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Diagnostic performance of SPECT/CT for identification of aseptic loosening after total knee and hip arthroplasty: a systematic review and meta-analysis

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Despite an increasing number of studies examining the effect of Single-Photon Emission Computed Tomography/ Computed Tomography (SPECT/CT) on improvement of diagnosis of aseptic loosening, there is still a great deal of uncertainty regarding its applicability in diagnostic algorithm. Therefore, in this meta-analysis, we aimed to investigate the diagnostic performance of SPECT/CT for identification of aseptic loosening in patients with persistent pain following the total knee arthroplasty (TKA) and total hip arthroplasty (THA).

Electronic databases including Medline, Scopus, Web of Science, Cochrane library, and Embase were systematically searched for identifying relevant published studies from their inception to April 2023. Quality evaluation of the included studies was carried out using Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2).

SPECT/CT had pooled sensitivity of 94% (95% CI: 92-95%) and pooled specificity of 86% (95% CI: 83-89%) for diagnosis of aseptic loosening. The pooled positive likelihood ratio (LR) was estimated as 6.92 (95% CI: 3.74-12.81), the pooled negative LR was estimated as 0.1 (95% CI: 0.06-0.16), and the pooled diagnostic odds ratio (DOR) was estimated as 89.82 (95% CI: 33.04- 244.21). The Summary receiver operating characteristics (SROC) analysis revealed high accuracy with an area under curve (AUC) of 0.96.

The findings of this meta-analysis revealed that SPECT/CT has high sensitivity and specificity for diagnosis of aseptic loosening in patients who underwent TKA or THA. Therefore, SPECT/CT can be considered as an encouraging diagnostic adjunct, particularly in cases with uncertain results of bone scan.

Keywords: Total knee arthroplasty, total hip arthroplasty, single-photon emission computed tomography, computed tomography, meta-analysis, Aseptic loosening.

INTRODUCTION

Hip and knee arthroplasties as elective surgical procedures are commonly performed for treatment of osteoarthritis that limits activities of daily living of the patients[1-3]. It has been reported that approximately 620000 knee arthroplasties and 285000 hip arthroplasties are performed annually in the USA which continue to increase in occurrence in the next few years[4] . It has also been estimated that by the year 2030, annual procedures of knee and hip in the USA rise to 3.48 million and 572000, respectively[5-7]. Although hip and knee arthroplasties commonly improve quality of life of the patients, persistent pain is reported in a significant proportion of the patients. This dissatisfaction due to recurrent or persistent pain can lead to some form of revision arthroplasty for approximately 10% of the patients[6,8]. Identification of a single cause for persistent pain following the total knee arthroplasty (TKA) and total hip arthroplasty (THA)

is challenging as there are different possible causes including aseptic loosening, infection, patellofemoral disorders, prosthetic malposition, instability, and arthrofibrosis. It is imperative to differentiate aseptic loosening which needs surgical management from other causes which may be managed non-surgically, thereby improving the treatment of patients[9,10]. Initial workup typically includes a detailed history, clinical examinations, and plain radiography. Moreover, in complex cases, other 3D imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), radionuclide arthrography, and bone scintigraphy can also be used for diagnosis of aseptic loosening. However, since these imaging modalities still fail to accurately diagnose aseptic loosening, a standardized diagnostic algorithms for evaluation of suspected cases has not yet been established[11]. For evaluation of suspected patients, combination of single photon emission tomography with computed tomography (SPECT/CT) as a recent advancement has been increasingly used to improve the diagnostic accuracy for identification of aseptic loosening. Hybrid imaging with SPECT/CT can accurately identify the increased metabolic activity of periprosthetic bone and correlate it to the morphological and anatomical information of CT[12,13].

Despite an increasing number of studies examining the effect of SPECT/CT on improvement of diagnosis of aseptic loosening, there is still a great deal of uncertainty regarding its applicability in diagnostic algorithm. Therefore, in this meta-analysis, we aimed to investigate the diagnostic performance of SPECT/CT for identification of aseptic loosening in patients with persistent pain following the TKA and THA.

METHODS

This systematic review and meta-analysis was carried out according to the recommendations of Preferred Reporting Items for Systematic reviews and Meta-analysis (PRISMA) extension for Diagnostic Test Accuracy (DTA) and also handbook of Cochrane. We did not register the protocol of this systematic review and meta-analysis in any public registration platform. Two independent authors (MF and SMK) systematically searched electronic databases including Medline, Scopus, Web of Science, Cochrane library, and Embase for identifying relevant published studies from their inception to April 2023. We used the following Medical Subject Heading (MeSH) terms, keywords, and their analogs to perform systematic search using Boolean operators: "single-photon emission computed tomography/computed tomography", "SPECT/CT", "SPECT", "prosthesis", "knee arthroplasty", "hip arthroplasty", "replacement", "prosthesis", "aseptic", and "loosening". Furthermore, reference list search of the eligible studies and similar systematic reviews was carried out manually to ensure all relevant studies could be included. No restriction on date, status, and language of publications was applied. Any disagreements between two authors during systematic search were resolved by consulting a third author.

Studies eligible for this systematic review and meta-analysis needed to fulfill the following criteria: (1) study design, diagnostic test accuracy study, (2) population, cases with suspected aseptic loosening following initial arthroplasty, (3) SPECT/CT was carried out, (4) the final diagnosis of aseptic loosening was confirmed by gold standard, reporting enough data to construct a 2 × 2 table of true positive (TP), true negative (TN), false positive (FP), and false negative (FN). The exclusion criteria were: (1) case reports, case series with less than 10 patients, conference abstracts, editorials, comments, letters, protocols, systematic reviews, and meta-analysis; (2) duplicated publications; (3) publications with insufficient data to construct a 2 × 2 table.

Two independent authors performed the data extraction (MF and SMK). The following data were extracted: first author, year of publication, country, study design, sample size, Male/Female, mean age, joint of arthroplasty, contrast agent, injection way, gold standard, TP, TN, FP, and FN. If we could not construct 2×2 table using the reported data, we back calculated the TP, TN, FP, and TN using the available variables. Data of some variables were also extracted from similar systematic reviews. Quality evaluation of the included studies was carried out using Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2). Any disagreements were resolved by a third author.

Statistical analysis was performed using Stata statistical software package (Stata Corp., College Station, TX, USA) (version 17.0) and meta-Disc software version 1.4 (Ramona Cajal Hospital, Madrid, Spain). The heterogeneity among the included studies was assessed using I^2 and Cochrane's-Q test. Significant heterogeneity was indicated by Cochrane's-Q $P<0.05$ or $I^2>50\%$. On the other hand, low heterogeneity was defined as Cochrane's-Q $P>0.05$ and $I^2<0.50\%$. Threshold effect, known as a source of heterogeneity in DTA meta-analysis, was evaluated using Spearman correlation coefficient. Publication bias was assessed using Begg's test and Funnel plot. Based on the results of heterogeneity, DerSimonian or Laird random effects model was used to estimate the pooled values

sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odd ratio (DOR).

RESULTS

After systematic search in the aforementioned five databases and other sources, we initially identified a total of 773 studies. A total of 431 duplicate papers were removed from these 773 articles, leaving 342 for title and abstract evaluation. A total of 44 articles were eligible for full-text paper review after evaluating the titles and abstracts. After evaluation of the full text of each paper in detail, 27 articles were excluded. Finally, a total of 17 papers were included in this systematic review and meta-analysis. The process of study selection is summarized in the PRISMA flowchart (Fig. 1).

Table I summarizes the characteristics of the 17 included studies published between 2010 and 2022 and conducted in 8 countries. Five studies recruited cases who underwent TKA, six studies recruited patients who underwent THA, and six studies assessed cases who underwent TKA or THA. The mean age of patients assessed in the included studies ranged from 46.8 to 71 years. In 14 studies patients received intravenous contrast and 3 used intraarticular contrast for imaging. Most of these studies used 99Tcm_methylene diphosphonate as a contrast agent.

The results of quality assessment using QUADAS-2 showed varying levels of risk of bias according to seven domains. The majority of included studies were classified as low risk. None of the studies were classified as high risk according to the criteria of index test. Table II summarizes the results of QUADAS-2 for evaluation of the quality assessment of the included studies. Investigation of publication bias using Funnel plot revealed that there is publication bias (Fig. 2). Similarly, Begg's test showed that there is significant publication bias (P=0.02).

Analysis of threshold effect using Spearmen correlation coefficient between logarithms of sensitivity and logarithms of 1-specificity showed no threshold effect in this meta-analysis (r=-0.07 and P=78). Moreover, evaluation of SROC revealed no "shoulder arm shape" indicating no significant threshold effect. Significant heterogeneity was found in sensitivity (I^2=54.4%, P=0.004), specificity (I^2=85.1%, P<0.01), PLR (I^2=87.1%, P<0.01), NLR (I^2=49.6%, P=0.01), and DOR (I^2=68.7%, P<0.01).

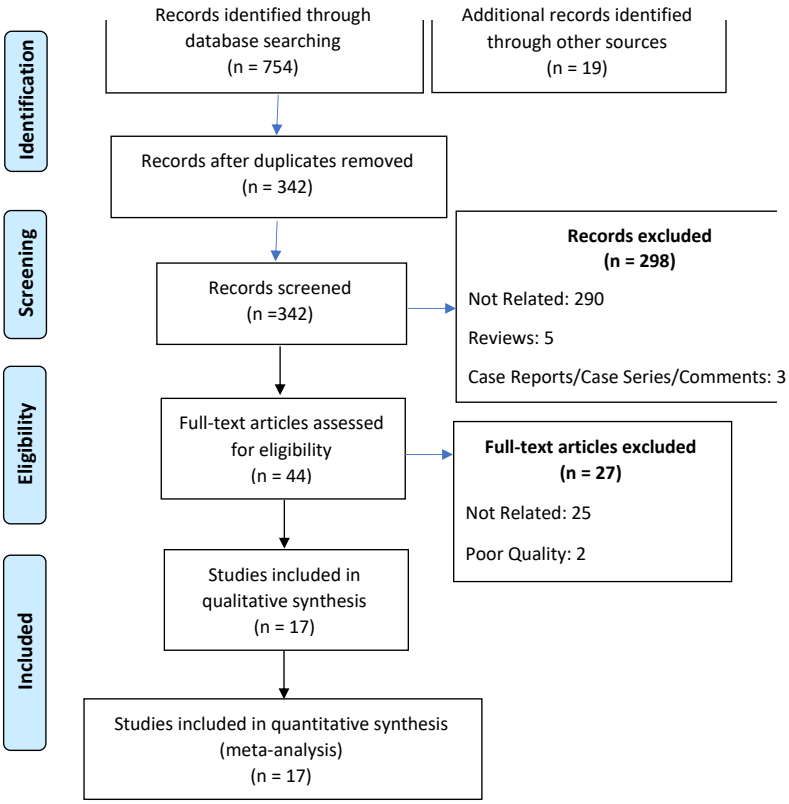

Figure 1. — PRISMA flowchart of the literature search and selection of studies that reported accuracy of SPECT/CT for diagnosis of aseptic loosening.

Table I. — Characteristics of the included studies

Author	Year	Country	Sample Size	M/F	Design	Joint	Contrast	Injection	Gold Standard	TP	FP	FN	TN
Aleksyniene et al.[19]	2022	Denmark	44	29/26	Prospective	Hip and Knee	In-labeled WBC/99mTc-Nanocoll	Intravenous	Operative Findings and Clinical and Radiographic Follow-up and Microbiologic Examinations	13	1	0	30
Bao et al.[20]	2021	Canada	63	26/37	Retrospective	Hip and Knee	99mTc-sulfur colloid	Joint	Operative Findings and Clinical and Radiographic Follow-up	6	1	1	55
Li et al.[21]	2020	China	69	31/27	Retrospective	Hip	99mTc-methylene diphosphonate	Intravenous	Operative Findings and Clinical and Radiographic Follow-up	61	3	0	5
Schuldt et al.[22]	2020	Switzerland	67	NA	Retrospective	Hip	99mTc-dicarboxypropane diphosphonate	Intravenous	Operative Findings	40	13	5	9
Murer et al.[14]	2019	Switzerland	166	79/123	Retrospective	Knee	99mTc-hydroxymethylene diphosphonate	Intravenous	Operative Findings	148	0	11	7
Backer et al.[23]	2019	Switzerland	35	14/21	Prospective	Hip	99mTc-dicarboxypropane diphosphonate	Intravenous	Clinical and Radiological Examinations	12	2	1	20
Zhang et al. (b)[24]	2019	China	33	23/28	Retrospective	Knee	99mTc-methylene diphosphonate	Intravenous	Operative Findings and Clinical and Radiographic Follow-up	14	3	0	16
Mandegaran et al.[8]	2018	India	33	18/31	Retrospective	Knee	99mTc-methylene diphosphonate	Intravenous	Operative and Histopathological/Cytological Findings and Clinical and Microbiologic Examinations	9	6	0	18
Zhang et al. (a)[15]	2018	China	230	103/82	Retrospective	Hip	99mTc-methylene diphosphonate	Intravenous	Operative Findings and Clinical and Radiographic Follow-up	123	0	3	104
Tang et al.[25]	2017	China	86	36/19	Retrospective	Hip and Knee	99mTc-methylene diphosphonate	Intravenous	Operative Findings	52	3	3	28
Abele et al.[17]	2015	Canada	38	NA	Retrospective	Hip and Knee	99mTc-sulfur colloid	Joint	Operative Findings and Clinical and Radiographic Follow-up	14	1	0	23
Hirschmann et al.[16]	2015	Switzerland	32	10/23	Prospective	Knee	99mTc-hydroxymethylene diphosphonate	Intravenous	Operative Findings	10	0	1	21
Arican et al.[18]	2015	Turkey	50	15/35	Retrospective	Hip and Knee	99mTc-methylene diphosphonate	Intravenous	Operative Findings	24	2	3	21
Yodong et al.[26]	2014	China	45	27/18	NA	Hip	99mTc-methylene diphosphonate	Intravenous	Operative Findings	34	5	3	3
Al-Nabhani et al.[27]	2013	UK	69	19/50	Retrospective	Knee	99mTc-hydroxymethylene diphosphonate	Intravenous	Operative Findings and Clinical and Radiographic Follow-up and Laboratory Examination	9	3	0	57
Yuke et al.[28]	2011	China	29	14/15	NA	Hip	99mTc-methylene diphosphonate	Intravenous	Operative Findings and Clinical and Radiographic Follow-up	20	2	2	5
Chew et al.[29]	2010	Australia	155	NA	Retrospective	Hip and Knee	99mTc-calcium phytate	Joint	Operative Findings	30	24	9	82

M/F: Male/Female ratio; TP: True positive; FP: False positive; FN: False negative; TN: True negative.

Table II. — Quality assessment of the include studies using QUADAS-2 tool

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Aleksyniene et al.	☺	☺	☺	☺	☺	☺	☺
Bao et al.	☺	?	☺	☺	☺	?	☺
Li et al.	☺	?	?	?	☺	?	☺
Schuldt et al.	☺	?	?	?	☺	?	?
Murer et al.	☺	☺	?	?	?	☹	?
Backer et al.	☺	☺	☹	☺	☺	☺	☹
Zhang et al. (b)	☺	☺	☺	☹	?	☹	☺
Mandegaran et al.	☺	☺	☺	☹	☺	☺	☺
Zhang et al. (a)	☺	☺	?	?	☺	☺	?
Tang et al.	☹	☺	?	?	☹	?	?
Abele et al.	☺	☺	?	☹	☺	☹	?
Hirschmann et al.	☺	?	☺	?	☺	?	?
Arican et al.	☺	☺	?	☺	☺	☺	?
Yodong et al.	☺	☺	☺	☺	?	☹	☺
Al-Nabhani et al.	☺	?	☺	?	☺	?	?
Yuke et al.	?	☺	☺	☺	?	☺	☺
Chew et al.	☺	☺	☺	☺	☺	?	☺

☺Low Risk; ☹High Risk; ? Unclear Risk.

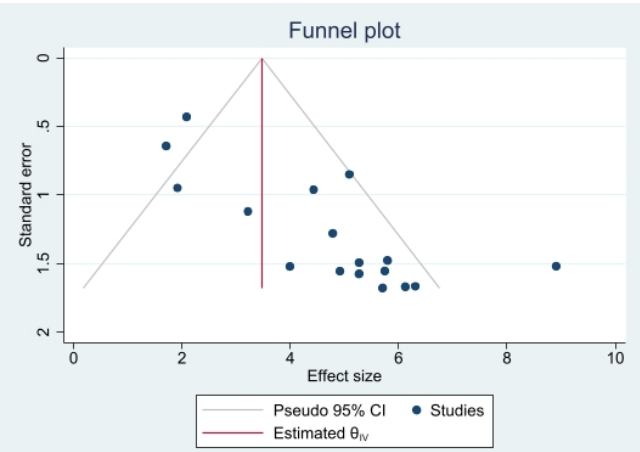

Figure 2. — Funnel plot of publication bias on the pooled DOR of SPECT/CT for diagnosis of aseptic loosening.

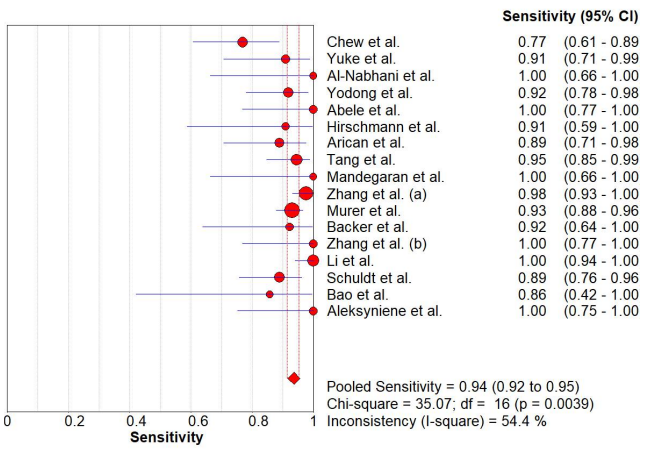

Figure 3. — Forest plot of the pooled sensitivity of SPECT/CT for diagnosis of aseptic loosening.

SPECT/CT had pooled sensitivity of 94% (95% CI: 92-95%) and pooled specificity of 86% (95% CI: 83-89%) for diagnosis of aseptic loosening. The pooled analyses on sensitivity and specificity of SPECT/CT are shown in figure 3 and 4, respectively. The pooled positive LR was estimated as 6.92 (95% CI: 3.74-12.81), the pooled negative LR was estimated as 0.1 (95% CI: 0.06-0.16), and the pooled DOR was estimated as 89.82 (95% CI: 33.04-244.21) (Fig. 5-7). The SROC analysis (Fig. 8) revealed high accuracy with an AUC of 0.96 for SPECT/CT as a diagnostic modality for identification of aseptic loosening.

Table III. — Subgroup analysis of the diagnostic performance of SPECT/CT for aseptic loosening

Subgroups	Covariates	No. of studies	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Pooled PLR (95% CI)	Pooled NLR (95% CI)	Accuracy	DOR (95% CI)	rDOR (95% CI)	P-value
Site of Arthroscopy	Hip	9	0.94 (0.91-0.97)	0.87 (0.82-0.91)	5.30 (1.96-14.32)	0.11 (0.05-0.25)	0.96	61.77 (13.55-281.48)	0.82 (0.09-7.15)	0.84
	Knee	8	0.92 (0.88-0.96)	0.88 (0.83-0.91)	6.67 (3.61-12.32)	0.14 (0.07-0.28)	0.94	54.6 (18.70-159.45)		
Injection Way	Intravenous	14	0.95 (0.93-0.96)	0.89 (0.85-0.92)	6.78 (3.16-14.54)	0.09 (0.06-0.14)	0.97	96.36 (32.64-284.46)	0.19 (0.02-1.54)	0.11
	Intraarticular	3	0.83 (0.71-0.92)	0.82 (0.75-0.87)	10.87 (1.42-83.44)	0.19 (0.06-0.62)	0.95	79.44 (3.66-1725.17)		

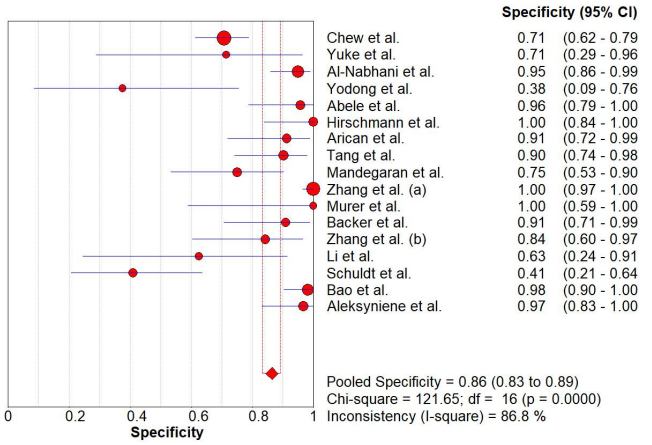

Figure 4. — Forest plot of the pooled specificity of SPECT/CT for diagnosis of aseptic loosening.

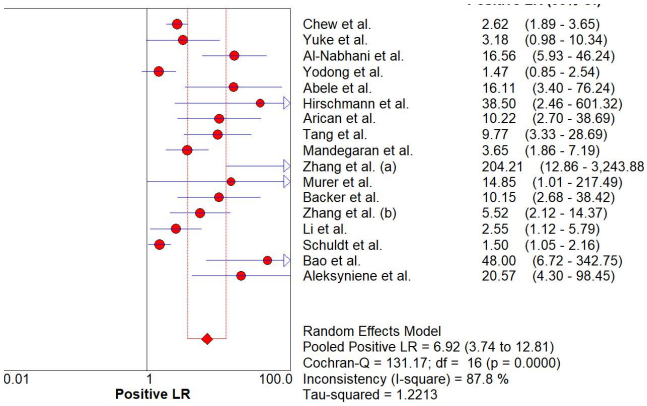

Figure 5. — Forest plot of the pooled positive likelihood ratio (PLR) of SPECT/CT for diagnosis of aseptic loosening.

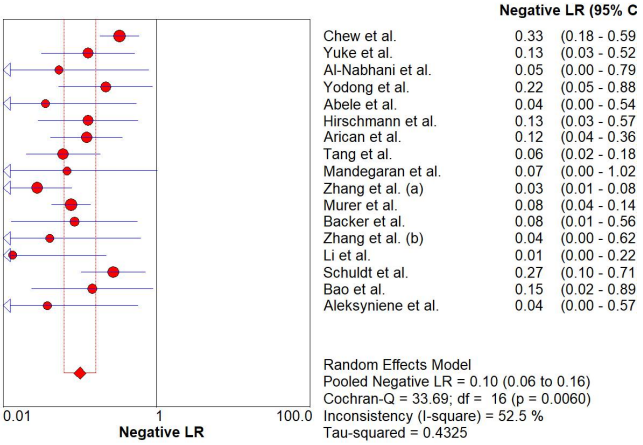

Figure 6. — Forest plot of the pooled negative likelihood ratio (NLR) of SPECT/CT for diagnosis of aseptic loosening.

Subgroup analysis revealed that location of contrast injection is not the source of heterogeneity for diagnostic accuracy of SPECT/CT between studies. Similarly, we found that type of joint did not influence diagnostic accuracy of SPECT/CT for identification of aseptic loosening. The results of meta-regression and subgroup analysis are summarized in table III.

DISCUSSION

This meta-analysis comprehensively investigated the diagnostic performance of SPECT/CT for identification of aseptic loosening in cases with persistent pain following the TKA and THA. Our findings showed that SPECT/CT had pooled sensitivity of 94% and pooled specificity of 86% for diagnosis of aseptic loosening. Moreover, SPECT/CT had excellent accuracy of 0.96 for identification of aseptic loosening. However, we found that location of contrast injection and type of joint did not affect the diagnostic performance of SPECT/CT for diagnosis of aseptic loosening.

Although these findings show that SPECT/CT as an imaging modality has excellent accuracy for diagnosis of aseptic loosening, this is in line with the results of

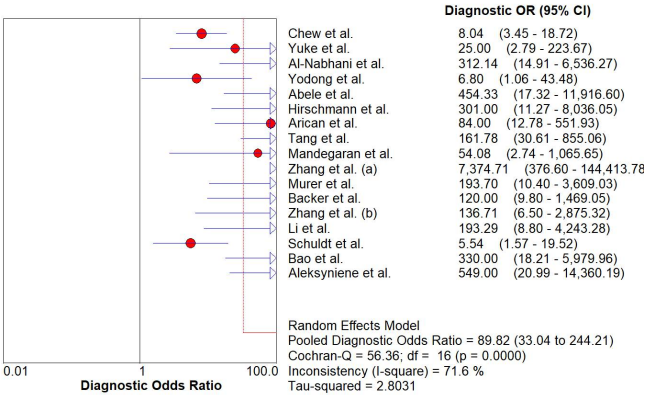

Figure 7. — Forest plot of the diagnostic OR (DOR) of SPECT/CT for diagnosis of aseptic loosening.

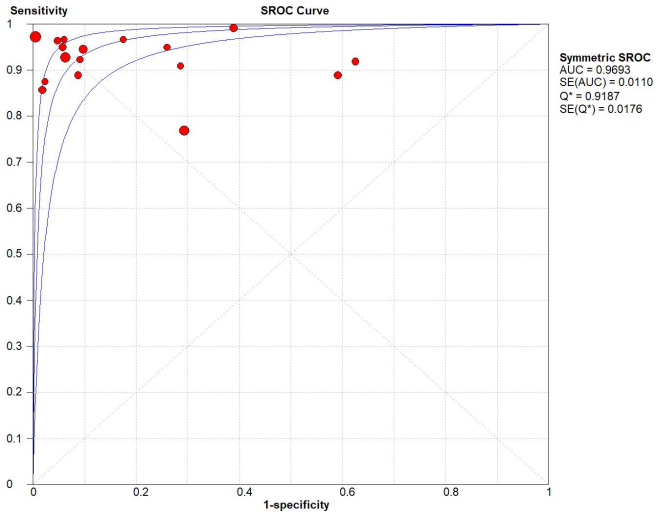

Figure 8. —Summary receiver-operating characteristic (SROC) of SPECT/CT for diagnosis of aseptic loosening.

previous studies[14-17]. However, we found significant heterogeneity in the diagnostic parameters including sensitivity, specificity, PLR, NLR, and DOR, and mete-regression suggested that the heterogeneity of included studies was not associated with type of joint and location of contrast injection. A possible explanation for these heterogeneities may lie in the fact that there are other factors affecting the diagnostic parameters of SPECT/CT for diagnosis of aseptic loosening which were not reported in the included studies. Therefore, these findings suggest a need for further diagnostic studies to standardize the imaging conditions of SPECT/CT for diagnosis of aseptic loosening.

In a similar study, Barnsley et al.[11] performed a systematic review and meta-analysis regarding diagnosis of aseptic loosening in patients who underwent TKA. In this meta-analysis, the authors conducted a systematic search in electronic databases such as MEDLINE, EMBASE, and Cochrane from inception to 2018 to find studies that used bone scintigraphy, 18F-FDG-PET, SPECT/CT, or radionuclide arthrogram for diagnosis of aseptic loosening. This study showed that SPECT/CT is the most accurate imaging tool for diagnosis of aseptic loosening in patients who underwent TKA. However, they included few studies and the pooled results of diagnostic accuracy for SPECT/CT were estimated based on the findings of only two papers. Another limitation of their study is that the majority of included papers had poor quality and according to the results of QUADAS-2, all studies had a high risk of bias in at least one domain. The small number of included studies in this meta-analysis and significant risk of bias preclude any definitive conclusions from their findings. Therefore, these limitations propose the need of future systematic reviews and meta-analysis based on further high quality studies. Compared with this study, our meta-analysis had some advantages. First, we included a considerably greater number of papers investigating the accuracy of SPECT/CT for diagnosis of aseptic loosening. Second, we also included the data of studies that evaluated diagnostic accuracy of SPECT/CT for diagnosis of aseptic loosening after THA. Finally, we investigated the source of heterogeneity using meta-regression.

Review of literature revealed that few studies investigated the effects of time between evaluation of patients with gold standard and SPECT/CT, or the time between SPECT/CT and TKA on the diagnostic performance of SPECT/CT for detection of aseptic loosening[16]. It seems that these data would be crucial for orthopedic surgeons to recommend the best time for SPECT/CT in order to achieve the highest diagnostic performance. Exposing the patients to high dose of radiation and being costly are two main limitations of SPECT/CT. Different imaging evaluation are commonly required to establish the final diagnosis of patients with painful prostheses. Although the comparison between other imaging modalities and SPECT/CT with respect to the cost-effectiveness was not reported in previous studies, SPECT/CT can reduce time between initiation of pain and treatment, and prevent other unnecessary diagnostic tests and management[18]. Therefore, despite the high cost of SPECT/CT, it can be considered as the first choice of imaging in cases with uncertain results of bone scan.

However, our study had some limitations. First, since meta-regression showed that type of joint and location of contrast injection did not affect diagnostic performance of SPECT/CT, the source of heterogeneity was not found using the extracted data. Second, the majority of included studies had an unclear

risk of bias in at least one domain. Third, most of the included studies were retrospective with small number of patients. Fourth, we found significant publication bias suggesting that further studies are required to be carried out and included in the meta-analysis. Finally, because of the low prevalence of aseptic loosening and the strict eligibility criteria used for this meta-analysis, the number of eligible studies was relatively small.

CONCLUSION

The findings of this meta-analysis revealed that SPECT/CT has high sensitivity and specificity for diagnosis of aseptic loosening in patients who underwent TKA or THA. Therefore, SPECT/CT can be considered as an encouraging diagnostic adjunct, particularly in cases with uncertain results of bone scan.

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Data Availability: Not applicable.

Using Artificial Intelligence Chatbots: None.

REFERENCES

1. Canovas F, Dagneaux L. Quality of life after total knee arthroplasty. Orthop Traumatol Surg Res. 2018;104(1s):S41-s6.
2. Van Manen MD, Nace J, Mont MA. Management of primary knee osteoarthritis and indications for total knee arthroplasty for general practitioners. J Am Osteopath Assoc. 2012;112(11):709-15.
3. Levine ME, Nace J, Kapadia BH, Issa K, Banerjee S, Cherian JJ, et al. Treatment of primary hip osteoarthritis for the primary care physician and the indications for total hip arthroplasty. J Long Term Eff Med Implants. 2013;23(4):323-30.
4. Murphy L, Helmick CG. The impact of osteoarthritis in the United States: a population-health perspective. Am J Nurs. 2012;112(3 Suppl 1):S13-9.
5. Beck RT, Illingworth KD, Saleh KJ. Review of periprosthetic osteolysis in total joint arthroplasty: an emphasis on host factors and future directions. J Orthop Res. 2012;30(4):541-6.
6. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am. 2007;89(4):780-5.
7. Piscitelli P, Iolascon G, Innocenti M, Civinini R, Rubinacci A, Muratore M, et al. Painful prosthesis: approaching the patient with persistent pain following total hip and knee arthroplasty. Clin Cases Miner Bone Metab. 2013;10(2):97-110.
8. Mandegaran R, Agrawal K, Vijayanathan S, Gnanasegaran G. The value of 99mTc-MDP bone SPECT/CT in evaluation of patients with painful knee prosthesis. Nucl Med Commun. 2018;39(5):397-404.
9. Apostu D, Lucaciu O, Berce C, Lucaciu D, Cosma D. Current methods of preventing aseptic loosening and improving osseointegration of titanium implants in cementless total hip arthroplasty: a review. J Int Med Res. 2018;46(6):2104-19.
10. van Otten TJM, van Loon CJM. Early aseptic loosening of the tibial component at the cement-implant interface in total knee arthroplasty: a narrative overview of potentially associated factors. Acta Orthop Belg. 2022;88(1):103-11.
11. Barnsley L, Barnsley L. Detection of aseptic loosening in total knee replacements: a systematic review and meta-analysis. Skeletal Radiol. 2019;48(10):1565-72.
12. Horger M, Bares R. The role of single-photon emission computed tomography/computed tomography in benign and malignant bone disease. Semin Nucl Med. 2006;36(4):286-94.
13. Hirschmann MT, Schön S, Afifi FK, Amsler F, Rasch H, Friederich NF, et al. Assessment of loading history of compartments in the knee using bone SPECT/CT: a study combining alignment and 99mTc-HDP tracer uptake/distribution patterns. J Orthop Res. 2013;31(2):268-74.
14. Murer AM, Hirschmann MT, Amsler F, Rasch H, Huegli RW. Bone SPECT/CT has excellent sensitivity and specificity for diagnosis of loosening and patellofemoral problems after total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2020;28(4):1029-35.
15. Zhang B SQ, Guo H. Diagnostic value of pain cause after hip prosthesis replacement by using SPECT/CT. J Chin Clin Med Imaging. 2018;29:59-61.
16. Hirschmann MT, Amsler F, Rasch H. Clinical value of SPECT/CT in the painful total knee arthroplasty (TKA): a prospective study in a consecutive series of 100 TKA. Eur J Nucl Med Mol Imaging. 2015;42(12):1869-82.
17. Abele JT, Swami VG, Russell G, Masson EC, Flemming JP. The Accuracy of Single Photon Emission Computed Tomography/Computed Tomography Arthrography in Evaluating Aseptic Loosening of Hip and Knee Prostheses. J Arthroplasty. 2015;30(9):1647-51.
18. Arıcan P, Okudan Tekin B, Şefizade R, Naldöken S, Baştuğ A, Özkurt B. The role of bone SPECT/CT in the evaluation of painful joint prostheses. Nucl Med Commun. 2015;36(9):931-40.
19. Aleksyniene R, Iyer V, Bertelsen HC, Nilsson MF, Khalid V, Schønheyder HC, et al. The Role of Nuclear Medicine Imaging with (18)F-FDG PET/CT, Combined (111)In-WBC/(99m)Tc-Nanocoll, and (99m)Tc-HDP SPECT/CT in the Evaluation of Patients with Chronic Problems after TKA or THA in a Prospective Study. Diagnostics (Basel). 2022;12(3).
20. Bao B, Liu CS, Masson ECO, Abele JT. Diagnostic accuracy of SPECT/CT arthrography in patients with suspected aseptic joint prostheses loosening. Eur J Hybrid Imaging. 2021;5(1):4.
21. Li L WB, Zhang B, Guo H. The diagnostic of SPECT/CT in aseptic prosthesis looseness after total hip replacement. J Med Imaging. 2020;30:308-11.
22. Schuldt A, Lehnick D, Agten CA, Beck M, Kist M, Bhure U, et al. Performance of radiography and single-photon emission computed tomography/computed tomography in painful total hip arthroplasty and impact on arthroplasty survival. Nucl Med Commun. 2020;41(9):875-82.
23. Bäcker HC, Steurer-Dober I, Beck M, Agten CA, Decking J, Herzog RF, et al. Magnetic resonance imaging (MRI) versus single photon emission computed tomography (SPECT/CT) in painful total hip arthroplasty: a comparative multi-institutional analysis. Br J Radiol. 2020;93(1105):20190738.
24. Zhang B SQ, Liu Y, Guo H. Diagnostic value of SPECT/CT for pain reason after total knee arthroplasty. J Chin Clin Med Imaging. 2019;30:437-40.

25. H T. Study on differential diagnosis of infection and loosening after arti ficial joint replacement by nuclear medicine imaging. J Tribune Grassroots Med. 2017:461-3.
26. Yudong J YL, Xiaodong Z, Xiantao C, Ying Z, Liyun L, et al. Value of SPECT/CT in the diagnosis of prosthesis loosening after hip replacement. Chin J Pract Diagn Ther. 2014;28:707-8.
27. Al-Nabhani K, Michopoulou S, Allie R, Alkalbani J, Saad Z, Sajjan R, et al. Painful knee prosthesis: can we help with bone SPECT/CT? Nucl Med Commun. 2014;35(2):182-8.
28. Yuke L MZ, Hongjun L, Huili G, Yalin C, Junhui W, et al. SPECT/CT imaging in the diagnosis of prosthesis loosening after hip arthroplasty. Chin J Nucl Med. 2011;31:348-9.
29. Chew CG, Lewis P, Middleton F, van den Wijngaard R, Deshaies A. Radionuclide arthrogram with SPECT/CT for the evaluation of mechanical loosening of hip and knee prostheses. Ann Nucl Med. 2010;24(10):735-43.