Are Patellofemoral Joint Alignment and Shape Associated With Structural Magnetic Resonance Imaging Abnormalities and Symptoms Among People With Patellofemoral Pain?

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Background: Patellofemoral malalignment has been observed among people with patellofemoral pain (PFP) and may be associated with the presence of imaging features of osteoarthritis, symptoms, and function.

Purpose: To determine whether patellofemoral joint alignment and bony shape are associated with (1) cartilage, bone, and soft tissue morphological abnormalities defined on magnetic resonance imaging (MRI) and (2) reported symptoms and function among people with PFP.

Study Design: Cross-sectional study; Level of evidence, 3.

Methods: Participants (mean ± SD age, 30.2 ± 9.5 years; range, 14-50 years; 78 females, 58.6%) completed questionnaires regarding demographics, pain, symptoms, and function and underwent a 3-T MRI scan of their more symptomatic eligible knee. Structural MRI abnormalities were scored with the MOAKS (Magnetic Resonance Imaging Osteoarthritis Knee Score), and MRI alignment and shape were measured with standardized methods. Associations among MOAKS features, PFP symptoms, and alignment and shape measures were evaluated with regression analyses (α = .05).

Results: Minor cartilage defects were present in 22 (16.5%) participants, patellar osteophytes in 83 (62.4%), anterior femur osteophytes in 29 (21.8%), Hoffa synovitis in 81 (60.9%), and prefemoral fat pad synovitis in 49 (36.8%). A larger Insall-Salvati ratio was significantly associated with the presence of patellar osteophytes (odds ratio [OR], 51.82; 95% CI, 4.20-640.01), Hoffa synovitis (OR, 60.37; 95% CI, 4.66-782.61), and prefemoral fat pad synovitis (OR, 43.31; 95% CI, 4.28-438.72) in the patellofemoral joint. A larger patellar tilt angle was significantly associated with the presence of minor cartilage defects (OR, 1.10; 95% CI, 1.00-1.20), the presence of patellar osteophytes (OR 1.12; 95%CI 1.02-1.22), and prefemoral fat pad synovitis (OR, 1.11; 95% CI, 1.03-1.20) in the patellofemoral joint. Finally, a larger bisect offset was significantly associated with the presence of minor cartilage defects (OR, 1.05; 95% CI, 1.00-1.11) and patellar osteophytes (OR, 1.07; 95% CI, 1.01-1.14) in the patellofemoral joint. The majority of patellofemoral alignment measures were not associated with symptoms or function.

Conclusion: For people with PFP, the presence of morphological abnormalities defined on MRI appears to be related to particular patellofemoral alignment measures, including higher Insall-Salvati ratio (indicating patella alta), larger patellar tilt angle (indicating greater lateral tilt), and larger bisect offset (indicating greater lateral displacement). Hardly any associations were found with symptoms or function. So there might be a distinct subgroup of PFP that is more prone to developing patellofemoral osteoarthritis later in life, as particular alignment measures seem to be associated with the presence of patellar osteophytes. Prospective studies are required to investigate the longitudinal relationship between alignment or bony shape and morphological abnormalities defined on MRI in this patient population.

Keywords: knee; alignment; imaging; patellofemoral

Patellofemoral pain (PFP) is a common knee condition accounting for 11% to 17% of all knee pain presentations in general practice.[34,37] PFP is characterized by pain around the patella that particularly arises during patellofemoral joint loading activities, such as squatting and

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walking up or down stairs,[11] as well as during prolonged sitting with the knees flexed.[7] While PFP typically affects relatively young, physically active people (aged <40 years), there is increasing evidence that PFP occurs at all stages of the life span, as well as among less physically active individuals.[9]

There is consensus that the etiology of PFP is multifactorial.[27] Elevated patellofemoral joint stress has frequently been postulated as a cause of pain and progression of symptoms.[11,14] One proposed cause of elevated joint stress is abnormal alignment of the patellofemoral joint. Several patellofemoral alignment and bone shape measures are associated with the presence of PFP, including a larger quadriceps angle, larger sulcus angle, larger patellar tilt angle, and greater lateral displacement.[12,22] However, there is very limited evidence from prospective studies to support a causal relationship.[12,23] Nevertheless, the proposed subgroup of patients with malaligned knees has been the subject of many studies because patellofemoral alignment features are potentially modifiable (eg, with taping[10] or bracing[1]) and can therefore have implications for the management and treatment of PFP.

Changes in patellofemoral load attributed to patellofemoral malalignment may exceed tissue capacity and potentially contribute to the development of chondral lesions and other imaging features of patellofemoral osteoarthritis (OA; eg, bone marrow lesions, osteophytes, synovitis).[24] Thuillier et al[32] reported differences in cartilage composition among women aged 18 to 45 years with PFP and patellar malalignment, as compared with pain-free controls. T1 rho values were significantly higher in the lateral patellar facet of those with PFP and patellar tilt, indicating greater proteoglycan loss.[32] Notably, T1 rho values approached those observed among people with early OA.[32] Furthermore, a recent systematic review found strong evidence of a relationship between trochlear bony shape and patellofemoral OA.[24] Patellofemoral malalignment has been linked to symptom severity among older people with knee OA, although results are inconsistent.[2,19] Thus, while there is literature suggesting that patellofemoral malalignment may be related to magnetic resonance imaging (MRI)–defined structural features of patellofemoral OA (eg, osteophytes and cartilage defects) among people with PFP, this relationship and the potential relationship with symptoms (ie, pain and function) are currently unknown. Therefore, the aim of this study was to determine whether patellofemoral joint alignment and bony shape are associated with (1) cartilage, bone, and soft tissue morphological abnormalities defined on MRI and (2) patient characteristics and reported symptoms among people with PFP.

METHODS

Study Design and Participants

Cross-sectional data from 2 separate but similar studies were used in this analysis: a cohort from Rotterdam, the Netherlands (TripleP study[33]; n = 64), and a cohort from Melbourne, Australia (Chronic Anterior Knee Pain [CAKP] Study[6]; n = 69). All participants with available baseline data were included in the current analyses. Both studies were approved by institutional review boards (Medical Ethical Committee of Erasmus MC, protocol MEC-2012-342; The University of Melbourne's Behavioural and Social Science Human Research Ethics Committee, ID 1136766).

The aggregated study population comprised participants with PFP (age range, 14-50 years) who were recruited by general practitioners, physical therapists, sports physicians, and local advertising. Inclusion and exclusion criteria for both studies were comparable (Table 1).

Measurements

After providing written informed consent, study participants were asked to complete questionnaires, which included the following: demographics (age, sex, body mass index [BMI], education level), knee complaints (duration of PFP, bilateral complaints), and pain severity on a 100-mm visual analog scale or 11-point numerical rating scale (usual pain and resting pain were combined into "usual pain," and worst pain and activity-related pain were combined into "worst pain"). Pain scores rated on a numerical rating scale were rescaled to a 0-100 visual analog scale to facilitate data pooling.[5] Knee symptoms and function were measured with the Anterior Knee Pain Scale (AKPS; 0-100)[20] and the Knee injury and Osteoarthritis Outcome Score (KOOS; 0-100),[28] including subscales of pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life.

All participants underwent an MRI scan of their (most) symptomatic eligible knee, positioned supine with the study knee in 20° to 30° of flexion. MRI in the TripleP study was performed at 3 T (Discovery MR750; GE Healthcare) with a dedicated 8-channel knee coil (Invivo Inc). The

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TABLE 1
Inclusion and Exclusion Criteria of the 2 Studies[a]

	TripleP Study	CAKP Study
Recruitment	Patients who visited a sports physician, physical therapist, or GP for PFP	Volunteers who responded to paid advertisements, flyers on community notice boards and university electronic bulletins, and referrals from health care practitioners
Age, y	14-40	26-50
Symptoms	Presence of at least 3 of the following: peri- or retropatellar pain while walking up or down stairs, squatting, running, cycling, sitting with knees flexed for a prolonged time, or grinding of the patella	Antero- or retropatellar knee pain aggravated by at least 2 activities that load the PFJ (eg, stair ambulation, squatting, rising from sitting) Pain during these activities present on most days during the past month
Pain severity	—	Knee pain severity of at least 30 mm on a 100-mm visual analog scale during aggravating activities
Duration of PFP	Longer than 2 mo but no longer than 2 y	Current symptoms >3 mo
Exclusion criteria	Knee OA, patellar tendinopathy, Osgood-Schlatter disease, or other defined pathological conditions of the knee Previous knee injuries or surgery Absolute and relative contraindications to undergo MRI	Concomitant pain from other knee structures, the hip, or the lumbar spine that may impede testing procedures Planned or previous knee surgery Moderate to severe concomitant TFJ OA (Kellgren-Lawrence grade >3 on posteroanterior radiograph) Recent knee injections (prior 3 months) Contraindications to radiograph or MRI Physical inability to undertake testing procedures

[a]CAKP, Chronic Anterior Knee Pain; GP, general practitioner; MRI, magnetic resonance imaging; OA, osteoarthritis; PFJ, patellofemoral joint; PFP, patellofemoral pain; TFJ, tibiofemoral joint.

MRI protocol comprised sagittal, axial, and coronal fast-spin echo proton density–weighted sequences with a slice thickness of 3 mm and sagittal and axial T2-weighted sequences with fat suppression and a slice thickness of 3 mm. In addition, a 3-dimensional high-resolution sagittal fat-suppressed spoiled gradient echo sequence was acquired with a slice thickness of 0.5 mm. CAKP Study MRI was acquired at 3 T (Achieva; Philips) with a 16-channel knee coil (Invivo Inc). The protocol consisted of a 3-dimensional proton density visualization of short relaxation time component sequence (ie, VISTA) acquired at 0.35-mm isotropic voxel size and reformatted in 3 planes. In addition, an axial proton density–weighted sequence with a slice thickness of 2.5 mm and fat saturation were performed.

All MRI scans from both studies were scored by a senior resident in radiology with a musculoskeletal subspecialization (J.L.K.), using the semiquantitative Magnetic Resonance Imaging Osteoarthritis Knee Score.[17] Since this score was primarily developed to evaluate the presence of OA in a relatively older population, specific patellofemoral features were added per the literature.[3] All findings were verified by an experienced musculoskeletal radiologist (E.H.O.). Scores of the most relevant and prevalent[33] items were used for this analysis, including minor patellar cartilage defects (present or not), patellar bone marrow lesions (present or not), patellar osteophytes (small to large), osteophytes at the anterior femur (small to large), and Hoffa synovitis and prefemoral fat pad synovitis (high signal intensity). High signal intensity was defined as abnormal high signal intensity on the T2-weighted images.

Alignment and bony shape were measured with methods described previously and were performed by the same radiologist (J.L.K.) in both studies.[3,30] These included the (1) Insall-Salvati (IS) ratio[18]; (2) patellar lateral translation relative to the femur, expressed in millimeters and dichotomized (absent <2 mm); (3) patellar tilt, expressed in degrees and dichotomized (present when >8°)[21]; (4) trochlear sulcus depth and angle, expressed in millimeters; (5) Wiberg classification for congruence (type I, facets are concave; type II, medial facet is rather smaller than lateral facet; type III, medial facet is markedly smaller than lateral facet[35]), dichotomized into symmetrical or not; and (6) tibial tuberosity–trochlear groove distance as an indicator of patellar lateralization.[36] The presence of a bipartite patella was also reported. All measures were performed by the same radiologist (J.L.K.) and confirmed by an experienced musculoskeletal radiologist (E.H.O.). One investigator (E.M.M.) performed 5 additional alignment and bony shape measurements following methods described by Stefanik et al[30] and Munch et al.[25] Lateral trochlear inclination was defined as the angle between the posterior condylar line and a line drawn along the surface of the lateral trochlear facet (degrees). Trochlear angle was defined as the angle between the posterior condylar line and a line passing along the most anterior margins of the medial and lateral trochlear facets (degrees). Bisect offset was defined as the percentage of the patella lateral to the line through the center of the trochlea. Patellar tilt angle was defined as the angle between the posterior condylar line and the line defining the maximal width of the patella (degrees). Patellar articular overlap was defined as the percentage of overlap of the length of patellar cartilage overlying the trochlear cartilage.[25] Details of alignment and bony shape measurements are presented in Figure 1.

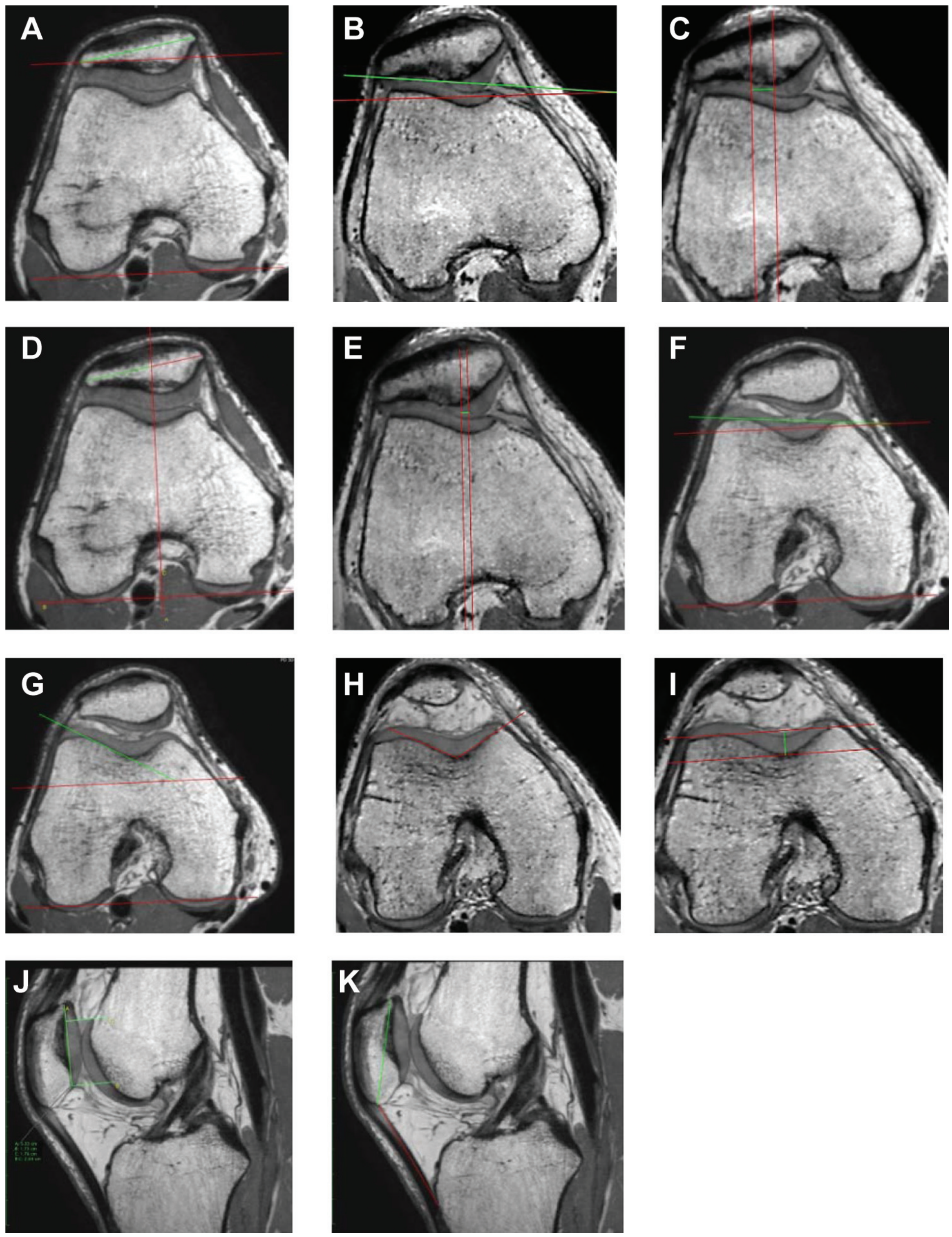

Figure 1. Alignment and bony shape measurements. (A) Patellar tilt angle: angle formed by line through the greatest width of the patella and posterior condylar line (PCL). (B) Lateral patellar tilt angle: the angle formed between the line drawn parallel to the lateral patellar facet and the line drawn connecting the most anterior points of the medial and lateral condyles. (C) Tibial tuberosity–trochlear groove distance: distance between lines drawn through the tibial tuberosity and trochlear groove in the axial plane (requires multiple magnetic resonance imaging slices). (D) Bisect offset: percentage of patella that lies lateral to the line bisecting the trochlear groove. (E) Patellar lateral translation: distance between lines from central medial ridge of patella and sulcus groove. (F) Trochlear angle: angle between anterior condylar line and PCL. (G) Lateral trochlear inclination: angle between lines through lateral trochlear facet and PCL. (H) Sulcus angle: angle between the condylar outsets. (I) Sulcus depth: depth of sulcus groove as compared with femoral condylar outsets (lines drawn). (J) Percentage articular overlap: amount of trochlear cartilage overlapping with patellar cartilage. (K) Insall-Salvati ratio: ratio of patellar tendon length to oblique patellar length (two lines drawn).

Statistical Analyses

Descriptive statistics were used to describe patient characteristics and morphological, alignment, and bony shape measures. Pearson χ^2 tests (dichotomous variables) and Student t tests (continuous variables) were used to evaluate potential differences between the cohorts. Analyses for cartilage, bone, and soft tissue morphological

TABLE 2
Patient Characteristics and Symptoms[a]

	Total Population (N = 133)	TripleP Study (n = 64)	CAKP Study (n = 69)	P Value[b]
Age, y	30.2 ± 9.5	23.4 ± 7.0	36.5 ± 6.6	<.001
Sex, female	78 (58.6)	35 (54.7)	43 (62.3)	.372
BMI, kg/m^2	24.4 ± 3.7	23.6 ± 3.8	25.0 ± 3.6	.025
High education level	102 (76.7)	37 (57.8)	65 (94.2)	<.001
Duration of complaints, mo				<.001
<6	26 (19.5)	20 (31.3)	6 (8.7)	
6-12	32 (24.1)	20 (31.3)	12 (17.4)	
13-24	28 (21.1)	23 (35.9)	5 (7.2)	
>24	47 (35.3)	1 (1.6)	46 (66.7)	
Bilateral complaints	80 (60.2)	33 (51.6)	47 (68.1)	.039
Pain, 0-100				
Usual	32.1 ± 23.3	39.2 ± 24.5	25.5 ± 20.1	.001
Worst	51.7 ± 26.5	65.8 ± 22.2	38.6 ± 23.4	<.001
AKPS, 0-100	70.1 ± 12.3	66.3 ± 11.6	73.6 ± 11.9	<.001
KOOS				
Pain	66.5 ± 18.0	59.7 ± 17.2	72.9 ± 16.3	<.001
Symptoms	63.2 ± 16.9	51.2 ± 11.8	74.2 ± 12.9	<.001
ADL	76.7 ± 17.4	71.4 ± 18.6	81.7 ± 14.7	.001
Sport/recreation	45.2 ± 26.0	39.4 ± 20.8	50.7 ± 29.2	.012
QoL	47.0 ± 16.3	46.1 ± 11.3	47.8 ± 19.9	.542

[a]Values are presented as mean ± SD or n (%). ADL, activities of daily living; AKPS, Anterior Knee Pain Scale; BMI, body mass index; CAKP, Chronic Anterior Knee Pain; KOOS, Knee injury and Osteoarthritis Outcome Score; QoL, quality of life.
[b]*P* value between the studies.

abnormalities defined on MRI, as well as alignment and bony shape measures, were adjusted for age. Correlations among the different alignment and bony shape measures were tested with Pearson correlations. Based on significant ($P < .10$) correlation coefficients and current literature, alignment and bony shape measures were selected for further analyses. Because of power issues, a preference was given to continuous measurements instead of dichotomized measures. Associations between morphological abnormalities defined on MRI and selected alignment and bony shape measures were tested with binary logistic regression analyses, adjusted for study, age, sex, and BMI. Specific items from the KOOS and AKPS were selected for the analyses of patellofemoral-specific symptoms. Item 6 from KOOS-pain was used to define pain while walking up or down stairs, dichotomized into no pain (no pain, some pain) and pain (moderate to severe). Items 2 and 6 were selected from KOOS-sport/recreation to define difficulties with squatting and running. These were both dichotomized into no difficulty (no, some difficulties) and difficulties (moderate to severe difficulties). Item 8 of the AKPS was used to define the presence of problems with prolonged sitting with knees flexed. Three categories were formed from 5 possible responses: no difficulty, pain after exercise, or problems with prolonged sitting (constant pain, pain forces to extend the knees temporarily, or unable).[7] Associations between PFP symptoms (usual pain; pain with stairs; problems with squatting, running, and prolonged sitting with knees flexed) and alignment and bony shape measures were evaluated with linear regression (usual pain), logistic regression (pain with stairs, problems squatting and running) and multinomal logistic regression (problems during prolonged sitting), adjusted for study, age, sex, and BMI. Differences between participant characteristics (age, sex, BMI, duration of PFP, bilateral PFP) and alignment and bony shape measures were tested with linear regression techniques (age, BMI), *t* tests (sex, bilateral PFP), and 1-way analysis of variance (duration of PFP). Associations were expressed in odds ratios (ORs) or betas with accompanying 95% CIs. All analyses were performed with SPSS for Windows (v 21; IBM), and *P* values <.05 were considered statistically significant.

RESULTS

The mean age of the total study population (N = 133) was 30 years (SD, 9.5) with 78 (59%) women (Table 2). Bilateral complaints were present among 60% of participants, and 56.4% had a minimum symptom duration of 12 months. Compared with the Australian CAKP Study, the Dutch TripleP study included a significantly younger PFP population with a lower BMI, shorter symptom duration, and fewer bilateral complaints (Table 2). Additionally, participants from the CAKP Study reported less severe symptoms on the visual analog scale for pain, AKPS, and KOOS (pain, symptoms, activities of daily living, and sport).

Minor cartilage defects were present in 22 (16.5%) participants, with more defects seen in the Dutch TripleP cohort (23.4%) versus the Australian CAKP cohort (10.1%) (Table 3). Patellar osteophytes were also more frequently present in the Dutch cohort (70.3%) as compared with the Australian cohort (55.1%). Hoffa synovitis and prefemoral fat pad synovitis were present among 60.9% and 36.8% of participants, respectively. Patellar

TABLE 3
Cartilage, Bone, and Soft Tissue Morphological Abnormalities Defined on Magnetic Resonance Imaging and Alignment and Bony Shape Measures[a]

	Total Population (N = 133)	TripleP Study (n = 64)	CAKP Study (n = 69)	*P* Value[b]
Abnormalities by MOAKS scoring				
Patella				
Minor cartilage defects	22 (16.5)	15 (23.4)	7 (10.1)	.003
Bone marrow lesions	74 (55.6)	34 (53.1)	40 (58.0)	.822
Osteophytes, small to large				
Patella	83 (62.4)	45 (70.3)	38 (55.1)	.003
Femur anterior	29 (21.8)	12 (18.8)	17 (24.6)	.136
Synovitis				
Hoffa	81 (60.9)	37 (57.8)	44 (63.8)	.437
Fat pad, prefemoral	49 (36.8)	24 (37.5)	25 (36.2)	.545
Alignment measures				
Insall-Salvati ratio	1.23 ± 0.18	1.21 ± 0.17	1.24 ± 0.18	.051
Patellar lateral translation				
mm	–0.02 ± 2.17	–0.30 ± 2.65	0.24 ± 1.57	.152
No.	22 (16.5)	20 (31.3)	2 (2.9)	.014
Patellar tilt				
Angle	8.5 ± 5.5	8.3 ± 6.0	8.7 ± 5.1	.660
No.	60 (45.1)	31 (48.4)	29 (42.0)	.815
Sulcus, deg				
Depth	6.40 ± 1.30	6.09 ± 1.03	6.69 ± 1.45	.746
Angle	134.9 ± 6.1[b]	137.3 ± 4.9	132.7 ± 6.3	.014
Wiberg classification				.994
Score 1	4 (3.0)	3 (4.7)	1 (1.4)	
Score 2	123 (92.5)	57 (89.1)	66 (95.7)	
Score 3	6 (4.5)	4 (6.3)	2 (2.9)	
TT-TG, lateralization	18 (13.5)	16 (25.0)	2 (2.9)	.152
Bisect offset, deg	57.62 ± 9.6	57.68 ± 9.9	57.56 ± 9.3	.876
Lateral patellar tilt angle, deg	12.10 ± 5.4	12.55 ± 5.7	11.67 ± 5.1	.340
Lateral trochlear inclination, deg	26.39 ± 4.8	25.46 ± 5.0	27.28 ± 4.5	.396
Trochlear angle, deg	0.45 ± 2.7[b]	1.17 ± 2.7	–0.23 ± 2.6	.008
Patellar articular cartilage, % (overlap)	0.49 ± 0.18[b]	0.35 ± 0.11	0.62 ± 0.15	<.001

[a]Values are presented as n (%) or mean ± SD. CAKP, Chronic Anterior Knee Pain; MOAKS, Magnetic Resonance Imaging Osteoarthritis Knee Score; TT-TG, tibial tubercle–trochlear groove.
[b]*P* value between studies, adjusted for age.

translation was present in 16.5% of participants and patellar tilt in 45.1%. A bipartite patella was seen in only 1 participant. Lateralization of the tibial tuberosity relative to the trochlear groove was present among 13.5% of participants. A significant difference between the cohorts was observed for patellar lateral translation (difference, 28.4%; 95% CI, 16.13-40.72), sulcus angle (mean difference [MD], –0.60; 95% CI, –1.04 to −0.17), trochlear angle (MD, 1.39; 95% CI, 0.48-2.31), and patellar articular overlap (MD, –0.26; 95% CI, –0.31 to 0.22).

Adjusted analyses (Table 4) showed that a larger IS ratio (indicating patella alta) was associated with the presence of bone marrow lesions of the patella (OR, 24.40; 95% CI, 2.63-226.79), patellar osteophytes (OR, 51.82; 95% CI, 4.20-640.01), Hoffa synovitis (OR, 60.37; 95% CI, 4.66-782.61), and prefemoral fat pad synovitis (OR, 43.31; 95% CI, 4.28-438.72). A larger patellar tilt angle (indicating greater lateral tilt) was associated with the presence of minor patellar cartilage defects (OR, 1.10; 95% CI, 1.00-1.20), patellar osteophytes (OR, 1.12; 95% CI, 1.02-1.22), and prefemoral fat pad synovitis (OR, 1.11; 95% CI, 1.03-1.20). Additionally, a larger bisect offset (indicating a more lateral patellar position) was associated with minor patellar cartilage defects (OR, 1.05; 95% CI, 1.00-1.11) and patellar osteophytes (OR, 1.07; 95% CI, 1.01-1.14). There was a significant association between a larger sulcus angle (indicating a shallower trochlea) and the presence of patellar osteophytes (OR, 1.10; 95% CI, 1.01-1.14). Finally, a larger patellar articular cartilage overlap was associated with fewer patellar osteophytes (OR, 0.03; 95% CI, 0.001-0.78) and less prefemoral fat pad synovitis (OR, 0.02; 95% CI, 0.001-0.52).

Table 5 presents the associations between alignment and bony shape measures and specific PFP symptoms. Sulcus angle was associated with usual pain (β = 0.77; 95% CI, 0.12-1.42) and problems while running (OR, 1.12; 95% CI, 1.03-1.23). Patellar articular cartilage overlap was associated with fewer problems while running (OR, 0.02; 95% CI, 0.00-0.84).

Some relationships were observed between participant characteristics and the alignment measures. Older age

TABLE 4
Association Between Morphological Abnormalities
Defined by Magnetic Resonance Imaging and Alignment and Bony Shape Measures[a]

	Patella		Osteophytes, Small to Large			Synovitis	
	Minor Cartilage Defects	Bone Marrow Lesions	Patella	Femur, Anterior	High Signal, Meniscus	Hoffa	Fat Pad, Prefemoral
Patellar tilt angle, deg	1.10[b] (1.00-1.20)	1.02 (0.96-1.10)	1.12[b] (1.02-1.22)	1.04 (0.96-1.14)	1.03 (0.95-1.11)	1.04 (0.97-1.13)	1.11[b] (1.03-1.20)
Patellar lateral translation, mm	1.08 (0.89-1.32)	0.99 (0.84-1.16)	1.06 (0.87-1.29)	0.99 (0.80-1.24)	1.02 (0.82-1.26)	0.94 (0.78-1.15)	1.04 (0.88-1.23)
Insall-Salvati ratio	11.60 (0.67-201.86)	24.40[b] (2.63-226.79)	51.82[b] (4.20-640.01)	3.73 (0.26-52.71)	0.53 (0.05-5.66)	60.37[b] (4.66-782.61)	43.31[b] (4.28-438.72)
Sulcus angle	0.98 (0.89-1.07)	1.04 (0.97-1.10)	1.10[b] (1.02-1.18)	1.04 (0.96-1.13)	1.01 (0.95-1.08)	1.04 (0.97-1.11)	1.09[b] (1.01-1.16)
Wiberg classification, medial < lateral	3.29 (0.66-16.36)	2.38 (0.57-10.01)	0.64 (0.16-2.55)	5.07 (0.99-25.75)	0.67 (0.12-3.87)	0.94 (0.24-3.70)	0.71 (0.17-3.00)
Lateral trochlear inclination	1.07 (0.97-1.19)	0.99 (0.92-1.09)	0.90 (0.82-0.98)	0.93 (0.84-1.03)	1.02 (0.93-1.11)	1.08 (0.99-1.18)	0.94 (0.87-1.02)
Trochlear angle	1.13 (0.94-1.36)	0.96 (0.84-1.10)	0.96 (0.83-1.10)	0.96 (0.80-1.16)	1.08 (0.92-1.25)	1.16 (0.99-1.35)	0.97 (0.84-1.11)
Bisect offset	1.05[b] (1.00-1.11)	1.01 (0.97-1.05)	1.07[b] (1.01-1.14)	1.02 (0.98-1.07)	1.01 (0.97-1.06)	1.04 (0.99-1.10)	1.04 (0.99-1.08)
Patellar articular cartilage, % (overlap)	0.18 (0.003-8.93)	0.89 (0.06-14.36)	0.03[b] (0.001-0.78)	0.87 (0.02-32.32)	2.36 (0.11-51.14)	0.09 (0.003-2.70)	0.02[b] (0.001-0.52)

[a]Values are presented as odds ratios (95% CI). All analyses are adjusted for study, age, sex, and body mass index.
[b]$P < .05$.

TABLE 5
Association Between Patellofemoral Pain Symptoms and Alignment and Bony Shape Measures[a]

		KOOS		AKPS: Prolonged Sitting[c]		AKPS
	Usual Pain[b] (0-100)	Pain Walking Stairs (n = 96)	Complaints While Squatting (n = 83)	Problems (n = 82)	Pain After Exercise (n = 24)	Problems While Running (n = 101)
Patellar tilt angle, deg	0.01 (–0.71 to 0.73)	0.956 (0.89 to 1.04)	0.94 (0.87 to 1.02)	1.04 (0.93 to 1.15)	0.96 (0.87 to 1.06)	0.97 (0.89 to 1.06)
Patellar lateral translation, mm	–0.73 (–2.48 to 1.02)	0.94 (0.77 to 1.14)	1.02 (0.85 to 1.23)	0.82 (0.58 to 1.17)	0.76 (0.55 to 1.04)	0.89 (0.72 to 1.09)
Insall-Salvati ratio	–8.77 (–30.32 to 12.78)	0.34 (0.03 to 3.46)	0.81 (0.08 to 7.85)	0.15 (0.004 to 5.40)	0.26 (0.01 to 5.06)	11.37 (0.83 to 155.94)
Sulcus angle, deg	0.77[d] (0.12 to 1.42)	1.01 (0.94 to 1.09)	0.99 (0.93 to 1.07)	0.94 (0.84 to 1.05)	0.98 (0.90 to 1.08)	1.12[d] (1.03 to 1.23)
Wiberg classification, medial < lateral	4.85 (–9.49 to 19.18)	4.77 (0.54 to 42.21)	2.56 (0.41 to 15.86)	1.86 (0.12 to 29.26)	1.16 (0.14 to 9.57)	0.56 (0.12 to 2.64)
Lateral trochlear inclination	–0.33 (–1.12 to 0.46)	0.99 (0.91 to 1.08)	0.98 (0.90 to 1.07)	1.09 (0.95 to 1.24)	0.98 (0.87 to 1.10)	1.04 (0.95 to 1.14)
Trochlear angle	–0.90 (–2.31 to 0.50)	0.97 (0.84 to 1.13)	1.07 (0.91 to 1.25)	1.06 (0.84 to 1.33)	1.02 (0.84 to 1.24)	1.16 (0.97 to 1.37)
Bisect offset	0.13 (–0.27 to 0.53)	0.96 (0.92 to 1.01)	0.99 (0.95 to 1.04)	0.95 (0.88 to 1.03)	0.98 (0.93 to 1.04)	0.96 (0.92 to 1.01)
Patellar articular cartilage, % (overlap)	0.07 (–21.11 to 37.83)	1.58 (0.07 to 35.55)	0.08 (0.003 to 2.18)	2.77 (0.07 to 115.85)	11.08 (0.10 to 1290.29)	0.02[d] (0.00 to 0.84)

[a]Values are presented as odds ratios (95% CI), unless otherwise noted. All analyses are adjusted for study, age, sex, and body mass index. AKPS, Anterior Knee Pain Scale; KOOS, Knee injury and Osteoarthritis Outcome Score.
[b]Values presented as β (95% CI).
[c]*No difficulty* reflects the reference group.
[d]$P < .05$.

was associated with a smaller patellar tilt angle ($P < .01$), smaller sulcus angle ($P < .01$), Wiberg classification indicating a concave facet ($P = .02$), larger lateral trochlear inclination ($P = .02$), and larger patellar articular cartilage overlap ($P < .01$). Female sex was associated with larger patellar tilt angle ($P < .01$), higher IS ratio ($P < .01$), and higher bisect offset ($P = .01$). Symptom duration >24 months was associated with higher IS ratio ($P = .04$), smaller sulcus angle ($P = .03$), and smaller trochlear angle ($P = .04$). The presence of bilateral PFP was associated with a larger patellar tilt angle ($P = .01$), larger IS ratio ($P < .01$), and smaller (negative) trochlear angle ($P < .01$) (see Appendix Table A1, available in the online version of this article).

DISCUSSION

Findings of this study highlight an apparent association between 5 measures of patellofemoral joint alignment and bony shape and the presence of cartilage, bone, and soft tissue morphological abnormalities of the patellofemoral joint among people with PFP. Those with a higher IS ratio (indicating patella alta), greater patellar tilt angle (indicating greater lateral tilt), greater bisect offset (indicating a more lateral patellar position), and greater sulcus angle (indicating a shallower trochlea) had higher odds of having features of patellofemoral OA on MRI, including patellar osteophytes, minor cartilage defects, and high fat pad signal. A lower percentage of patellar articular cartilage overlap was associated with having osteophytes and fat pad synovitis. Age, sex, duration of PFP, and bilateral PFP were associated with several alignment and bony shape measures of the patellofemoral joint. However, only a few associations were found between patellofemoral joint alignment and bony shape and patient-reported symptoms and function.

A higher IS ratio, a measure of patella alta, had the strongest association with morphological abnormalities of the patellofemoral joint, including the presence of patellar bone marrow lesions, patellar osteophytes, and Hoffa synovitis. A simpler alternative, the patellar articular overlap, confirmed these associations for patellar osteophytes and fat pad synovitis. The importance of the IS ratio as a measure of alignment was acknowledged by Stefanik et al,[30] although in an older population, for its relationship to patellofemoral joint dysfunction. A high-riding patella may result in delayed engagement of the patella in the trochlea during knee flexion and a reduced articular cartilage contact area. It was also shown that lateral patellar maltracking is more prevalent among people with PFP and patella alta as compared with those with PFP and normal patellar height,[26] possibly because a high-riding patella has less bony constraint to mediolateral patellar movement in low knee flexion angles. Changes in local joint loading attributed to patella alta with or without lateral maltracking may lead to increased patellofemoral joint stress and may initiate or perpetuate OA processes. Indeed, Stefanik et al[30] found that a high IS ratio was a risk factor for worsening of patellofemoral cartilage damage and bone marrow lesions over 30 months. Interestingly, we also found a positive association between (1) a higher IS ratio and (2) the presence of Hoffa synovitis and prefemoral fat pad synovitis as well as less patellar articular cartilage overlap and prefemoral pat pad synovitis. Although the role of the fat pad in the etiology of PFP remains unclear,[11] recent studies described the fat pad as an active joint tissue capable of modulating inflammatory and destructive responses in knee OA.[4] Findings of the present study are supported by Subhawong et al,[31] who found that several markers of patellar instability were associated with superolateral Hoffa fat pad edema among patients with knee pain. This implies that abnormal alignment and aberrant movement may contribute to high signal intensity of the fat pad, indicating fat pad edema and synovitis.

We also found that a more lateral patellar position (tilt, displacement) was associated with greater odds of morphological abnormalities defined on MRI in the patellofemoral joint. Abnormal patellar alignment is proposed to reduce the contact area between the patella and trochlea, resulting in increased patellofemoral joint stress, particularly in the lateral patellofemoral joint.[14,16] Elevated loading of the patellofemoral joint was hypothesized to result in reduced patellar cartilage thickness and reduced deformational behavior of patellar articular cartilage.[13] Salsich and Perman[29] found that only 17% of the variance in contact area was explained by patellar width and that patellar tilt angle did not contribute to patellofemoral joint contact area. These results are contrary to literature linking patellar alignment to patellofemoral contact area.[14,15] Irrespective of the mechanism, our findings do suggest that patellofemoral joint alignment or bony shape may contribute to increased patellofemoral joint stress, as a greater lateral patellar tilt angle and bisect offset were associated with cartilage defects of the patella. However, these measures were not associated with PFP intensity or symptoms.

The findings of this study are in line with previous findings of patellofemoral OA populations, in which associations were found between knee alignment and imaging features of patellofemoral OA.[24] As described here, it is plausible that patellofemoral malalignment may lead to higher patellofemoral joint stress, potentially leading to structural morphological changes in the joint (ie, early OA features). However, the cross-sectional nature of the presented data means that conclusions cannot be made regarding causation. Although we did not find an association between (1) specific PFP symptoms and function and (2) alignment and bony shape measures, we did find that specific patient characteristics were associated with particular alignment measures, including age, sex, bilaterality and duration of PFP. It was apparent that patients with a relatively long symptom duration and the presence of bilateral PFP were more likely to have a higher IS ratio and larger sulcus angle as compared with those with a shorter symptom duration and unilateral knee pain. This indicates that these patients might represent a distinct subgroup of PFP that is more prone to developing patellofemoral OA later in life, as these alignment measures seem to be associated with the presence of patellar osteophytes. Long-term follow-up of patients with PFP will provide better insight into the often-suggested patellofemoral OA continuum for young PFP patients[8] and whether malalignment is associated with the progression of structural MRI features in the patellofemoral joint.

The cross-sectional nature of our findings means that clinical implications need to be made with caution. Based on current findings, people with PFP who have patella alta or a shallow trochlea may be at risk of more persistent symptoms given the associations with early OA features.[24] It is important to distinguish between modifiable and nonmodifiable factors that are related to patellofemoral joint structural morphology. For example, patella alta and lateral patellar tilt and displacement may be amenable to nonsurgical interventions, such as patellar taping, bracing, and exercise.[1] In comparison, surgery is required to increase the depth of a shallow trochlea. Until the longitudinal relationship between alignment or bony shape and morphological abnormalities is established, it is difficult to recommend surgical intervention when the sulcus angle is not strongly related to patient-reported symptoms or function.

Strengths and Limitations

This cross-sectional study used data from 2 of the largest PFP cohorts with MRI. Although the cohorts were similar, there are differences that should be noted. Patients recruited in the Netherlands were, on average, younger, had a shorter symptom duration, and reported worse pain and symptoms as compared with those recruited in Australia. This is likely related to the recruitment methods applied. While participants in the Netherlands were recruited in primary care settings (general practice, physical therapy, and sports medicine clinics), participants in Australia were recruited by means of local advertising. To address this, all analyses were adjusted for "study." Furthermore, our research questions centered on within-participant relationships rather than between-group differences. Thus, the effect of these differences on study outcomes is likely to be marginal.

While our cohort represents a relatively large sample size, we evaluated many associations, and it is plausible that a type I error may have occurred. Our analyses were hypothesis generating, and as physiologically expected, consistent associations were found between particular alignment measures and morphological abnormalities. This strengthens our confidence that the results are less likely to be by chance owing to multiple testing issues. To enhance statistical power, we chose to analyze all alignment measures as continuous variables. Clinical cutoff values were proposed in the literature and may be worth considering in future MRI studies of larger PFP cohorts.

CONCLUSION

For people with PFP, particular alignment and bony shape measures—including higher IS ratio (indicating patella alta), smaller percentage of patellar articular overlap, larger patellar tilt angle (indicating greater lateral tilt), and larger bisect offset (indicating greater lateral displacement)—are associated with the presence of patellar osteophytes, minor cartilage defects, or Hoffa and prefemoral fat pad synovitis. Patellofemoral alignment and bony shape measures do not appear to be related to symptoms and function. Prospective studies are required to investigate the longitudinal relationship between alignment or bony shape and cartilage, bone, and soft tissue morphological abnormalities defined on MRI in this patient population.

REFERENCES

1. Callaghan MJ, Guney H, Reeves ND, et al. A knee brace alters patella position in patellofemoral osteoarthritis: a study using weight bearing magnetic resonance imaging. *Osteoarthritis Cartilage*. 2016;24(12):2055-2060.
2. Chang CB, Han I, Kim SJ, Seong SC, Kim TK. Association between radiological findings and symptoms at the patellofemoral joint in advanced knee osteoarthritis. *J Bone Joint Surg Br*. 2007;89(10):1324-1328.
3. Chhabra A, Subhawong TK, Carrino JA. A systematised MRI approach to evaluating the patellofemoral joint. *Skeletal Radiol*. 2011;40(4):375-387.
4. Clockaerts S, Bastiaansen-Jenniskens YM, Runhaar J, et al. The infrapatellar fat pad should be considered as an active osteoarthritic joint tissue: a narrative review. *Osteoarthritis Cartilage*. 2010;18(7):876-882.
5. Collins NJ, Bierma-Zeinstra SM, Crossley KM, van Linschoten RL, Vicenzino B, van Middelkoop M. Prognostic factors for patellofemoral pain: a multicentre observational analysis. *Br J Sports Med*. 2013;47(4):227-233.
6. Collins NJ, Oei EHG, de Kanter JL, Vicenzino B, Crossley KM. Prevalence of radiographic and MRI features of patellofemoral osteoarthritis in young and middle-aged adults with persistent patellofemoral pain [published online August 23, 2018]. *Arthritis Care Res (Hoboken)*. doi:10.1002/acr.23726
7. Collins NJ, Vicenzino B, van der Heijden RA, van Middelkoop M. Pain during prolonged sitting is a common problem in persons with patellofemoral pain. *J Orthop Sports Phys Ther*. 2016;46(8):658-663.
8. Crossley KM. Is patellofemoral osteoarthritis a common sequela of patellofemoral pain? *Br J Sports Med*. 2014;48(6):409-410.
9. Crossley KM, Callaghan MJ, van Linschoten R. Patellofemoral pain. *BMJ*. 2015;351:H3939.
10. Crossley KM, Marino GP, Macilquham MD, Schache AG, Hinman RS. Can patellar tape reduce the patellar malalignment and pain associated with patellofemoral osteoarthritis? *Arthritis Rheum*. 2009;61(12):1719-1725.
11. Crossley KM, Stefanik JJ, Selfe J, et al. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester: part 1. Terminology, definitions, clinical examination, natural history, patellofemoral osteoarthritis and patient-reported outcome measures. *Br J Sports Med*. 2016;50(14):839-843.
12. Drew BT, Redmond AC, Smith TO, Penny F, Conaghan PG. Which patellofemoral joint imaging features are associated with patellofemoral pain? Systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2016;24(2):224-236.
13. Farrokhi S, Colletti PM, Powers CM. Differences in patellar cartilage thickness, transverse relaxation time, and deformational behavior: a comparison of young women with and without patellofemoral pain. *Am J Sports Med*. 2011;39(2):384-391.
14. Farrokhi S, Keyak JH, Powers CM. Individuals with patellofemoral pain exhibit greater patellofemoral joint stress: a finite element analysis study. *Osteoarthritis Cartilage*. 2011;19(3):287-294.
15. Heino Brechter J, Powers CM. Patellofemoral stress during walking in persons with and without patellofemoral pain. *Med Sci Sports Exerc*. 2002;34(10):1582-1593.
16. Ho KY, Keyak JH, Powers CM. Comparison of patella bone strain between females with and without patellofemoral pain: a finite element analysis study. *J Biomech*. 2014;47(1):230-236.

17. Hunter DJ, Guermazi A, Lo GH, et al. Evolution of semi-quantitative whole joint assessment of knee OA: MOAKS (MRI Osteoarthritis Knee Score). *Osteoarthritis Cartilage*. 2011;19(8):990-1002.
18. Insall J, Salvati E. Patella position in the normal knee joint. *Radiology*. 1971;101(1):101-104.
19. Kalichman L, Zhu Y, Zhang Y, et al. The association between patella alignment and knee pain and function: an MRI study in persons with symptomatic knee osteoarthritis. *Osteoarthritis Cartilage*. 2007; 15(11):1235-1240.
20. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. *Arthroscopy*. 1993; 9(2):159-163.
21. Kujala UM, Kormano M, Osterman K, et al. Magnetic resonance imaging analysis of patellofemoral congruity in females. *Clin J Sport Med*. 1992;2(1):21-26.
22. Lankhorst NE, Bierma-Zeinstra SM, van Middelkoop M. Factors associated with patellofemoral pain syndrome: a systematic review. *Br J Sports Med*. 2013;47(4):193-206.
23. Lankhorst NE, Bierma-Zeinstra SM, van Middelkoop M. Risk factors for patellofemoral pain syndrome: a systematic review. *J Orthop Sports Phys Ther*. 2012;42(2):81-94.
24. Macri EM, Stefanik JJ, Khan KK, Crossley KM. Is tibiofemoral or patellofemoral alignment or trochlear morphology associated with patellofemoral osteoarthritis? A systematic review. *Arthritis Care Res (Hoboken)*. 2016;68(10):1453-1470.
25. Munch JL, Sullivan JP, Nguyen JT, et al. Patellar articular overlap on MRI is a simple alternative to conventional measurements of patellar height. *Orthop J Sports Med*. 2016;4(7):2325967116656328.
26. Pal S, Besier TF, Beaupre GS, Fredericson M, Delp SL, Gold GE. Patellar maltracking is prevalent among patellofemoral pain subjects with patella alta: an upright, weightbearing MRI study. *J Orthop Res*. 2013;31(3):448-457.
27. Powers CM, Bolgla LA, Callaghan MJ, Collins N, Sheehan FT. Patellofemoral pain: proximal, distal, and local factors: 2nd International Research Retreat. *J Orthop Sports Phys Ther*. 2012;42(6):A1-A54.
28. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee injury and Osteoarthritis Outcome Score (KOOS)—development of a self-administered outcome measure. *J Orthop Sports Phys Ther*. 1998;28(2):88-96.
29. Salsich GB, Perman WH. Patellofemoral joint contact area is influenced by tibiofemoral rotation alignment in individuals who have patellofemoral pain. *J Orthop Sports Phys Ther*. 2007;37(9):521-528.
30. Stefanik JJ, Zumwalt AC, Segal NA, Lynch JA, Powers CM. Association between measures of patella height, morphologic features of the trochlea, and patellofemoral joint alignment: the MOST study. *Clin Orthop Relat Res*. 2013;471(8):2641-2648.
31. Subhawong TK, Eng J, Carrino JA, Chhabra A. Superolateral Hoffa's fat pad edema: association with patellofemoral maltracking and impingement. *AJR Am J Roentgenol*. 2010;195(6):1367-1373.
32. Thuillier DU, Souza RB, Wu S, Luke A, Li X, Feeley BT. T1rho imaging demonstrates early changes in the lateral patella in patients with patellofemoral pain and maltracking. *Am J Sports Med*. 2013; 41(8):1813-1818.
33. van der Heijden RA, de Kanter JL, Bierma-Zeinstra SM, et al. Structural abnormalities on magnetic resonance imaging in patients with patellofemoral pain: a cross-sectional case-control study. *Am J Sports Med*. 2016;44(9):2339-2346.
34. van Middelkoop M, van Linschoten R, Berger MY, Koes BW, Bierma-Zeinstra SM. Knee complaints seen in general practice: active sport participants versus non-sport participants. *BMC Musculoskelet Disord*. 2008;9:36.
35. Wiberg G. Roentgenographic and anatomic studies on the patellofemoral joint with special reference to chondromalacia patellae. *Acta Orthop Scand*. 1941;12:319-410.
36. Wittstein JR, Bartlett EC, Easterbrook J, Byrd JC. Magnetic resonance imaging evaluation of patellofemoral malalignment. *Arthroscopy*. 2006;22(6):643-649.
37. Wood L, Muller S, Peat G. The epidemiology of patellofemoral disorders in adulthood: a review of routine general practice morbidity recording. *Prim Health Care Res Dev*. 2011;12(2):157-164.