# Medial Meniscal Extrusion in Patients With Medial Meniscus Root Tears

# **A Systematic Review and Meta-analysis**

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**Background:** Medial meniscal extrusion (MME) has received significant interest because of its correlation with medial meniscus root tears (MMRTs), its potential as a diagnostic tool, and its significance in the progression of knee osteoarthritis (OA).

Purpose: To (1) evaluate if MMRTs significantly increase MME compared with nonroot tears (NRTs) and no tears and (2) determine the clinical outcomes of increased MME.

Study Design: Systematic review; Level of evidence, 4.

**Methods:** Electronic database searches of PubMed, Embase, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials were conducted on June 6, 2022, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist criteria. The searches were conducted using the keywords "meniscus tear" and "extrusion." No restrictions were placed on the date of publication. Quality and sensitivity assessments were conducted on included studies. Major MME was defined as an extrusion  $\geq 3$  mm.

**Results:** Twenty-two studies involving 7882 knees were included. Compared with patients with NRTs, those with MMRTs had a 1.12-mm greater mean absolute meniscal extrusion (AME) and were 3.45 times more likely to have major MME (P < .001 for both). Compared with patients with no tears, those with MMRTs had a 2.13-mm greater AME (P < .001). Within patients with MMRT, those with widely displaced MMRT had a 1.01-mm greater AME compared with nondisplaced MMRT (P < .001). Patients with OA had a 0.73-mm greater AME and were 3.86 times more likely to have major MME compared with patients without OA (P < .001 for both). Within patients who were not stratified according to MMRT, NRT, or no tears, those who eventually developed OA had a 0.79-mm greater AME than those who did not have OA (P = .02).

**Conclusion:** Patients with MMRTs had higher MME values compared with those with other types of meniscal tears and those without any meniscal tears. Patients with knee OA were more likely to have higher MME compared with those without OA.

Keywords: knee; meniscal extrusion; osteoarthritis; meniscus root tear

The Orthopaedic Journal of Sports Medicine, 11(3), 23259671231151698 DOI: 10.1177/23259671231151698 © The Author(s) 2023 There is interest in the study of medial meniscal extrusion (MME) because of its association with medial meniscus root tears (MMRTs)<sup>35</sup> and its predictive value in the early diagnosis of knee osteoarthritis (OA).<sup>40,47</sup> MME is defined as the significant medial displacement of the medial meniscus with respect to the central margin of the medial tibial plateau. The amount of extrusion is significant when the meniscus extends beyond the tibial margin. MME commonly occurs because of the disruption of collagen fibers within the meniscus that provide hoop tension strength.<sup>1</sup> The circumferential fibers in the meniscus provide hoop tension to resist tensile stress and prevent outward extrusion.<sup>25</sup> When a meniscal tear occurs, there is a potential loss of meniscus hoop stresses. This results in increased MME and progressive degeneration of the articulation cartilage with loading. Thus, MME has also been associated with

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Inclusion Criteria	Exclusion Criteria					
<ul> <li>Clinical studies</li> <li>Studies with comparative data on MME of the knee</li> <li>Studies that only included data from nonoperative or preoperative knees</li> </ul>	<ul> <li>Studies with no comparative data</li> <li>Studies that did not utilize MRI to evaluate medial meniscal extrusions</li> <li>Biomechanical studies</li> <li>Cadaveric studies</li> <li>In vitro studies</li> <li>Animal studies</li> <li>Review articles, case reports, conference papers, and letters that do not contain original data</li> <li>Non-English-language articles</li> <li>Unpublished studies</li> <li>Studies in which patients received prior surgical treatment before imaging</li> <li>Studies with an NOS score &lt;7</li> </ul>					

 $\begin{array}{c} {\rm TABLE \ 1} \\ {\rm Study \ Inclusion \ and \ Exclusion \ Criteria}^{a} \end{array}$ 

<sup>a</sup>MME, medial meniscal extrusion; MRI, magnetic resonance imaging; NOS, Newcastle-Ottawa Scale.

joint effusions, meniscal tears, and degenerative joint disease.  $^{4,41}$ 

Patients with MMRT are evaluated with sudden-onset pain at the back of the knee, which worsens with knee flexion; there is usually posteromedial joint line tenderness.<sup>27,34</sup> However, root tears may be hard to visualize on imaging because of the tear size and orientation. MME has been strongly correlated with meniscus root tears<sup>5,38</sup> and have potential clinical utility to improve the detection of meniscus root tears. Currently, there is a lack of consensus on whether a greater MME would indicate MMRTs over nonroot tears (NRTs) or no meniscal tears.

The primary aim of this meta-analysis was to compare the amount of MME among MMRTs, NRTs, and no meniscal tears to determine if a greater MME can be correlated with MMRTs. Our secondary aim was to evaluate the clinical implications arising from increased MME, in particular the association between the severity of MME and incidence of knee OA. We hypothesized that MMRT would result in the greatest MME compared with other meniscal tears or no tears and that increased MME would result in a greater incidence of knee OA.

### METHODS

### Literature Search

Comprehensive searches of published literature were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist criteria.<sup>44</sup> Clinical articles reporting either the respective cause of a patient's MME or clinical outcomes of patients with MME were identified via electronic database searches of PubMed, Scopus, Cochrane Central Register of Controlled Trials, Embase, and Web of Science conducted on June 6, 2022. The searches were conducted using the keywords "meniscus tear" and "extrusion." The detailed search strategy can be found in Appendix Table A1. There were no restrictions placed on the publication date.

### Study Selection and Data Extraction

After eliminating duplicates, study evaluation was performed by an independent blinded pair of authors (F.J.Y.F. and B.W.L.O.). Full texts of potentially eligible articles were extracted, and further analysis was conducted. Backward chaining of references from final retrieved papers was also undertaken to further identify potential articles. Only articles that met the predefined inclusion and exclusion criteria (Table 1) were included in the final analysis. Any discrepancies were resolved by achieving consensus with an independent author (Y.H.D.L.).

# Data Collection

Data from the included studies were extracted by the same pair of independent investigators (F.J.Y.F. and B.W.L.O.) using a standardized protocol and reporting form. Data extraction was performed to extract study characteristics (study period, location, number of knees, age, and body mass index [BMI]) and clinical outcome data (type of meniscal tear and MME). Means and standard deviations were pooled for the collection of continuous data. When means and standard deviations were not available, and medians with ranges were presented instead, we used previously established models by Wan et al<sup>49</sup> to convert data into means and standard deviations.

The following six comparative data were collected:

- 1. Major MME: We accepted both definitions of major MME by Costa et  $al^{10}$  (>3 mm) and Lerer et  $al^{35}$  (>3 mm).
- 2. Widely displaced MMRT (WD-MMRT): Defined as measurable tear gap on magnetic resonance imaging (MRI).<sup>3</sup>
- 3. Nondisplaced MMRT (ND-MMRT): Defined as no measurable tear gap on MRI. $^3$
- 4. Non-OA knees: Defined by the OA Initiative as Kellgren and Lawrence (KL) grade 0 or  $1.^5$



**Figure 1.** In the coronal slices method, the medial meniscal extrusion (arrows) is measured as the horizontal distance between the most medial aspect of the tibia and the meniscus, respectively (black lines).

- 5. OA knees: Defined by the OA Initiative as KL grades 2 to  $4.^{48}$
- 6. Absolute MME: Defined as MME recorded during weightbearing MRI.

### Methods of Measuring MME

Jones et al<sup>23</sup> previously described the various methodologies of assessing MME on MRI scans. The reference standard for assessing MME is the "circular edge of tibia to circular edge of meniscus" (CETCEM) method, in which a 3-dimensional analysis of the meniscus is achieved by segmenting the tibia and the meniscus. Only 1 study included in this paper utilized this method.<sup>15</sup> The majority of the studies included in this review utilized the "coronal slices" method, in which MME was measured using the coronal MRI slice, which showed the greatest extrusion measured using the horizontal distance between the most medial aspect of the tibia and the meniscus, respectively (Figure 1).

# Methodological Quality Assessment and Statistical Analysis

The methodological quality of each included article was assessed using the Newcastle-Ottawa Scale (NOS) for the assessment of nonrandomized studies in meta-analyses.<sup>50</sup> The NOS grades each article based on 3 domains: selection of study groups, comparability of groups, and ascertainment of outcome. All 22 studies were of good quality according to the NOS, with a mean score of 8.43 (range, 8-9) (Appendix Table A2).

Comparisons of continuous data such as the mean absolute MME were summarized using the absolute mean

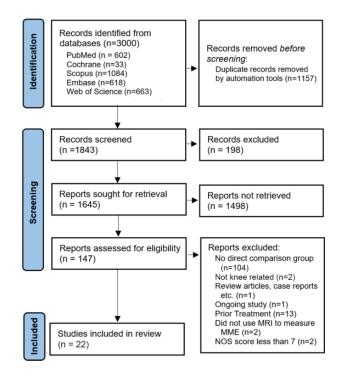


Figure 2. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) diagram of study inclusion and exclusion. MME, medial meniscal extrusion; MRI, magnetic resonance imaging; NOS, Newcastle-Ottawa Scale.

difference between groups. For binary data such as incidence of major MME, the odds ratio was summarized using the incidence between groups. All statistical analyses were performed using Review Manager Version 5.3 (RevMan; Cochrane Information Management System) software. Random-effects models were used in all metaanalyses. Heterogeneity between articles was assessed using the  $I^2$  statistic. Interpretations of  $I^2$  were adopted from the Cochrane Handbook, where values of 0% to 50% indicate that heterogeneity might not be important, and 50% to 100% may represent heterogeneity. As all the analyses did not meet the minimum number of studies (>10) required to conduct a meta-regression or funnel plots, subgroup and sensitivity analyses were instead performed to evaluate potential sources of heterogeneity.

### RESULTS

Our search strategy yielded 1645 articles after the removal of duplicates. Of these, 1498 articles were excluded based on the title and abstract review. The remaining 147 articles underwent full-text review, of which 22 articles were included in the meta-analysis (Figure 2). All 22 articles selected were retrospective studies. A summary of the study characteristics can be found in Table 2.

Lead Author (Year)	Indications	No. of Patients (M/F)	Knees per Group, n	Patient Age, y, mean $\pm$ SD	BMI	Patients With Major MME (>3 mm), n
Costa (2004) <sup>10</sup>	MMRT vs NRT and no tear	105 (12/93)	MMRT: 31 NRT: 52	$57.25\pm8.17$	NR	58
Lerer $(2004)^{35}$	MMRT vs NRT and no tear	205 (92/113)	No tear: 22 MMRT: 61 NRT: 167	$48.75\pm12.17$	NR	93
Choi (2010) <sup>5</sup>	MMRT vs NRT	248 (98/150)	No tear: 106 MMRT: 66 NRT: 182	$50.75\pm11$	NR	127
Lee (2011) <sup>33</sup>	MMRT vs NRT	102 (30/72)	MMRT: 17 NRT: 85	$52.25 \pm 5.83$	NR	57
Park (2012) <sup>45</sup>	MMRT vs NRT and no tear	67 (32/35)	MMRT: 24 NRT: 18	MMRT: $53.7 \pm 10.6$ NRT: $48.8 \pm 10.9$	NR	NR
Ohishi (2014) <sup>42</sup>	MMRT vs NRT and no tear	188 (89/99)	No tear: 25 MMRT: 44 NRT: 72 No tear:72	No tear: $36.3 \pm 16.4$ MMRT: $62.5 \pm 11.6$ NRT: $59.1 \pm 15.3$ No tear: $41.1 \pm 20.0$	NR	NR
MacFarlane (2017) <sup>37</sup>	MMRT vs NRT	224 (93/131)	MMRT: 42 NRT: 182	MMRT: $59 \pm 8$ NRT: $58.5 \pm 7.45$	MMRT: $30 \pm 6$ NRT: $29.83 \pm 6.28$	85
Goto (2019) <sup>18</sup>	<ul><li>MMRT vs NRT</li><li>OA vs no OA</li></ul>	190 (69/121)	<ul> <li>MMRT: 136, NRT: 54</li> <li>OA: 148, no OA: 42</li> </ul>	$59.4 \pm 11.1$	$24.1\pm3$	136
Liu (2020) <sup>36</sup>	MMRT vs NRT	115 (66/49)	MMRT: 11 NRT: 104	MMRT: $53 \pm 5.5$ NRT: $50.5 \pm 5.5$	MMRT: $26.4 \pm 3.2$ NRT: $25.9 \pm 3.5$	55
Kim (2020) <sup>25</sup>	MMRT vs no tear	40 (20/20)	MMRT: 23 No tear: 17	MMRT: $63.5 \pm 7.7$ NRT: $26.5 \pm 6.4$	MMRT: $24.6 \pm 24$ NRT: $23.4 \pm 2.7$	NR
Hisashi (2022) <sup>21</sup>	MMRT vs NRT	151 (42/109)	MMRT: 48 NRT: 103	MMRT: $67.9 \pm 8.2$ NRT: $65.8 \pm 8.3$	NR	NR
Yoon (2022) <sup>51</sup>	MMRT vs NRT and no tear	124 (62/62)	MMRT: 36 NRT: 31	MMRT: $49.79 \pm 10.87$ NRT: $45.14 \pm 10.48$	NR	MMRT: 35/36 NRT: 22/31
Bin (2016) <sup>3</sup>	WD-MMRT vs ND-MMRT	44 (36/8)	No tear: 57 WD-MMRT: 20 ND-MMRT: 24	No tear: 41.78 ± 11.48 WD-MMRT: 59.8 ± 10.2 ND-MMRT: 55.1 ± 7.4	WD-MMRT: 25.2 ± 2.5 ND-MMRT: 25.3 ± 2.8	No tear: 4/57 WD-MMRT: 20/20 ND-MMRT: 10/24
Kim (2019) <sup>29</sup>	WD-MMRT vs ND-MMRT	109 (26/83)	WD-MMRT: 79 ND-MMRT: 30	$58.14 \pm 9.64$	$26.02 \pm 3$	WD-MMRT: 72/79 ND-MMRT: 17/30
Kim (2019) <sup>28</sup>	WD-MMRT vs ND-MMRT	97 (19/78)	WD-MMRT: 86 ND-MMRT: 11	$58.60 \pm 8.90$	$25.98 \pm 2.89$	NR
Ding (2007) <sup>14</sup>	OA vs non-OA	294 (192/102)	OA: 21 Non-OA: 273	OA: 47.2 ± 5.4 Non-OA: 45.0 ± 6.6	OA: 31.3 ± 7.0 Non-OA: 26.8 ± 4.5	OA: 11 Non-OA: 41
Crema (2010) <sup>11</sup>	OA vs non-OA	152 (52/100)	OA: 58 Non-OA: 94	OA: 57.3 ± 8.2 Non-OA: 56.3 ± 8.29	OA: 36.7 ± 5.4 Non-OA: 24.8 ± 4.4	NR
Emmanuel (2016) <sup>15</sup>	OA vs non-OA	438 (163/275)	OA: 206 Non-OA: 232	OA: 61.5 ± 8.7 Non-OA: 61.0 ± 9.0	OA: $29.1 \pm 4.2$ Non-OA: $27.6 \pm 0.3$	NR
Teichtahl (2017) <sup>48</sup>	OA vs non-OA	4369 (1834/2535)	OA: 2249 Non-OA: 2120	OA: 62.7 ± 9.0 Non-OA: 59.9 ± 9.1	OA: 29.8 ± 4.8 Non-OA: 27.6 ± 4.5	OA: 771 Non-OA: 207
Özdemir (2019) <sup>43</sup>	OA vs non-OA	306 (116/190)	OA: 274 Non-OA: 32	OA: 70.96 ± 4.7 Non-OA: 68.25 ± 3.9	NR	OA: 177 Non-OA: 16
Jeon (2021) <sup>22</sup>	OA vs non-OA	86 (27/59)	OA: 57 Non-OA: 29	$61 \pm 7$	$26.2\pm3.7$	NR
Kim (2020) <sup>26</sup>	OA vs non-OA	99 (15/84)	OA: 59 Non-OA: 40	$55.54 \pm 7.5$	NR	NR

 TABLE 2

 Summary Characteristics of Included Articles<sup>a</sup>

<sup>a</sup>All studies were retrospective cohort studies. BMI, body mass index; F, female; M, male; MME, medial meniscal extrusion; MMRT, medial meniscus root tear; ND-MMRT, nondisplaced medial meniscus root tear; NR, not recorded; NRT, nonroot tear; OA, osteoarthritis; WD-MMRT, widely displaced medial meniscus root tear.

A total of 7882 knees were included in the meta-analysis. Twelve studies<sup>§</sup> (n = 1888 knees; 37.34% male patients) compared MME between MMRT and NRT or no tears. There were 539 knees in the MMRT, 1050 knees in the NRT, and 299 knees in the no-tear groups. Three papers<sup>3,28,29</sup> (250 knees; 32.4% male patients) reported WD-MMRT versus ND-MMRT, with 185 knees in the WD-MMRT group and 65 knees in the ND-MMRT group. Seven papers<sup>11,14,15,22,26,43,48</sup> (n = 5744 knees; 41.77% male patients), reported OA versus non-OA. There were 2924 knees in the OA group and 2820 knees in the non-OA group.

# Subgroup Analysis Involving Patients With MMRT Versus NRT

Mean AME. The pooled mean absolute meniscal extrusion (AME) from 5 studies<sup>5,33,42,45,51</sup> (n = 575) was 4.00 ± 1.82 mm for the MMRT group (n = 187) and 2.79 ± 1.47 mm for the NRT group (n = 388). Calculating the standard difference in means of AME between MMRT versus NRT from these studies resulted in a pooled estimate of 1.12 (95% CI, 0.48-1.76; P < .001;  $I^2 = 81\%$ ) (Figure 3). This finding indicates that the mean AME was significantly greater by 1.12 mm for patients with MMRT versus NRT.

Incidence of Major MME. The pooled number of knees with major MME from 8 studies<sup>5,10,18,33,35-37,51</sup> (n = 1381) was 275 for the MMRT group (n = 349) and 533 for the NRT

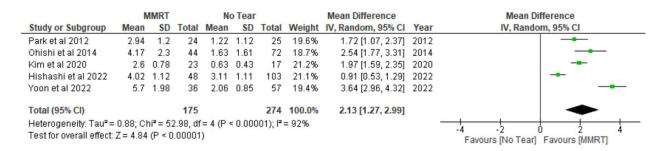
<sup>&</sup>lt;sup>§</sup>References 5, 10, 18, 21, 25, 33, 35–37, 42, 45, 51.

	N	MRT	NRT Mean Differe					Mean Difference	e Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI		
Choi et al 2010	3.8	1.4	66	2.7	1.3	182	23.2%	1.10 [0.71, 1.49]	2010	+		
Lee et al 2010	3	1	17	3	2	85	20.3%	0.00 [-0.64, 0.64]	2010	+		
Park et al 2012	2.94	1.2	24	1.28	0.72	18	21.0%	1.66 [1.08, 2.24]	2012	-		
Ohishi et al 2014	4.17	2.3	44	3.4	1.75	72	18.3%	0.77 [-0.02, 1.56]	2014			
Yoon et al 2022	5.7	1.98	36	3.52	1.68	31	17.2%	2.18 [1.30, 3.06]	2022			
Total (95% CI)			187			388	100.0%	1.12 [0.48, 1.76]		◆		
Heterogeneity: Tau <sup>2</sup> = 0.42; Chi <sup>2</sup> = 21.45, df = 4 (P = 0.0003); l <sup>2</sup> = 81% Test for overall effect: Z = 3.42 (P = 0.0006)										-10 -5 0 5 10 Favours [NRT] Favours [MMRT]		

#### Figure 3. Mean AME between MMRT and NRT. IV, inverse variance.

	MMRT NRT			Г		Odds Ratio		Odds Ratio				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	r M-H, Random, 95% Cl				
Costa et al 2004	30	31	42	52	4.1%	7.14 [0.87, 58.82]	2004	۱.				
Lerer et al 2004	39	61	40	167	20.5%	5.63 [2.99, 10.59]	2004	·				
Choi et al 2010	50	66	77	182	20.4%	4.26 [2.26, 8.04]	2010	) ——				
Lee et al 2010	10	17	47	85	11.9%	1.16 [0.40, 3.32]	2010	) —				
MacFarlane et al 2017	22	42	63	182	19.3%	2.08 [1.05, 4.09]	2017	· · · · · · · · · · · · · · · · · · ·				
Goto et al 2018	80	85	196	229	13.2%	2.69 [1.02, 7.15]	2018	3				
Liu et al 2020	9	11	46	104	6.6%	5.67 [1.17, 27.55]	2020	) —				
Yoon et al 2022	35	36	22	31	4.0%	14.32 [1.70, 120.93]	2022	2				
Total (95% CI)		349		1032	100.0%	3.45 [2.20, 5.43]		•				
Total events	275		533									
Heterogeneity: Tau <sup>2</sup> = 0.	16; Chi <sup>2</sup> =	11.81,	df = 7 (P	= 0.11)	; I <sup>≈</sup> = 41%							
Test for overall effect: Z	= 5.37 (P <	< 0.000	01)					0.01 0.1 1 10 100 Favours [NRT] Favours [MMRT]				





#### Figure 5. Mean AME between MMRT and NRT.

group (n = 1032). Calculating the pooled odds ratio of knees that had major MME from these studies resulted in a pooled estimate of 3.45 (95% CI, 2.20-5.43; P < .001;  $I^2 = 41\%$ ) (Figure 4). This finding indicates that patients who had MMRT were 3.45 times more likely to have major MME compared with those who had NRT.

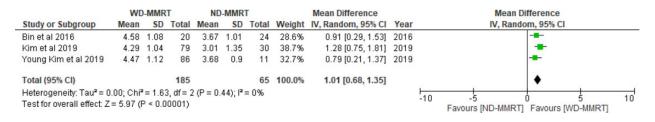
# Subgroup Analysis Involving Patients With MMRT Versus No Meniscal Tears

*Mean AME.* The pooled mean AME from 5 studies<sup>21,25,42,45,51</sup> (n = 449) was  $4.07 \pm 1.93$  mm for the MMRT group (n = 175) and  $2.18 \pm 1.43$  mm for the no-tear group (n = 274). Calculating the standard difference in means of AME between MMRT versus no tears from these studies resulted in a pooled estimate of 2.13 (95% CI, 1.27-2.99;

 $P < .001; I^2 = 92\%$ ) (Figure 5). The finding indicates that the mean AME was significantly greater by 2.13 mm for patients with MMRT versus no tears.

# Subgroup Analysis Involving Patients With WD-MMRT vs ND-MMRT

*Mean AME.* The pooled AME from 3 studies<sup>3,28,29</sup> (n = 250) was 4.41 ± 1.08 mm for the WD-MMRT group (n = 185) and 3.67 ± 1.20 mm for the ND-MMRT group (n = 65). Calculating the standard difference in means of AME between WD-MMRT versus ND-MMRT from these studies resulted in a pooled estimate of 1.01 (95% CI, 0.68-1.35;  $P < .001; I^2 = 0\%$ ) (Figure 6). The finding indicates that the mean AME was significantly greater by 1.01 mm in patients with WD-MMRT versus ND-MMRT.





Non-OA OA Mean Difference Mean Difference Study or Subgroup SD Total Mean SD Total Weight IV, Random, 95% Cl Year IV. Random, 95% CI Mean 2.3.1 Studies that did not stratify according to type of mensical tears Crema et al 2010 3.5 1.1 94 4.5 1.8 58 18.3% -1.00 [-1.51, -0.49] 2010 Emmaneul et al 2016 1.29 0.99 232 1.56 1.22 206 23.1% -0.27 [-0.48, -0.06] 2016 21.0% Goto et al 2018 3 0.9 42 4.17 1.47 148 -1.17 [-1.53, -0.81] 2018 412 Subtotal (95% CI) 368 62.5% -0.79 [-1.44, -0.14] Heterogeneity: Tau<sup>2</sup> = 0.29; Chi<sup>2</sup> = 21.14, df = 2 (P < 0.0001); l<sup>2</sup> = 91% Test for overall effect: Z = 2.39 (P = 0.02) 2.3.2 Studies that stratified into MMRT Joen et al 2019 366 0.91 29 3.9 1 57 20.0% -0.24 [-0.66, 0.18] 2019 Dong et al 2020 59 17.5% -1.07 [-1.63, -0.51] 2020 3.97 1.35 40 5.04 1.45 69 116 37.5% -0.63 [-1.45, 0.18] Subtotal (95% CI) Heterogeneity: Tau<sup>2</sup> = 0.28; Chi<sup>2</sup> = 5.41, df = 1 (P = 0.02); I<sup>2</sup> = 82% Test for overall effect: Z = 1.53 (P = 0.13) Total (95% CI) 528 100.0% 437 -0.73 [-1.17, -0.29] Heterogeneity: Tau<sup>2</sup> = 0.21; Chi<sup>2</sup> = 26.55, df = 4 (P < 0.0001); l<sup>2</sup> = 85% -10 10 -5 5 Ô Test for overall effect: Z = 3.23 (P = 0.001) Favours [OA] Favours [Non-OA] Test for subgroup differences: Chi<sup>2</sup> = 0.09, df = 1 (P = 0.76), I<sup>2</sup> = 0%

Figure 7. Mean AME between OA and non-OA.

Subgroup Analysis Involving Patients With OA Versus Non-OA

*Mean AME*. The pooled AME for non-OA from 5 studies<sup>11,15,18,22,26</sup> (n = 965) was  $2.33 \pm 1.53$  mm for the non-OA group (n = 437) and  $3.27 \pm 1.95$  mm for the OA group (n = 528). Calculating the standard difference in means of AME between non-OA and OA from these studies resulted in a pooled estimate of -0.73 mm (95% CI, -1.17 to -0.29; *P* = .001; *I*<sup>2</sup> = 85%) (Figure 7). The finding suggests that the mean AME was significantly smaller by 0.73 mm in non-OA patients versus those with OA.

In a subgroup analysis of 3 studies<sup>11,15,18</sup> (n = 780) comparing the mean AME between non-OA and OA patients who were not specified to have MMRT, NRT, or no tears, the baseline AME for non-OA was significantly lower compared with OA (-0.79 mm; 95% CI, -1.44 to -0.14; P = .02;  $I^2 = 91\%$ ).

In a subgroup analysis of 2 studies<sup>22,26</sup> (n = 185) comparing AME between non-OA and OA patients with MMRT, the baseline AME in non-OA was not significantly lower compared with OA (-0.63 mm; 95% CI, -1.45 to 0.18;  $P = .13; I^2 = 82\%$ ).

#### Incidence of Major Meniscal Extrusion

The pooled number of knees that had major MME from 3 studies  $^{14,48}\,(n=4969)$  was 595 for the OA group (n=2544)

and 264 for the non-OA group (n = 2425). Calculating the pooled odds ratio of MME between the OA and non-OA groups from these studies resulted in a pooled estimate of  $3.86 (95\% \text{ CI}, 2.04\text{-}7.28; P < .001; I^2 = 70\%)$  (Figure 8). This finding indicates that patients with OA were 3.86 times more likely to have major MME compared with those who did not have OA.

### DISCUSSION

The most important finding of this study was that MMRTs had a significantly greater mean AME compared with NRTs and no tears. Furthermore, MMRTs had a 3.45 times higher likelihood of major MME compared with NRTs.

For patients with MMRTs, WD-MMRTs had a significantly greater mean AME compared with ND-MMRTs. A cadaveric biomechanical study found that when physiological loading (1800 N) was applied, the torn meniscus root had a wider gap compared with an absence of a load (0 N).<sup>20</sup> The results highlight that prolonged weightbearing after an MMRT results in greater displacement of the tear gap and MME, which exposes the tibial articular surface, increasing the risk of chondral wear progression. Although some previous studies have reported a lack of correlation between major MME and MMRTs,<sup>3,33</sup> Bin et al<sup>3</sup> hypothesized that these differences arose due to MMRTs having different stages depending on tear site displacement. Hence, these studies could have assessed the knee in

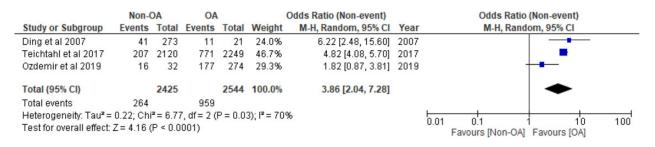


Figure 8. Incidence of MME between OA and non-OA.

different time points after an MMRT. Overall, the majority of the studies show that MME is sensitive for MMRTs.<sup>10,39</sup>

Patients with no meniscal tears and knees without OA had mean meniscal extrusions of  $2.18 \pm 1.43$  and  $2.33 \pm 1.53$  mm, respectively. This may be related to a variety of possible origins that result in meniscal extrusion, including meniscus degeneration. With meniscus degeneration, the meniscus increases in size due to the formation of microcysts and separation of fibrils. This alteration in meniscal morphology affects the meniscus' ability to resist hoop strain,<sup>19</sup> stretching the fibers outward and causing MME.<sup>10</sup> Krych et al<sup>31</sup> also observed that isolated meniscal extrusions are associated with meniscotibial ligament abnormality.

It has been suggested that varus malalignment is a risk factor for increased MME.<sup>16,18</sup> There were insufficient papers to perform a proper subanalysis, and therefore, we were unable to draw conclusions for it as a risk factor. Both Erquicia et al<sup>16</sup> and Goto et al<sup>18</sup> reported that there was no significant correlation between the degree of meniscal extrusion and varus alignment in non-OA knees and nonmajor MME knees, respectively.<sup>16</sup> However, both Crema et al<sup>12</sup> and Goto et al<sup>18</sup> noted correlation between the degree of MME and varus alignment in knees with major MME. When structurally intact, the meniscus can offset the influence of the varus alignment. However, once the structural integrity of the meniscus is compromised, such as in meniscus degeneration or with a root tear, the varus malalignment becomes significant, increasing the risk of OA progression.<sup>30</sup>

Ding et al<sup>14</sup> reported that obese individuals had nearly a 5-fold increased risk of having MME. They also reported that those with past knee injury were nearly 4 times more likely to have increased MME. Further studies are required to investigate the effect of these risk factors (varus malalignment, obesity, and previous knee injury) on MME. These factors could account for the incidence of meniscal extrusion seen in the patients with no MMRTs in this review study.

For patients who had MMRTs, there was no significant difference in mean AME between OA and non-OA knees. Therefore, increased MME is a pathognomonic finding of MMRTs (regardless of the OA severity) and aids the diagnosis of MMRTs.

In this study, we also report that patients with knee OA had a greater mean AME than non-OA knees; OA knees tended to have 3.86 times more likelihood of having major

MME. For studies that did not stratify patients according to types of meniscal tears, those who had OA knees had a significantly greater mean AME compared with those who had non-OA knees. This reinforces the relationship we know that exists between MME, cartilage degeneration, and OA development.

Increased MME in an MMRT can be likened to a "total meniscectomy" in terms of knee joint contact pressure and kinematics.<sup>2</sup> The nonoperative treatment for MMRTs often leads to poor treatment outcomes in patients with large meniscal extrusion ratio.<sup>32</sup> Clinicians should consider routinely measuring MME with serial repeat MRI scans to aid in the treatment decision. When treating MMRTs, meniscal repairs have been shown to achieve superior clinical outcomes compared with partial meniscectomy.<sup>9</sup> A recent cadaveric biomechanical study found that the utilization of an anatomic transtibial pull-out root repair with centralization suture techniques achieved better restoration of the contact mechanics of the knee and meniscal extrusion when compared with nonanatomic repairs.<sup>13</sup>

However, there are studies that have shown that meniscus root repair does not significantly decrease postoperative  $\mathrm{MME}^{6,24,46}$  or OA progression.<sup>8</sup> A recent metaanalysis found that 33.5% of patients treated via meniscal repair underwent conversion to total knee arthroplasty within 10 years.<sup>17</sup> Chung et al<sup>7</sup> observed that preoperative varus alignment and increased postoperative meniscal extrusions were poor prognostic factors of meniscal repair. Future studies are required to investigate the efficacy of meniscus root repair in decreasing meniscal extrusions and preventing OA progression.

### Limitations

We acknowledge several limitations in this study. First, all included articles were retrospective in nature. To minimize the inherent bias of retrospective studies, we utilized the NOS to appraise the methodology of each included article. Two articles that scored less than 7 were excluded. The final articles included had a mean score of 8.43 (range, 8-9). Second, high heterogeneity was observed between the studies. This could be due to the differences in the way papers report their data. A majority of papers utilized the coronal slices method when measuring MME, and a study by Jones et al<sup>23</sup> found that the coronal slices method tends to overestimate maximal extrusion compared with the reference CETCEM method, reducing the accuracy of the values measured. However, as most of the studies utilized the same coronal slices method to measure MME in NRTs and no tears, the inaccuracy of the conclusions drawn from the results is minimized. All efforts were taken to standardize the data analyzed, and subgroup analysis was undertaken, when appropriate, to further minimize the  $I^2$  values. Third, as there were inadequate studies investigating the temporal relationship between MME and the risk of development of knee OA, it is challenging to form a temporal relationship between MME and the development of OA.

### CONCLUSION

Patients with MMRT have higher MME compared with other types of meniscal tears and those without any meniscal tears. Patients who had OA were more likely to have higher meniscal extrusion compared with patients who did not have knee OA.

### REFERENCES

- Adams JG, McAlindon T, Dimasi M, Carey J, Eustace S. Contribution of meniscal extrusion and cartilage loss to joint space narrowing in osteoarthritis. *Clin Radiol*. 1999;54(8):502-506.
- Allaire R, Muriuki M, Gilbertson L, Harner CD. Biomechanical consequences of a tear of the posterior root of the medial meniscus. Similar to total meniscectomy. J Bone Joint Surg Am. 2008;90(9):1922-1931.
- Bin SI, Jeong TW, Kim SJ, Lee DH. A new arthroscopic classification of degenerative medial meniscus root tear that correlates with meniscus extrusion on magnetic resonance imaging. *Knee*. 2016;23(2): 246-250.
- Breitenseher MJ, Trattnig S, Dobrocky I, et al. MR imaging of meniscal subluxation in the knee. Acta Radiol. 1997;38(5):876-879.
- 5. Choi CJ, Choi YJ, Lee JJ, Choi CH. Magnetic resonance imaging evidence of meniscal extrusion in medial meniscus posterior root tear. *Arthroscopy*. 2010;26(12):1602-1606.
- Chung KS, Ha JK, Ra HJ, Kim JG. A meta-analysis of clinical and radiographic outcomes of posterior horn medial meniscus root repairs. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(5):1455-1468.
- Chung KS, Ha JK, Ra HJ, Kim JG. Preoperative varus alignment and postoperative meniscus extrusion are the main long-term predictive factors of clinical failure of meniscal root repair. *Knee Surg Sports Traumatol Arthrosc.* 2021;29(12):4122-4130.
- Chung KS, Ha JK, Ra HJ, et al. Pullout fixation for medial meniscus posterior root tears: clinical results were not age-dependent, but osteoarthritis progressed. *Knee Surg Sports Traumatol Arthrosc.* 2019; 27(1):189-196.
- Chung KS, Ha JK, Ra HJ, Yu WJ, Kim JG. Root repair versus partial meniscectomy for medial meniscus posterior root tears: comparison of long-term survivorship and clinical outcomes at minimum 10-year follow-up. *Am J Sports Med*. 2020;48(8):1937-1944.
- Costa CR, Morrison WB, Carrino JA. Medial meniscus extrusion on knee MRI: is extent associated with severity of degeneration or type of tear? AJR Am J Roentgenol. 2004;183(1):17-23.
- Crema MD, Guermazi A, Li L, et al. The association of prevalent medial meniscal pathology with cartilage loss in the medial tibiofemoral compartment over a 2-year period. Osteoarthritis Cartilage. 2010;18(3):336-343.
- Crema MD, Roemer FW, Felson DT, et al. Factors associated with meniscal extrusion in knees with or at risk for osteoarthritis: the multicenter osteoarthritis study. *Radiology*. 2012;264(2):494-503.
- Daney BT, Aman ZS, Krob JJ, et al. Utilization of transtibial centralization suture best minimizes extrusion and restores tibiofemoral contact mechanics for anatomic medial meniscal root repairs in a cadaveric model. *Am J Sports Med*. 2019;47(7):1591-1600.

- Ding C, Martel-Pelletier J, Pelletier JP, et al. Knee meniscal extrusion in a largely non-osteoarthritic cohort: association with greater loss of cartilage volume. *Arthritis Res Ther*. 2007;9(2):R21.
- Emmanuel K, Quinn E, Niu J, et al. Quantitative measures of meniscus extrusion predict incident radiographic knee osteoarthritis—data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2016;24(2): 262-269.
- Erquicia J, Gelber PE, Cardona-Munoz JI, et al. There is no relation between mild malalignment and meniscal extrusion in trauma emergency patients. *Injury*. 2012;43(suppl 2):S68-S72.
- Faucett SC, Geisler BP, Chahla J, et al. Meniscus root repair vs meniscectomy or nonoperative management to prevent knee osteoarthritis after medial meniscus root tears: clinical and economic effectiveness. Am J Sports Med. 2019;47(3):762-769.
- Goto N, Okazaki K, Akiyama T, et al. Alignment factors affecting the medial meniscus extrusion increases the risk of osteoarthritis development. *Knee Surg Sports Traumatol Arthrosc.* 2019;27(8): 2617-2623.
- Hajek PC, Gylys-Morin VM, Baker LL, et al. The high signal intensity meniscus of the knee. Magnetic resonance evaluation and in vivo correlation. *Invest Radiol.* 1987;22(11):883-890.
- Hein CN, Deperio JG, Ehrensberger MT, Marzo JM. Effects of medial meniscal posterior horn avulsion and repair on meniscal displacement. *Knee*. 2011;18(3):189-192.
- Hisashi K, Muneta T, Kohno Y, et al. MRI study of medial meniscus degeneration of osteoarthritic knees with or without posterior root tear. *J Exp Orthop*. 2022;9(1):38.
- Jeon SW, Jung M, Choi CH, Kim SG, Kim SH. Factors related to meniscal extrusion and cartilage lesions in medial meniscus root tears. *J Knee Surg.* 2021;34(2):178-186.
- Jones LD, Mellon SJ, Kruger N, et al. Medial meniscal extrusion: a validation study comparing different methods of assessment. *Knee Surg Sports Traumatol Arthrosc.* 2018;26(4):1152-1157.
- Kaplan DJ, Alaia EF, Dold AP, et al. Increased extrusion and ICRS grades at 2-year follow-up following transtibial medial meniscal root repair evaluated by MRI. *Knee Surg Sports Traumatol Arthrosc.* 2018; 26(9):2826-2834.
- Kim C, Bin SI, Lee BS, et al. Volumetric assessment of extrusion in medial meniscus posterior root tears through semi-automatic segmentation on 3-tesla magnetic resonance images. *Orthop Traumatol Surg Res.* 2020;106(5):963-968.
- Kim DH, Lee GC, Kim HH, Cha DH. Correlation between meniscal extrusion and symptom duration, alignment, and arthritic changes in medial meniscus posterior root tear: research article. *Knee Surg Relat Res.* 2020;32(1):2.
- Kim JH, Chung JH, Lee DH, et al. Arthroscopic suture anchor repair versus pullout suture repair in posterior root tear of the medial meniscus: a prospective comparison study. *Arthroscopy*. 2011;27(12): 1644-1653.
- Kim JY, Bin SI, Kim JM, et al. A novel arthroscopic classification of degenerative medial meniscus posterior root tears based on the tear gap. Orthop J Sports Med. 2019;7(3):2325967119827945.
- Kim JY, Bin SI, Kim JM, et al. Tear gap and severity of osteoarthritis are associated with meniscal extrusion in degenerative medial meniscus posterior root tears. Orthop Traumatol Surg Res. 2019;105(7):1395-1399.
- Kozaki T, Fukui D, Yamamoto E, et al. Medial meniscus extrusion and varus tilt of joint line convergence angle increase stress in the medial compartment of the knee joint in the knee extension position—finite element analysis. J Exp Orthop. 2022;9(1):49.
- Krych AJ, Bernard CD, Leland DP, et al. Isolated meniscus extrusion associated with meniscotibial ligament abnormality. *Knee Surg Sports Traumatol Arthrosc.* 2020;28(11):3599-3605.
- Kwak YH, Lee S, Lee MC, Han HS. Large meniscus extrusion ratio is a poor prognostic factor of conservative treatment for medial meniscus posterior root tear. *Knee Surg Sports Traumatol Arthrosc.* 2018;26(3): 781-786.
- Lee DH, Lee BS, Kim JM, et al. Predictors of degenerative medial meniscus extrusion: radial component and knee osteoarthritis. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(2):222-229.

- 34. Lee JH, Lim YJ, Kim KB, Kim KH, Song JH. Arthroscopic pullout suture repair of posterior root tear of the medial meniscus: radiographic and clinical results with a 2-year follow-up. Arthroscopy. 2009:25(9):951-958.
- 35. Lerer DB, Umans HR, Hu MX, Jones MH. The role of meniscal root pathology and radial meniscal tear in medial meniscal extrusion. Skeletal Radiol. 2004;33(10):569-574.
- 36. Liu X, Ding R, Liu C, Yang B, Wang W. Factors associated with medial meniscal subluxation in knees with medial meniscus tears: a crosssectional study. Research Square. Preprint posted online August 11, 2020. doi:10.21203/rs.3.rs-35269/v2
- 37. MacFarlane LA, Yang H, Collins JE, et al. Associations among meniscal damage, meniscal symptoms and knee pain severity. Osteoarthritis Cartilage. 2017;25(6):850-857.
- 38. Magee T. MR findings of meniscal extrusion correlated with arthroscopy. J Magn Reson Imaging. 2008;28(2):466-470.
- 39. Magee T, Shapiro M, Williams D. Prevalence of meniscal radial tears of the knee revealed by MRI after surgery. AJR Am J Roentgenol. 2004;182(4):931-936.
- 40. Mahmoudian A, Lohmander LS, Jafari H, Luyten FP. Towards classification criteria for early-stage knee osteoarthritis: a population-based study to enrich for progressors. Semin Arthritis Rheum. 2021;51(1): 285-291.
- 41. Miller TT, Staron RB, Feldman F, Cepel E. Meniscal position on routine MR imaging of the knee. Skeletal Radiol. 1997;26(7):424-427.
- 42. Ohishi T, Suzuki D, Yamamoto K, et al. Medial extrusion of the posterior segment of medial meniscus is a sensitive sign for posterior horn tears. Knee. 2014;21(1):112-118.
- 43. Özdemir M, Kavak R. Meniscal lesions in geriatric population: prevalence and association with knee osteoarthritis. Curr Aging Sci. 2019; 12(1):67-73.

- 44. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
- 45. Park HJ, Kim SS, Lee SY, et al. Medial meniscal root tears and meniscal extrusion transverse length ratios on MRI. Br J Radiol. 2012; 85(1019):E1032-E1037.
- 46. Perry AK, Lavoie-Gagne O, Knapik DM, et al. Examining the efficacy of medial meniscus posterior root repair: a meta-analysis and systematic review of biomechanical and clinical outcomes. Am J Sports Med. Published online April 6, 2022. doi:10.1177/ 3635465221077271
- 47. Sasaki E, Ota S, Chiba D, et al. Early knee osteoarthritis prevalence is highest among middle-aged adult females with obesity based on new set of diagnostic criteria from a large sample cohort study in the Japanese general population. Knee Surg Sports Traumatol Arthrosc. 2020;28(3):984-994.
- 48. Teichtahl AJ, Cicuttini FM, Abram F, et al. Meniscal extrusion and bone marrow lesions are associated with incident and progressive knee osteoarthritis. Osteoarthritis Cartilage. 2017;25(7):1076-1083.
- 49. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14:135.
- 50. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa scale (NOS) for assessing the quality of non-randomised studies in metaanalyses. Accessed January 3, 2023. http://www.ohri.ca/programs/ clinical\_epidemiology/oxford.asp
- 51. Yoon SJ, Ahn JM, Kang Y, Kim BR, Kang HS. Morphological changes in the superficial medial collateral ligament on knee MR imaging: association with medial meniscal extrusion and posterior root medial meniscus abnormality. Skeletal Radiol. 2022;51(7):1399-1405.

# APPENDIX

### TABLE A1 Search Strategy

PICO	MeSH	Keywords					
Meniscus Tear	"Tibial Meniscus Injuries" [MeSH]	"Menisc* injur*" / "Menisc* tear*" / "Menisc* torn*" / "Flap tear*" / "Flap torn*" / "Bucket Handle Tear*" / "Bucket handle torn*"					
Extrusion	—	extrusion* / sublux* / protru*					
Databases Searched							

### PubMed, Embase, Web of Science:

(1) 'Meniscus injury' OR 'Meniscal injury' OR 'Meniscus tear' OR 'Meniscus tears' OR 'Meniscal tear' OR 'Meniscal tears' OR 'Meniscus tear' OR 'Meniscus torn' OR 'Flap tear' OR 'Flap tears' OR 'Flap torn' OR 'Bucket Handle Tear' OR 'Bucket Handle tears' OR 'Bucket handle torn' OR 'Meniscus Root Tear' OR 'Meniscus Root Torn' OR 'Meniscal Root Tear' OR 'Meniscal Root Torn' (2) extrusion\* OR sublux\* OR protru\* (3) #1 AND #2

#### Scopus:

(1) TITLE-ABS-KEY ("Meniscus injury" OR "Meniscal injury" OR "Meniscus tear" OR "Meniscus tears" OR "Meniscus tear" OR "Meniscal tears" OR "Meniscus torn" OR "Meniscus torn" OR "Flap tear" OR "Flap tears" OR "Flap torn" OR "Bucket Handle Tear" OR "Bucket Handle tears" OR "Bucket handle torn" OR "Meniscus Root Tear" OR "Meniscus Root Torn" OR "Meniscal Root Tear" OR "Meniscal Root Torn") (2) extrusion\* OR sublux\* OR protru\*

(3) #1 AND #2 = 1084

#### **Cochrane:**

(1) MeSH descriptor: [Tibial Meniscus Injuries] explode all trees

(2) 'Meniscus injury' OR 'Meniscal injury' OR 'Meniscus tear' OR 'Meniscus tears' OR 'Meniscal tear' OR 'Meniscal tears' OR 'Meniscus tear' OR 'Meniscus torn' OR 'Flap tear' OR 'Flap tears' OR 'Flap torn' OR 'Bucket Handle Tear' OR 'Bucket Handle tears' OR 'Bucket handle torn' OR 'Meniscus Root Tear' OR 'Meniscus Root Torn' OR 'Meniscal Root Tear' OR 'Meniscal Root Torn' (3) extrusion\* OR sublux\* OR protru\* = 2515

(4) (#1 OR #2) AND #3 = 33

	Newcastle-Ottawa Scale.											
		Sele	ction		Comparability							
Lead Author (Year)	1	2	3	4	5	6	7	8	Total			
Costa (2004) <sup>10</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Lerer (2004) <sup>35</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Choi (2010) <sup>5</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Lee (2011) <sup>33</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Park (2012) <sup>45</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Ohishi (2014) <sup>42</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond \diamond$	$\diamond$	$\diamond$	$\diamond$	9			
MacFarlane (2017) <sup>37</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Goto (2019) <sup>18</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Liu (2020) <sup>36</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond \diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Kim (2020) <sup>25</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Hisashi (2022) <sup>21</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond\diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Yoon (2022) <sup>51</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Bin (2016) <sup>3</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond\diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Kim (2019) <sup>29</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Kim (2019) <sup>28</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond\diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Ding (2007) <sup>14</sup>	ò	$\diamond$	$\diamond$	$\diamond$	$\diamond\diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Crema (2010) <sup>11</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Emmanuel (2016) <sup>15</sup>	ò	$\diamond$	$\diamond$	$\diamond$	$\diamond\diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Teichtahl (2017) <sup>48</sup>	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond\diamond$	$\diamond$	$\diamond$	$\diamond$	9			
Özdemir (2019) <sup>43</sup>	ò	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	$\diamond$	8			
Jeon (2021) <sup>22</sup>	ò	ò	$\diamond$	$\diamond$	$\diamond \diamond$	ò	ò	ò	9			
Kim (2020) <sup>26</sup>	ò	$\diamond$	$\diamond$	$\diamond$	$\diamond$	ò	ò	$\diamond$	8			

 $\begin{array}{c} {\rm TABLE~A2} \\ {\rm Newcastle-Ottawa~Scale.}^{a} \end{array}$ 

"One diamond indicates 1 point. A maximum of 2 diamonds can be awarded for the "Selection" and "Outcome" categories (columns 1-4 and 6-8). A maximum of 2 diamonds can be awarded for "Comparability" (column 5). Newcastle-Ottawa Scale items: 1 = representativeness of exposed cohort; 2 = selection of nonexposed cohort; 3 = ascertainment of exposure; 4 = demonstration that outcome of interest was not present at start of study; 5 = comparability of cohorts based on basis of design or analysis; 6 = assessment of outcomes; 7 = follow-up long enough for outcomes to occur; 8 = adequacy of follow-up of cohorts.