

# Radiographic Osteoarthritis Prevalence Over Ten Years After Anterior Cruciate Ligament Reconstruction

## Authors

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## Key words

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## ABSTRACT

The purpose of this study was to conduct an up-to-date systematic review and meta-analysis of radiographic knee osteoarthritis (OA) over minimal ten years after ACL reconstruction. The database of Pubmed and the Ovid was adopted. The radiographic knee OA over minimal ten years after ACL reconstruction was systematically reviewed. Both the ipsilateral and contralateral knees were evaluated referring to the tibiofemoral joint (TFJ), the patellofemoral joint (PFJ), and the overall knee OA prevalence. Nineteen studies were included for review, with nine screened for the meta-analysis. The overall knee OA rate ranged from 8.3–79.2 %, meanly 51.6 % on the ipsilateral side; ranged from 3.6–35.7 %, meanly 15.5 % on the contralateral side. Compared to the contralateral side, the RR of developing radiographic OA was 3.73 ( $P < 0.01$ ) for the overall knee, 2.88 ( $P < 0.01$ ) for TFJ, and 2.42 ( $P < 0.01$ ) for PFJ. Ipsilaterally, the RR of developing TFJ radiographic OA was 1.15 ( $P < 0.01$ ) compared to that of the PFJ. Over a minimum of 10 years after surgery, more than half the cases developed overall radiographic OA on the ipsilateral knee, which was nearly four times higher than the contralateral side. On the ipsilateral knee, the TFJ was most affected.

## Introduction

The long-term clinical outcomes of ACL reconstruction are richly reported in the literature [1–12]. Interestingly, the occurrence of radiographicosteoarthritis (OA) varies among those researchers, ranging from 10–90 % [13–16]. The inclusion of cases, evaluation methods, and follow-up period might be a good explanation for that inconsistency. Falciglia et al. reported follow-up research at meanly 13.6 years after ACL reconstruction among the adolescent population [17], in which the radiographic OA rate was merely 8.3 %. While Lohmander et al. reported that the radiographic OA rate was 50 % at 10–20 years after ACL injury [13]. In contrast,

Gillquist et al. reported that rate could reach as high as over 70 % at 15–20 years after ACL surgeries [18].

In 2009, Oiestad et al. systematically reviewed the rate of knee OA after ACL injury [19], concluding that the prevalence of knee OA was low for isolated ACL injury and higher for subjects with combined injuries. However, the insufficient data from the included studies rendered it difficult to reach a firm conclusion on the prevalence of knee OA for more than 10 years. In 2013, Claes et al. reported a meta-analysis of knee radiographic OA after ACL surgery [20], suggesting that the knee OA prevalence after ACL reconstruction is lower than commonly perceived. The same year, Ajuied et al.

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reported the other meta-analysis on this topic [21], concluding that ACL reconstruction had a role in reducing the risk of developing degenerative changes at 10 years. Remarkably, in the meta-analysis abovementioned, only a limited number of studies were included. Additionally, the evidence quality was lower with many as retrospective cohorts or case series, which inevitably affect the efficacy of conclusion.

During the past several years, studies concerning the long-term clinical outcomes of the ACL reconstruction were successively reported [1, 6, 7, 17, 22–34]. Some were randomized control trials or prospective cohort studies [1, 22, 23, 26, 27, 29, 34] of relatively higher evidence quality compared with previous reports. Due to standardized reporting strategy and better design, more detailed OA information could be attained, including those of the ipsilateral and contralateral sides, as well as those of the tibiofemoral joint (TFJ) and patellofemoral joint (PFJ). Over the long term after ACL

reconstruction, the OA development could be observed in both the TFJ and PFJ. Although the OA rate was as anticipated a higher level in the TFJ, it was also reported that the OA of the PFJ had been under-recognized, which could be prevalent after ACLR and was associated with worse symptoms and function [25, 35]. Considering the differences of clinic manifestation, treating methods, as well as the etiology between the OA of the TFJ and the PFJ, a meta-analysis of the OA development between the TFJ and PFJ could be meaningful for clinicians to better recognize the OA development in the long term after ACLR. So far, no investigation has compared the radiographic OA of the TFJ with that of the PFJ by meta-analysis. In addition, no study ever compared the radiographic OA of TFJ or PFJ between the ipsilateral and contralateral sides.

The purpose of this study was to conduct an up-to-date systematic review and meta-analysis of the knee radiographic OA over a minimum of ten years after ACL reconstruction. Both the ipsilateral and contralateral knees were evaluated referring to the TFJ, the PFJ, and the overall knee OA prevalence.

► **Table 1a** Searching Strategy and Outcomes from PubMed.

Search Step	Search Terms	Number
1	Anterior cruciate ligament [MeSH]	9 869
2	Knee joint [MeSH]	52 908
3	Ligaments, articular [MeSH]	27 786
4	Knee joint OR Ligaments, articular	73 171
5	Knee injuries [MeSH]	22 325
6	Osteoarthritis, knee [MeSH]	15 539
7	Osteoarthritis [MeSH]	54 274
8	Epidemiologic studies [MeSH]	2 120 577
9	Epidemiology	2 124 510
10	2 or 7	97 604
11	1 or 4 or 5	81 314
12	6 or 10	97 604
13	8 or 9	3 536 969
14	11 and 12 and 13	13 564
15	Limits: humans, English	12 014

► **Table 1b** Searching Strategy and Outcomes from Ovid.

Search Step	Search Terms	Number
1	ligaments or ligaments, articular	122 764
2	Anterior Cruciate Ligament	66 387
3	Knee Joint	128 822
4	Knee Injuries	27 067
5	Osteoarthritis	321 405
6	Osteoarthritis, Knee	27 003
7	Epidemiology	2 388 942
8	Epidemiologic studies	126 831
9	7 or 8	2 477 116
10	3 or 5	418 964
11	1 or 3	241 184
12	2 or 4 or 11	297 730
13	6 or 10	418 964
14	9 and 12 and 13	3 458
15	Limit 14 to English language	3 297
16	Limit to humans	3 248

## Materials and Methods

The systematic review was initiated on December 12, 2017. The retrieval platform included the Pubmed and the Ovid. The database included the Medline (since inception to December 12, 2017), the Embase (since 1974 to December 12, 2017), the Global Health Archive (from 1910 to 1972). The searching strategy used in the Pubmed and the Ovid was presented in ► **Tables 1a, b**. For all returned studies, the titles and abstracts were respectively reviewed and assessed by inclusion and exclusion criteria, presented in ► **Table 2**. If the titles and abstracts provided vague or insufficient information, the full texts were then reviewed. The references of included studies were reviewed for additional sources. The reviewing and screening process was respectively fulfilled by two investigators. Given disagreement on including or excluding of study, the discussion was required. If necessary, a professor specialized in sports medicine was invited to join the discussion. The registration number of the study is CRD42018084786. The study meets the ethical standards of Harriss et al. [36].

## Study Quality Assessment

The Modified Coleman Methodology Score (MCMS) was applied for study quality evaluation. The original CMS was derived from the Consolidated Standards Of Reporting Trials (CONSORT) statement and applied for the review of patellar and Achilles tendinopathy [37, 38]. In 2009, Oiestad modified the CMS for cohort studies, and adopted it in reviewing the long-term radiographic OA after ACL injuries [19]. In the modified CMS, questions 2, 3, 6, and 7 in part A were altered or removed, resulting in a maximum score of 50; question 1, criterion of sensitivity and the reliability of radiographic assessment in part B were altered or removed, resulting in a maximum score of 40. Therefore the maximum score of the modified CMS was 90. In this study, we adopted the same version as Oiestad et al. We compared the MCMS of the studies of different designs, published before and after December 31, 2013, and included it or did not include it in the meta-analysis.

► **Table 2** Study Selection Criteria.

Inclusion criteria	Exclusion criteria
1. Prospective or retrospective design	1. Follow-up period less than ten years
2. Patients with ACL tear surgically treated	2. No radiographic exam performed
3. ACL reconstruction (Arthroscopically, Extra-articular and Intra-articular, Open surgery)	3. No Kellgren&Lawrence classification adopted
4. Radiographic exam at final follow-up	4. No radiographic evaluation method was adopted
5. Adopting the Kellgren&Lawrence classification	5. The study involved the same subjects
6. Isolate ACL injury and ACL injury combined with meniscal, cartilage, and medial collateral ligament injuries	6. No ACL reconstruction was performed
7. Minimal follow-up period of 10 years	
8. Written in English	

► **Table 3** Inclusion criteria for meta-analysis.

Inclusion criteria
1. Reporting the overall knee radiographic OA on both ipsilateral and contralateral sides;
2. Reporting the TFJ radiographic OA on both ipsilateral and contralateral sides;
3. Reporting the PFJ radiographic OA on both ipsilateral and contralateral sides;
4. Reporting the TFJ and the PFJ radiographic OA on the ipsilateral side;
5. Reporting the TFJ and the PFJ radiographic OA on the contralateral side.

## Data extraction and statistical analysis

The data were sorted and compiled with the Excel (Office 365, Microsoft). The authors, country, journal, study design, publish year, patients demographics, follow-up period, evaluation rate (subjects radiographically evaluated/subjects included), surgical technique, graft, meniscus injury, cartilage injury, radiographic outcomes, and position radiograph were extracted. The inclusion criteria for meta-analysis were presented in ► **Table 3**.

For the scarce number of randomized control studies that adopted the Kellgren&Lawrence classification [1, 23, 29], this study included the non-randomized prospective cohort studies in meta-analysis. This method has been successfully adopted in previous studies [21, 39].

The grade II of Kellgren&Lawrence classification was set as the cut-off point for radiographic OA. The grading algorithm of the TFJ, the PFJ, and overall knee radiographic OA was consistent with previous reports. For unreported data necessitated for the meta-analysis, requesting emails were sent to the corresponding authors.

The Review Manager 5 (Revman) was adopted for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and meta-analysis. The risk ratios (RR) with its 95% Confidential Interval (CI) were calculated based on the data extracted in the meta-analysis using the Review Manager 5 (Revman). The publication bias was visually inspected by funnel plots for asymmetry within the comparison of interest. The random effects model and fixed effects model were adopted for data pooling. The random effects model was used to reduce bias from systematic errors given higher heterogeneity of the included studies. Heterogeneity was quantified by the  $I^2$  statistic, with  $P < 0.10$  being statistically significant. We performed a sensitivity analysis, in which one study was

in turn removed at a time while the others were analyzed to estimate whether the  $I^2$  result could be affected markedly by the study removed.

## Results

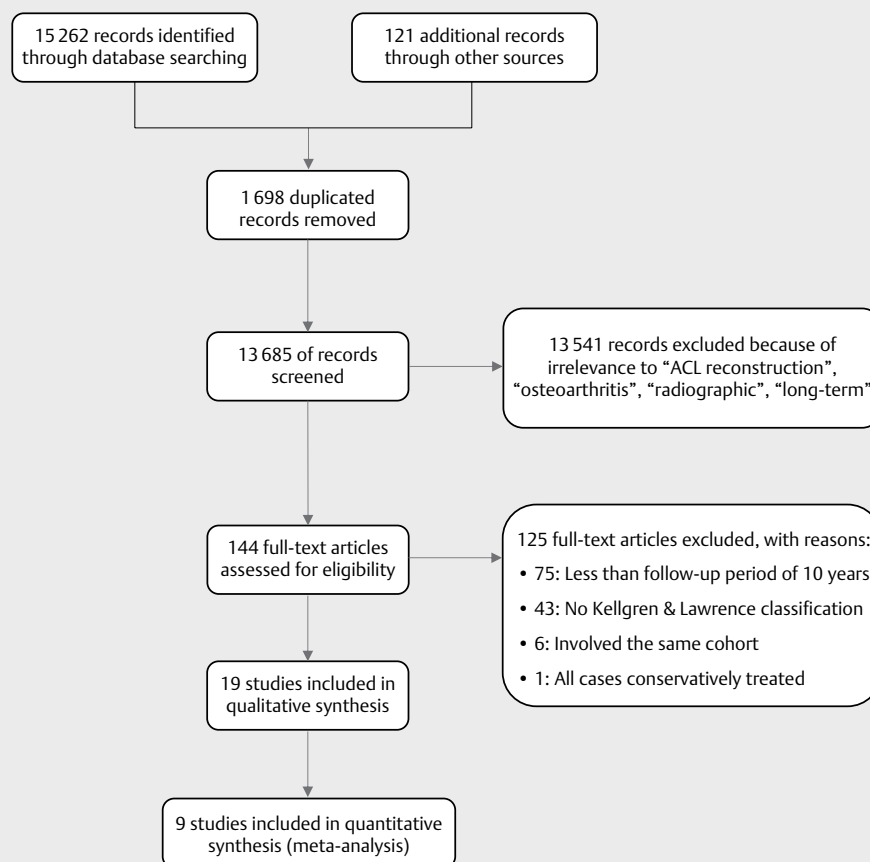
### General information

A total of 15 383 studies were obtained from the database. With all duplicates removed, 13 685 articles were screened using the inclusion and exclusion criteria. Then 144 studies were identified and carefully read. Eventually, 19 articles were finally included in the systematic review [1, 4–6, 8, 16, 17, 22, 27, 29, 31, 34, 40–46], and nine articles were included in the meta-analysis [1, 5, 22, 27, 29, 40, 41, 45, 46] (► **Fig. 1**).

For the articles included, 4 were randomized controlled trials [1, 22, 34, 41], 8 were cohort studies [5, 27, 29, 31, 40, 44–46], 5 were case series [4, 6, 16, 17, 42], and 2 were case-control studies [8, 43]. One group of subjects from a case-control study was not included because the follow-up period was less than ten years [43]. In the other case-control study, one group of subjects was excluded for conservative treatment [8]. The corresponding authors of four studies (26.7% response rate) replied to our request for unpublished data [1, 22, 27, 29].

### Study characteristics

In the 19 articles included, the sample size ranged from 12 [17] to 210 [29]. A total of 1 642 cases were included in the analysis, and 1,273 of these were radiographically evaluated, with evaluation rate ranging from 58.5% [34] to 100% [4, 6, 8, 16, 17, 42]. The follow-up period ranged from 10 years [5, 8, 42, 45] to 23 years [27], with a mean follow-up period of 15.4 years. Regarding the graft choice, the autologous hamstring (HT) was applied in all cases from four articles [6, 17, 27, 42]; the autologous bone patella tendon bone (BPTB) in all cases from seven articles [4, 8, 16, 41, 44–46]; the autologous HT or BPTB, respectively, in one group of cases from five articles [1, 5, 22, 29, 34]; synthetic ligament in some cases from two articles [31, 40]; the BPTB allografts were applied in one group of cases from one article [43]. Arthroscopic single bundle ACL reconstruction was adopted in 18 articles. Among them, one group of cases from one article was treated additionally by extra-articular ACL reconstruction using iliotibial tract, namely the Macintosh technique modified by Cocker Arnold [27]; in another article, open



► **Fig. 1** PRISMA flow diagram of the search strategy.

ACL reconstruction was performed in one group of cases. The open ACL reconstruction was performed in all cases in one article [41].

The details of combined meniscus injuries were not reported in 5 articles [4–6, 31, 45]. One article expelled the cases of combined meniscus injuries [16]. The remaining 13 articles described the details of combined meniscus injuries. The rate of combined injuries ranged from 16.7% [17] to 72.1% [42] with a mean rate of 49.5%. One article expelled the cases of combined cartilage injuries; in addition, only five articles described the combined cartilage injuries. More details are presented in ► **Tables 4a, b**.

### Methodological Quality

The details of the methodology used to evaluate the quality of the included studies, the studies with different designs, the studies published before and after December 31, 2013, and the studies included or not in the meta-analysis, were presented in ► **Tables 5a–d**.

### Radiographic OA rate

Sixteen articles reported the knee radiographic OA on the ipsilateral side [1, 4, 5, 8, 16, 17, 22, 27, 31, 34, 40–42, 44–46]. Seven articles reported the knee radiographic OA on the contralateral side [1, 5, 22, 40, 41, 45, 46].

Four articles reported the radiographic OA of the ipsilateral TFJ [22, 27, 29, 40]. Three articles reported the radiographic OA of the contralateral TFJ [22, 29, 40].

Four articles reported the radiographic OA of the ipsilateral PFJ [22, 27, 29, 40]. Three articles reported the radiographic OA of the contralateral PFJ [22, 29, 40]. More details were presented in ► **Tables 6a–e**.

One study included in this study reported the OA rate of the TFJ and the PFJ, but failed in reporting the outcomes of the overall knee OA rate, resulting in the higher OA rate of TFJ and PFJ compared with that of the overall knee joint. The definition of radiographic OA was atypical in two studies [6, 43]. One did not set the cut-off point for radiographic OA, simply concluding that the radiographic OA rate of the ipsilateral TFJ was significantly higher than the contralateral side [6]. The other one defined the radiographic OA as a side-to-side difference of Grade II or worse in 1 or more compartments or a side-to-side difference of Grade I in 2 or more compartments according to the Kellgren-Lawrence classification [43]. On that basis, the radiographic knee joint OA rate was 52.9%.

### Meta-analysis

A total of nine articles were eligible for meta-analysis [1, 5, 22, 27, 29, 40, 41, 45, 46]. Of these, seven compared the overall OA rate between ipsilateral and contralateral sides [1, 5, 22, 40, 41, 45, 46];

► **Table 4a** Summary of Studies Included.

Authors	Year	Country	Mean F/U Time	No. of Subjects	Evaluation cases/rate	Radiographic exam cases/rate	Description	Surgical Technique	Graft	Meniscal injuries cases/rate	Position radiograph
TW Chen et al.	2017	China	10.2	133	111/83.5%	89/66.9%	Synthetic group: 10 female, 28 male, mean age at surgery 27.6; Auto-HT group, 9 female, 64 male, mean age at surgery 28.8	Arthroscopic singe-bundle	Synthetic, Auto-HT	80/60.2%	Weight-bearing, 30° flexion, PA, lateral, patella axial
Björnsson H et al.	2016	Sweden	16	193	147/76.2%	147/76.2%	Auto-BPTB group: 19 female, 42 male, mean age at surgery 28.2; Auto-HT group: 33 female, 53 male, mean age at surgery 26.8	Arthroscopic singe-bundle	Auto-BPTB, Auto-HT	97/50.3%	Standard weight-bearing
Webster K et al.	2016	Australia	15.3	65	47/72.3%	38/58.5%	Auto-HT group: 20 male, 5 female, mean age at surgery 26.1; Auto-BPTB group: 16 male, 6 female, mean age at surgery 26.6	Arthroscopic trans-tibial singe-bundle	Auto-BPTB, Auto-HT	35/53.8%	Weight-bearing, 15° flexion, PA, full extension lateral
Ferretti A et al.	2016	Italy	10.4/33.9	150	140/93.3%	91/60.7%	Intra-articular reconstruction: 20 female, 51 male, mean age at surgery 27.3; Intra & Extra-articular reconstruction: 12 female, 56 male, mean age at surgery 25.7	Arthroscopic singe-bundle; Intra & Extra-articular	Auto-HT	51/34.0%	Weight-bearing, extension, AP, lateral, patella axial
Risberg M et al.	2016	N. way	17.8	210	168/80.0%	167/79.5%	95 male, 73 female, mean age at F/U 45.1	Arthroscopic singe-bundle	Auto-BPTB, Auto-HT	106/50.5%	weight-bearing, 20° flexion, 5° external rotation, AP, 40° flexion, patella axial
Falciglia F et al.	2016	Italy	10.4	12	12/100.0%	12/100.0%	10 male, 1 female, age at surgery 12.2–14.6	Arthroscopic singe-bundle	Auto-HT	2/16.7%	NA
Barenius B et al.	2014	Sweden	14.1	164	134/81.7%	134/81.7%	Auto-BPTB group: 35 male, 34 female, mean age at F/U 39.2; Auto-HT group: 44 male, 21 female, mean age at F/U 41.6	Arthroscopic singe-bundle	Auto-BPTB, Auto-HT	56/34.1%	Weight bearing, extension, AP, lateral, 30° flexion, lateral, patellar axial
Tengman E et al.	2014	Sweden	23	42	33/78.6%	NA/NA	21 male, 12 female, mean age at F/U 45.6	Arthroscopic singe-bundle	Synthetic, Auto-BPTB, Combined	NA/ NA	NA
Leiter JR et al.	2014	Canada	14.6	68	68/100.0%	68/100.0%	43 male, 25 female, mean age at surgery 31.2	Arthroscopic singe-bundle	Auto-HT	NA/ NA	Standard weight-bearing
Janssen RP et al.	2013	Netherlands	10	86	86/100%	86/100%	57 male, 29 female, mean age at surgery 31.2	Arthroscopic singe-bundle	Auto-HT	62/72.1%	Weight-bearing, 45° flexion, AP, lateral, patellar axial

► **Table 4b** Summary of Studies Included.

Authors	Year	Country	Mean F/U Time	No. of Subjects	Evaluation cases/rate	Radiographic exam cases/rate	Description	Surgical Technique	Graft	Meniscal injuries cases/rate	Position radiograph
Gerhard P et al.	2013	Switzerland	16	63	63/100%	63/100%	54 male, 9 female, mean age at surgery 27.0	Arthroscopic single-bundle	Auto-BPTB	NA	Weight-bearing, full-length, Rosenberg view, AP, lateral, skyline view
Holm I et al.	2012	Norway	12	67	53/79.1%	53/79.1%	26 female, 41 male, mean age at surgery: arthroscopic surgery 27.0, open surgery 29.2	Arthroscopic transtibial single-bundle, Open single-bundle	Auto-BPTB	34/50.7%	Weight-bearing, 20° flexion, 5° feet external rotation, PA, lateral, patellar axial
Hoffelner T et al.	2012	Austria	10	32	28/87.5%	28/87.5%	Skiing athletes: 6 female, 6 male, mean age at F/U 31.5. Soccer athletes: 1 female, 15 male, mean age at F/U 32.8	Arthroscopic transtibial single-bundle	Auto-BPTB, Auto-HT	NA	Weight-bearing, AP, Rosenberg view
Struwer J et al.	2012	Germany	13.5	73	73/100%	73/100%	46 male, 27 female, mean age at F/U 43	Arthroscopic single-bundle	Auto-BPTB	Excluded	/
Sutherland AG et al.	2010	Britain	10	126	79/62.7%	79/62.7%	16 female, 63 male, mean age at F/U 41	Open single-bundle	Auto-BPTB	NA	Weight-bearing, AP, lateral
Mascarenhas R et al.	2010	US	9.1/10.3	19	17/89.5%	17/89.5%	Auto-BPTB: 7 female, 12 male, mean age at surgery 27.9; Allo-BPTB 7 female, 12 male, mean age at surgery 28.1	Arthroscopic single-bundle	Auto-BPTB, Allo-BPTB	12/63.2%	Long leg cassette, flexion weight bearing, lateral, and Merchant views
Meuffels DE et al.	2009	Netherlands	10	25	25/100%	25/100%	Surgical treated: 19 male, 6 female, mean age at F/U 37.6; Conservative treated: 19 male, 6 female, mean age at F/U 37.8	Arthroscopic single-bundle	Auto-BPTB	17/68.0%	Weight-bearing, PA, Rosenberg view
van der Hart et al.	2008	Netherlands	10.3	44	28/63.6%	28/63.6%	11 female, 17 male, mean age at surgery 30.5	Arthroscopic transtibial single-bundle	Auto-BPTB	13/29.5%	Weight-bearing, 40° flexion, AP, lateral, skyline view
Jong Keun Seon et al.	2006	South Korea	11.2	70	58/82.9%	58/82.9%	55 male, 3 female, mean age at surgery 30.4	Arthroscopic single-bundle	Auto-BPTB	33/47.1%	Weight-bearing, AP, lateral

► **Table 5a** Modified Coleman Methodology Score (MCMS) of the studies included.

Author	Meta-analysis	Design	Year	MCMSA	MCMSB	MCMS
TW Chen et al.	Ipsilateral vs. contralateral TFJ vs. PFJ	Cohort	2017	48	38	86
Bjornsson H et al.	Ipsilateral vs. contralateral	RCT	2016	40	33	73
van der Hart et al.	Ipsilateral vs. contralateral	Cohort	2008	24	24	48
Barenius B et al.	Ipsilateral vs. contralateral TFJ vs. PFJ	RCT	2014	30	40	70
Holm I et al.	Ipsilateral vs. contralateral	RCT	2012	44	30	73
Sutherland AG et al.	Ipsilateral vs. contralateral	Cohort	2010	28	32	60
Hoffelner T et al.	Ipsilateral vs. contralateral	Cohort	2012	24	29	53
Ferretti A et al.	TFJ vs. PFJ	Cohort	2016	33	30	63
Risberg M et al.	TFJ vs. PFJ	Cohort	2016	38	38	76
Falciglia F et al.	Not included	Case series	2016	25	13	38
Webster K et al.	Not included	RCT	2016	44	26	70
Struwer J et al.	Not included	Case series	2012	35	18	53
Mascarenhas R et al.	Not included	Case control	2010	24	30	54
Meuffels DE et al.	Not included	Case control	2009	27	37	64
Seon JK et al.	Not included	Cohort	2006	32	25	57
Tengman E et al.	Not included	Cohort	2014	48	19	67
Leiter JR et al.	Not included	Case series	2014	33	26	59
Janssen RP et al.	Not included	Case series	2013	28	29	57
Gerhard P et al.	Not included	Case series	2013	35	20	55

RCT: randomized control study

► **Table 5b** Modified Coleman Methodology Score (MCMS) of studies included with different designs.

Study Design	No. of articles	MCMSA (Mean, range)	MCMSB (Mean, range)	MCMS (Mean, range)
RCT	4	40; 30–44	32; 26–40	72; 70–73
Cohort	8	34; 24–48	29; 19–38	64; 48–86
Case control	2	26; 24–27	34; 30–37	59; 54–64
Case series	5	31; 25–35	21; 13–29	52; 38–59

► **Table 5c** Modified Coleman Methodology Score (MCMS) of studies published before and after the 31<sup>st</sup> December 2013.

Publication Year	No. of articles	MCMSA (Mean, range)	MCMSB (Mean, range)	MCMS (Mean, range)
2014–2017	9	38; 25–48	29; 13–40	67; 38–86
2006–2013	10	30; 24–44	27; 18–37	57; 48–73

► **Table 5d** Modified Coleman Methodology Score (MCMS) of the studies included/not included in the meta-analysis.

Meta-analysis	No. of articles	MCMSA (Mean, range)	MCMSB (Mean, range)	MCMS (Mean, range)
Ipsilateral Vs contralateral	7	34; 24–48	32; 24–40	66; 48–86
TFJ Vs PFJ	4	37; 30–48	37; 30–40	74; 63–86
Not included	10	33; 24–48	24; 13–37	57; 38–70

three compared the TFJ OA rate between ipsilateral and contralateral sides [22, 29, 40]; three compared the PFJ OA rate between ipsilateral and contralateral sides [22, 29, 40]; four compared the TFJ OA with the PFJ OA on the ipsilateral side [22, 27, 29, 40]; three compared the TFJ OA with the PFJ OA on the contralateral side [22, 29, 40]. The extracted data was insufficient to perform the meta-analysis relating to the combined meniscus and cartilage injuries. (► **Table 6g**)

Compared with contralateral control, the risk ratio of developing overall knee radiographic OA was 3.73 (range, 2.66–5.22;  $P < 0.00001$ ) on the ipsilateral side; the risk ratio of developing PFJ radiographic OA was 2.42 (range, 1.60–3.67;  $P < 0.0001$ ) on the ipsilateral side; the risk ratio of developing TFJ radiographic OA was 2.88 (range, 2.15–3.87;  $P < 0.00001$ ) on the ipsilateral side. Compared with the PFJ, the risk ratio of developing radiographic OA in the TFJ was 1.15 (range, 1.03–1.28;  $P = 0.01$ ) on the ipsilateral side. While on the contralateral side, the risk ratio was not statistically different between the PFJ and TFJ ( $P = 0.38$ ). By the sensitivity analysis, the studies by Risberg, Barenius, and Hoffelner et al. were removed from meta-analysis. In all five meta-analyses, the heterogeneity of the  $I^2$  index ranged from 0–50%. For details, ► **Fig. 2a–e**.

## Discussion

The systematic review and meta-analyses of the radiographic OA rate at a minimum of ten years after ACL reconstruction was performed in this study. For the radiographic OA, in addition to the comparison between the ipsilateral and the contralateral side, the comparison between the tibiofemoral and the patellofemoral joint was also made.

In the systematic reviews and meta-analysis previously reported, researchers focused on the minimal ten-year knee OA rate after



► **Table 6a** The Overall Knee Radiographic OA Rate of the Ipsilateral Knee from the Studies Included.

Author	Year	Kellgren & Lawrence Classification					Radiographic OA rate
		0	I	II	III	IV	
Bjornsson H et al.	2016	43	39	45	14	6	44.2 %
Ferretti A et al.	2016	9	49	22	10	1	36.3 %
Barenius B et al.	2014	51		83			61.9 %
TW Chen et al.	2017	23	18	43	5	0	53.9 %
Tengman E et al.	2014	2	5	12	10	4	78.8 %
Falciglia F et al.	2016	7	4	1	0	0	8.3 %
Gerhard P et al.	2013	8	30	5	9	4	32.1 %
Struwer J et al.	2012	3	30	24	12	4	54.8 %
Janssen RP et al.	2013	7	16	17	41	5	73.3 %
van der Hart et al.	2008	3	12	8	3	2	46.4 %
Sutherland AG et al.	2010	43		36			45.6 %
Hoffelner T et al.	2012	19	2	1	2	4	24.1 %
Meuffles DE et al.	2009	4	9	9	3	0	48.0 %
Seon JK et al.	2006	33		20	5	0	43.1 %
Webster K et al.	2016	11		27			28.9 %
Holm I et al	2012	4	7	23	14	5	79.2 %

► **Table 6b** The Overall Knee Radiographic OA Rate of the Contralateral Knee from the Studies Included.

Author	Year	Kellgren & Lawrence Classification					Radiographic OA rate
		0	I	II	III	IV	
Bjornsson H et al.	2016	117	16	9	0	1	7.0 %
Barenius B et al.	2014	108		26			19.4 %
TW Chen et al.	2017	46	25	18	0	0	20.2 %
van der Hart et al.	2008	20	7	1	0	0	3.6 %
Sutherland AG et al.	2010	73		6			7.6 %
Hoffelner T et al.	2012	17	1	4	2	4	35.7 %
Holm I et al.	2012	26	12	11	2	2	28.3 %

► **Table 6c** The Tibiofemoral Joint Radiographic OA Rate of the Ipsilateral Knee from the Studies Included.

Author	Year	Kellgren & Lawrence Classification					Radiographic OA rate
		0	I	II	III	IV	
Ferretti A et al.	2016	11	49	20	10	1	34.10 %
Risberg M et al.	2016	10	12	99	35	11	86.80 %
Barenius B et al.	2014	54		80			59.70 %
TW Chen et al.	2017	45		44			49.40 %

► **Table 6d** The Tibiofemoral Joint Radiographic OA Rate of the Contralateral Knee from the Studies Included.

Author	Year	Kellgren & Lawrence Classification					Radiographic OA rate
		0	I	II	III	IV	
Risberg M et al.	2016	49	32	68	15	3	51.50 %
Barenius B et al.	2014	109		25			18.70 %
TW Chen et al.	2017	71		18			20.20 %

ACL injury, while they did not exclude the cases conservatively treated [19–21]. In comparison, we only investigate the cases of ACL reconstruction in this study. For the portion of cases conservatively treated in some studies, they were specifically excluded from the analysis to minimize the heterogeneity of data.

The ipsilateral knee was affected more often than the contralateral side, and meanly over half proportion of the ACL reconstruction cases demonstrated radiographic degeneration a minimum of ten years after surgery.



► **Table 6e** The Patellofemoral Joint Radiographic OA Rate of the Ipsilateral Knee from the Studies Included.

Author	Year	Kellgren & Lawrence Classification					Radiographic OA rate
		0	I	II	III	IV	
Ferretti A et al.	2016	15	48	21	6	1	30.80 %
Risberg M et al.	2016	13	20	123	10	1	80.20 %
Barenius B et al.	2014	101		33			23.60 %
TW Chen et al.	2017	64		25			28.10 %

► **Table 6f** The Patellofemoral Joint Radiographic OA Rate of the Contralateral Knee from the Studies Included.

Author	Year	Kellgren & Lawrence Classification					Radiographic OA rate
		0	I	II	III	IV	
Risberg M et al.	2016	46	27	89	5	0	56.30 %
Barenius B et al.	2014	122		12			9.00 %
TW Chen et al.	2017	75		14			15.70 %

► **Table 6g** The Osteoarthritis Rates on Ipsilateral and Contralateral Sides.

Position	No. of article	OA rate (Mean, range)
Ipsilateral overall knee	16	51.6%, 8.4%–79.2%
Contralateral overall knee	7	15.5%, 3.6%–35.7%
Ipsilateral TFJ	4	62.4%, 34.1%–86.8%
Contralateral TFJ	3	33.1%, 18.7%–51.5%
Ipsilateral PFJ	4	46.8%, 28.1%–80.2%
Contralateral PFJ	3	30.8%, 9.0%–56.3%

Ajuied et al. once performed a meta-analysis on the radiographic OA rate at a minimum of ten years after ACL reconstruction [21]. In their study, the risk ratio of developing moderate to severe OA (grade III or IV, according to the Kellgren&Lawrence classification) on the ipsilateral knee was 3.62 compared to that of the contralateral side. In this study, the risk ratio of developing overall radiographic OA ( $\geq$  grade II, according to the Kellgren&Lawrence classification) on the ipsilateral knee was 3.73 compared to that of the contralateral side. The cut-off point was grade II, which was widely accepted in the radiographic degeneration evaluation using the Kellgren & Lawrence classification. Among 19 studies included herein, 17 adopted grade II as the cut-off point for radiographic evaluation [1, 4, 5, 8, 16, 17, 20, 22, 27, 29, 31, 34, 41, 42, 44–46].

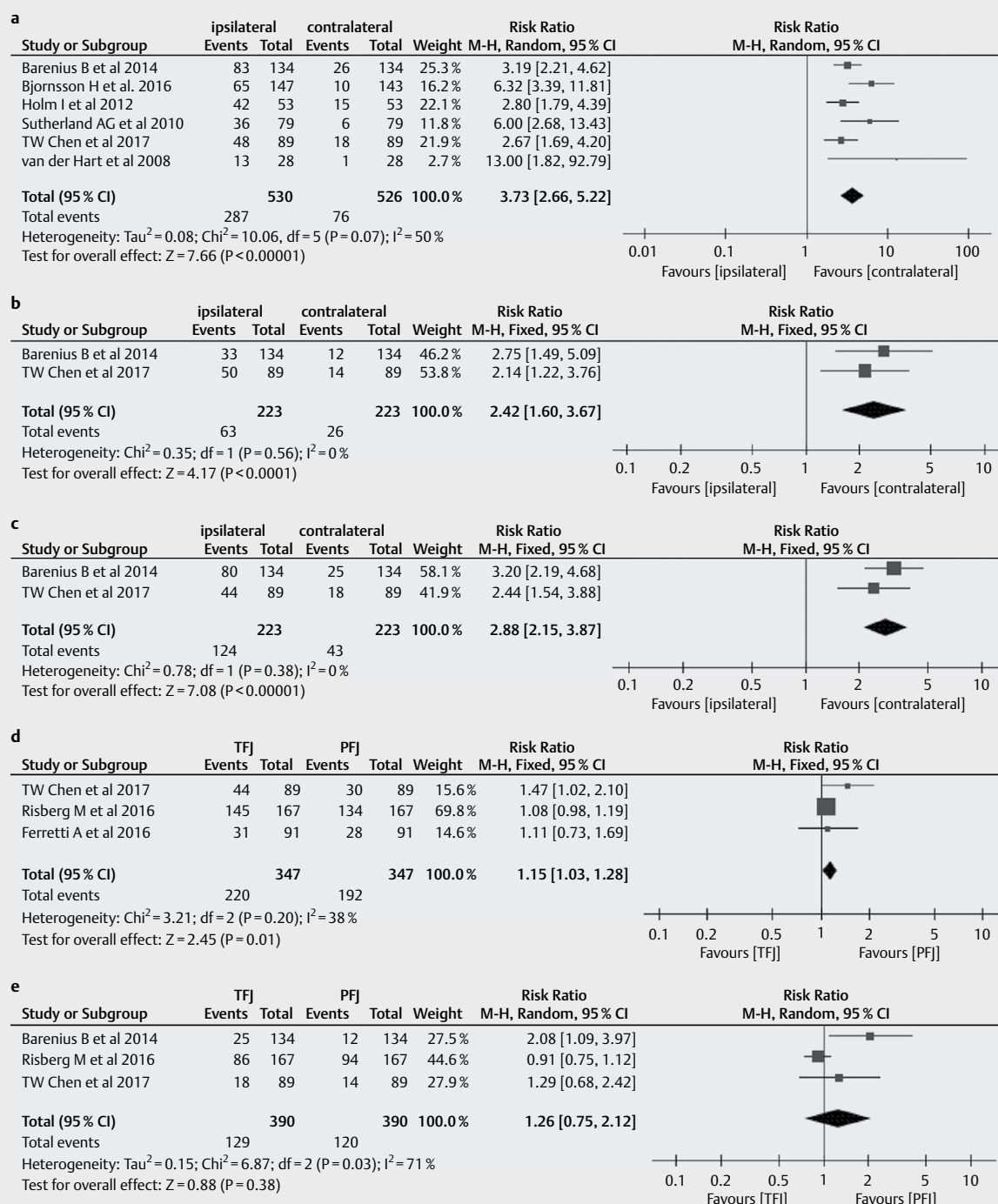
Harris et al. systematically reviewed the radiographic OA rate on the tibiofemoral joint long-term after ACL injury that was either surgically or conservatively treated [47]. A total of 380 cases from four retrospective studies were investigated with a mean follow-up period of 11.8 years. The radiographic tibiofemoral OA rate on the ipsilateral knee ranged from 32.6–51.2% for cases surgically treated, and ranged from 24.5–42.3% for cases conservatively treated. The researchers suggested that surgical treatment not be back by any definitive evidence to prevent tibiofemoral OA after ACL injury. In this study, the radiographic tibiofemoral OA rate ranged from 34.1–86.8% and was on average 62.4% for the ipsilateral knee. In contrast, it ranged from 18.7–51.5% and was a mean of 33.1% for the contralateral side. The risk ratio of developing tibiofemoral radiographic OA was 2.88 on the ipsilateral knee compared with that of the contralateral side. To the best of our knowledge, it was for

the first time that the tibiofemoral radiographic OA rate between the ipsilateral and contralateral sides was meta-analyzed.

In the study reported by Risberg et al., the posttraumatic tibiofemoral OA was associated with combined meniscus injuries, while the extracted data in this study could not support further analysis about meniscal conditions [29].

The OA occurred in the PFJ was different from that in the TFJ regarding the clinic manifestation, treating methods, as well as the etiology. Although it was anticipated that risk of OA was higher in the TFJ for the nature of ACL tear, an injury mostly involving the other structures between the tibia and femur menisci and subchondral bones, the results were inconsistent in literature. Oiestad et al. reported the PFJ OA rate on the ipsilateral knee long-term after ACL reconstruction [48]. Their study involved 210 cases with a mean follow-up period of 12.3 years, and the PFJ radiographic OA rate was 26 %. While in a narrative review by Culvenor et al., the researchers concluded that PFJ OA might be an under-recognized outcome of ACL reconstruction, and be at least as common as TFJ OA.[35].. In this systematic review, the PFJ OA rate of the ipsilateral knee ranged from 28.1–80.2% and meanly at 46.8%. For the contralateral side, it ranged from 9.0–56.3% and meanly at 30.8%. On the ipsilateral side, the risk ratio of developing OA in the TFJ was merely 1.15 compared with that in the PFJ. And compared with contralateral side, the risk ratio of developing PFJ radiographic OA was 2.42 on the ipsilateral knee. These outcomes indicated that we should stay vigilant of the OA developed in the PFJ on the ipsilateral side, which could result in anterior knee pain and knee function impairment long-term after ACL reconstruction [25, 26]. In this study, the PFJ radiographic OA between the ipsilateral side and contralateral side and the ipsilateral OA between the TFJ and PFJ was for the first time meta-analyzed.

There was an interesting phenomenon in the literature about the long-term clinical results of ACL reconstruction. Briefly, despite many described radiographic evaluation methods respectively on TFJ and PFJ, only very few of them did report the radiographic OA outcomes individually for PFJ and TFJ. Instead, the overall knee OA rates, the summarization of both PFJ and TFJ OA outcomes, were simply reported [4–6, 16, 17, 42, 46]. This rendered it difficult to perform a meta-analysis on the PFJ and the TFJ radiographic OA



► **Fig. 2** **a** Forest plot of ipsilateral versus contralateral knees in developing overall knee radiographic OA. Risk ratio = 3.73 ( $P < 0.00001$ ), with heterogeneity of 50%, ( $P = 0.07$ ); **b** Forest plot of ipsilateral versus contralateral knees in developing patellofemoral joint radiographic OA. Risk ratio = 2.42 ( $P < 0.0001$ ), with heterogeneity of 0%, ( $P = .56$ ); **c** Forest plot of ipsilateral versus contralateral knees in developing tibiofemoral joint radiographic OA. Risk ratio = 2.88 ( $P < 0.00001$ ), with heterogeneity of 0%, ( $P = .38$ ); **d** Forest plot of tibiofemoral joint versus patellofemoral joint in developing radiographic OA on the ipsilateral side. Risk ratio = 1.15 ( $P = 0.01$ ), with heterogeneity of 38%, ( $P = .20$ ); **e** Forest plot of tibiofemoral joint versus patellofemoral joint in developing radiographic OA on the contralateral side. Risk ratio = 1.26 ( $P = 0.38$ ), with heterogeneity of 71%, ( $P = 0.03$ ).

after ACL reconstruction. In previous studies by Ajuied et al. [21], Claes et al. [20], and Oiestad et al. [19], the researchers only fulfilled the meta-analysis on the overall knee OA. As Claes et al. mentioned, “it was decided to pool all available data in one general

group of ‘knee OA’”. In this study, unpublished data of the TFJ and PFJ OA were shared by some researchers whose studies were therefore included in the meta-analysis, allowing further exploration.

The methodology quality of evidence in meta-analysis is vital. In 2009, Oiestad et al. adopted the modified Coleman Methodology Score (MCMS) for the quality evaluating of included studies in their research. It was concluded that the MCMS was low for the included studies without a universal methodological radiologic classification. Thus it was difficult to compare the studies reporting the knee OA prevalence more than ten years after ACL injury, as well as to state firm conclusions on that. Herein, only the studies adopting the Kellgren&Lawrence classification, a richly applied and widely reported grading system for knee OA evaluation, were included for analysis. Moreover, we performed the methodological quality assessment on all included studies. In 2014, Ajuied et al. reported the meta-analysis on radiographic knee OA at minimal ten years after ACL injury, extracting data from the studies published before 2013. To the best of our knowledge, there has not been any meta-analysis on the topic since 2013. In the meantime, several studies on the long-term clinical outcomes of ACL reconstruction were successively reported. It should be highlighted that the average MCMS of the nine studies published between 2014 and 2017 was 10 points higher than those published earlier than 2014. Owing to the merits of better study design and standardized reporting strategy, we were able to analyze the OA between the ipsilateral and contralateral sides, and furtherly investigated the OA between the TFJ and PFJ in this meta-analysis.

There were some limitations in this study. Firstly, only four studies reporting the TFJ or PFJ radiographic OA included in this study. Secondly, the analysis of combined injuries like meniscus or cartilage lesion herein was not performed due to insufficient data from the included studies. Thirdly, the attrition of subjects was high. In some study the radiographic evaluation was merely about 60 % or even not reported. Fourthly, the response rate was lower than expected.

There were also some advantages. Firstly, the study provided an up to date, in-depth view of the long-term radiographic OA at minimal ten years after ACL reconstruction. Owing to better quantity and quality of the evidence, this review stated firm conclusion on the long-term OA prevalence over 10 years after ACL reconstruction. Secondly, compared with previous researches, the study focused on a more specific group of the ACL reconstructed cases by excluding those conservatively treated. Thirdly, previous meta-analysis failed to investigate in detail the OA rate in ACL reconstruction, and studies of higher quality recently published made it possible to further analyze the OA prevalence long-term ACL reconstruction, especially in different joints (TFJ and PFJ). The OA in the PFJ was reportedly prevalent and associated with worse symptoms and function impairment long-term after ACL reconstruction like dramatic swelling, valgus deformity, markedly reduced quadriceps strength, and pain on the PFJ compression, while the TFJ OA were associated with bony enlargement or deformity, reduced flexion range of movement, mediolateral instability and varus deformity [49]. For the differences of symptoms and signs between the PFJ OA and the TFJ OA, the health care providers need to remain vigilant to risk factors of both. This meta-analysis compared, for the first time, the radiographic OA of the TFJ between ipsilateral and contralateral sides, as well as that of the PFJ. Also, the study for the first time compared the radiographic OA of the PFJ and that of the TFJ, respectively, on ipsilateral and contralateral sides.

## Conclusion

The current evidence suggested that the ACL reconstruction cannot spare the knee from developing radiographic OA long-term postoperative. Over a minimum of 10 years after surgery, about half the cases developed overall radiographic OA on the ipsilateral knee, which is nearly four times higher than the contralateral side. On the ipsilateral knee, the TFJ was mostly affected, which is about 1.15 times higher than the PFJ.

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## Conflict of Interest

Authors declare that they have no conflict of interest.

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