

Original Article

Is patellar denervation circumferentially effective in reducing anterior knee pain and improving knee function after total knee arthroplasty? A meta-analysis of randomized controlled trials

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Abstract: The aim of this meta-analysis was to evaluate whether patellar denervation with electrocautery (PD) without resurfacing after total knee arthroplasty (TKA) had an advantage over no patellar denervation (NPD) regarding postoperative anterior knee pain (AKP) and knee function. The electronic databases including PubMed, Embase, Web of Science and the Cochrane Library were systematically searched up to June 2017. Four hundred and eleven papers were identified and 8 randomized controlled trials containing 881 knees (796 patients) were finally eligible for meta-analysis. GRADE approach was used to assess the overall quality of evidence. The pooled results showed that PD could reduce the incidence of AKP and improve WOMAC score in early period (within 12 months) ($P=0.0001$), but not maintain after 12 months follow-up ($P=0.12$). In addition, we found better knee functional outcomes in range of motion (ROM) ($P=0.02$) and Knee Society Score knee score (KSSKS) ($P=0.002$) and the results did not change over time. We also identified PD was associated with better Oxford Knee Score (OKS) after 12 months follow-up. However, there was no significant difference between the two groups in visual analogue scale score (VAS), patella score (PS), and other outcomes. Based on this meta-analysis of all currently published RCTs, the findings have important implications for the medical community, namely, that PD is a safe procedure to reduce the incidence of AKP in early period and improve the knee function with similar rates of adverse events compared with NPD.

Keywords: Total knee arthroplasty, patellar denervation, meta-analysis, anterior knee pain

Introduction

Total knee arthroplasty (TKA) has been proven to be a reliable mean to relieve pain and improve postoperative knee function [1, 2]. However, an estimated 4-49% of patient post-TKA complained of anterior knee pain (AKP) [3-5], the occurrence of which negatively affected the quality of life, postoperative satisfaction,

and knee mobility [6, 7]. Although the mechanism of AKP remains unclear, the presence of substance-P nociceptive afferent fibers in peripatellar soft tissues and the infra-patellar fat pad have been implicated as the origin of AKP [8, 9]. Therefore, in theory, some orthopedic surgeons produced a thermal lesion using circumferential electrocautery to achieve denervation of the anterior knee, thereby blocking the

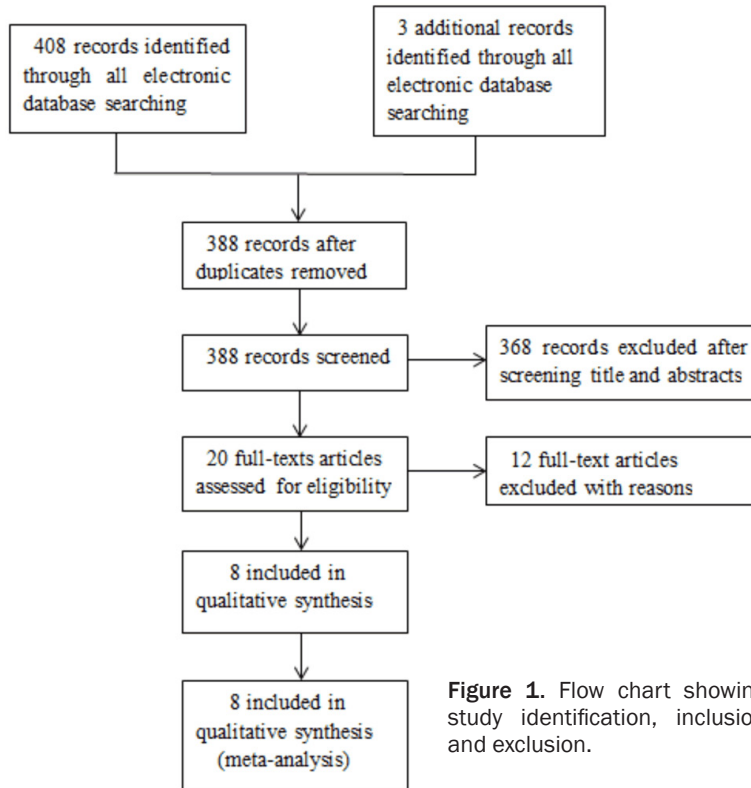


Figure 1. Flow chart showing study identification, inclusion and exclusion.

clear advice on whether to or not to conduct electrocautery during TKA. Recently, a new RCT [14] on this topic was published with a low risk of bias and showed no difference between the two groups. Moreover, an updated report [15] with longer follow-up time was published recently, so we could conduct subgroup analysis to evaluate whether the clinical effect of electrocautery changes with time.

Thus, we conducted this current meta-analysis to evaluate whether the PD is superior to the NPD regarding the incidence of AKP, clinical outcomes, and complications. We hypothesized that no difference was seen in all outcomes between patellar denervation and no denervation.

Materials and methods

Literature search and study selection

The electronic databases including PubMed, Embase, Web of Science and the Cochrane Library were searched for information from their inception to June 2017 with the following search terms: (electrocautery OR patellar denervation) AND (total knee arthroplasty OR total knee replacement OR TKA OR TKR). A final check that no relevant articles were missed was conducted by searching manually all references of included studies and by performing citation tracking on the included articles. Moreover, ongoing prospective RCTs were searched in the *ClinicalTrials.gov* website. There were no restrictions on the date or language of publication.

Two review authors screened the titles and abstracts of all studies identified by the search strategy. Then, we retrieved the studies for full-text review and evaluated again according to the inclusion criteria: (1) the trial had to be the primary TKA comparing PD with NPD without resurfacing due to osteoarthritis; (2) Follow-up had to be at least 12 months; (3) Studies had to be randomized controlled trials. Any non-RCTs, quasi-RCTs, retrospective studies, cadaver studies, comments, letters, editorials, proto-

pain pathways and reducing the prevalence of AKP [10]. Some studies demonstrated the reduction of AKP incidence in favor of patellar denervation (PD) [11-13]. However, other studies drew opposite conclusions [14-18].

A Dutch survey demonstrated that surgeons differ in their practice, with 56% of surgeons performed PD with electro-cautery during TKA when not resurfacing the patella and 32% use electrocautery when resurfacing the patella [4]. Other surgeons never conduct PD by reason of not believing in this technique. Nevertheless, whether the electrocautery is effective in reducing AKP and improving function was controversial. A previous meta-analysis [19] demonstrated that PD showed no benefits compared with non-patellar denervation (NPD). Unfortunately, the meta-analyses lacked adequate reporting of methodological quality assessment and included a retrospective study. A more recent meta-analysis [20] found a significantly decreased incidence of AKP in favor of PD. However, the review had several errors with respect to study inclusion, data abstraction, and analyses. In addition, the quality of the evidence in these meta-analysis was not appraised by a validated approach, such as GRADE. Considering all these issues, it was hard to give

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Table 1. Characteristics of the included studies

	Year	Country	Knee (n)		Gender (M/F)		Age		BMI		Cement	Surgical approach	Electrocautery depth	Follow-up (Months)
			PD	NPD	PD	NPD	PD	NPD	PD	NPD				
Kwon et al.	2015	Korea	50	50	0/50	0/50	66	67	25.9	26.1	NA	MP	1 mm	64 (60-70)
Van Jonbergen et al.	2014	Netherlands	103	99	28/75	34/65	70	71	30.3	29.2	Yes	MP	≤1 mm	42 (13-50)
Pulavarti et al.	2014	England	63	63	31/32	27/36	70	70	29.1	29.3	Both	MP	NA	26.4
Yim et al.	2012	Korea	50	50	0/50	0/50	70	70	NA	NA	Yes	MP	2-3 mm	21 (12-48)
Baliga et al.	2012	England	91	94	51/41	42/52	69	69	NA	NA	Yes	MP	≤1 mm	9-12
Altay et al.	2012	Turkey	35	35	9/26	9/26	68	68	NA	NA	Yes	MV	2-3 mm	36 (24-60)
Van Jonbergen et al.	2011	Netherlands	131	131	95/36	84/47	71	72	30.1	29.4	Yes	MP	≤1 mm	12
Saoud et al.	2004	Egypt	19	19	NA	NA	NA	NA	NA	NA	NA	MP	1 mm	9-12

PD patellar denervation with electrocautery; NPD no patellar denervation with electrocautery; BMI body mass index; MP medial parapatellar approach, MV midvastus approach, NA not available.

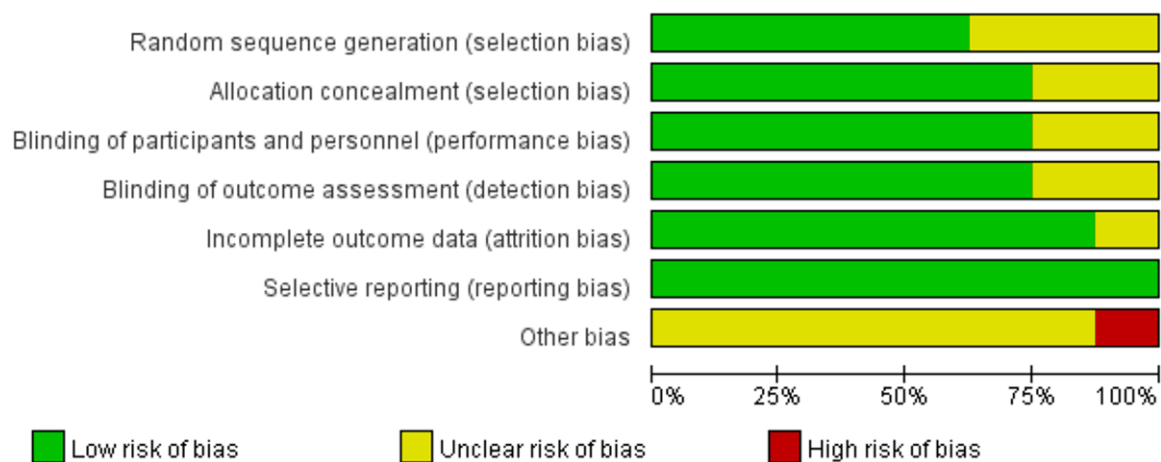


Figure 2. Risk of bias graph.

cols, guidelines, surgical registries, and review papers were excluded. Disagreements were resolved by consensus.

Data extraction

Predefined data collection form was developed to extract data from the eligible studies by two independent reviewers. Items collected were authors, publication date, patient demographics, depth of electrocautery, surgical approach, the use of cement, follow-up duration, and all the outcome measurements reported in both PD and NPD groups. The primary outcome was AKP, including the incidence of AKP and VAS score. The improvement in clinical knee function and complications was regarded as secondary outcomes. The difference of validated clinical knee scores (such as Knee Society Score [KSS], the Western Ontario and McMaster Universities Arthritis Index [WOMAC], the Oxford Knee Score [OKS] and patellar score

[PS]) and range of motion (ROM) was used to evaluate the improvement of knee function. Corresponding authors of included studies were contacted via e-mail for relevant information if the available data were insufficient. Discrepancies were resolved by consensus. When no consensus could be reached, a third reviewer cast the decisive vote.

Assessment of study quality

Two review authors use the Cochrane Collaboration tool to assess the risk of bias of every included study in six domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of assessors, incomplete data, selective reporting and other bias. Possible judgments were low risk of bias, high risk of bias, or unclear risk of bias for each study.

The quality of the evidence was assessed using the GRADE approach. The RCTs was con-

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Altay et al. 2012	?	+	+	+	+	+	?
Baliga et al. 2012	+	+	+	+	+	+	-
Kwon et al. 2015	+	+	+	+	+	+	?
Pulavarti et al. 2014	+	+	+	+	+	+	?
Saoud et al. 2004	?	?	?	?	+	+	?
Van Jonbergen et al. 2014	+	+	+	+	?	+	?
Van Jonbergen et al. 2011	+	+	+	+	+	+	?
Yim et al. 2012	?	?	?	?	+	+	?

Figure 3. Risk of bias summary (“+” indicates a low risk of bias, “-” indicates a high risk of bias, “?” indicates unclear or unknown risk of bias).

sidered as high-quality evidence, which could be degraded to moderate, low, or very low quality for five reasons. The reasons were high risk of bias, inconsistent results, indirect evidence, imprecision and publication bias. Any disagreements were resolved through discussion.

Statistical analysis

The statistical analysis was performed using Review Manager 5.3 software and a P -value < 0.05 was considered statistically significant. For each eligible study, we calculated the odds

ratios (OR) for dichotomous variables with 95% confidence intervals (CI). If outcomes were measured in the same way between studies, we calculated mean differences (MD) and 95% CI for continuous variables. Heterogeneity of the mean difference across studies was checked using the chi-squared test and I^2 statistic. If significant ($P < 0.1$ or $I^2 > 50\%$), a random effects model was used to estimate the overall effect sizes and a sensitivity analysis was performed to investigate the potential sources of heterogeneity. Otherwise, fixed effects model was adopted. Moreover, Publication bias among the studies was assessed by funnel plots.

Results

Study characteristics

The process of study selection is showed in **Figure 1**. We totally identified 411 articles with our search strategy. After removing duplications, scanning titles and abstracts and reading the full-text, eight RCTs were eligible based on our inclusion and exclusion criteria, including 881 knees (796 patients) in this current meta-analysis. We used data reporting a change from baseline as our effect index. All

included trials were in English and published after 2004. The detailed characteristics of the studies are displayed in **Table 1**.

Risk of bias and quality of evidence

The risk-of-bias assessments were displayed below and in **Figures 2** and **3**. We took the following measures to evaluate the methodological quality of the eight RCTs. Five articles [12, 14-16, 18] described the sequence generation (randomization scheme used) fairly well. The method of allocation concealment was done

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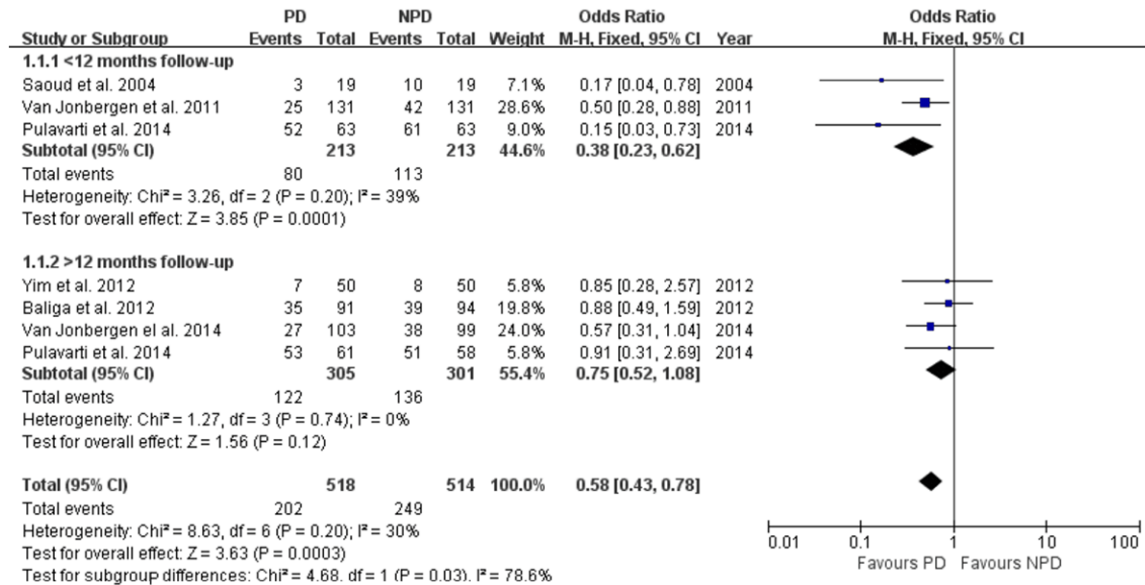


Figure 4. Forest plot of comparison: total incidence of AKP (PD patellar denervation with electrocautery, NPD no patellar denervation with electrocautery, CI Confidence interval, df degrees of freedom).

Table 2. Results of meta-analyses in included randomized controlled trials

Subgroup (follow-up)	Variables	Studies (n)	Knee (n)	Overall Effect		Heterogeneity P Value (I²)	Model
				P value	MD/OR (95% CI)		
Less than 12 months	AKP	3	426	0.0001*	0.38 (0.23, 0.62)	0.20 (39%)	Fixed
	Sensitivity of AKP*	2	164	0.001*	0.16 (0.05, 0.48)	0.94 (0%)	Fixed
	VAS pain scores	2	226	0.58	0.28 (-0.70, 1.26)	0.18 (44%)	Random
	ROM improvement	1	126	0.02*	2.90 (0.47, 5.33)	NA	Fixed
	Patella score	2	226	0.06	0.78 (-0.04, 1.60)	0.47 (0%)	Fixed
	KSSKS	3	488	0.002*	3.00 (1.07, 4.93)	0.17 (44%)	Fixed
	KSSFSS	2	388	0.07	2.57 (-0.19, 5.32)	0.61 (0%)	Random
	WOMAC	1	262	0.005*	4.90 (1.48, 8.32)	NA	Fixed
	WOMAC function score	2	362	0.42	2.60 (-3.77, 8.97)	0.02 (80%)	Random
	OKS	2	311	0.36	1.38 (-1.56, 4.31)	0.09 (65%)	Random
	AKP	4	606	0.12	0.75 (0.52, 1.08)	0.74 (0%)	Fixed
	VAS pain scores	4	474	0.63	0.15 (-0.45, 0.75)	0.06 (59%)	Random
More than 12 months	Sensitivity of VAS*	2	304	0.55	0.09 (-0.21, 0.40)	0.87 (0%)	Fixed
	ROM improvement	3	289	< 0.00001*	3.50 (1.82, 5.18)	0.4 (0%)	Fixed
	Patella score	4	389	0.02*	0.55 (0.07, 1.02)	0.25 (26%)	Fixed
	KSSKS	5	597	0.002*	2.24 (0.84, 3.64)	0.21 (32%)	Fixed
	KSSFSS	4	497	0.32	1.87 (-1.80, 5.55)	0.02 (80%)	Random
	Sensitivity of KSSFSS*	2	327	0.18	2.12 (-0.94, 5.18)	0.8 (0%)	Fixed
	WOMAC	2	302	0.02*	2.65 (0.47, 4.83)	0.49 (0%)	Fixed
	WOMAC function score	2	302	0.7	0.72 (-3.00, 4.44)	0.23 (31%)	Random
	OKS	2	310	0.01*	1.92 (0.18, 3.66)	0.47 (0%)	Random
	AKP	4	606	0.12	0.75 (0.52, 1.08)	0.74 (0%)	Fixed

AKP anterior knee pain; KSSKS Knee Society Score; KSSFSS KSS function score; ROM range of motion; VAS visual analogue scale; OKS Oxford Knee Score; PS patellar score; WOMAC Western Ontario and McMaster Universities Arthritis Index; MD mean difference; CI confidence interval; OR odds ratio. *Significant difference.

and reported in six studies [11, 12, 14-16, 18]. With respect to blinding of the outcome assessor and participants, six trials [11, 12, 14-16, 18] illustrated and conducted the blinding explicitly. The dropout or withdraw patients rate

was less than 20% except one [15]. In addition, all trials reported the outcomes planned previously. One trial [18] received commercial funding to support their research, but other trials did not receive any financial grants. We did not

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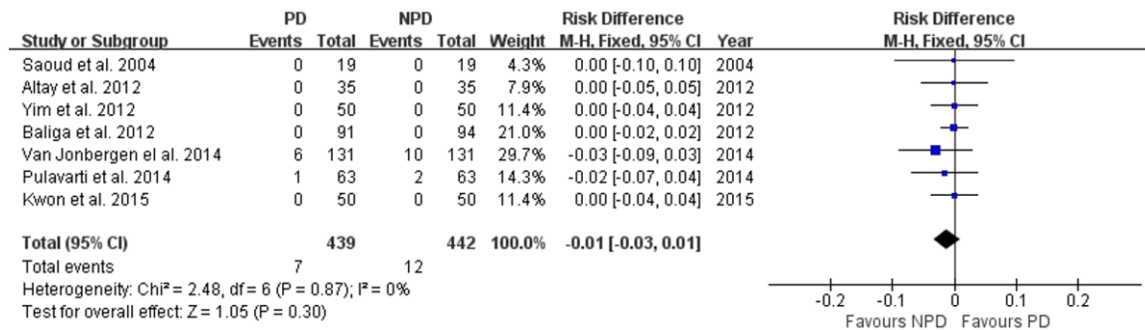


Figure 5. Forest plot of comparison: total incidence of complications (PD patellar denervation with electrocautery, NPD no patellar denervation with electrocautery, CI confidence interval, df degrees of freedom).

find any other apparent bias in each eligible study. After careful examination, five of the eight included studies were evaluated as having a low risk of bias, two of them had an unclear risk of bias, and one was assessed as having a high risk of bias.

We also used the GRADE approach to grade these trials reporting the primary outcomes of AKP. These studies were considered as being of moderate quality. The presence of studies with unclear risk of bias and one study with high risk of bias downgraded the quality of evidence. In addition, these studies reporting the secondary outcomes were graded as being of moderate to high quality (data not shown).

Meta-analysis of AKP

AKP incidence: There was moderate quality of evidence from 6 [12, 13, 15-18] studies (711 knees) that PD was associated with lower incidence of AKP (OR=0.58, 95% CI: 0.43-0.78; $P=0.0003$) with moderate heterogeneity ($I^2=30\%$, $P=0.20$). Considering that the origin of heterogeneity may be attributed to the duration of follow-up, subgroup analysis was conducted based on different follow-up time (Group A: less than 12 months follow-up; Group B: more than 12 months follow-up). The results showed that PD may significantly reduce the incidence of AKP compared with NPD in Group A (OR=0.38, $P=0.0001$; $I^2=39\%$), but not in Group B (OR=0.75, $P=0.12$; $I^2=0\%$) (**Figure 4**). Furthermore, we performed a sensitivity analysis by excluding one study [12] in Group A, and the result showed no heterogeneity ($P=0.94$; $I^2=0\%$). Statistically similar result was obtained, suggesting the stability of this finding in this meta-analysis (**Table 2**).

VAS: VAS score was used to evaluate AKP postoperatively. There was moderate quality of evidence from 4 studies [11, 14, 16, 18] (530 knees) that no significant difference was seen between PD and NPD with respect to VAS score in Group A (MD=0.45, $P=0.1$; $I^2=44\%$) and Group B (MD=0.18, $P=0.19$; $I^2=59\%$). Furthermore, a sensitivity analysis was conducted by excluding two trials [11, 14] in Group B, and then no heterogeneity was identified ($P=0.87$; $I^2=0\%$). The result was consistent with previous analysis (MD=0.09, $P=0.55$), indicating this finding was stable and credible (**Table 2**).

Meta-analysis of knee function improvement

ROM: ROM value represented the mobility of the knee after operation. The ROM score was used in 3 studies [11, 16, 17] (296 knees). There was moderate quality of evidence that the ROM improvement in PD group was better than these in NPD group at any follow-up time with no heterogeneity (**Table 2**).

Patella score: There was moderate quality of evidence from 4 studies [11, 14, 16, 17] (396 knees) that PD was associated with significant better score with moderate heterogeneity in Group B (MD=0.55, $P=0.02$; $I^2=26\%$), but not in Group A with no heterogeneity (MD=0.78, $P=0.06$; $I^2=0\%$) (**Table 2**).

OKS: OKS was used to assess pain and function from the patients' perspective. There was low quality of evidence from 2 studies [16, 18] (311 knees) that the PD group displayed higher OKS score than those in NPD group in more than 12 months follow-up (MD=1.92, $P=0.03$; $I^2=0\%$), while no difference was seen in less than 12 months follow-up (MD=0.138, $P=0.36$; $I^2=65\%$) (**Table 2**).

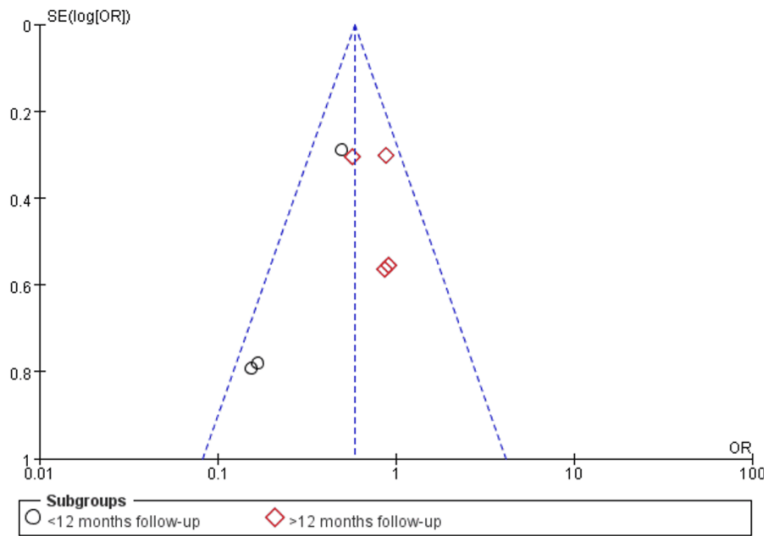


Figure 6. Funnel plot: AKP.

KSS: The KSS comprised a Knee Score (KSSKS) and a Function Score (KSSFS). There was moderate quality of evidence from 6 studies [11, 12, 14-17] (658 knees) that the PD was associated with significantly higher KSSKS score with moderate heterogeneity at any follow-up time (**Table 2**). However, patients were assessed with use of KSSFS (558 knees) in 5 studies [11, 12, 15-17] and the result revealed no significant difference in either Group A (MD=2.57, $P=0.07$; $I^2=0\%$) or Group B (MD=1.87, $P=0.32$; $I^2=80\%$) with moderate quality of evidence. In addition, sensitivity analysis was conducted after excluded two studied [11, 17] in Group B and the result was in line with previous result with no heterogeneity (**Table 2**).

WOMAC: There was moderate quality of evidence from 3 studies [12, 15, 17] (362 knees) that a higher WOMAC score was observed with no heterogeneity in PD group at any follow-up time (MD=4.9, $P=0.005$; MD=2.65, $P=0.02$, respectively). Nevertheless, no significant difference was identified With regard to WOMAC function score (362 knees) at any follow-up time (**Table 2**).

Meta-analysis of satisfaction and complications

As we know, no validated clinical scores can displace patient satisfaction. However, only one study provided data demonstrating that The PD was related to higher patient satisfaction with a higher proportion of patients rating the procedure as excellent ($P < 0.05$).

There were 7 studies [11, 13-18] (881 knees) reporting complications, such as osteonecrosis, infection, revision and reoperation. Analysis with moderate quality of evidence demonstrated that the risk of complications between PD and NPD revealed no statistically significant difference (**Figure 5**).

Publication bias

Funnel plot analyses on AKP (**Figure 6**), KSSKS, ROM, VAS, and complications indicated symmetry, suggesting that bias was minimal.

Discussion

The most important finding of the present study was that PD was associated with decreasing incidence of AKP within 12 months follow-up time, but not after 12 months. In addition, the results consistently demonstrated that PD without patellar resurfacing could improve knee function in postoperative ROM and KSS over follow-up time with no significant complications in TKA. The findings of the present study have important implications that the PD without patellar resurfacing is a safe procedure and could be used in many cases, with better clinical outcome.

TKA is an effective intervention for relieving pain and restoring knee function associated with end-stage osteoarthritis. However, the AKP was reported to occur in up to one half of all patients following primary TKR, which may result in patients' dissatisfaction and lower levels of quality of life. Considering this worrisome problem, an increasing number of orthopedic surgeons took various measures to reduce AKP incidence, such as patellar resurfacing and reshaping. A randomized prospective trial by Liu et al. [21] showed no significant difference between the groups treated with patellar reshaping and patellar resurfacing with regard to the KSS, AKP and radiographs. Recently, Calvisi et al. [22] and Pavlou et al. [23] demonstrated that No significant difference in clinical outcome can be expected with or without patellar resurfacing. Furthermore, the patellar resur-

facing was associated with patellar fracture, aseptic loosening and wear of the patellar polyethylene, thereby leading to a higher incidence of revision [24]. Therefore, no consensus on the optimal treatment of patella was reached to reduce AKP rate during primary TKA.

Based on the above results, we could choose not to apply patella replacement in TKA. Although the exact mechanism of the residual AKP remains unclear, the patellar cartilage erosion, peripatellar soft tissue, and symptomatic patellar maltracking may be related to residual pain [25]. The presence of substance-P fibers distributed in the peripatellar soft tissues may also contribute to the AKP [8, 9]. Additionally, an anatomical study [26] demonstrated that the patella was innervated by the medial and the lateral patellar nerves, coursing within the substance of the vastus medialis and lateralis. Thus, some researchers suggested that disabling selectively these nerves could reduce AKP and improve knee function. On the basis of the data above, many orthopaedic surgeons conducted peripatellar denervation by electrocautery to treat patients with intractable patellofemoral pain. Several studies found that PD is beneficial to the clinical outcome of primary TKA operation [11-13]. In the Netherlands, a postal survey by van Jonbergen et al. [4] found that 56% of orthopedic surgeons favored the application of circumpatellar electrocautery without resurfacing in TKA. However, other studies yielded conflicting results [14-18]. Furthermore, the benefits of PD have not yet been validated through previous meta-analysis due to inconsistent results.

In this current meta-analysis, we adopted two parameters of AKP to evaluate the effectiveness of PD in TKA. The results indicated that PD could reduce the incidence of AKP in the early period (within 12 months), but no significant difference was identified with regard to VAS at any follow-up time. Interestingly, these findings were inconsistent with the previous two meta-analyses [19, 27] and might be interpreted by the following reasons: Firstly, we enrolled two recent RCTs [14, 16] on this topic with low risk of bias, which had a longer follow-up time than previous RCTs did. In addition, an updated report [15] with high quality was published recently, which demonstrated that improved clinical outcome with PD was not maintained at a mean of 3.7 years' follow-up.

These results suggested that the clinical outcome and the prevalence of AKP may change over time. Therefore, it is necessary to conduct subgroup analysis based on follow-up duration. Secondly, the effect variable "postoperative VAS change from baseline" was more accurate than "postoperative VAS level". Thirdly, the previous meta-analysis by Cheng et al. [19] pooled the results from RCTs and non-RCTs with high heterogeneity. However, they did not use sensitivity analysis or subgroup to investigate the origin of heterogeneity, thereby leading to an unstable result. Xie's meta-analysis falsely included two RCTs which are from the same trial [20].

To assess the effectiveness of PD in TKA, post-operative knee function is another important parameter. Since different validated scoring systems may lead to unclear functional assessment findings and moderate heterogeneity, we evaluate the functionality with the use of more complete scoring systems than previous meta-analyses, including ROM, KSS, OKS, PS and WOMAC. In addition, we used the change in knee functional assessments from baseline as our effect index to assess actual improvement in knee function, which eliminated the influence of different baselines. The pooled results found better outcomes regarding the ROM, OKS and KSSKS with low heterogeneity in PD group, suggesting greater improvement in knee function. Furthermore, sensitivity analysis was conducted and the result was consistent with previous results with no heterogeneity.

As for complications, a retrospective study [28] found that the presence of substance-P fibers may include pain/pressure reception, which may affect the proprioception and induce increased pain. However, no abnormal proprioception was reported. In addition, the pooled results showed no significant difference in complications between PD and NPD with no heterogeneity, which was in accord with the previous meta-analysis.

Our study had several strengths: Firstly, this is a comprehensive review of Level-I evidence on this topic with stricter inclusion criteria. (That is, the studies were all prospective randomized trials). Secondly, this study included two new high-quality RCTs and contained a larger sample size than the previous meta-analysis [19, 27], making possible a more robust conclusion.

Thirdly, we adopted the variable “postoperative scores change”, which was more accurate than the “postoperative scores level”. Fourthly, sensitivity analysis was conducted to evaluate the stability of our study. In addition, subgroup analysis was performed to assess the results. Fifthly, we adopted the GRADE approach to assess the quality of evidence.

The limitations of this analysis include the relatively low numbers for the WOMAC and OKS scores of at different time points. In addition, another limitation is the lack of high-quality evidence in several articles. Furthermore, we found that heterogeneity may come from these risk factors, such as the age, gender, and depth of circumpatellar electrocautery. However, we cannot perform further analysis by subgroup analysis due to insufficient data on this topic.

Conclusion

Although the overall quality of the evidence can be considered “average”, we objectively assessed the benefits and risk of PD. Based on this meta-analysis of all currently published RCTs, the findings have important implications for the medical community, namely, that PD is a safe procedure to reduce the incidence of AKP in early period and improve the knee function with similar rates of adverse events compared with NPD.

Disclosure of conflict of interest

None.

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