CRITICALLY APPRAISED TOPIC

FOCUSED CLINICAL QUESTION

For a 40 year old female with painful knee joint hypermobility, is strength training more effective than proprioceptive training to improve pain as measured by the Numeric Pain Rating Scale?

AUTHOR

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CLINICAL SCENARIO

This patient is a 40 year old female who was a competitive gymnast in her childhood and active in various other sports and activities throughout adolescence and into adulthood. Her painful knee joint range of motion measurements indicate hyperextension and she has scored a 6 out of 9 on the Beighton test[12], which is indicative of general hypermobility. All lower extremity manual muscle tests are 5/5. She reports daily intermittent knee joint pain in particular during the stance phase of walking beginning with heel strike and relieved with off loading.

Strengthening the muscles around involved joints is a typical treatment in this instance however, those with hypermobility, be it generalized or falling on a scale of hypermobility syndrome, may be experiencing contributing proprioception deficiencies. Proprioceptors provide feedback from muscles, tendons, joint capsules and ligaments responsible for stabilizing joints to ensure limbs are positioned and ready for joint loading. If this is compromised, joints may be in biomechanically unsound positions with ensuing micro-trauma at the joint, which could lead to pain and potentially osteoarthritis[4].

SUMMARY OF SEARCH

Of the eight articles reviewed, two were highly relevant RCTs, one was a highly relevant quasi-experiment and the remaining five articles were observational, cross-sectional studies. As a whole, there was a general mid to low range quality of the studies with regards to addressing the focused clinical question.

Proprioception, balance and strength all seem to contribute to joint hypermobility and were addressed in the intervention studies. Outcomes of these interventions showed significant reductions in pain levels for participants with a potential for increased positive outcomes according to the order in which interventions were performed. However, no study specifically compared strength training to proprioception interventions in those with joint hypermobility.

Future studies should address dosing and timing of each of these aspects of interventions in the adult population to alleviate joint pain.

CLINICAL BOTTOM LINE

The currently reviewed evidence suggests that both proprioception and strength training may be beneficial to those with painful joint hypermobility. Some evidence suggests that the timing of the proprioception intervention may be more or less beneficial per patient however, the overarching consensus is that both interventions aid those with painful joint hypermobility in pain reduction and should be utilized for rehabilitation. Further research is necessary, as the return of applicable evidence based research on this focused clinical question is limited for studies in the adult population as well as management of painful hypermobility.

This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor

SEARCH STRATEGY

Terms used to guide the search strategy			
Patient/Client Group	**I**ntervention (or Assessment)	**C**omparison	**O**utcome(s)
Knee Hypermobility Knee Hypermobile Knee Hyperlaxity Knee Laxity Knee Instability	Strength training Resistance training Therapeutic exercise Physical exercise Strengthen	Proprioceptive training Proprioception Kinesthesia	Pain Pain Relief Analgesia Numeric Pain Rating Scale

Final search strategy (history):

1. Knee AND (hypermobility OR hyperlaxity OR hypermobile OR laxity)
2. Strength training OR resistance training OR therapeutic exercise OR physical exercise
3. Proprioceptive training OR proprioception
4. Pain OR pain relief OR analgesia OR Numeric Pain Rating Scale
5. #1 AND #2 AND #3 AND #4
6. #1 OR (knee AND instability)
7. #2 OR strengthen
8. #3 OR kinesthesia
9. #6 AND #7 AND #8 AND #4
10. #6 NOT anterior cruciate ligament
11. #10 AND #7 AND #8 AND #4

Databases and Sites Searched	**Number of results**	**Limits applied, revised number of results (if applicable)**
PubMed	**17**	
CINHAL	**9**	**To increase results:** **-added 'joint laxity' and 'joint instability'** **-added 'strengthening exercise', 'kinesiotherapy' and 'exercise' to intervention** **-added 'joint propriocpetion' to comparison** **-added 'WOMAC score' and 'joint stiffness' to outcomes**
Embase	**14**	**To increase results per the site dropdown recommendations:** **-added 'joint laxity' and 'joint instability' to population** **-added 'strengthening exercise', 'kinesiotherapy' and 'exercise' to intervention** **-added 'joint propriocpetion' to comparison** **-added 'WOMAC score' and 'joint stiffness' to outcomes**

INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
Randomized controlled trials, clinical trials, meta-analysis, systematic reviews Published in English
Exclusion Criteria
Abstracts, conference proceedings, letters to the editor, dissertations, narrative review articles

RESULTS OF SEARCH

Summary of articles retrieved that met inclusion and exclusion criteria

Author (Year)	Risk of bias (quality score)*	Level of Evidence**	Relevance	Study design
Ferrel (2004)[1]	Modified Downs and Black Score: 17/29	IIb	High	Quasi-experimental: Repeated pretest – post test design
Sahin (2008)[2]	PedRo Scale: 4/11	Ib	High	RCT
Knoop (2014)[3]	PedRo Scale: 9/11	Ib	High	Subgroup Analysis of Single-blinded RCT
Hall (1995)[4]	Modified Downs and Black Score: 12/29	IV	Moderate	Observational, cross sectional study
Van der Esch (2016)[5]	RoBANS: Low Risk of Bias (5 Low, 1 Unclear)	IIb	Moderate	Observational, prospective, longitudinal Cohort Study
Pacey (2014)[6]	Modified Downs and Black Score: 22/29	IV	Low	Observational, cross sectional study
Sanchez-Ramirez (2013)[7]	Modified Downs and Black Score: 21/29	IV	Low	Observational, cross sectional study
Bayramoglu (2007)[8]	Modified Downs and Black Score: 19/29	IV	Low	Observational, cross sectional study

*Indicate tool name and score

**Use Portney & Watkins Table 16.1 (2009); if downgraded, indicate reason why

BEST EVIDENCE

The following 2 studies were identified as the 'best' evidence and selected for critical appraisal. Rationale for selecting these studies were:

- **Knoop (2014)[3]: PedRO 9/11, 1b Level of Evidence and High Relevance. This article was selected for critical appraisal because it was one of the articles most closely related to the focused clinical question with a well-designed study and low bias. It compares a group of participants with an intervention of strength and proprioception training (through stabilization exercises) to a group with just strength training, which most closely addresses the focused clinical question intervention and comparison groups.**
- **Ferrel (2004)[1]: Downs & Black 19/29, 2b Level of Evidence and High Relevance. This article was selected for critical appraisal because it was also an article most closely related to the focused clinical question with a well-designed study and low bias. It utilized a subgroup of participants to act as their own control and incorporated progressive strength and balance exercises over an eight week period for all participants.**

SUMMARY OF BEST EVIDENCE

(1) Description and appraisal of "Knee joint stabilization therapy in patients with osteoarthritis of the knee and knee instability: Subgroup analyses in a randomized, controlled trial." by Knoop J, Leeden M, Roorda L et al. 2014

Aim / Objective of the Study / Systematic Review:
The purpose of this study was to compare the effects of knee stabilization therapy prior to strength/functional training to that of strength/functional training alone for added benefit in knee activity limitations for those with knee osteoarthritis and knee instability accompanied by either decreased leg strength, impaired knee proprioception, increased knee laxity or frequent episodes of knee instability.
Study Design
This study was a subgroup analysis of a previous single-blinded randomized controlled trial called STABILITY. This trial report[9] was accessed and used to verify details pertaining to this subgroup analysis. Participants were measured at baseline, 6 weeks (midway through treatment), 12 weeks (end of treatment), and 38 weeks (post treatment follow up) Blinding: One trained research assistant was blinded for measurement assessment and group allocation. Randomization: Prior to interventions, groups were randomly allocated via computer using a permutated block randomization procedure to ensure equal sample sizes of the two treatment groups. Allocation: Group allocation was concealed through use of opaque, sealed envelopes that were numbered consecutively. Data collection/Analysis methods: Data was analyzed with an intention to treat approach using a generalized estimating equation (GEE) analysis model. The GEE model calculated significant interactions by including the treatment group or control group along with the subgroup factor to analyze effect modification. Estimates of p-values and unstandardized regression coefficients with 95% confidence intervals (CI) were included with a p-value of < 0.05 indicating statistical significance. The primary outcome for this study was the WOMAC score however, the numeric rating for pain was a secondary outcome measure that correlates with the focused clinical questions.
Setting
Reade, centre for rehabilitation and rheumatology, Amsterdam, the Netherlands, an outpatient rehabilitation center.
Participants
Participants were recruited over a 25-month period via advertisements in newspapers as well as rheumatologist or rehab physician referrals from the Reade center. Every three months, a new group of sixteen participants were selected and randomly allocated to an experimental and control group (8 participants in each group) per session. This study was comprised of 11 trial sessions in total. Potential participants were first screened via questionnaire and phone call by the researcher along with a physical exam. Participants were then included in the study if they had been diagnosed with knee osteoarthritis using the American College of Rheumatology criteria. Participants were also included only if they were between the ages of 40 and 75 years old with the presence of knee instability in the past three months. The knee instability could be self-reported or biomechanically assessed. Participants were excluded if they were found to have forms of arthritis other than osteoarthritis, severe activity limitations as a result of comorbidity, or have had or would soon have a total knee arthroplasty. A total of 159 participants were included in this study. 5 participants were lost to follow up and not included in the analysis, 2 participants in the experimental group discontinued the intervention while 2 participants from the control group and 2 participants from the intervention group underwent knee surgery after treatment.

Experimental group:

n=80 (1 was lost to follow-up before the first follow-up measurement and not analyzed, 2 discontinued intervention, 2 underwent knee surgery after treatment)

mean age: 62.1 $\pm$7.6

66% women

mean BMI: 28.8 $\pm$4.8 kg/m^2

61% K/L grade $\geq$2 (radiographic severity of knee)

WOMAC score: 25.2 $\pm$11.8 (physical function)

NRS score: 4.8 $\pm$2.2 (knee pain severity)

Get Up and Go test: 10.6 $\pm$1.8 sec

Upper leg muscle strength: 0.83 $\pm$0.35 Nm/kg^2

Proprioceptive accuracy of knee: 2.7 $\pm$2.2

Varus-valgus laxity of knee: 7.0 $\pm$3.1

30% patient-reported knee instability in previous 6 weeks

Control group:

n=79 (4 were lost to follow-up before the first follow-up measurement and not analyzed and 2 underwent knee surgery after treatment)

mean age: 61.8 $\pm$6.6

56% women

mean BMI: 28.3 $\pm$4.5

68% K/L grade $\geq$2 (radiographic severity of knee)

WOMAC score: 27.1 $\pm$12.7 (physical function)

NRS score: 5.2 $\pm$2.0 (knee pain severity)

Get Up and Go test: 10.8 $\pm$2.5 sec

Upper leg muscle strength: 0.85 $\pm$0.43 Nm/kg^2

Proprioceptive accuracy of knee: 3.7 $\pm$2.6

Varus-valgus laxity of knee: 7.1 $\pm$4.5

30% patient-reported knee instability in previous 6 weeks

Intervention Investigated

Control

Each week patients participated in two 60-minute exercise sessions supervised by two physical therapists and were given home exercises to be performed the other five days of the week. Physical therapists did not provide feedback or instructions regarding knee positioning.

Week 1 focused on muscle strengthening exercises of low intensity with minimal loading of the knee similar to the experimental group. This weeks sessions were performed in the pool. This group also received education on knee OA.

Weeks 2-4 focused on muscle strengthening/muscle endurance exercises with minimal loading of the knee similar to the experimental group. This weeks sessions (and all weeks after) were performed on land. This group also received education on knee OA.

Weeks 5-8 continued with muscle strengthening/muscle endurance exercises but with an increase in the amount of load on the knee as well as training intensity.

Weeks 9-12, focused on muscle strengthening/maximal muscle power exercises. There was also an addition of functional and aerobic exercises, which were similar to the experimental group.

Experimental

Each week patients participated in two 60-minute exercise sessions supervised by two physical therapists

and were given home exercises to be performed the other five days of the week. Physical therapists provided verbal and tactile cues for proper knee positioning as well as visual cues via mirrors.

Week 1 focused on knee joint stabilization exercises of low intensity with minimal loading of the knee similar to the control group consisting of 3 sets of 15 reps that focused on knee position perception, motions that improve proprioceptive accuracy and neuromuscular control. This weeks sessions were performed in the pool.

Weeks 2-4 were similar to week one however, all exercises were land based. There were also three sessions providing patients with information about OA, risk factors and how to self-manage OA.

Weeks 5-8 consisted of sessions and exercises with increased difficulty from the previous weeks stabilization training while also incorporating muscle strengthening/endurance exercises similar to those of the control group. Exercises intensity and loading increased during the weeks along with an increase in reps from 15 to 20 by week 8.

Weeks 9-12 consisted of sessions and exercises with increased difficulty from the previous weeks stabilization training once again while also incorporating muscle strengthening/maximal muscle power exercises similar to those of the control group at 3 sets of 10 reps. Additionally, patients were given tailored exercises that were specific to daily activities the individuals believed were problematic along with aerobic training.

The original study had a supplementary file attachment that was available to download containing each exercise performed by those in the experimental group.

Outcome Measures

One trained research assistant assessed each outcome measure.

Primary Outcome Measure:

- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale physical function: The WOMAC is a self-reported questionnaire pertaining to pain, stiffness and function in those with osteoarthritis of the hip or knee. The subscale of physical function consists 17 questions related to difficulty performing activities such as don/doff socks, shopping, sitting, standing, lying down, or navigating stairs. A Likert Scale version was used and each of these questions was given a numeric value according to a scaled rating. No difficulty receives a score of 0 while extreme difficult receives a score of 4. The scores were then summed together with 0 being the lowest possible score indicating no limitations of physical function and 68 being the highest score possible indicating maximal physical function limitations.

Secondary Outcome Measures:

- Numeric rating for knee pain severity: Participants were asked “What was your average knee pain during the last week?” and asked to reply with a number on a scale of 0-10 in which 0 represents no pain and 10 represents the worst pain imaginable.
- Get Up and Go (GUG) Test: This is a timed performance test in which the participant rises from a standard height chair and walks for 15 meters over an even, level surface as quickly as possible. Time is recorded in seconds.

Main Findings

Unstandardized regression coefficients (B) were used to notate change difference in primary and secondary outcomes between stratified subgroups as a result of the experimental intervention. Statistically significant differences were found for the following as noted by the p-values:

- WOMAC, physical function subcategory
    - Baseline upper leg muscle strength
        - B = -7.07
        - 95% Confidence Interval (CI) = -12.39 to -1.75
        - P-value=0.01
- NRS pain scale
    - Baseline varus-valgus knee joint laxity
        - B = 0.18
        - 95% CI = 0.07 to 0.29
        - P-value < 0.001
- GUG test
    - Baseline patient-reported knee instability
        - B = -0.58

        - 95% CI = -1.13 to -0.02
        - P-value = 0.04

No data is offered however, Figure 1 provides visual representation, through graphs of the effect sizes of the control or experimental interventions for stratified subgroups. They are plotted per significant outcome measure findings (WOMAC or NRS) at each time of measurement (baseline, 6 weeks, 12 weeks and 38 week follow up).

Estimated values from the graphs are as follows:

- WOMAC (physical function subscale) Score
    - Low muscle strength subgroup
        - Control group
            - Baseline (T0) = 31
            - 6 weeks (T6) = 24.5
            - 12 weeks (T12) = 20.5
            - 38 week follow up (T38) = 21
                - Estimated absolute effect size from baseline to end of intervention = 10.5
                - Estimated absolute effect size from baseline to follow up = 10
        - Experimental group
            - T0 = 26
            - T6 = 24
            - T12 = 20
            - T 38 = 20
                - Estimated absolute effect size from baseline to end of intervention = 6
                - Estimated absolute effect size from baseline to follow up = 6
    - High muscle strength subgroup
        - Control group
            - T0 = 23
            - T6 = 20
            - T12 = 17
            - T38 = 16
                - Estimated absolute effect size from baseline to end of intervention = 6
                - Estimated absolute effect size from baseline to follow up = 7
        - Experimental group
            - T0 = 24
            - T6 = 19.5
            - T12 = 14
            - T 38 = 15
                - Estimated absolute effect size from baseline to end of intervention = 10
                - Estimated absolute effect size from baseline to follow up = 9

    - These findings indicate that for those with low baseline muscle strength, there was no difference in WOMAC score changes for those in the control or experimental groups. However, for those with high baseline muscle strength, there was greater improvement in WOMAC scores for those who received the experimental intervention than for those who were in the control group. Minimal Detectable Change (MDC) reports for the WOMAC varies according to study and joint assessed however, one report is a MDC90 of pain is 3.94 points in which all subgroups in each group achieved. However, another report assessed an MDC95 for knee OA at 2 months to be 14.1 points[13], in which no group or subgroup achieved.
- NRS Pain Score
    - High laxity subgroup
        - Control group
            - T0 = 4.5
            - T6 = 4
            - T12 = 3
            - T38 = 3.5
                - Estimated absolute effect size from baseline to end of intervention = 1.5

        - Estimated effect size from baseline to follow up = 1
    - Experimental group
        - T0 = 5
        - T6 = 4
        - T12 = 3
        - T38 = 3.5
            - Estimated absolute effect size from baseline to end of intervention = 2
            - Estimated absolute effect size from baseline to follow up = 1.5
- Low laxity subgroup
    - Control group
        - T0 = 5.2
        - T6 = 4
        - T12 = 3.5
        - T38 = 3.8
            - Estimated absolute effect size from baseline to end of intervention = 1.7
            - Estimated absolute effect size from baseline to follow up = 1.4
    - Experimental group
        - T0 = 4.2
        - T6 = 3
        - T12 = 2.5
        - T38 = 2.1
            - Estimated absolute effect size from baseline to end of intervention = 1.7
            - Estimated absolute effect size from baseline to follow up = 2.1
- High-frequent instability subgroup
    - Control group
        - T0 = 5
        - T6 = 4.2
        - T12 = 3.5
        - T38 = 4
            - Estimated absolute effect size from baseline to end of intervention = 1.5
            - Estimated absolute effect size from baseline to follow up = 1
    - Experimental group
        - T0 = 6
        - T6 = 3.9
        - T12 = 3.5
        - T38 = 3
            - Estimated absolute effect size from baseline to end of intervention = 2.5
            - Estimated absolute effect size from baseline to follow up = 3
- Low-frequent instability subgroup
    - Control group
        - T0 = 5
        - T6 = 3.9
        - T12 = 3
        - T38 = 3.2
            - Estimated absolute effect size from baseline to end of intervention = 2
            - Estimated effect size from baseline to follow up = 1.8
    - Experimental group
        - T0 = 4
        - T6 = 3.4
        - T12 = 2.3
        - T38 = 2.9
            - Estimated absolute effect size from baseline to end of intervention = 1.7
            - Estimated absolute effect size from baseline to follow up = 1.1

- These findings indicate that for those with lower knee joint laxity or more frequent episodes of knee instability, there were greater improvements in NAS pain scores for those who received the experimental intervention than for those who were in the control group. According to one source, there is no established MDC or MCID for this patient population to assess significance of change in pain[14].

Original Authors' Conclusions

The original authors concluded that knee stabilization exercises prior to strengthening exercises may be beneficial for those who already had strong upper leg muscles. However, for those with weaker upper leg muscle strength, strength training prior to knee stabilization training may be more effective. The authors also concluded that for those with knee instability but minimal knee joint laxity, stabilization training may be beneficial prior to strengthening. And finally, for patients with frequent knee instability episodes, stabilization training prior to strength training may be more beneficial.

Critical Appraisal

Validity

PEDro Scale score: 9/11 based on Edibility Criteria: yes; Random Allocation: yes; Concealed Allocation: yes; Baseline Comparison: yes; Blind Subjects: no; Blind Therapist: no; Blind Assessors: yes; >85% Participant Outcomes: yes; Intention to Treat Analysis: yes; Between-Group Comparison: yes; Point Estimates and Variability: yes

A score of 9/11 on the PEDro scale is relatively high and therefore it can be assumed that this trial has high internal validity and that there was enough statistical information provided in the study for interpretation.

A limitation of this study, as reported by the authors, is that fact that although the original study had sufficient power, this study was not adequately powered for the subgroup analysis.

There is also a potential for confounding as the interventions for both groups required the participants to perform at home exercises four days a week. Compliance or improper execution of the exercises may affect the outcomes.

Another limitation of this study is the absence of numerical data for the outcome scores and standard deviations used to generate the information presented in Figure 1. Means plotted could be estimated however, without the standard deviation information, assessment by readers for statistical significance was lacking.

As a strength, although they were unable to be blinded for this study, the physical therapists were assigned to just one treatment arm and were specifically trained for those interventions. They also received booster training after each 12 week session that may limit confounding.

The random allocation of participants to control and experimental groups is also a strength of their study.

It is unclear if the interventions for the control group were appropriate in comparison to the interventions for the experimental group. The original study had a supplementary file that could be downloaded listing the exact exercises and regime for those in the experimental group, however there was no such attachment for the control group exercises. Generalizations made in this study as to the control interventions lead the reader to think that these exercises were similar.

Good

Interpretation of Results

The results of the study suggest those with greater upper leg strength would benefit more from initial proprioceptive training prior to strength training while those with lower leg strength would benefit from the opposite. This indicates a potential hierarchy of importance in rehabilitation for those with joint instability as if sufficient strength is essential to facilitate proprioception, however, none of the articles analyzed refer to this so further study is essential.

While a main limitation noted by the authors of this study is insufficient power, there was a statistically significant result for those with high leg muscle strength benefiting from proprioceptive training prior to strength training. So for this observed effect, there was sufficient power.

As previously stated, the lack of numerical data is of concern and limits further ability of the reader to determine meaningfulness of the change in pain values, however, the plot graphs are a helpful way to

portray the findings. Using MCDs from other studies, it could be inferred that there was a significant clinical change for the WOMAC scores in relation to the muscle strength subgroups. I would question the author's use of "high" and "low" to describe the stratified subgroups as this makes it difficult to compare and apply these findings to particular patients, as there is no scale for the amount of difference there were between the two.

Applicability of Study Results

An issue with utilizing the results from this study as an answer to the focused clinical question is that the patient demonstrates knee hypermobility while the study addresses knee instability along with other knee joint issues. While many patients with joint hypermobility may also experience joint instability, they may not be successfully substituted for one another with the hopes of producing the same outcomes. Further investigation and conversations with the patient may reveal that there are knee instability sensations and episodes that contribute to knee pain.

The observed effect of proprioceptive training prior to strength training is clinically relevant to the focused clinical question in the fact that the scenario involves an active individual with 5/5 tested leg muscle strength. Compared to the baseline characteristics of the study group, this patient is quite a bit younger than the mean age of each group by about 20 years, which should be taken into consideration. However, the patient is female as were a majority of those in the study. The patient BMI should be assessed and compared for similarity to those in the study as well.

The interventions were at-home and clinic based exercises that were described as being similar to if not exactly the same exercises typically prescribed in physical therapy. There seems to be little to no risk of injury and only potential benefits of decreasing pain with these exercises. With the exception of the hydrotherapy session requiring a pool, there was no special equipment required so the intervention would be extremely practical and feasible to implement into practice.

The measure of change for which this effect was most relevant was in the WOMAC subscale for physical function. While this doesn't directly address alleviation of pain, it does address daily functional movements. It would be important to understand the patient's individual thoughts about the ways her knee issues interfere with her life and her goals for physical therapy to ensure that her values and expectations align with the intervention potential outcomes.

(2) Description and appraisal of "Amelioration of symptoms by enhancement of proprioception in patients with joint hypermobility syndrome." by Ferrel et al. 2004

Aim / Objective of the Study / Systematic Review:

The aim of this study was determine if a home-based exercise program could improve knee joint proprioception and alleviate symptoms reported by those with joint hypermobility syndrome (JHS).

Study Design

This study was a quasi-experimental study with a repeated pretest / post-test design. There was no blinding or randomization noted for subjects, assessors or data analysis.

All participants were to complete an 8 week at home exercise program consisting of various proprioception, balance and strengthening exercises.

Half of the participants (10), the subgroup, were assessed after recruitment and then again 2-8 weeks later, before the treatment intervention began. They were assessed one more time after completion of the 8 week home exercise program.

The other half of the participants (10) were assessed after recruitment and then again after completion of the 8 week home exercise program.

There was no mention of who performed the assessments or who prescribed the home-exercises to the patients.

During the period between assessment and treatment, patients in both the subgroup and treatment group were given similar attention to that provided during treatment via phone access to medical and physiotherapy staff as well as advice regarding exercise and analgesia.

There was one follow-up meeting between participants and physiotherapy to assess compliance, which was tracked via individual exercise diaries.

Comparisons of normally distributed data were performed by paired t-test. Comparisons of non-normally distributed data used the median as the measure of central tendency while interquartile range showed the variability. For paired before and after treatment comparisons, the Wilcoxon signed rank test was used.

The primary outcome for this study appears to be proprioception acuity however, the visual analog scale for pain was a secondary outcome measure that correlates with the focused clinical questions.

Setting

Although patients were recruited from a hypermobility clinic, it is assumed assessment activities also occurred at this outpatient facility. Patients were given exercises to be performed at home.

Participants

Participants were recruited from the Glasgow Royal Infirmary hypermobility clinic.

Eligibility Criteria: Patients recruited to the program required the presence of 2 major criteria from the revised Brighton or 1 major and at least 2 minor criteria. Major criteria included joint hypermobility >4 (this was based on the Beighton scoring system) or arthralgia in $\geq$4 joints for more than 3 months. Minor criteria included the dislocation/subluxation of joints, skin signs considered to be abnormal relative to joint hypermobility syndrome, hernia or prolapse, or soft tissue rheumatism. Additionally, patients had to be experiencing knee joint pain. No exclusion criteria were listed.

There were originally 20 participants however, 2 did not complete the study because they relocated.

Baseline Characteristics:

n=18

gender: 2 male, 16 female

mean age: 27.3 $\pm$10.4 years (range 16-49 years)

mean Beighton score: 6.3 $\pm$ 1.7 (range 4-9)

mean Contompasis score: 33.4 $\pm$ 5.6 (range 23-42)

Intervention Investigated

Control

This was a single group study therefore, there was no control group.

Experimental

Subset treatment group: After initial assessments, a group of 10 patients returned 2-8 week later for reassessment. These patients then proceeded with the same 8 week treatment as the treatment group listed below.

Treatment group: After initial assessments, this group participated in a standardized 8 week physiotherapy program to be performed at home for 4 out of 7 days. This program included closed kinetic chain and static hamstring exercises during the timeline as follows:

Week 1: 1 set of 5 reps of squats, pliés and bridges

Week 2: 2 sets of 5 reps of squats, pliés and bridges

Week 3: 2 sets of 5 reps of squats, pliés, bridges and front lunges

Week 4: 4 sets of 5 reps of squats, pliés, bridges and front lunges

Week 5: 1 sets of 10 reps of squats, pliés, bridges, front lunges, static hamstring exercise and balance board exercise for 2 minutes/3 reps

Week 6: 2 sets of 10 reps of squats, pliés, bridges, front lunges, static hamstring exercise and balance board exercise for 2 minutes/4 reps

Week 7: 1 sets of 15 reps of squats, pliés, bridges, front lunges, static hamstring exercise, side lunge and balance board exercise for 2 minutes/3 reps

Week 8: 2 sets of 15 reps of squats, pliés, bridges, front lunges, static hamstring exercise, side lunge and balance board exercise for 2 minutes/3 reps

During the period between assessment and treatment, patients were given similar attention to that provided during treatment via phone access to medical and physiotherapy staff as well as advice regarding exercise and analgesia.

There was one follow-up meeting between participants and physiotherapy to assess compliance however, there is no mention of exactly when this took place during the 8 week intervention.

Outcome Measures

It is unclear who administered these measures or if they were blinded to the study.

Knee joint proprioception using Threshold Angle (degrees): The authors referenced the method used in an article by Hall[10]. In general, knee joint proprioception was assessed on the painful knee only using a device that rotates at a constant velocity via a computerized stepper motor. The participant is in side lying with a fixed thigh and an aircast around the lower leg. They are given a device to stop the motor once they detect movement of the lower leg and knew in which direction it was being moved. The angular displacement at this point was recorded. A decrease in the angular displacement before detection is favorable.

Balance using an instrumented balance board: Participants were assessed on their ability to hold an instrumented balance board within eight degree of horizontal in both the anterior-posterior and medial-lateral directions. They were allowed 3 trials consisting of 30 seconds each with their final value being an average of the trials quantified as percent time out of balance. The ability to hold the board within eight degrees of horizontal for each of the 30 seconds trials is favorable.

Muscle strength using an isokinetic dynamometer: Peak and average strength of both the quadriceps and hamstring muscles were tested three times at a setting of 60 degree/minute and 120 degree/minute. Values at each speed were averaged for a final outcome.

The Short Form 36[15] (SF 36) was used as a measure of quality of life. It is a self-reported questionnaire addressing 8 subscales of physical functioning, physical and emotion limitations, general health perception, vitality, social functioning, mental health and health transition. Scores range from 0-100 with a lower score indicating more disability and a higher score indicating less disability.

Knee joint pain using a visual analog scale (VAS) of 0-10. A score of 0 represents no pain and a score of 10 represents the worst imaginable pain.

Main Findings

To rule out a learning effect of assessments for proprioception, balance, muscle strength as well as quality of life and pain perception, a subset of 10 patients were re-tested after initial assessments (2-8 weeks later) but before treatments began. There were no significant differences in any scores between the two pretests for the subset treatment group indicating no learning effect for measures.

Paired t-tests were used to compare differences from baseline to subset retest to 8 weeks after home exercise program began.

Significant differences found for proprioception:

- Mean difference was reduced from 1.07 ($\pm$ 0.07) degrees to 0.79 ($\pm$ 0.04) degrees = 0.28 degree difference
- P-value < 0.001
- The largest improvements were made by those participants with poorest initial proprioception scores signifying a significant correlation between percentage changes after treatment (r=0.45, P=0.006)
    - Indicating a medium to large effect size using standardized effect size for correlation

Significant differences found for balance:

- Mean difference was reduced from 8.5 ($\pm$ 1.6)% to 4 ($\pm$ 0.7)% = 4.5% difference
- P-value < 0.001
- The largest improvements were made by those participants with poorest initial balance scores signifying a significant correlation between percentage changes after treatment (r=0.43, P=0.008)
    - Indicating a medium to large effect size using standardized effect size for correlation

Significant differences found for muscle strength:

- Median difference for quadriceps peak torque was increased from 144 (111-127 interquartile range) Nm to 147 (105-172) Nm = 3 Nm difference
- P-value for quadriceps peak torque increase was 0.038
- Median difference for quadriceps average torque was increased from 107 Nm (79-127) Nm to 120.6 (92-147) Nm = 13.6 Nm difference

- P-value for quadriceps average torque increase was 0.0002
- Median difference for hamstring peak torque was increased from 90.5 (76-119) Nm to 103.5 (86-123) Nm = 13 Nm
- P-value for hamstring peak torque increase was 0.002
- Median difference for hamstring average torque increase was 70 (58-80) Nm to 75 (64-82) Nm = 5 Nm difference
- P-value for hamstring average torque increase was 0.0065

Significant differences found for SF-36:

- Physical functioning domain:
    - Overall summary median score increase from 43.5 (28.1-64.0) to 52.6 (42.0-75.3) points = 9.1 points difference
    - Overall summary median score increase p-value=0.029
        - Role limitation due to physical problems median score increase from 12.5 (0.0-50.0) to 37.5 (33.3-70.8) = 25 points difference
        - Role limitation due to physical problems median score increase p-value =0.016
        - Bodily pain median score increase from 44.4 (25.0-55.6) to 55.6 (30.0-70.8) = 11.6 points difference
        - Bodily pain median score increase p-value=0.039
- Mental health domain:
    - Overall summary median score increase from 50.1 (39.6-77.5) to 77.9 (65.9-90.0) = 27.8 points difference
    - Overall summary median score p-value=0.008
        - Role limitation due to emotional problems median score increase from 66.7 (33.3-100) to 100.0 (75.0-100.0) = 33.3 points difference
        - Role limitation due to emotional problems median score increase p-value=0.019
        - Mental health median score increase from 68.8 (57.0-79.0) to 80.0 (73.0-88.0) = 11.2 points difference
        - Mental health median score increase p-value=0.0023

Significant differences found for joint pain using VAS:

- Mean difference using the VAS decreased from 4.2 ($\pm$ 0.4) to 2.5 ($\pm$ 0.5) = 1.7 difference
- P-value = 0.003

Original Authors' Conclusions

The original authors concluded that physiotherapy can improve knee joint proprioception, improve balance, decrease symptoms of pain and improve physical function and mental health. They go on to note the proprioceptive and balance performances of the patients after exercises matched those found in subjects with normal mobility.

Critical Appraisal

Validity

Downs and Black Checklist Score: 17/29 based on clearly described Aim of Study: yes; Main Outcomes Measured; yes; Characteristics of Patients: yes; Interventions: yes; Principal Confounders: no; Main Findings: yes; Estimates of Random Variability: yes; Adverse Events Reported: yes; Characteristics of Patients Lost to Follow Up: yes; Actual Probability Values: yes; Subjects Asked Representative of Population: unable to determine; Subjects Prepared Representative of Population: unable to determine; Majority of Treatment Represented: yes; Attempt to Blind Subjects: no; Attempt to Blind Assessors: no; Results from Data Dredging: yes; Time Period Considerations: yes; Appropriate Tests: yes; Reliable Compliance: yes; Accurate Main Outcome Measures: yes; Same Population Recruitment: yes; Recruitment Over Same Time: unable to determine; Randomization to Intervention: no; Concealed Randomization: no; Confounding Analyses Adjustment: unable to determine; Accounting for Loss to Follow-up: yes; Power Analysis Reported: no

This score of 17/29 which could be interpreted as a fair score however, it can be noted that the area of the checklist with the lowest score were those concerned with internal validity.

The authors recognized that a limitation of the study was not having a control group who did not participate in exercises and that more information could be acquired if future research included a larger sample size.

The authors also report on normal mobility values and referenced previous studies[11] as well as unpublished observations as sources raising question of the validity of this correlation.

There are several areas of concern for the internal validity of this study.

- There was no mention of blinding of assessors. In fact, there is no mention as to who the assessors were, if the initial assessors also performed the subgroup intermediate assessment measurements or the final post-intervention assessment.
- There is also no mention of randomization of those who were part of the subgroup treatment group or if there was blinding of participants as to if they were part of the subgroup or general treatment group.
- It was noted that during the 8 week intervention program, there was a follow-up meeting between staff and patient. However, there is no mention as to where this occurred, what was discussed during this meeting and whether or not all patients received the same information during this meeting or any information at all that may have influenced performance and outcomes. There is also no mention as to when this meeting occurred during the intervention.
- There is a potential for confounding that was not addressed. There is no mention of how the participants were instructed to perform their home exercises. They could have received written, verbal and/or visual instruction in various forms from various instructors or resources that influenced the exercise performance and therefore the results.

In general, aspects of the external validity of the study that could be considered strengths:

- The entire 8 week intervention program consisted of exercises able to be performed at home.
- Aside from a balance board that is relatively easy to obtain, there was no special equipment required to perform the at-home exercises.

Interpretation of Results

The results of this study suggest that closed kinetic chain and balance exercises significantly improve knee joint proprioception, balance, strength, quality of life and pain in those with joint hypermobility. There was a lack of information provided about the participant allocation and the manner in which they received their instruction however, considering a worst case scenario in which the participants received poor instruction and performed the at-home exercises incorrectly, the results were still significant. For the best-case scenario in which they received excellent instruction and feedback and performed ever at-home exercise perfectly, which is what should be utilized in an outpatient PT setting, the results were still significant.

There was no mention of the power for this study however, there were statistically significant results therefore, it can be concluded that it was sufficiently powered. There is concern for the small amount of participants as well as the wide variance for some of the reported data in particular to that concerning the SF-36 outcomes. These elements could impact the effect size demonstrated in the results.

There is no known MCID or MDC for clinical significance with regards to the proprioception, balance or strength tests however, the p-values reported show a statistically significant difference for all three. The SF-36 has been noted as having a MCID for chronic musculoskeletal pain[15] of 1. If this is used as a clinical significance standard, then it definitely has clinical significance. For clinical significance of changes in pain, it would be essential to find out what

These results suggest that a home exercise program for patients with painful knee joint hypermobility may be beneficial for gains of strength, proprioception and balance. They may also be beneficial for improving the patient's quality of life and significantly decreasing pain.

Applicability of Study Results

As previously mentioned, the results of this study showed significant improvements in all aspects studied. The described interventions and duration of treatment (4 days a week for 8 weeks) were practical and feasible to easily implement into treatment sessions as well as home exercise programs. With regards to the focused clinical question, this study does not discern between the results of proprioception training versus the results of strength training however it is still clinically relevant with reduction in pain and all other aspects of improvement. The closed kinetic chain exercises used for muscular strengthening were chosen for this intervention because they required lower extremity muscular co-contraction to perform these exercises known to promote knee joint stability. These exercises are also thought to increase the knee joint intraarticular pressure, which in turn stimulates Ruffini nerve endings that detect joint position to facilitate joint proprioception.

The subjects utilized for this study were mostly female with a mean Beighton score of 6.3 which correlates well with the focused clinical question patient. However, there is a difference in the mean age with the study participants being approximately 12 years younger than the patient but the age range did extend to 49 years. Being that the listed exercises are similar if not exactly the same exercises as those typically utilized in physical therapy sessions, it could be assumed that these exercises are in general safe to perform with a minimal amount of pain inflicted. The benefits certainly outweigh the risks of having this patient perform

these exercises to potentially decrease knee joint pain. It would be important include the patient on the plan to use these types of exercises for similar potential improvements and ensure they align with her values and expectation of physical therapy.

SYNTHESIS AND CLINICAL IMPLICATIONS

Evidence Synthesis:

Of the evidence reviewed in this analysis, no study specifically compared strength training to proprioception interventions in those with joint hypermobility. As a whole, there was a general mid to low range quality of the studies with regards to addressing areas of the focused clinical question. A majority of the articles reviewed were cross-sectional studies that were lower level evidence and by nature did not include interventions. However, they did note the current levels of strength, balance and proprioception for those with joint hypermobility as concern and potential sources for intervention. Overall the evidence in support of proprioceptive over strength training is lacking and poor.

Implications for Clinical Practice:

The studies reviewed implied that those with hypermobile joints could benefit from proprioception, balance and strength training for alleviation of pain. The studies listing interventions utilized exercises that employed each of these through methods that were easy to execute in a clinic or for use in home exercise programs. They would be relatively easy for most patients to learn and understand and could be modified to match the current abilities of patients and progressed when gains are made as appropriate. The fact that there was a heavy reliance of home exercises contributing to positive results also speaks to the applicability of these exercises to be included in home exercise programs.

Implications for Future Research:

Future research would benefit from assessing outcomes for proprioception only compared to balance training only and strength training only for this population, as these are the major areas of concern for those with hypermobile joints. This information could be helpful to assess which aspect is the greatest contributor to symptoms associated with hypermobility. Cross-over design studies could also be beneficial to assess variations in order or dosing as potential ways to improve patient outcomes. A majority of research articles for hypermobility in an initial search returned participants who were children with an obvious lack of valid studies on adults, so this too could be an area to address. Future research could also benefit from unifying or clarification of classification for those with joint hypermobility. This was found to be a source of confusion in comparison of participants per study. The terms used were joint hypermobility syndrome, benign joint hypermobility syndrome, generalized hypermobility and hypermobility syndrome, yet the distinctions between these were often not discernable or varied from study to study. In general, there is a lack of evidence for effective interventions in the adult population in which future research could address in a multitude of ways.

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