020, 75, 104989. [CrossRef]

31. Proessl, F.; Ketelhut, N.B.; Rudroff, T. No association of leg strength asymmetry with walking ability, fatigability, and fatigue in multiple sclerosis. Int. J. Rehabil. Res. 2018, 41, 267–269. [CrossRef]

32. Impellizzeri, F.M.; Rampinini, E.; Maffiuletti, N.; Marcora, S.M. A vertical jump force test for assessing bilateral strength asymmetry in athletes. Med. Sci. Sports Exerc. 2007, 39, 2044–2050. [CrossRef] [PubMed]

33. Croisier, J.L.; Reveillon, V.; Ferret, J.M.; Cotte, T.; Genty, M.; Popovich, N.; Filho, M.; Faryniuk, J.E.; Ganteaume, S.; Crielard, J.M. Isokinetic assessment of knee flexors and extensors in professional soccer players. Isokinet. Exerc. Sci. 2003, 11, 61–62. [CrossRef]

34. Cohen, J. Statistical Power Analysis for the Behavioral Sciences. Available online: https://books.google.si/books?id=2v9zDfArsLtvAo&pg=P1&redir_esc=y#v=onepage&q&f=false (accessed on 10 May 2021).

35. Akoglu, H. User’s guide to correlation coefficients. Turk. J. Emerg. Med. 2018, 18, 91–93. [CrossRef]
36. Ferber, R.; Bolgla, L.; Earl-Boehm, J.E.; Emery, C.; Hamstra-Wright, K. Strengthening of the hip and core versus knee muscles for the treatment of patellofemoral pain: A multicenter randomized controlled trial. J. Athl. Train. 2015, 50, 366–377. [CrossRef] [PubMed]

37. Ismail, M.M.; Gamaleldein, M.H.; Hassa, K.A. Closed Kinetic Chain exercises with or without additional hip strengthening exercises in management of Patellofemoral pain syndrome: A randomized controlled trial. Eur. J. Phys. Rehabil. Med. 2013, 49, 687–698. [PubMed]

38. Crowe, M.A.; Bampouras, T.M.; Walker-Small, K.; Howe, L.P. Restricted Unilateral Ankle Dorsiflexion Movement Increases Interlimb Vertical Force Asymmetries in Bilateral Bodyweight Squatting. J. Strength Cond. Res. 2020, 34, 332–336. [CrossRef]

39. Macrum, E.; Bell, D.R.; Boling, M.; Lewek, M.; Padua, D. Effect of limiting ankle-dorsiflexion range of motion on lower extremity kinematics and muscle-activation patterns during a squat. J. Sport Rehabil. 2012, 21, 144–150. [CrossRef]

40. Nakagawa, T.H.; dos Santos, A.F.; Lessi, G.C.; Petersen, R.S.; Silva, R.S. Y-Balance Test Asymmetry and Frontal Plane Knee Projection Angle during Single-Leg Squat as Predictors of Patellofemoral Pain in Male Military Recruits. Phys. Ther. Sport 2020, 44, 121–127. [CrossRef]

41. Brechter, J.H.; Powers, C.M. Patellofemoral joint stress during stair ascent and descent in persons with and without patellofemoral pain. Gait Posture 2002, 16, 115–123. [CrossRef]

42. Noehren, B.; Scholz, J.; Davis, I. The effect of real-time gait retraining on hip kinematics, pain and function in subjects with patellofemoral pain syndrome. Br. J. Sports Med. 2011, 45, 691–696. [CrossRef]

43. Rabelo, N.D.D.A.; Lima, B.; Reis, A.C.D.; Bley, A.S.; Yi, L.C.; Fukuda, T.Y.; Costa, L.O.P.; Lucareli, P.R.G. Neuromuscular training and muscle strengthening in patients with patellofemoral pain syndrome: A protocol of randomized controlled trial. BMC Musculoskelet. Disord. 2014, 15, 157. [CrossRef] [PubMed]

44. Saad, M.C.; de Vasconcelos, R.A.; de Mancinelli, L.V.; de Munno, M.S.; Liporaci, R.F.; Grossi, D.B. Is hip strengthening the best treatment option for females with patellofemoral pain? A randomized controlled trial of three different types of exercises. Braz. J. Phys. Ther. 2018, 22, 408–416. [CrossRef] [PubMed]

45. Ebert, J.R.; Edwards, P.; Preez, L.D.; Furzer, B.; Joss, B. Knee extensor strength, hop performance, patient-reported outcome and inter-test correlation in patients 9–12 months after anterior cruciate ligament reconstruction. Knee 2021, 30, 176–184. [CrossRef] [PubMed]

46. Piva, S.R.; Fitzgerald, G.K.; Irrgang, J.J.; Fritz, J.M.; Wisniewski, S.; McGinty, G.T.; Childs, J.D.; Domenech, M.A.; Jones, S.; Delitto, A. Associates of Physical Function and Pain in Patients with Patellofemoral Pain Syndrome. Arch. Phys. Med. Rehabil. 2009, 90, 285–295. [CrossRef] [PubMed]

47. Magalhães, E.; Silva, A.P.; Sacramento, S.N.; Martin, R.L. FT Isometric strength ratios of the hip musculature in females with patellofemoral pain: A comparison to pain-free controls. J. Strength Cond. Res. 2013, 27, 2165–2170. [CrossRef]

48. Şahin, M.; Ayhan, F.F.; Borman, P.; Atasoy, H. The effect of hip and knee exercises on pain, function, and strength in patients with patellofemoral pain syndrome: A randomized controlled trial. Turk. J. Med. Sci. 2016, 46, 265–277. [CrossRef]

49. Ferber, R.; Kendall, K.D.; Farr, L. Changes in Knee Biomechanics after a Hip-Abductor Strengthening Protocol for Runners with Patellofemoral Pain Syndrome. J. Athl. Train. 2011, 46, 142–149. [CrossRef]

50. Barton, C.J.; Lack, S.; Malliaras, P.; Morrissey, D. Gluteal muscle activity and patellofemoral pain syndrome: A systematic review. Br. J. Sports Med. 2013, 47, 207–214. [CrossRef]

51. Rathleff, M.S.; Richter, C.; Brushøj, C.; Benceke, J.; Bandholm, T.; Hölmich, P.; Thorborg, K. Increased medial foot loading during drop jump in subjects with patellofemoral pain. Knee Surg. Sport. Traumatol. Arthrosc. 2014, 22, 2301–2307. [CrossRef]

52. Molgaard, C.M.; Rathleff, M.S.; Andreassen, J.; Christensen, M.; Lundbye-Christensen, S.; Simonsen, O.; Kaalund, S. Foot exercises and foot orthoses are more effective than knee focused exercises in individuals with patellofemoral pain. J. Sci. Med. Sport 2018, 21, 10–15. [CrossRef]

53. Barton, C.J.; Lack, S.; Hemmings, S.; Tufail, S.; Morrissey, D. The “Best Practice Guide to Conservative Management of Patellofemoral Pain”: Incorporating level 1 evidence with expert clinical reasoning. Br. J. Sport. Med. 2015, 923–934. [CrossRef] [PubMed]