IS QUALITY OF LIFE REDUCED IN PEOPLE WITH PATELLOFEMORAL OSTEOARTHRITIS AND DOES IT IMPROVE WITH TREATMENT? A SYSTEMATIC REVIEW, META- ANALYSIS AND REGRESSION

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ABSTRACT

Purpose: To determine if quality of life is reduced in individuals with patellofemoral osteoarthritis, whether it can be improved with treatment, and potential factors associated with quality of life in individuals with patellofemoral osteoarthritis.

Materials and Methods: Published articles were identified by using electronic and manual searches. Studies reporting quality of life in individuals with patellofemoral osteoarthritis relative to a comparator group (e.g. no osteoarthritis) and intervention studies reporting quality of life in patellofemoral osteoarthritis following treatment relative to baseline/control group were included.

Results: Seventeen studies (7 cross-sectional, 10 intervention) were included in this systematic review. Relative to those without osteoarthritis, individuals with patellofemoral osteoarthritis had worse knee-related quality of life (5 studies) and health-related quality of life (2 studies). Non-surgical treatments appear to improve knee-related quality of life compared to pre-treatment (3 studies) but not control (3 studies). Surgical-treatments also improved knee-related quality of life compared to pre-treatment (5 studies). Worse knee-related quality of life was associated with younger age, worse pain, symptoms, function in activities of daily living, and function in sport and recreation.

Conclusion: Individuals with patellofemoral osteoarthritis had worse knee-related and health-related quality of life compared to those without knee osteoarthritis. Non-surgical and surgical interventions may be effective in improving knee-related quality of life in individuals with patellofemoral osteoarthritis, but the intervention results are based on limited studies, and further research is needed to determine optimal strategies.

Key Words: Osteoarthritis; Quality of life; Patellofemoral Joint; Surgery; Non-surgical Treatment

INTRODUCTION

Quality of life is a multi-dimensional concept that focuses on physical, psychological and social aspects associated with a disease or its treatment [1]. It has been described as an individual's perception of how an illness or condition and its treatment affect the physical, mental and social aspects of his or her life [2]. Individuals with knee osteoarthritis have among the lowest quality of life compared with other chronic diseases [3]. Of the three knee compartments, the patellofemoral joint is commonly affected by osteoarthritis [4, 5] and is implicated in the progression osteoarthritis in tibiofemoral joint compartments [6, 7]. Patellofemoral osteoarthritis can cause considerable knee pain and functional impairment [8] and is associated with greater disability than tibiofemoral osteoarthritis [9].

Over the past few years, awareness of the importance of patellofemoral osteoarthritis within clinical practice and knee osteoarthritis research is increasing. A number of studies have investigated quality of life, either as a primary or secondary outcome, in individuals with patellofemoral osteoarthritis. However, the evidence on quality of life and the impact of specific treatment strategies on quality of life in individuals with patellofemoral osteoarthritis has not been systematically evaluated. Thus, there is a need to synthesize this evidence to provide a clearer understanding of quality of life in people with patellofemoral osteoarthritis. Identification of factors that contribute to quality of life impairment in people with patellofemoral osteoarthritis may guide the development of treatment strategies to improve quality of life in this patient-population. Therefore, the objective of the current study was to perform a systematic review, meta-analysis and regression to (i) determine the quality of life in individuals with patellofemoral osteoarthritis compared with those without knee osteoarthritis controls, (ii) evaluate the effect of

specific treatment strategies on quality of life in individuals with patellofemoral osteoarthritis, and (iii) identify factors associated with quality of life in individuals with patellofemoral osteoarthritis.

METHODS

The study is reported with reference to the Preferred Reporting Items for Systematic Reviews and Meta-analyses Checklist. The protocol was prospectively registered on the PROSPERO International Prospective Register for Systematic Reviews website (Registration #: CRD42016046354) (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016046354).

Literature Search Strategy

Using guidelines provided by the Cochrane Collaboration, a comprehensive search strategy was devised from the following electronic databases with no date restrictions: (i) MEDLINE via OVID; (ii) EMBASE via OVID; (iii) CINAHL via EBSCO; (iv) Scopus; (v) Web of Science; (vi) SPORTDiscus, and (vii) Cochrane Central Register of Controlled Trials. The primary search strategy included a search for original publications. The search strategy was deliberately simplified to ensure inclusion of all relevant papers, with all terms searched as free text and keywords (where applicable). *Concept 1*, Patellofemoral (patellofemoral, patello-femoral, PF, PFJ, knee joint); *Concept 2*, Osteoarthritis (osteoarthritis, OA, arthritis, degenerative arthritis, bone marrow lesion); and *Concept 3*, Health-related quality of life (QOL, quality of life, HRQoL, Knee Injury and Osteoarthritis Outcome Score, KOOS, 36 Item Short-Form Health Survey, SF-36, EuroQoL). All search terms were exploded and scope notes from each database were examined for other possible terms for modification of search strategies. The MEDLINE search strategy was adapted for other

databases (supplementary table 1). The search strategy was limited to English language and full-text. All potential references were imported into Endnote X7 (Thomson Reuters, Carlsbad, California, USA) and duplicates were removed. Two teams of two reviewers (total of 4: SC and SRF; HFH and PS) reviewed all titles returned by the database searches and retrieved eligible abstracts. Where abstracts suggested that papers were potentially eligible, the full-text versions were screened (HFH) and included in the review if they fulfilled the selection criteria. Reference lists of all publications considered for inclusion were hand-searched recursively and citation tracking was completed using Google Scholar until no additional eligible publications were identified. A third reviewer was consulted in case of disagreements (KMC).

Selection Criteria

Study eligibility was determined using the following inclusion criteria: (i) cross-sectional and observational studies comparing quality of life between individuals with and without patellofemoral osteoarthritis; or (ii) intervention studies reporting quality of life in individuals with patellofemoral osteoarthritis relative to baseline or comparator group. Patellofemoral osteoarthritis definition included symptomatic or imaging-defined features of patellofemoral damage. Cross-sectional and observational studies reporting quality of life in individuals with patellofemoral osteoarthritis without a comparator group were ineligible. When intervention studies reported quality of life data at multiple time points post-treatment for patellofemoral osteoarthritis, data from the first follow-up time-point was included. There was no restriction placed on type of osteoarthritis (e.g. post-traumatic, idiopathic), sex, age, type of intervention (e.g. surgical, non-surgical, unconventional care), period of intervention or method of recruitment. If multiple studies presented data from one cohort, the study with the most complete data was included.

Assessment of Reported Methodological Quality and Risk of Bias

Two independent reviewers (HFH, JC), who remained blind to authors, affiliations, and the publishing journal, rated the methodological quality of included cross-sectional and non-randomized studies using the modified Downs and Black checklist [10]. A 23-item checklist was utilized for cross-sectional and intervention studies (supplementary table 2). All items, except item 4, were scored as 'Yes' (score = 1), 'No' (score = 0), or "Not Applicable' (items removed from scoring). Item 4 'presence of selection bias' was scored as 'Yes' (score = 0) or 'No' (score = 1). A normalized score ranging from 0 to 2 was calculated for each study to assign a level of methodological quality. Studies were then classified as high quality (≥1.4), moderate quality (1.1 - 1.4) or poor quality (<1.1) based on normalized scores.[11] The Cochrane Risk of Bias Tool was used to assess risk of bias in the randomized controlled intervention studies. A 7-item checklist was utilized to assess selection bias (2 items), performance bias (1 item), detection bias (1 item), attrition bias (1 item), reporting bias (1 item), and other bias (1 item). Items were recorded as low risk of bias (score = 1), high risk of bias (score = 0) or risk of bias unclear (score = 0). Studies were classified as having a low risk of bias (score at least 6 of the 7 criteria), moderate risk (4 or 5), or high risk (≤3). Any inter-rater disagreement was discussed in a consensus meeting and unresolved items were taken to a third reviewer (KMC) for consensus.

Heterogeneity was assessed based on X2 ($p < 0.05$) and I^2. The magnitude of heterogeneity was interpreted based on Higgins et al., [12] where $I^2 = 0\%$ is no heterogeneity, $I^2 = 25\%$ low heterogeneity, $I^2 = 50\%$ moderate heterogeneity, and $I^2 = 75\%$ high heterogeneity. A level of evidence was assigned for pooled data using the X2 and I^2 and the reported methodological quality ratings. Definitions for 'levels of evidence' were guided by recommendations as per van Tulder et

al., [13]: (i) strong evidence provided by pooled results derived from three or more studies, including a minimum of two high-quality studies (low risk of bias), which were statistically homogenous ($p > 0.05$) (may be associated with a statistically significant or non-significant pooled result); (ii) moderate evidence provided by statistically significant pooled results derived from multiple studies that were statistically heterogeneous ($p < 0.05$), including at least one high-quality study (low risk of bias); or from multiple low-quality studies (high risk of bias), which were statistically homogenous ($p > 0.05$); (iii) limited evidence provided by results from one high-quality study (low risk of bias) or multiple low-quality studies (high risk of bias) that are statistically heterogeneous ($p < 0.05$); (iv) very limited evidence provided by results from one low-quality study (high risk of bias); and (v) conflicting evidence provided by pooled results that are insignificant and derived from multiple statistically heterogeneous studies ($p < 0.05$) (regardless of quality).

Data management

Data pertaining to participant characteristics (e.g. age, sex, body mass index), quality of life, patellofemoral osteoarthritis disease pattern (e.g. isolated patellofemoral osteoarthritis, combined patellofemoral and tibiofemoral osteoarthritis) and treatment (only for intervention studies) were extracted and entered into an Excel spreadsheet. If sufficient data were not reported in the published article or supplementary material provided, the corresponding author was contacted to request further data.

Quality of life instruments

The Knee Injury and Osteoarthritis Outcome Score, an instrument to assess knee-related health, consists of five subscales: Pain, Symptoms, function in activities of daily living, function in sport and recreation, and quality of life. The Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale is a disease-specific instrument to assess knee-related quality of life, whereas 36 Item Short-Form Health Survey and 12 Item Short-Form Health Survey are generic measures of health-related quality of life. The Knee Injury and Osteoarthritis Outcome Score – quality of life, 36 Item Short-Form Health Survey, and 12 Item Short-Form Health Survey are scored on a scale from 0 (worst possible score) to 100 (best possible score).

Statistical analysis

Methodological heterogeneity was evaluated for all quality of life measures and data were pooled in a meta-analysis (Review Manager Version 5.3. Copenhagen) based on quality of life measure: (i) Knee Injury and Osteoarthritis Outcome Score – quality of life, (ii) 36 Item Short-Form Health Survey, and (iii) 12 Item Short-Form Health Survey. Quality of life data were compared between individuals with any patellofemoral osteoarthritis compared to those without knee osteoarthritis. In addition, comparisons were made between isolated patellofemoral osteoarthritis and combined patellofemoral osteoarthritis and tibiofemoral osteoarthritis, where possible. The intervention studies were divided into surgical and non-surgical (e.g. taping, manual therapy) treatments within each quality of life measure. Where possible comparisons of quality of life were made between pre- and post- treatment and between post-treatment and control group. Standardized mean differences (SMD) with 95% confidence intervals (CI) were calculated for variables of interest and random effects models were used for each analysis. Meta-analyses were only conducted when

at least two studies were available. The magnitude of the pooled SMD was interpreted based on Cohen's criteria, where SMD ≥ 0.8 was interpreted as a large effect, > 0.5 and < 0.8 a moderate effect, and > 0.2 and < 0.5 a weak effect. Mean differences (MD) with 95% CI are also presented for the pooled data to enable interpretation of the SMD in the unit of the original outcome measure. Quality of life data from cross-sectional and intervention studies (baseline data) were used to conduct meta-regression analyses. Random-effects models were used for each analysis to evaluate potential associations between quality of life and other factors: age, body mass index, Knee Injury and Osteoarthritis Outcome Score – Pain, Symptoms, Sport and Recreation and Activities of Daily Living subscales. (Comprehensive Meta-Analysis Version 3, Biostat, New Jersey). Data from a minimum of four studies were required to conduct meta-regression analyses. The significance was set at $p < 0.05$.

RESULTS

Search strategy, methodological quality and risk of bias

The comprehensive search strategy identified 3401 titles, with the final search conducted on September 20th 2016, and repeated on October 9th 2017. Following removal of duplicate publications, titles of 3365 publications were evaluated. The full text of 333 articles were retrieved, and 17 (7 cross-sectional, 10 intervention) studies [14-30] met the eligibility criteria (supplementary figure 1). Tables 1 and 2 present characteristics of the included cross-sectional and intervention studies, respectively. The reported methodological quality scores ranged from 0.7 to 2 (out of 2), with a median score of 1.6. There were 9 studies of high quality, 6 were moderate quality and 2 were low quality (supplementary table 3). There were three randomized controlled trials included in this systematic review [16, 25, 30]. The risk of bias assessment revealed that

there was one low risk of bias [16] and two moderate risk of bias studies [25, 30] supplementary table 4).

INSERT table 1

INSERT table 2

Is quality of life lower in individuals with patellofemoral osteoarthritis?

Knee-related quality of life

Five studies reported knee-related quality of life in individuals with patellofemoral osteoarthritis [19, 21, 24, 26, 27] (figure 1). Pooled data from five studies provided moderate level evidence of significantly lower knee-related quality of life in individuals with any patellofemoral osteoarthritis (irrespective of presence or absence of tibiofemoral osteoarthritis) (SMD presented in figure 1; equivalent to MD [95% CI]: -18 [-38 to -2]) compared to those without osteoarthritis [19, 21, 24, 26, 27]. Two studies reported the Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale scores for individuals with isolated patellofemoral osteoarthritis and combined patellofemoral and tibiofemoral osteoarthritis relative to those without knee osteoarthritis [19, 26]. Pooled data provided moderate evidence of reduced knee-related quality of life (SMD presented in figure 1; equivalent to MD: -43 [-56 to -31]) in individuals with combined patellofemoral and tibiofemoral osteoarthritis relative to those without knee osteoarthritis. However, there was moderate level evidence of no significant differences in knee-related quality of life between individuals with isolated patellofemoral osteoarthritis (SMD presented in figure 1; equivalent to MD: -29 [-84 to 26]) and those without knee osteoarthritis [19, 26]. Further to this, there was moderate level evidence of no significant differences in knee-related quality of life (SMD [95% CI]: 0.57 [-1.46 to 2.59]; equivalent to MD: 14 [-28 to 57]) between individuals with isolated patellofemoral osteoarthritis and combined patellofemoral and tibiofemoral osteoarthritis [19, 26]. The results indicate that individuals with patellofemoral osteoarthritis have worse knee-related quality of life compared to those without osteoarthritis.

INSERT figure 1

Health-related quality of life

Two studies reported health-related quality of life in individuals with patellofemoral osteoarthritis [15, 23] (figure 2). Pooled data from two studies [15, 23] provided moderate level evidence of significantly lower physical function (SMD presented in figure 2; equivalent to MD: -7 [-12 to -3]), physical role functioning (SMD presented in figure 2; equivalent to MD: -11 [-19 to -3]), bodily pain (SMD presented in figure 2; equivalent to MD: -5 [-9 to -2]), social function (SMD presented in figure 2; equivalent to MD: -3 [-7 to -0.03]), and emotional role functioning (SMD presented in figure 2; equivalent to MD: -6 [-12 to -0.12]) in individuals with any patellofemoral osteoarthritis compared to individuals without knee osteoarthritis [15, 23]. There was also a moderate level of evidence that individuals with isolated patellofemoral osteoarthritis have significantly lower physical function (SMD: -0.21 [-0.41 to -0.01]; equivalent to MD: -5 [-10 to -1]) and physical role functioning (SMD: -0.20 [-0.40 to -0.00]; equivalent to MD: -7 [-15 to 0]) compared to individuals without knee osteoarthritis [15, 23]. A single study reported health-related QOL in those with combined patellofemoral and tibiofemoral osteoarthritis relative to individuals without OA [23]: physical function (SMD: -0.40 [-0.61 to -0.18]), physical role functioning (SMD: -0.44 [-0.65 to -0.22]), bodily pain (SMD: -0.55 [-0.76 to -0.33]), general health (SMD: -0.28 [-0.50 to -0.07]), vitality (SMD: -0.22 [-0.44 to -0.01]), social function (SMD: -0.46 [-0.68 to -0.25]) and emotional role functioning (SMD: -0.28 [-0.49 to -0.06]). The results indicate that individuals with patellofemoral osteoarthritis have worse health-related quality of life compared to those without osteoarthritis.

INSERT figure 2

Health-related quality of life data comparing individuals with isolated patellofemoral osteoarthritis [15, 23] to those with combined patellofemoral and tibiofemoral osteoarthritis [23] revealed worse physical function (SMD: -0.34 [-0.60 to -0.08]; equivalent to MD: -8 [-14 to -2]), physical role functioning (SMD: -0.60 [-0.86 to -0.33]; equivalent to MD: -24 [-34 to -14]), bodily pain (SMD: -0.83 [-1.10 to -0.55]; equivalent to MD: -16 [-21 to -11]), social function (SMD: -0.62 [-0.89 to -0.35]; equivalent to MD: -13 [-18 to -8]) and emotional role functioning (SMD: -0.53 [-0.79 to -0.26]; equivalent to MD: -22 [-33 to -11]) in individuals with combined patellofemoral and tibiofemoral osteoarthritis relative to individuals with isolated patellofemoral osteoarthritis, however no differences were observed in general health (SMD: 0.07 [-0.19 to 0.33]), vitality (SMD: 0.05 [-0.21 to 0.31]) or mental health (SMD: 0.12 [-0.14 to 0.38]) domains. A single study reported 36 Item Short-Form Health Survey mental and physical component summary scores in individuals with patellofemoral osteoarthritis [15]. This study found no differences in mental component summary (SMD: -0.22 [-0.61 to 0.18]) and physical component summary (SMD: -0.25 [-0.64 to 0.15]) between individuals with isolated patellofemoral osteoarthritis and those without knee osteoarthritis. The results indicate that individuals with combined patellofemoral and tibiofemoral osteoarthritis have worse health-related quality of life compared to those with isolated patellofemoral osteoarthritis.

Does quality of life improve following treatment for patellofemoral osteoarthritis?

Knee-related quality of life

Eight studies that investigated treatments for patellofemoral osteoarthritis evaluated knee-related quality of life [16-18, 20, 22, 25, 29, 30]. Three non-surgical studies reported the Knee Injury and

Osteoarthritis Outcome Score – Quality of Life subscale score compared to pre-treatment and control group.[16, 25, 30] Pooled data provided moderate level evidence of significant improvements in knee-related quality of life in patellofemoral osteoarthritis individuals post non-surgical treatment (e.g. bracing, taping, exercise, manual therapy – manual patellofemoral, tibiofemoral and soft tissue mobilization to the local knee and thigh area) compared to pre-treatment (SMD: 0.43 [0.20 to 0.67]; equivalent to MD: 7 [3 to 12]) (figure 3A).

INSERT figure 3

There was limited level evidence from three studies [16, 25, 30] that non-surgical treatments do not significantly improve knee-related quality of life relative to control/education alone (SMD presented in figure 4; equivalent to MD: 3 [-0.31 to 6]). Pooled data from five studies provided moderate level evidence of significant improvements in knee-related quality of life (SMD presented in figure 3A; equivalent to MD: 20 [5 to 35]) with surgical treatments [17, 18, 20, 22, 29]. No surgical studies assessed quality of life in comparison to a control group. The results indicate that non-surgical and surgical treatments can improve knee-related quality of life post-treatment relative to pre-treatment.

INSERT figure 4

Health-related quality of life

Five studies reported health-related quality of life pre- and post- treatment in individuals with patellofemoral osteoarthritis [14, 20, 22, 28, 29]. Data from a single study [14] reported

improvements in 36 Item Short-Form Health Survey domains: physical function (SMD: 0.77 [0.27 to 1.27]), physical role functioning (SMD: 0.89 [0.38 to 1.40]), bodily pain (SMD: 0.90 [0.39 to 1.41]), vitality (SMD: -0.66 [0.16 to 1.16]), social function (SMD: 0.62 [0.12 to 1.11]) and emotional role functioning (SMD: 0.76 [0.26 to 1.26]) with autologous osteochondral transplantation but no differences were observed in general health (SMD: 0.24 [-0.24 to 0.72]) and mental health (SMD: 0.43 [-0.05 to 0.92]) domains. Pooled data from three studies provided limited evidence of no significant improvements in 36 Item Short-Form Health Survey mental (SMD presented in figure 3B) and physical (SMD presented in figure 3B) component summary scores following surgical intervention compared to pre-treatment [20, 28, 29]. One study [22] reported improvements in 12 Item Short-Form Health Survey physical component summary scores (SMD: 0.43 [0.04 to 0.81]) following autologous chondrocyte implantation treatment but no improvement in mental component summary scores (SMD: 0.36 [-0.03 to 0.75]). The results indicate that surgical treatments do not significantly improve health-related quality of life post-treatment relative to pre-treatment.

What factors influence quality of life in individuals with patellofemoral osteoarthritis?

Meta regression analysis revealed that knee-related quality of life positively correlated with age (slope = 1.43, 95% CI: 0.27 to 2.58, Q*model* = 5.84, p = 0.0157; Tau^2 = 294, R^2 = 51%) [16, 18-22, 24-27, 29, 30], but not with body mass index (slope = -2.98, 95% CI: -11.51 to 5.55, Q*model* = 0.47, p = 0.4935; Tau^2 = 625, R^2 = 0%) [16, 18-22, 24-27, 29, 30] (figure 5). Worse knee-related quality of life also correlated with worse Knee Injury and Osteoarthritis Outcome Score – Pain subscale (slope = 1.28, 95% CI: 0.78 to 1.77, Q*model* = 25.53 p < 0.0001; Tau^2 = 125, R^2 = 79%) [16-18, 20-22, 24-26, 29, 30], Knee Injury and Osteoarthritis Outcome Score – Symptoms subscale

(slope = 1.51, 95% CI: 0.75 to 2.26, Q*model* = 15.16, p = 0.0001; Tau^2 = 197, R^2 = 67%) [16-18, 20-22, 24, 26, 29, 30], Knee Injury and Osteoarthritis Outcome Score – Activities of Daily Living subscale (slope = 1.29, 95% CI: 0.68 to 1.90, Q*model* = 17.37, p <0.0001; Tau^2 = 166, R^2 = 72%) [16-18, 20-22, 24-26, 29, 30], and Knee Injury and Osteoarthritis Outcome Score – Sport and Recreation subscale (slope = 0.98, 95% CI: 0.90 to 1.06, Q*model* = 532.09, p <0.0001; Tau^2 = 4, R^2 = 99%) [16-18, 20-22, 24, 26, 29, 30] (figure 5). The results indicate that younger individuals with worse pain and symptoms, and poorer function have worse knee-related quality of life.

INSERT figure 5

DISCUSSION

Summary of findings

This systematic review with meta-analysis evaluated quality of life in individuals with patellofemoral osteoarthritis and determined the effect of patellofemoral osteoarthritis treatment on quality of life. There were seven cross-sectional studies (5 high and 2 low reported methodological quality), 7 non-randomized controlled (2 high, 3 moderate, and 2 low reported methodological quality), 3 randomized controlled (1 low and 2 moderate risk of bias) studies. Based on the limited number of studies (i.e. two to five), there is moderate evidence that individuals with patellofemoral osteoarthritis have lower knee-related and health-related quality of life compared to those without knee osteoarthritis. Surgical treatments appear to improve knee-related but not health-related quality of life compared to pre-treatment. Non-surgical treatments showed improvement in knee-related quality of life compared to pre-treatment but not compared to controls. Worse knee-related quality of life was related to younger age but not body mass index.

Worse self-reported pain and symptoms, and worse function in activities of daily living and sports/recreation were also related with worse knee-related quality of life in individuals with patellofemoral osteoarthritis.

Quality of life is reduced in individuals with patellofemoral osteoarthritis

Individuals with any patellofemoral osteoarthritis had worse knee-related quality of life (Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale MD = 18) and health-related quality of life (36 Item Short-Form Health Survey domains MD range 3 to 11) compared to those without knee osteoarthritis. From two studies, it appears that individuals with combined patellofemoral and tibiofemoral osteoarthritis had worse health-related quality of life relative to those with isolated patellofemoral osteoarthritis (36 Item Short-Form Health Survey domains MD range 8 to 24), but no significant between-group differences were observed in knee-related quality of life. Potential explanations include a combined disease pattern reflecting worsening disease in both the patellofemoral and tibiofemoral joints, or tibiofemoral osteoarthritis may be associated with worse health-related quality of life compared with isolated patellofemoral osteoarthritis. Future research may consider evaluating quality of life, using both health- and knee- related quality of life measures, in longitudinal studies, to evaluate the progression of quality of life over time, and its association with changing disease severity in both the patellofemoral and tibiofemoral joints.

Patellofemoral osteoarthritis is a dominant source of symptoms in knee osteoarthritis and contributes significantly to disability [8, 9]. Quality of life is a strong predictor of mortality and morbidity [31-33] and has emerged as an important clinical endpoint to determine treatment

efficacy. This systematic review and meta-analysis revealed that individuals with patellofemoral osteoarthritis have lower knee-related and health-related quality of life. The difference in the Knee Injury and Osteoarthritis Outcome Score - quality of life represents substantially (8-10 points) lower knee-related quality of life, which is greater than the minimal perceptible clinically decline [34]. Furthermore, the mean score for the Knee Injury and Osteoarthritis Outcome Score – quality of life, across all studies (Knee Injury and Osteoarthritis Outcome Score – Quality of Life subcale 63±21) is substantially lower than previously published normative data in healthy individuals aged 50-59 years (Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale 85±16) [35] indicating that individuals with patellofemoral osteoarthritis are greatly impacted by their condition. Whilst the differences in 36 Item Short-Form Health Survey domains are significant between individuals with patellofemoral osteoarthritis and those without knee osteoarthritis, the magnitude of the differences are small (e.g. social function MD: 3; emotional function MD: 6). This suggests that non knee-related factors may be driving health-related quality of life in individuals with patellofemoral osteoarthritis. This systematic review highlights that people with patellofemoral osteoarthritis have worse knee- and health- related quality of life. However, we do urge the readers to practice caution when interpreting the findings presented, as some of these are based on data from as few as two studies.

QOL can be improved with treatments for patellofemoral osteoarthritis

Surgical treatments appear to enhance knee-related quality of life in individuals with patellofemoral osteoarthritis (Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale MD improvement: 20), but not health-related quality of life. Due to the paucity of studies, data from different surgical patellofemoral osteoarthritis treatments were pooled together, and no

conclusions can be drawn from individual surgical procedures. Post-treatment follow-up in the surgical studies ranged from 3 months to 4 years and thus, change in quality of life may reflect a response shift. Further to this, surgical studies included in this systematic review did not include a control group, increasing the risk of study bias contributing to the positive benefits observed in quality of life. Placebo effects will influence patient-reported outcomes after any treatment that the clinician and patient believe is effective and can result in high rates of improvement [36]. Further research is needed to determine whether surgical treatments are effective in improving quality of life in individuals with patellofemoral osteoarthritis relative to no-treatment and placebo comparator groups.

Non-surgical treatments including bracing, combined treatment (exercise, education, taping, manual therapy – manual patellofemoral, tibiofemoral and soft tissue mobilization to the local knee and thigh area), and exercise alone can result in improved knee-related quality of life compared to pre-treatment (Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale MD improvement: 7). However, these studies found no significant improvements in knee-related quality of life when compared to a control group (education alone/control). This highlights the importance of a control group to determine whether a treatment is truly affecting quality of life or merely having a placebo effect. As there were few studies to include in this review, no conclusions can be drawn regarding the effect of individual treatments (e.g. bracing vs. exercise) on quality of life.

Interestingly, these non-surgical intervention studies showed statistically significant improvements in knee pain in the treatment group compared to no-treatment comparator group (Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale MD improvement: 4). The discrepancy between pain and quality of life may reflect that future studies may need to specifically target quality of life.

This systematic review also suggests based on limited evidence that surgical treatments are effective in improving knee-related quality of life but not health-related quality of life when compared to pre-treatment. Since it is not known whether surgical treatments are more effective than placebo/education in improving knee-related quality of life – this should be investigated in future research. Additionally, the lack of improvements in health-related quality of life with surgical treatments indicates the need for new approaches.

Approaches that are likely to address factors that are specific to the patient might influence a person's health-related quality of life. For example, in addition to treatment elements with biological plausibility to reduce pain and improve function (e.g. bracing, exercise, taping and manual therapy – treating knee-specific impairment), discussing the burden of patellofemoral osteoarthritis with patients, mechanisms to overcome such burdens, as well as education on physical and mental health, are likely to be effective. Some evidence for this approach was demonstrated in a clinical trial by Crossley et al. [16] who found improvements in knee-related quality of life in individuals with patellofemoral osteoarthritis who received an education-only intervention.

Factors that influence quality of life in individuals with patellofemoral osteoarthritis

Current evidence suggests that individuals with patellofemoral osteoarthritis have a higher body mass index compared to healthy controls [37]. We anticipated that knee-related quality of life would be significantly worse in those with higher body mass index, as a consequence of heightened load on the patellofemoral joint and resultant functional limitations. However, body mass index did not significantly correlate with Knee Injury and Osteoarthritis Outcome Score – Quality of Life subscale. The World Health Organization guidelines define obesity as body mass index $\geq 30 kg/m^2$ and $\geq 25 kg/m^2$ as overweight [38]. The pooled mean body mass index of the studies included in the analyses was 27 (range 24 to 31) kg/m^2. Perhaps, the relationship between body mass index and knee-related quality of life would be more evident in obese individuals ($\geq 30 kg/m^2$). Younger age significantly correlated with worse knee-related quality of life. This finding may reflect older individuals with patellofemoral osteoarthritis adapting to their restricted lifestyle, or younger individuals desiring participation in more demanding sport and recreational activities, limitations in desired activities has potential to negatively impact quality of life. Younger and older individuals with patellofemoral osteoarthritis may have different needs; thus may benefit from different intervention strategies. Worse pain and symptoms, and poor function in activities of daily living and sport and recreation significantly correlated with worse quality of life. This finding is not surprising, as pain during activities such as kneeling and squatting and symptoms such as stiffness and swelling are common in individuals with patellofemoral osteoarthritis [39, 40]. Individuals with patellofemoral osteoarthritis often reduce or restrict their physical activity due to pain. Thus, lifestyle modifications, knee-related difficulties, and impairments in knee confidence were anticipated in individuals with worse functional limitations. The results suggest that addressing functional impairments and improving pain may aid in improving knee-related quality

of life in individuals with patellofemoral osteoarthritis. Future research is needed to explore other modifiable factors associated with health-related quality of life in individuals with patellofemoral osteoarthritis and strategies to improve them.

Study limitations

There are several limitations that should be considered when interpreting the findings of this systematic review. Firstly, a number of studies reporting quality of life data were not included because estimates of variability were not provided, which could alter the outcomes. Secondly, risk of bias assessment could only be performed on randomized controlled trials. For case-control, case-series and cross-sectional studies reported methodological quality was assessed with the modified Downs and Black checklist, which included two items on risk of bias. Cut-off scores were used to categorize studies into high, moderate and low reported methodological quality. It is possible that studies with good reported methodological quality also have a high risk of bias (e.g. score = 0 on risk of bias items). Thirdly, all relevant studies were included in this systematic review, regardless of reported methodological quality. Therefore, this systematic review may be subject to bias through the inclusion of low-quality studies. The levels of evidence were applied to the pooled data in an attempt to take quality and quantity of studies into accountFourthly, most research studies are based on other studies that were done in the past ('historical inertia'). As we are not able to statistically measure the interaction between studies within the meta-analysis, this may have influenced the results. Fifthly, publication bias may have resulted in over estimation of effect sizes. Sixthly, due to limited translation resources, this systematic review only included studies published in English. Thus, consideration of data from non-English language studies could also alter the outcomes. Seventhly, we only considered a few variables in the meta-regression.

There are a number factors that may influence quality of life in individuals with patellofemoral osteoarthritis (e.g. radiographic severity and presence of comorbidities). Eighthly, this systematic review only included full-text articles. Exclusion of data from unpublished or gray literature may have overestimated the effects. However, a recent systematic review shows that this is only the case in a minority of reviews [41]. Lastly, a very small number of studies (i.e., 2-4 studies) contributed to each meta-analysis, and thus, the results of this systematic review should be interpreted with caution.

Recommendations

We recommend that future studies more clearly describe quality of life data and provide estimates of variability. Further to this, studies presenting data based on subgroups (e.g. no osteoarthritis, isolated patellofemoral osteoarthritis, isolated tibiofemoral osteoarthritis, combined patellofemoral and tibiofemoral osteoarthritis) should consider presenting demographic data based on subgroups. We also recommend that studies should calculate and report scores based on the quality of life instrument scoring instructions. For example, 36 Item Short-Form Health Survey scores should be calculated and reported as individual domains or mental and physical component summaries rather than total score. Different quality of life instruments assess different dimensions of health; thus, direct comparisons between these instruments are not appropriate. Additionally, future studies may consider utilizing the same health instruments in patellofemoral osteoarthritis research. Finally, we recommend that intervention studies should include a control group to determine true effectiveness of a treatment.

Conclusions

Patellofemoral osteoarthritis is associated with lower knee-related and health-related quality of life compared with individuals without osteoarthritis. Combined patellofemoral and tibiofemoral osteoarthritis disease patterns appear to be associated with worse health-related quality of life than isolated patellofemoral osteoarthritis. Further to this, surgical (e.g. matrix-induced autologous chondrocyte implantation, multipotent stem cells implantation) and non-surgical treatments (e.g. bracing, manual therapy) appear to improve quality of life in individuals with patellofemoral osteoarthritis compared to pre-treatment. Non-surgical treatments did not improve knee-related quality of life compared to control group, and the effects of surgical treatment options against a control group are unknown. Younger age, worse pain and symptoms, and functional limitations are related to worse knee-related quality of life. Addressing pain and functional impairments may aid in improving knee-related quality of life in individuals with patellofemoral osteoarthritis.

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DECLARATION OF INTEREST

The authors report no conflicts of interest

FIGURE CAPTIONS

Figure 1: Comparisons of knee-related quality of life

Figure 2: Comparisons of health-related quality of life

Figure 3: Effects of surgical and non-surgical treatments on knee-related quality of life (A) and health-related quality of life (B)

Figure 4: Effects of non-surgical treatments on knee-related quality of life in individuals with patellofemoral osteoarthritis compared to no treatment group

Figure 5: Relationship between knee-related quality of life (Knee Injury Osteoarthritis Outcome Score – Quality of Life subscale) and other factors. Slope (bolded dashed line) and 95% confidence (solid black lines) data are presented.

TABLE CAPTIONS

Table 1: Characteristics of the included cross-sectional studies

Table 2: Characteristics of the included intervention studies

SUPPLEMENTARY MATERIAL

Supplementary Table 1: Search strategy for MEDLINE

Supplementary Table 2: Modified Downs and Black Scale

Supplementary Table 3: Reported methodological quality of the included studies

Supplementary Table 4: Risk of bias of included randomized controlled intervention studies

Supplementary Figure 1: Flowchart of the study selection process

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1 **Table 1. Characteristics of the included cross-sectional studies**

Study	Population	OA pattern	Comparator	PFOA	Comparator	KOOS subscales (PFOA)	KOOS-QOL scores
KOOS Quality of life subscale							
Fok 2013 [26]		Isolated PFOA	Healthy controls	N = 17 Age: 56 (11) years Sex, F: 13 BMI: 27 (3) kg/m^2	N = 21 Age: 56 (11) years Sex, F: 13 BMI: 25 (4) kg/m^2	Pain: 65 (16) Symptoms: 65 (18) ADL: 73 (16) Sport/rec: 47 (20)	PFOA: 42 (16) Comparator: 99 (4)
		Combined PFOA	Healthy controls	N = 13 Age: 60 (11) years Sex, F: 10 BMI: 28 (3) kg/m^2	N = 21 Age: 56 (11) years Sex, F: 13 BMI: 25 (4) kg/m	Pain: 70 (18) Symptoms: 67(23) ADL: 70 (2) Sport/rec: 47 (29)	PFOA: 49 (25) Comparator: 99 (4)
Jensen 2012 [19]	Floor layers and graphic designers	Isolated PFOA	Healthy controls	N = 13 Age: 59 (8) years Sex, F: 0 BMI: 29 (5) kg/m^2	N = 91 Age: 54 (7) years Sex, F: 0 BMI: 26 (4) kg/m^2		PFOA: 73 (20) Comparator: 74 (23)
		Combined PFOA	No PFOA	N = 2 Age: 58 (7) years Sex, F: 0 BMI: 26 (2) kg/m^2	N = 91 Age: 54 (7) years Sex, F: 0 BMI: 26 (4) kg/m^2		PFOA: 38 (9) Comparator: 74 (23)
Neuman 2009 [27]	15 years post-acute ACL injury	PFOA +/- TFOA	No PFOA	N = 12 Age: 45 (9) years Sex, F: 4 BMI: 27 (4) kg/m^2	N = 63 Age: 41 (7) years Sex, F: 24 BMI: 26 (4) kg/m^2		PFOA: 74 (27) Comparator: 76 (20)
Oiestad 2013 [21]	12 years post ACL reconstruction	PFOA +/- TFOA	No OA	N = 48 Age: 44 (8) years Sex, F: NR BMI: 24 (3) kg/m^2	N = 46 Age: NR Sex, F: NR BMI: NR	Pain: 84 (19) Symptoms: 80 (18) ADL: 91 (12) Sport/rec: 66 (30)	PFOA: 67 (15) Comparator: 75 (20)

Study	Population	OA pattern	Comparator	PFOA	Comparator	KOOS subscales (PFOA)	KOOS-QOL scores
Teng 2016 [24]		PFOA +/- TFOA	Healthy controls	N = 56 Age: 55 (10) years Sex, F: 42 BMI: 25 (4) kg/m^2	N = 43 Age: 48 (11) years Sex, F: 20 BMI: 25 (3) kg/m^2	Pain: 84 (17) Symptoms: 85 (17) ADL: 90 (14) Sport/rec: 78 (24)	PFOA: 74 (15) Comparator: 80 (20)
Study	**Population**	**OA pattern**	**Comparator**	**PFOA**	**Comparator**	**SF-12 domain**	**SF-12 score**
12 Item Short Form Health Survey							
Cho 2016 [15]	Elderly Koreans	Isolated PFOA	No OA	N = 26 Age: ≥65 years Sex, F: NR BMI: NR	N = 431 Age: ≥65 years Sex, F: NR BMI: NR	Physical function	PFOA: 60 (28) Comparator: 68 (24)
						Role physical	PFOA: 73 (33) Comparator: 78 (24)
						Bodily pain	PFOA: 66 (28) Comparator: 69 (28)
						General health	PFOA: 46 (20) Comparator: 45 (23)
						Vitality	PFOA: 54 (22) Comparator: 56 (21)
						Social function	PFOA: 80 (27) Comparator: 84 (20)
						Role emotional	PFOA: 82 (29) Comparator: 87 (21)
						Mental health	PFOA: 66 (25) Comparator: 70 (19)

Study	Population	OA pattern	Comparator	PFOA	Comparator	SF-12 domain	SF-12 score
Cho 2016 [15] (continued)						Mental component	PFOA: 57 (14) Comparator: 54 (9)
						Physical component	PFOA: 57 (14) Comparator: 60 (12)
Tangtrakulwanich 2006 [23]		Isolated PFOA	No OA	N = 91 Age: NR Sex, F: NR BMI: NR	N = 348 Age: NR Sex, F: NR BMI: NR	Physical function	PFOA: 56 (24) Comparator: 60 (27)
						Role physical	PFOA: 44 (42) Comparator: 53 (42)
						Bodily pain	PFOA: 57 (19) Comparator: 56 (20)
						General health	PFOA: 61 (14) Comparator: 59 (15)
						Vitality	PFOA: 62 (14) Comparator: 63 (16)
						Social function	PFOA: 79 (19) Comparator: 76 (20)
						Role emotional	PFOA: 57 (42) Comparator: 59 (42)
						Mental health	PFOA: 70 (16) Comparator: 70 (16)
		Combined PFOA	No OA	N = 111 Age: NR Sex, F: NR BMI: NR	N = 348 Age: NR Sex, F: NR BMI: NR	Physical function	PFOA: 50 (24) Comparator: 60 (27)

Study	Population	OA pattern	Comparator	PFOA	Comparator	SF-12 domain	SF-12 score
Tangtrakulwanich 2006 [23] (continued)		Combined PFOA	No OA	N = 111 Age: NR Sex, F: NR BMI: NR	N = 348 Age: NR Sex, F: NR BMI: NR	Role physical	PFOA: 35 (40) Comparator: 53 (42)
						Bodily pain	PFOA: 45 (19) Comparator: 56 (20)
						General health	PFOA: 55 (16) Comparator: 59 (15)
						Vitality	PFOA: 59 (18) Comparator: 63 (16)
						Social function	PFOA: 66 (21) Comparator: 76 (20)
						Role emotional	PFOA: 47 (43) Comparator: 59 (42)
						Mental health	PFOA: 70 (17) Comparator: 70 (16)

Data are presented as mean (standard deviation), unless otherwise stated. Abbreviations as follows: OA, osteoarthritis; QOL, quality of life; KOOS, Knee Injury and Osteoarthritis Outcome Score; PFOA, patellofemoral osteoarthritis; TFOA, tibiofemoral osteoarthritis; F, female; BMI, body mass index; NR, not reported; ADL, function in activities of daily living; Sport/rec, function in sport and recreation activities

1 **Table 2. Characteristics of the included intervention studies**

Study	Population	Treatment	Duration	Follow-up	Demographics	Sample size (n)	KOOS subscales (PFOA)	KOOS-QOL scores
KOOS-Quality of life subscale								
Non-surgical interventions								
Callaghan 2015 [25]	PFOA	Brace	6 weeks	6 weeks	Age: 55 (7) years Sex, F: 40 BMI: 31 (6) kg/m^2	Pre-treatment: 63 Post-treatment: 60	Pain: 48 (18) ADL: 53 (22)	Pre-treatment: 32 (20) Post-treatment: 38 (14)
		No brace (Control)		6 weeks	Age: 56 (8) years Sex, F: 32 BMI: 31 (5) kg/m^2	Pre-treatment: 63 Post-treatment: 60	Pain: 51 (18) ADL: 57 (19)	Pre-treatment: 34 (17) Post-treatment: 34 (12)
Crossley 2015 [16]	PFOA	Manual therapy, exercise, education and taping	3 months	3 months	Age: 56 (10) years Sex, F: 24 BMI: 27 (4) kg/m^2	Pre-treatment: 44 Post-treatment: 39	Pain: 64 (15) Symptoms: 65 (15) ADL: 72 (15) Sport/rec: 42 (20)	Pre-treatment: 44 (14) Post-treatment: 55 (20)
		Education (Control)	3 months	3 months	Age: 53 (10) years Sex, F: 29 BMI: 28 (5) kg/m^2	Pre-treatment: 48 Post-treatment: 41	Pain: 63 (14) Symptoms: 61 (18) ADL: 71 (17) Sport/rec: 43 (22)	Pre-treatment: 40 (16) Post-treatment: 50 (14)
Koli 2015 [30]	PFOA	Exercise	12 months	12 months	Age: 58 (4) years Sex, F: 36 BMI: 27 (3) kg/m^2	Pre-treatment: 36 Post-treatment: 36	Pain: 86 (10) Symptoms: 78 (12) ADL: 92 (8) Sport/rec: 78 (16)	Pre-treatment: 77 (15) Post-treatment: 83 (16)
		Control	12 months	12 months	Age: 59 (4) years Sex, F: 40 BMI: 27 (4) kg/m^2	Pre-treatment: 40 Post-treatment: 40	Pain: 87 (7) Symptoms: 83 (10) ADL: 93 (6) Sport/rec: 78 (13)	Pre-treatment: 79 (15) Post-treatment: 83 (13)

Surgical interventions								
Study	**Population**	**Treatment**	**Duration**	**Follow-up**	**Demographics**	**Sample size (n)**	**KOOS subscales (PFOA)**	**KOOS-QOL scores**
Dhollander 2010 [17]	PF chondral lesions	Autologous matrix-induced chondrogenesis		1 year	Age: 18 to 50 years Sex, F: NR BMI: NR	Pre-treatment: 5 Post-treatment: 5	Pain: 64 (range: 39-92) Symptoms: 39 (range: 36-86) ADL: 65 (range: 38-76) Sport/rec: 15 (range: 0-20)	Pre-treatment: 25 (3) Post-treatment: 25 (14)
Ebert 2017 [29]	PF chondral lesions	PF matrix-induced autologous chondrocyte implantation		3 months	Age: 38 (range: 20 to 65) years Sex, F: 24 BMI: 26 (range: 19 -37) kg/m^2	Pre-treatment: 67 Post-treatment: 67	Pain: 62 (15) Symptoms: 66 (17) ADL: 70 (16) Sport/rec: 26 (21)	Pre-treatment: 23 (17) Post-treatment: 30 (18)
Gobbi 2015 [18]	Lateral PF chondral lesions	Matrix-induced autologous chondrocyte implantation		2 years	Age: 43 (6) years Sex, F: 10 BMI: 24 (1) kg/m^2	Pre-treatment: 19 Post-treatment: 19	Pain: 44 (14) Symptoms: 51 (13) ADL: 50 (13) Sport/rec: 32 (17)	Pre-treatment: 33 (18) Post-treatment: 76 (19)
		Multipotent stem cells		2 years	Age: 46 (8) years Sex, F: 8 BMI: 25 (3) kg/m^2	Pre-treatment: 18 Post-treatment: 18	Pain: 56 (14) Symptoms: 56 (19) ADL: 64 (17) Sport/rec: 33 (22)	Pre-treatment: 34 (11) Post-treatment: 79 (15)

Study	Population	Treatment	Duration	Follow-up	Demographics	Sample size (n)	KOOS subscales (PFOA)	KOOS-QOL scores
Meyerkort 2014 [20]	PF chondral defects	Matrix-induced autologous chondrocyte implantation		3 months	Age: 42 (12) years Sex, F: 10 BMI: 26 (4) kg/m^2	Pre-treatment: 23 Post-treatment: 23	Pain: 61 (3) Symptoms: 64 (3) ADL: 71 (5) Sport/rec: 21 (7)	Pre-treatment: 20 (5) Post-treatment: 23 (5)
Pascul-Garrido 2009 [22]	PF articular cartilage defects	Autologous chondrocyte implantation		4 years	Age: 32 (9) years Sex, F: 26 BMI: 30 (8) kg/m^2	Pre-treatment: 52 Post-treatment: 52	Pain: 48 (14) Symptoms: 51 (16) ADL: 60 (21) Sport/rec: 25 (16)	Pre-treatment: 24 (19) Post-treatment: 49 (29)

Study	Population	Treatment	Duration	Follow-up	Demographics	Sample size (n)	SF-36 domain	SF-36 score
36 Item Short Form Health Survey								
Astur 2014 [14]	Full thickness patellar chondral lesion	Autologous osteochondral transplantation		2 years	Age: <60 years Sex, F: NR BMI: NR	Pre-treatment: 33 Post-treatment: 33	Physical function	Pre-treatment: 46 (13) Post-treatment: 64 (29)
							Role physical	Pre-treatment: 44 (35) Post-treatment: 75 (32)
							Bodily pain	Pre-treatment: 52 (21) Post-treatment: 72 (24)
							General health	Pre-treatment: 74 (18) Post-treatment: 78 (18)
							Vitality	Pre-treatment: 62 (22) Post-treatment: 76 (18)
							Social function	Pre-treatment: 62 (16) Post-treatment: 74 (22)

Study	Population	Treatment	Duration	Follow-up	Demographics	Sample size (n)	Short-Form Domains	SF-36 score
Astur 2014 [14] (continued)							Role emotional	Pre-treatment: 44 (37) Post-treatment: 74 (41)
							Mental health	Pre-treatment: 66 (17) Post-treatment: 74 (11)
Ebert 2017 [29]	PF chondral lesions	PF matrix-induced autologous chondrocyte implantation56		3 months	Age: 38 (range: 20 to 65) years Sex, F: 24 BMI: 26 (range: 19 -37) kg/m^2	Pre-treatment: 67 Post-treatment: 67	Mental component	Pre-treatment: 52 (9) Post-treatment: 55 (9)
							Physical component	Pre-treatment: 37 (11) Post-treatment: 37 (9)
Meyerkort 2014 [20]	PF chondral defects	Matrix-induced autologous chondrocyte implantation		3 months	Age: 42 (12) years Sex, F: 10 BMI: 26 (4) kg/m^2	Pre-treatment: 23 Post-treatment: 23	Mental component	Pre-treatment: 51 (2) Post-treatment: 56 (3)
							Physical component	Pre-treatment: 36 (3) Post-treatment: 35 (4)
Patel 2017 [28]	Isolated patellofemoral arthrosis	HemiCap Wave patellofemoral prosthesis		24 months	Age: 63 (range: 46 to 83) years Sex, F: 8 BMI: 27 (range: 6 to 34) kg/m^2	Pre-treatment: 16 Post-treatment: 16	Mental component	Pre-treatment: 42 (range: 18 to 55) Post-treatment: 45 range: 20 to 62)
							Physical component	Pre-treatment: 32 (range: 19 to 40) Post-treatment: 53 (range: 19 to 70)

Study	Population	Treatment	Duration	Follow-up	Demographics	Sample size (n)	SF-12 domain	SF-12 score
12 Item Short Form Health Survey								
Pascul-Garrido 2009 [22]	PF articular cartilage defects	Autologous chondrocyte implantation		4 years	Age: 32 (9) years Sex, F: 26 BMI: 30 (8) kg/m^2	Pre-treatment: 52 Post-treatment: 52	Mental component	Pre-treatment: 50 (12) Post-treatment: 54 (10)
							Physical component	Pre-treatment: 37 (7) Post-treatment: 41 (7)

1 Data are presented as mean (standard deviation), unless otherwise stated. Abbreviations as follows: QOL, quality of life; KOOS, Knee Injury and Osteoarthritis
2 Outcome Score; PFOA, patellofemoral osteoarthritis; PF, patellofemoral; F, female; NR, not reported; BMI, body mass index; ADL, function in activities of daily
3 living; Sport/rec, function in sport and recreation activities

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