Arthroplasty Today 15 (2022) 182–187

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Systematic review

Routine Pathologic Examination of Femoral Head Specimens from Total Hip Arthroplasty May Not Be Indicated or Cost-effective: A Systematic Review

Sumon Nandi, MD, MBA [a, *], Ran Schwarzkopf, MD, MSc [b], Antonia Chen, MD, MBA [c], Thorsten Seyler, MD, PhD [d], Lauren Wheeler, MLIS [e], Javad Parvizi, MD [f], AAHKS Research Committee

[a] University of Maryland School of Medicine, Baltimore, MD, USA
[b] NYU Grossman School of Medicine, New York, NY, USA
[c] Harvard Medical School; Boston, MA, USA
[d] Duke University School of Medicine, Durham, NC, USA
[e] University of Maryland, Baltimore, Baltimore, MD, USA
[f] Rothman Institute, Thomas Jefferson University, Philadelphia, PA, USA

ARTICLE INFO

Article history:
Received 6 December 2021
Received in revised form
5 March 2022
Accepted 15 March 2022
Available online 9 May 2022

Keywords:
Femoral head
Hip
Arthroplasty
Pathology
Routine
Cost

ABSTRACT

Background: There is considerable disparity in institutional practices surrounding routine pathologic examination of femoral heads removed during total hip arthroplasty (THA). Multiple groups have studied the merits of routine femoral head pathology in THA, without clear consensus. We sought to further investigate the existing evidence on routine pathologic examination of femoral heads retrieved during THA to determine if this practice provides additional clinical value and is cost-effective.
Material and methods: To conduct a systematic review of the literature, a medical librarian was consulted to develop and perform comprehensive searches in PubMed (1809-present), Embase (embase.com 1974-present), CINAHL (EBSCO, 1937-present), and the Cochrane Central Register of Controlled Trials (Wiley). Final searches resulted in 727 references. Through multiple reviewer screenings and assessments of eligible full-text articles, we included 14 articles for review.
Results: Our systematic review yielded pathologic examination results from 17,388 femoral head specimens collected during THA. In 0.85% of cases, the pathologic diagnosis differed in a meaningful way from the preoperative clinical diagnosis. Routine pathology changed patient management in approximately 0.0058% of cases. The average cost for pathologic examination of each specimen was $126.38.
Conclusion: Routine pathologic examination of femoral heads retrieved during THA has limited impact on patient management. With an estimated 500,000 THAs performed in 2019, the economic feasibility of routine femoral head pathology is limited at an annual cost of up to $63,000,000 and cost per quality-adjusted life-year approaching infinity. However, surgeon discretion on a patient-specific or practice-specific basis should be used to make the final determination on the need for femoral head pathology.

Introduction

Approximately 500,000 total hip arthroplasties (THAs) were estimated to be performed in 2019 in the United States alone, and this number is increasing exponentially over time [1,2]. Intraoperative practices during THA are thus consequential in terms of quality of care provided to patients as well as cost incurred by health-care systems. While osteoarthritis, inflammatory arthritis, and avascular necrosis are the most common indications for THA, occult diagnoses such as malignancy or infection may have significant implications for postoperative management, patient outcomes, as well as cost [3].

To determine if routine pathologic examination of the femoral head retrieved during THA is indicated and/or cost-effective, it is

PROSPERO registration application #293599.

* Corresponding author. University of Maryland School of Medicine, 110 S. Paca St., Suite 300, Baltimore, MD 21201, USA. Tel.: +1 410 683 2130.
E-mail address: sumon.nandi@gmail.com

https://doi.org/10.1016/j.artd.2022.03.016

necessary to determine the frequency with which the pathologic diagnosis differs from the preoperative diagnosis as well as the cost of pathologic examination of the femoral head. While multiple studies have strived to make this determination, the conclusions are widely disparate [4–7].

Several reports have found that the routine pathologic examination of femoral head specimens retrieved during THA provides little additional diagnostic value and is an unnecessary and costly practice [4,5]. Others report routine femoral head pathology is critical to the diagnosis of occult disease, such as malignancy, and is cost-effective in terms of quality-adjusted life-years (QALY) [6,7]. As a result, it is not surprising that institutional policies and clinical practices surrounding pathologic examination of femoral head specimens are quite variable.

The purpose of the study was to further investigate the existing evidence on routine pathologic examination of femoral head specimens retrieved during THA through systematic review in order to determine if this practice provides additional diagnostic value and, if so, evaluate associated costs.

Material and methods

Literature search strategy

A medical librarian (L.W.) was consulted to develop and conduct comprehensive searches in PubMed (1809-present), Embase (embase.com 1974-present), CINAHL (EBSCO, 1937-present), and the Cochrane Central Register of Controlled Trials (Wiley). Search strategies were individually developed for each database utilizing database-appropriate controlled vocabulary (see below). Controlled vocabulary and text words encompassed *hip arthroplasty*, *routine diagnostic test*, and *femur* terms.

Database-specific searches

PubMed (1809-present): 321 references retrieved

Single-line search run in the "New PubMed" interface:

((("arthroplasty, replacement, hip"[mh] OR (((hip joint*[tiab]) AND (replacement*[tiab] OR arthroplast*[tiab])) OR ((hip[tiab]) AND (implantation*[tiab] OR replacement*[tiab] OR arthroplasty [tiab])))))) AND ("diagnostic tests, routine"[mh] OR "pathology, clinical"[mh] OR "pathology, surgical"[mh] OR "histology"[mh] OR (diagnostic test*[tiab] OR ((histopatholog*[tiab] OR histolog*[tiab] OR pathologic*[tiab]) AND (examin*[tiab])))))) AND (("femur head"[mh] OR (femoral[tiab]OR femur*[tiab] OR caput-femoris [tiab])))

Embase (Embase.com): 372 references retrieved

Single-line search run in "Results" tab of Embase.com interface:

('hip replacement'/exp OR ((('hip joint') NEAR/3 (replacement* OR arthroplast*)) OR ((hip) AND (implantation* OR replacement* OR arthroplast*))):ti,ab) AND ('diagnostic test'/exp OR (((clinical OR surgical) NEAR/3 (pathology)) OR 'diagnostic test*' OR ((histopatholog* OR histolog* OR pathologic*) NEAR/3 (examin*))):ti,ab) AND ('femoral head'/exp OR (femoral OR femur* OR 'caput femoris'):ti,ab)

CINAHL (EBSCOhost): 30 references retrieved

Search run in Advanced Search interface by entering each line into separate search box with each search box combined with AND:

((MH "Arthroplasty, Replacement, Hip") OR ("hip replacement*" OR "hip joint replacement*" OR "hip joint arthroplast*" OR "hip implantation*" OR "hip replacement*" OR "hip arthroplast*")) AND ((MH "Diagnostic Tests, Routine" OR MH "Pathology, Clinical" OR MH "Histology") OR ("diagnostic test*" OR "histopatholog* examin*" OR "histolog* examin*" OR "pathologic* examin*")) AND ((MH "Femur Head") OR (femoral OR femur* OR "caput femoris"))

Cochrane Library (WileyOnline; Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register): 4 references retrieved

Using Search Manager in Advanced Search:

(hip NEAR/3 (arthroplasty OR replacement OR (joint NEXT arthroplasty) OR (joint NEXT replacement) OR implantation)) AND (diagnostic NEAR/3 test) OR (clinical pathology) OR (histopathology NEAR/3 examin*) OR (pathologic NEXT examin*) AND (femur NEXT head) OR femoral OR (caput femoris) OR femur

Article selection and data collection protocol

Final searches were run on November 24, 2020, resulting in 727 total references. After removing duplicates, 587 references remained. Two reviewers (S.N. and R.S.) independently performed title and abstract screening of the references. Conflicts were resolved by a third reviewer (A.C.) to arrive at 19 articles. Article screening was performed using Covidence (Melbourne, Australia) systematic review management software. After full-text review, 14 of these articles were confirmed to meet study inclusion and exclusion criteria (Table 1) and comprised our final cohort for data extraction [4–17]. Figure 1, illustrating the aforementioned process, is the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram [18].

Data points collected from each article by a single reviewer (S.N.), if available, were as follows: title, authors, journal, year of publication, study design, country of origin, source population, number of femoral head specimens, pathologic diagnosis, discrepancies between clinical and pathologic diagnoses, cost analysis, and article conclusion regarding routine pathologic examination. A discordant diagnosis was defined as a pathologic diagnosis that both differed from the clinical diagnosis and altered patient management according to the majority of authors of the articles reviewed.

Statistical analysis

Descriptive statistics were utilized for data analysis, including the calculation of frequencies, percentages, and means (Microsoft Excel, Redmond, WA).

Results

A summary of data extracted from included articles is provided in Table 2.

OA, osteoarthritis. Our systematic review yielded pathologic examination results from a total of 17,388 femoral head specimens collected during primary THA performed for any indication. All specimens were fixed, decalcified, sectioned, and stained with hematoxylin and eosin for histologic evaluation. Immunohistochemistry and flow cytometry were performed as needed. Only in 147 of these cases, or 0.85% of the time, did the authors believe that the pathologic diagnosis differed from the preoperative clinical diagnosis in a manner that affected patient management (discordant diagnosis). The frequency of each discordant diagnosis is listed in Table 3. Inflammatory arthritis and B-cell lymphoma were the 2 most common discordant diagnoses.

We re-evaluated all femoral head pathologic diagnoses labeled as discordant in the literature. Final pathologic diagnoses are only available postoperatively. As a result, the value of each discordant pathologic diagnosis following THA was considered. For most discordant diagnoses in Table 3, THA is a definitive treatment,

routine postoperative surveillance is sufficient for the condition, or management is dictated by clinical symptoms alone. As a result, patient care or prognosis did not benefit from these pathologic data. Previously undiagnosed metastatic carcinoma was the only truly discordant diagnosis. As a result, routine pathology changed patient management in approximately 0.0058% (1 out of 17,388) of cases.

Eight studies conducted in the United States provided cost-analyses of routine pathologic examination of femoral head specimens obtained from THA [4–8,10,12,15]. The mean cost per specimen was $126.38 (range $60 to $283), based on available data from 7 of these articles [4–6,8,10,12,15]. If 500,000 THAs are performed annually [1,2], the cost of routine femoral head pathology is $126.38/femoral head × 500,000 femoral heads/year = $63,190,000/y. While DiCarlo and Klein reported routine pathologic examination of femoral heads accounted for just 0.5% of total costs at a single musculoskeletal specialty hospital, Campbell et al. reported the absolute annual cost of routine pathology examination of femoral heads in 1997 was $17.5 to $25 million [7,8]. In order to arrive at 1 discordant case, 2 of the articles found pathology costs approached $123,000 [5,6]. The cost per QALY for routine pathologic examination of femoral heads was highly disparate in the articles that reported this metric. Liow et al. calculated a cost of $49,569.74 per QALY after assuming a benefit in QALY with routine femoral head pathology [6]. Lin et al. arrived at essentially infinite cost per QALY by not finding any gain in QALY (QALY = 0) with routine pathology [4,6].

Of the articles that commented on the need for routine pathologic examination of femoral heads retrieved during THA, 58% (7 of 12 articles) advised against this practice as it was not found to change patient management [4,5,8,10,12,13,15]. It is our opinion that the remaining 5 articles that favored routine pathologic examination did so after mischaracterizing many pathologic diagnoses that did not impact patients' clinical course as discordant [6,7,9,11,17]. This resulted in an overvaluation of routine femoral head pathology, which skewed analyses of cost-effectiveness and ultimately these articles' conclusions.

Discussion

There is a disparity in institutional practices surrounding routine pathologic examination of femoral heads obtained during THA. Multiple groups have studied the merits of routine pathology in THA, but the conclusions are conflicting [4–7]. We conducted a systematic review of existing evidence to determine if routine pathologic examination of femoral head specimens obtained during THA is indicated and, if so, cost-effective. The results of our study demonstrate that routine femoral head pathology seldom impacts patient management and is a significant economic burden.

Table 1
Article inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
English language manuscript	Review article
Routine pathology/histology of femoral head	Meeting abstract
Specimens obtained during total hip arthroplasty	Cadaveric study
	Case report
	Repeat publication of same patient cohort
	Patients younger than 18
	Specimens obtained during hemiarthroplasty

When femoral head specimens from THA were routinely sent for pathologic examination, we found that the pathologic diagnosis meaningfully differed from the preoperative clinical diagnosis 0.85% of the time. Cases in which the pathologic diagnosis differed from the clinical diagnosis, resulting in a change in patient management, were described as discordant. While less than 1% of cases were labeled discordant in the papers reviewed, patient management was rarely, if ever, changed by routine pathology in these cases.

The most common discordant diagnosis was inflammatory arthritis. A patient with a single joint affected by inflammatory arthritis that has undergone joint replacement requires little further intervention. Without involvement of any other joints, initiation of disease-modifying antirheumatic drugs would be undesirable due to the increased risk of infection and malignancy [19]. Thus, a diagnosis of inflammatory arthritis on routine pathology does not significantly change patient management.

B-cell lymphoma was the second most common discordant diagnosis. Many of the included studies assumed an improvement in clinical outcome with early diagnosis of B-cell lymphoma in patients who were otherwise asymptomatic. However, even with early diagnosis, indolent subtypes of this condition are often left untreated unless patients are symptomatic or there are aberrations on physical examination, radiographs, or laboratory studies such as complete blood count [20–27]. As there is no clinical benefit to early diagnosis of asymptomatic indolent B-cell lymphoma , there is little utility in its detection on routine pathologic examination of femoral heads. While high-grade B-cell lymphomas do benefit from early diagnosis, patients with bone marrow involvement detectable on femoral head pathology would likely present with significant constitutional symptoms, rapidly growing mass, laboratory abnormalities, and/or radiographic findings [28].

The third most common discordant diagnosis was pigmented villonodular synovitis (PVNS). The endpoint of this aggressive, benign condition that causes the destruction of primarily a single joint is arthroplasty [29]. As a result, a finding of PVNS on routine pathology after THA does not alter a patient's treatment course. The definitive treatment has already been performed, and monitoring occurs through routine postoperative surveillance even without the diagnosis of PVNS.

Infection (septic arthritis, osteomyelitis) is another discordant diagnosis made with permanent pathology of femoral head specimens in THA. One would assume if THA is performed in the setting of an active infection, then management with debridement, antibiotics, irrigation, and retention of implants or one- or two-stage revision will likely be required whether infection is diagnosed clinically or through pathologic examination. Thus, routine pathology does not likely impact patient management. There is also evidence that femoral head pathology is insufficiently specific for diagnosing acute infection. O'Connell et al. histologically identified sterile subchondral acute inflammation in femoral head specimens with severe arthritis that could easily be mistaken for infection [14]. Furthermore, Raab et al. noted that a pathologic diagnosis of chronic osteomyelitis in a femoral head specimen resulted in unnecessary administration of antibiotics for 6 weeks; revisiting the histologic findings demonstrated that they were in fact consistent with degenerative joint disease, and there was no evidence of infection in clinical follow-up [15]. Others have also found initial femoral head histology to yield false-positive diagnoses of infection [13].

Out of the 17,388 femoral head pathologic examinations reported in the included studies, approximately 1 was a discordant diagnosis of metastatic carcinoma. If a primary malignancy is unknown at the time of pathologic diagnosis of metastatic disease, then routine pathology proves beneficial in 0.0058% of cases.

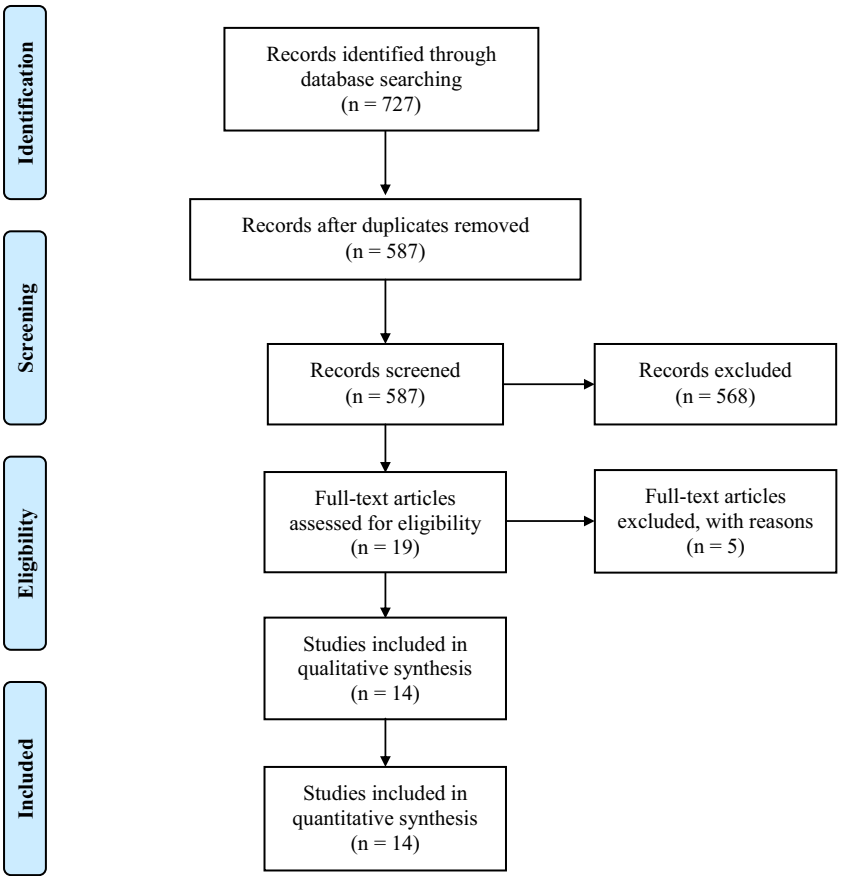

Figure 1. PRISMA flow diagram.

Table 2
Summary of data extraction from articles selected for review.

Authors	Year of publication	Study design	Country of origin	Source population	Femoral head specimens	Discordant diagnoses	Cost analysis	Conclusion on routine pathology
Campbell et al. [8]	1997	Multicenter, retrospective	US	THA for any indication	283	1.06%	$140-$200 per specimen; $17.5-25 million in savings without routine pathology	Against
Dermawan et al. [9]	2021	Multicenter, retrospective	US	Elective THA	1722	0%	None	For
DiCarlo et al. [7]	2014	Single center, retrospective	US	THA for any indication	7968	1.46%	Less than 0.5% of total costs saved without routine pathology	For
Kocher et al. [5]	2000	Single center, retrospective	US	THA for OA	471	0.21%	$89.08 per specimen; $122,728 per discordant case	Against
Lawrence et al. [10]	1999	Single center, retrospective	US	THA for any indication	562	0%	$102.59 per specimen	Against
Layfield et al. [11]	2020	Single center, retrospective	US	THA for OA	953	0.52%	None	For
Lin et al. [4]	2012	Single center, retrospective	US	Elective THA	457	0.22%	$102.37 per specimen; no gain in QALY	Against
Liow et al. [6]	2017	Single center, retrospective	US	Elective THA	3200	0.16%	$185.14 per specimen; $122,932.96 per discordant case; $49,569.74/QALY	For
Meding et al. [12]	2000	Single center, retrospective	US	THA for any indication	313	0%	$60-$283 per specimen	Against
Niggemeyer et al. [13]	2011	Single center, prospective	Germany	THA for inflammatory arthritis or OA	100	0%	None	Against
O'Connell et al. [14]	1999	Single center, retrospective	US	THA for any indication	164	1.22%	None	None
Raab et al. [15]	1998	Single center, retrospective	US	Elective THA	79	0%	$64 per specimen	Against
Sissons et al. [16]	1992	Single center, retrospective	US	THA for idiopathic osteonecrosis	264	0%	None	None
Zwitser et al. [17]	2009	Single center, prospective	Netherlands	Elective THA	852	1.64%	None	For

OA, osteoarthritis.

Table 3
Frequency table of discordant diagnoses.

Diagnosis	Frequency
Inflammatory arthritis	82
B-cell lymphoma	22
Pigmented villonodular synovitis (PVNS)	19
Unenumerated malignancies (most commonly B-cell lymphoma, includes metastatic carcinoma)	14
Septic arthritis	5
Osteomyelitis	3
Metastatic carcinoma	1
Granulomatous inflammation	1
	Total = 147

Nonetheless, even metastatic disease detected by routine femoral head pathology may have limited impact on management or prognosis if the presence of a primary malignancy was known preoperatively. Patients with a history of malignancy often undergo routine oncologic monitoring to evaluate for metastases, which are unlikely to be limited to the femoral head and have often already occurred by the time of pathologic examination.

With an estimated 500,000 THAs performed in 2019 [1,2], the cost of routine pathologic examination of femoral heads for the year was up to $63,000,000. The cost per QALY is a measure of cost-effectiveness of an intervention. QALY for an intervention is calculated using the following formula: years of life gained × utility value gained. Utility value is 0 in death and 1 in perfect health. Based on our systematic review, routine pathology in THA infrequently impacts patient management and as a result, does little to increase lifespan or quality of life. Cost per QALY thus approaches infinity for routine pathologic examination of femoral heads given the high cost (numerator) and low QALY (denominator), as Lin et al. also reported [4]. Liow et al. calculated a low cost per QALY of $49,569.74 for routine pathology based on the flawed assumption that presymptomatic diagnosis of B-cell lymphoma benefitted prognosis [6].

We understand that our work has limitations. First, the quality of our data and conclusions is limited by that of the papers we included for review, particularly given that 12 of 14 papers were retrospective. For example, while DiCarlo and Klein reported approximately 14 malignancies that were discordant diagnoses, the text only noted B-cell lymphoma as the most common diagnosis without individually enumerating each malignancy type [7]. Additional potential limitations of the retrospective studies in our review include inconsistent criteria for pathologic diagnoses and incomplete past medical histories, both of which hamper the accurate identification of discordant diagnoses. Second, it is possible our search terms did not capture all relevant articles although a medical librarian performed our comprehensive search of multiple databases. Third, our calculated costs may vary with geographic location, practice setting, and year. Finally, our conclusions are not generalizable to routine pathologic examination in all orthopedic surgeries, only in THA which was the subject of our study.

Conclusions

Our review of the existing literature, although largely retrospective with inherent limitations, demonstrates routine pathologic examination of femoral head specimens collected during THA results in a change in patient management in approximately 0.0058% of cases. Articles advocating for routine femoral head pathology label several pathologic diagnoses as discordant, which, upon closer examination, affect neither treatment nor prognosis. At a cost of up to $63,000,000 per year and a cost per QALY approaching infinity, the economic feasibility of routine pathology of femoral heads in THA is limited. However, surgeon discretion on a patient-specific or practice-specific basis is essential in making the final determination on need for femoral head pathology. Future studies are needed to evaluate the cost-effectiveness of selective femoral head pathologic examination in THA.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: S. Nandi is in the editorial or governing board of *Journal of Arthroplasty* and is a board member in AAHKS and AAOS. R. Schwarzkopf receives royalties from Smith & Nephew; is a paid consultant for Smith & Nephew and Intellijoint; has stock or stock options in Intellijoint, Gauss Surgical, and PSI; receives research support as a principal investigator from Smith & Nephew and Intellijoint; receives financial or material support from Smith & Nephew; is in the editorial or governing board of JOA and *Arthroplasty Today*; and is a board member in AAHKS and AAOS. A. Chen receives royalties from Stryker; is a paid consultant for 3M, Avanos, BICMD, bOne, Convatec, Ethicon, GLG, Guidepoint, Heraeus, IrriMax, Pfizer, PhagoMed, and Stryker; has stock or stock options in bOne, Graftworx, Hyalex, IrriMax, Joint Purification Systems, and Sonoran; receives financial or material support from SLACK Inc. and UpToDate; is in the editorial or governing board of *Journal of Arthroplasty*, *Clinical Orthopaedics and Related Research*, *Journal of Bone and Joint Surgery*, and *Journal of Orthopaedic Research*; and is a board member in AAOS, AJRR, AAHKS, and European Knee Association. T. Seyler receives royalties from Total Joint Orthopaedics, Pattern Health, MiCare Path, and Restor3D; is a paid consultant for Total Joint Orthopaedics, Smith & Nephew, and Heraeus Medical; is an unpaid consultant for Next Science; has stock or stock options in Extrel Therapeutics and MiCare Path; receives research support as a principal investigator from Zimmer Biomet; receives financial or material support from Lippincott Williams and Wilkins; and is a board member in Musculoskeletal Infection Society and the American Association of Hip and Knee Surgeons. J. Parvizi receives royalties from Corentec; is a paid consultant for Zimmer Biomet, Corentec, Ethicon, Tenor, KCI/3M (Acelity), Heraeus, MicroGenDx, Jointstem, Peptilogics, and Fidia Pharm; has stock or stock options in Parvizi Surgical Innovations and Subsidiaries, Hip Innovation Technologies, Corentec, Alphaeon/Strathsby Crown, Joint Purification Systems, Ceribell, Acumed, PRN-Veterinary, MD-valuate, Intellijoint, MicroGenDx, Nanooxygenic, Sonata, Moleculae Surface Technologies; and receives financial or material support from Data Trace, Elsevier, Jaypee Publishers, SLACK Inc., Wolters Kluwer, and Becton Dickenson.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2022.03.016.

References

[1] Singh JA, Yu S, Chen L, Cleveland JD. Rates of total joint replacement in the United States: future projections to 2020-2040 using the National Inpatient Sample. J Rheumatol 2019;46:1134–40.
[2] Sloan M, Premkumar A, Sheth NP. Projected volume of primary total joint arthroplasty in the U.S., 2014 to 2030. J Bone Joint Surg Am 2018;100:1455–60.
[3] Pivec R, Johnson AJ, Mears SC, et al. Hip arthroplasty. Lancet 2012;380:1768–77.
[4] Lin MM, Goldsmith JD, Resch SC, et al. Histologic examinations of arthroplasty specimens are not cost-effective: a retrospective cohort study. Clin Orthop Relat Res 2012;470:1452–60.
[5] Kocher MS, Erens G, Thornhill TS, et al. Cost and effectiveness of routine pathological examination of operative specimens obtained during primary total hip and knee replacement in patients with osteoarthritis. J Bone Joint Surg Am 2000;82:1531–5.

[6] Liow MHL, Agrawal K, Anderson DW, et al. Unsuspected malignancies in routine femoral head histopathologic examination during primary total hip arthroplasty: cost-effectiveness analysis. J Arthroplasty 2017;32:735–42.
[7] DiCarlo EF, Klein MJ. Comparison of clinical and histologic diagnoses in 16,587 total joint arthroplasties: implications for orthopedic and pathologic practices. Am J Clin Pathol 2014;141:111–8.
[8] Campbell ML, Gregory AM, Mauerhan DR. Collection of surgical specimens in total joint arthroplasty. Is routine pathology cost effective? J Arthroplasty 1997;12:60–3.
[9] Dermawan JK, Goldblum A, Reith JD, et al. Accurate and reliable diagnosis of avascular necrosis of the femoral head from total hip arthroplasty specimens requires pathologic examination. Am J Clin Pathol 2021;155:565–74.
[10] Lawrence T, Moskal JT, Diduch DR. Analysis of routine histological evaluation of tissues removed during primary hip and knee arthroplasty. J Bone Joint Surg Am 1999;81:926–31.
[11] Layfield LJ, Crim JR, Oserowsky A, et al. Pathology assessment of femoral head resection specimens: an important quality assurance procedure. Arch Pathol Lab Med 2020;144:580–5.
[12] Meding JB, Ritter MA, Jones NL, et al. Determining the necessity for routine pathologic examinations in uncomplicated total hip and total knee arthroplasties. J Arthroplasty 2000;15:69–71.
[13] Niggemeyer O, Steinhagen J, Zustin J, et al. The value of routine histopathology during hip arthroplasty in patients with degenerative and inflammatory arthritis. Hip Int 2011;21:98–106.
[14] O'Connell JX, Nielsen GP, Rosenberg AE. Subchondral acute inflammation in severe arthritis: a sterile osteomyelitis? Am J Surg Pathol 1999;23:192–7.
[15] Raab SS, Slagel DD, Robinson RA. The utility of histological examination of tissue removed during elective joint replacement. A preliminary assessment. J Bone Joint Surg Am 1998;80:331–5.
[16] Sissons HA, Nuovo MA, Steiner GC. Pathology of osteonecrosis of the femoral head. A review of experience at the Hospital for Joint Diseases, New York. Skeletal Radiol 1992;21:229–38.
[17] Zwitser EW, de Gast A, Basie MJ, et al. B-cell lymphoma in retrieved femoral heads: a long term follow up. BMC Musculoskelet Disord 2009;10:53.
[18] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
[19] Sepriano A, Kerschbaumer A, Smolen JS, et al. Safety of synthetic and biological DMARDs: a systematic literature review informing the 2019 update of the EULAR recommendations for the management of rheumatoid arthritis. Ann Rheum Dis 2020;79:760–70.
[20] Freedman A, Jacobsen E. Follicular lymphoma: 2020 update on diagnosis and management. Am J Hematol 2020;95:316–27.
[21] Lumish M, Falchi L, Imber BS, et al. How we treat mature B-cell neoplasms (indolent B-cell lymphomas). J Hematol Oncol 2021;14(1):5.
[22] Advani R, Rosenberg SA, Horning SJ. Stage I and II follicular non-Hodgkin's lymphoma: long-term follow-up of no initial therapy. J Clin Oncol 2004;22:1454–9.
[23] Brice P, Bastion Y, Lepage E, et al. Comparison in low-tumor-burden follicular lymphomas between an initial no-treatment policy, prednimustine, or interferon alfa: a randomized study from the Groupe d'Etude des Lymphomes Folliculaires. Groupe d'Etude des Lymphomes de l'Adulte. J Clin Oncol 1997;15:1110–7.
[24] Ardeshna KM, Smith P, Norton A, et al. Long-term effect of a watch and wait policy versus immediate systemic treatment for asymptomatic advanced-stage non-Hodgkin lymphoma: a randomised controlled trial. Lancet 2003;362:516–22.
[25] Rosenberg SA. Karnofsky memorial lecture. The low-grade non-Hodgkin's lymphomas: challenges and opportunities. J Clin Oncol 1985;3:299–310.
[26] Armitage JO, Longo DL. Is watch and wait still acceptable for patients with low-grade follicular lymphoma? Blood 2016;127:2804–8.
[27] Zelenetz AD, Gordon LI, Wierda WG, et al. Non-Hodgkin's lymphomas, version 4.2014. J Natl Compr Canc Netw 2014;12:1282–303.
[28] Padala SA, Kallam A. Diffuse large B cell lymphoma. In: StatPearls. Treasure Island, FL: StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC; 2021.
[29] Yoo JJ, Kwon YS, Koo KH, et al. Cementless total hip arthroplasty performed in patients with pigmented villonodular synovitis. J Arthroplasty 2010;25:552–7.

Appendix

PRISMA 2020 for abstracts checklist.

Section and topic	Item #	Checklist item	Reported (yes/no)
Title			
Title	1	Identify the report as a systematic review.	Line 2
Background			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Lines 7-10
Methods			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Table 1
Information sources	4	Specify the information sources (eg, databases, registers) used to identify studies and the date when each was last searched.	Lines 11-14
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Lines 14-15
Synthesis of results	6	Specify the methods used to present and synthesise results.	Lines 14-15
Results			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Line 15
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (ie, which group is favored).	Lines 16-20
Discussion			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (eg, study risk of bias, inconsistency and imprecision).	Lines 24-26
Interpretation	10	Provide a general interpretation of the results and important implications.	Lines 21-24
Other			
Funding	11	Specify the primary source of funding for the review.	None
Registration	12	Provide the register name and registration number.	Title Page

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71, For more information, visit: http://www.prisma-statement.org/

PRISMA 2020 checklist.

Section and topic	Item #	Checklist item	Location where item is reported
Title			
Title	1	Identify the report as a systematic review.	Line 2
Abstract			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	See abstract checklist
Introduction			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Lines 45-50
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Lines 52-55
Methods			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Table 1
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Lines 59-61, 100
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Lines 66-97
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Lines 101-106, Table 1
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Lines 110-115
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (eg, for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Lines 110-115
	10b	List and define all other variables for which data were sought (eg, participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	NA
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Line 111
Effect measures	12	Specify for each outcome the effect measure(s) (eg, risk ratio, mean difference) used in the synthesis or presentation of results.	Lines 118-119
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (eg, tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	NA
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	NA
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Lines 110-115, Table
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	NA
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (eg, subgroup analysis, meta-regression).	NA
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	NA
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	NA
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Line 111
Results			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Lines 100-108
Study characteristics	17	Cite each included study and present its characteristics.	Table 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Table 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (eg, confidence/credible interval), ideally using structured tables or plots.	Lines 124-161
Results of syntheses	20a	For each synthesis, briefly summarize the characteristics and risk of bias among contributing studies.	NA
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (eg, confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	NA
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	NA
	20d		NA

(*continued on next page*)

(*continued*)

Section and topic	Item #	Checklist item	Location where item is reported
		Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 2
Discussion			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Lines 179-226
	23b	Discuss any limitations of the evidence included in the review.	Lines 239-250
	23c	Discuss any limitations of the review processes used.	Line 239-250
	23d	Discuss implications of the results for practice, policy, and future research.	Line 253-261
Other information			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Title page
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Lines 103-104
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	None
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	None
Competing interests	26	Declare any competing interests of review authors.	None
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	With corresponding author

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71, For more information, visit: http://www.prisma-statement.org/.