

is highly effective at pain relief. In many cases of late shoulder PJI, including those with unexpected positive cultures, a change in patient pain and dysfunction are often the only clinical manifestation. On the other hand, when pain does not normally diminish in the early recovery period after surgery (first few weeks), PJI should also be suspected. Two hundred fifty patients among 276 (90.6%) reported in 10 studies [1,5,6,8,10,14,19,20,23,24], suffered from shoulder pain and impairment at the time of diagnosis, making pain a sensitive symptom. Pain can be associated with other local signs (inflammatory wound, swelling, collection, fistula), or may be present in isolation. In the case of a painful shoulder arthroplasty, establishing a diagnosis of infection is often difficult and should be based on further investigation. Nevertheless, infection should be strongly considered in the case of a painful shoulder arthroplasty. In less than 10% of cases, an infected shoulder prosthesis can be painless, but in these cases, there is always local evidence for an infection (inflammatory wound, swelling, collection, fistula).

Stiffness

Limited range of motion is classically associated with shoulder periprosthetic infection, but was specifically reported in only one study (30 out of 44 patients; 68.2%) [5]. It frequently occurs in conjunction with pain, another nonspecific symptom.

REFERENCES

- [1] Braman JP, Sprague M, Bishop J, Lo IK, Lee EW, Flatow EL. The outcome of resection shoulder arthroplasty for recalcitrant shoulder infections. *J Shoulder Elbow Surg.* 2006;15:549–553. doi:10.1016/j.jse.2005.11.001.
- [2] Buchalter DB, Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Two-stage revision for infected shoulder arthroplasty. *J Shoulder Elbow Surg.* 2017;26:939–947. doi:10.1016/j.jse.2016.09.056.
- [3] Jawa A, Shi L, O'Brien T, Wells J, Higgins L, Macy J, et al. Prosthesis of antibiotic-loaded acrylic cement (PROSTALAC) use for the treatment of infection after shoulder arthroplasty. *J Bone Joint Surg Am.* 2011;93:2001–2009. doi:10.2106/JBJS.J.00833.
- [4] Achermann Y, Sahin F, Schwyzer H, Kolling C, Wüst J, Vogt M. Characteristics and outcome of 16 periprosthetic shoulder joint infections. *Infection.* 2013;41:613–620. doi:10.1007/s15010-012-0360-4.
- [5] Amaravathi RS, Kany J, Melet M, Katz D, Sauzieres P, Valenti P, et al. Analysis of infection in shoulder arthroplasty: a multicentre study. *Eur J Orthop Surg Traumatol.* 2012;22:145–150. doi:10.1007/s00590-011-0806-x.
- [6] Assenmacher AT, Alentorn-Geli E, Dennison T, Baghdadi YMK, Cofield RH, Sánchez-Sotelo J, et al. Two-stage reimplantation for the treatment of deep infection after shoulder arthroplasty. *J Shoulder Elbow Surg.* 2017;26:1978–1983. doi:10.1016/j.jse.2017.05.005.
- [7] Beekman PDA, Katusic D, Berghs BM, Karelse A, De Wilde L. One-stage revision for patients with a chronically infected reverse total shoulder replacement. *J Bone Joint Surg Br.* 2010;92:817–822. doi:10.1302/0301-620X.92B6.23045.
- [8] Coste JS, Reig S, Trojani C, Berg M, Walch G, Boileau P. The management of infection in arthroplasty of the shoulder. *J Bone Joint Surg Br.* 2004;86:65–69.
- [9] Cuff DJ, Virani NA, Levy J, Frankle MA, Derasari A, Hines B, et al. The treatment of deep shoulder infection and glenohumeral instability with debridement, reverse shoulder arthroplasty and postoperative antibiotics. *J Bone Joint Surg Br.* 2008;90-B:336–342. doi:10.1302/0301-620X.90B3.19408.
- [10] Dennison T, Alentorn-Geli E, Assenmacher AT, Sperling JW, Sánchez-Sotelo J, Cofield RH. Management of acute or late hematogenous infection after shoulder arthroplasty with irrigation, débridement, and component retention. *J Shoulder Elbow Surg.* 2017;26:73–78. doi:10.1016/j.jse.2016.05.018.
- [11] Dodson CC, Craig EV, Cordasco FA, Dines DM, Dines JS, Dicarlo E, et al. Propionibacterium acnes infection after shoulder arthroplasty: a diagnostic challenge. *J Shoulder Elbow Surg.* 2010;19:303–307. doi:10.1016/j.jse.2009.07.065.
- [12] Ghijssels S, Stuyck J, Debeer P. Surgical treatment algorithm for infected shoulder arthroplasty: a retrospective analysis of 17 cases. *Acta Orthop Belg.* 2013;79:626–635.
- [13] Ince A, Seemann K, Frommelt L, Katzer A, Loehr JF. One-stage exchange shoulder arthroplasty for peri-prosthetic infection. *J Bone Joint Surg Br.* 2005;87:814–818. doi:10.1302/0301-620X.87B6.15920.
- [14] Jacquot A, Sirveaux F, Roche O, Favard L, Clavert P, Molé D. Surgical management of the infected reversed shoulder arthroplasty: a French multicentre study of reoperation in 32 patients. *J Shoulder Elbow Surg.* 2015;24:1713–1722. doi:10.1016/j.jse.2015.03.007.
- [15] Jerosch J, Schneppenheim M. Management of infected shoulder replacement. *Arch Orthop Trauma Surg.* 2003;123:209–214. doi:10.1007/s00402-003-0497-9.
- [16] Klatte TO, Junghans K, Al-Khateeb H, Rueger JM, Gehrke T, Kendoff D, et al. Single-stage revision for peri-prosthetic shoulder infection: outcomes and results. *Bone Joint J.* 2013;95-B:391–395. doi:10.1302/0301-620X.95B3.30134.
- [17] Levy JC, Triplett J, Everding N. Use of a functional antibiotic spacer in treating infected shoulder arthroplasty. *Orthopedics.* 2015;38:e512–e519. doi:10.3928/01477447-20150603-60.
- [18] Mahure SA, Mollon B, Yu S, Kwon YW, Zuckerman JD. Definitive treatment of infected shoulder arthroplasty with a cement spacer. *Orthopedics.* 2016;39:e924–930. doi:10.3928/01477447-20160623-07.
- [19] Ortmaier R, Resch H, Hitzl W, Mayer M, Stundner O, Tauber M. Treatment strategies for infection after reverse shoulder arthroplasty. *Eur J Orthop Surg Traumatol.* 2014;24:723–731. doi:10.1007/s00590-013-1251-9.
- [20] Romanò CL, Borens O, Monti L, Meani E, Stuyck J. What treatment for periprosthetic shoulder infection? Results from a multicentre retrospective series. *Int Orthop.* 2012;36:1011–1017. doi:10.1007/s00264-012-1492-y.
- [21] Sabesan VJ, Ho JC, Kovacevic D, Iannotti JP. Two-stage reimplantation for treating prosthetic shoulder infections. *Clin Orthop Relat Res.* 2011;469:2538–2543. doi:10.1007/s11999-011-1774-5.
- [22] Sperling JW, Kozak TK, Hanssen AD, Cofield RH. Infection after shoulder arthroplasty. *Clin Orthop Relat Res.* 2001;206–216.
- [23] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. *J Bone Joint Surg Br.* 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.
- [24] Weber P, Utzschneider S, Sadoghi P, Andress H-J, Jansson V, Müller PE. Management of the infected shoulder prosthesis: a retrospective analysis and review of the literature. *Int Orthop.* 2011;35:365–373. doi:10.1007/s00264-010-1019-3.
- [25] Zavala JA, Clark JC, Kissenberth MJ, Tolan SJ, Hawkins RJ. Management of deep infection after reverse total shoulder arthroplasty: a case series. *J Shoulder Elbow Surg.* 2012;21:1310–1315. doi:10.1016/j.jse.2011.08.047.
- [26] Hsu JE, Somerson JS, Vo KV, Matsen FA. What is a “periprosthetic shoulder infection”? A systematic review of two decades of publications. *Int Orthop.* 2017;41:813–822. doi:10.1007/s00264-017-3421-6.
- [27] Parvizi J, Gehrke T, International Consensus Group on Periprosthetic Joint Infection. Definition of periprosthetic joint infection. *J Arthroplasty.* 2014;29:1331. doi:10.1016/j.arth.2014.03.009.
- [28] Kelly JD, Hobgood ER. Positive culture rate in revision shoulder arthroplasty. *Clin Orthop Relat Res.* 2009;467(9):2343–2348. doi:10.1007/s11999-009-0875-x



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QUESTION 2: What radiographic findings are concerning for shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Radiographic findings concerning for shoulder PJI include component loosening or migration, radiolucent lines, osteolysis, endosteal scalloping and new bone formation. Specifically, humeral loosening should significantly raise the suspicion for shoulder PJI.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

A formal comprehensive literature search was performed to address this subject. PubMed, conference proceedings and Google scholar were searched using the following terms and keywords: infection, periprosthetic, prosthesis, arthroplasty, low-grade, total shoulder, shoulder arthroplasty, radiology, X-rays and imaging.

Plain Radiographs

The typical clinical presentation of an acutely infected shoulder arthroplasty includes (1) local symptoms, such as shoulder pain, decreased range of motion, erythema, swelling, wound drainage, draining sinus, purulence and warmth; and (2) systemic symptoms, such as fever, chills and malaise and positive markers (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)). In the presence of these obvious signs of infection, any radiographic change will be attributed to periprosthetic shoulder infection (PSI). However, depending on the virulence of the infecting organisms and the intensity of the host immune response, an infected arthroplasty can have subtle or even no clinical signs. This is true of most subacute and chronic PSI and almost universally true in revision of cases of apparently aseptic failure that are subsequently determined to be infected. Plain radiographs may help to determine the diagnosis of PSI. If any of the following are present, infection should be considered: non-traumatic periprosthetic fracture, fracture of the arthroplasty material, implant loosening, osteolysis without loosening, periosteal new bone formation, subluxation due to cuff failure from infection or dislocation.

Detection of periprosthetic lucency, loosening of the prosthesis components, effusion, adjacent soft tissue gas or fluid collection, or periosteal new bone formation around the hip arthroplasty may suggest infection, but none are either sensitive or specific [1]. A study of 65 patients with painful hip arthroplasties found that the presence of either lucency or periosteal new bone formation was 75% sensitive but only 28% specific for diagnosis of PJI [2]. Periosteal new bone formation alone was 100% specific but occurred in only 16% of patients with PJI. Serial radiographs with progressively expanding lucency over several months may also suggest PJI.

Plain radiographs are essential for the evaluation of any painful shoulder arthroplasty but are neither sensitive nor specific for the diagnosis of low-grade indolent infection. Typical radiographic findings that suggest periprosthetic infection include radiolucent lines around the components, osteolysis, bone erosion, endosteal scalloping, new periosteal bone formation and shift of the components. These findings are, however, often absent in indolent or low-grade infection.

In a review of 193 revision shoulder arthroplasty patients without obvious clinical evidence of infection, Pottinger et al. [3] reported a 56% incidence of unexpected positive intraoperative culture, with *C. acnes* being identified most commonly in 69% of the positive cultures. They found that humeral component loosening and humeral osteolysis on plain radiographs were associated with 3-fold and 10-fold increases, respectively, in the risk of a positive *C. acnes* culture.

Radiolucent lines around the glenoid component have been reported to be common even in the immediate postoperative period [4–6]. Interpretation of these radiolucent lines in the absence of clinical symptoms or signs should be done with caution so as not to inappropriately assume that there is an infection. However, radiolucent lines that appear relatively early after surgery and those that are significant enough to cause loosening of the component should

always raise a high index of suspicion of infection, especially in the presence of pain or stiffness.

Computed Tomography (CT) Scans

CT scans are often used in revision shoulder arthroplasty for evaluation of the remaining bone stock, implant position and loosening, glenoid component wear, soft tissue swelling, fluid collection, and rotator cuff tendon and muscle pathology. However, the value of CT scan as a direct diagnostic modality for infection is limited to the identification of the same structural changes as observed in plain radiographs, and the metal artifact from the implants can make the interpretation difficult.

If there is a need for computed tomography arthrography, such as for evaluation of rotator cuff integrity or glenoid loosening, a joint aspiration can be performed concomitantly for synovial fluid analysis and culture.

CT has the advantages of high spatial resolution and allows for the evaluation of signs of infection in the periprosthetic tissues. One study found that detection of joint distention upon CT imaging was highly sensitive (83%) and specific (96%) for suspected hip arthroplasty infection [2]. However, the added benefit of these findings beyond history, physical examination and plain radiographs is unclear. The same study found no difference in the evaluation of the bony structures compared to the use of plain radiographs.

Magnetic Resonance Imaging (MRI)

MRI is of little value in the diagnosis of infection because of metal artifact from implants and is seldom used. Adjustments in the image acquisition parameters can lessen but not eliminate these artifacts. The metal artifact reduction sequence (MARS) can be helpful in some occasions. The MARS technique allows visualization of structures adjacent to metal implants and may improve visualisation of periprosthetic bone and soft-tissue structures near total shoulder arthroplasty [7,8].

Nuclear imaging

Currently, little is known about the diagnostic accuracy of nuclear imaging for indolent or low-grade periprosthetic shoulder joint infection (PSJI). It is reported to have a limited direct role in diagnosis of lower extremity PJI [9,10].

Technetium Tc99m bone scintigraphy is sensitive for identifying a failed arthroplasty but cannot differentiate between infection and aseptic failure. Neither periprosthetic uptake patterns nor performance of the test as a 3-phase study significantly improves the accuracy, which is only about 50% to 70% [9].

Three-phase bone scintigraphy is one of the most widely utilized imaging techniques in the diagnosis of PJI. The intensity of uptake following injection of the radiopharmaceutical is measured at three different time points, corresponding to blood flow (immediate), blood pool (at 15 min) and late (at 2 to 4 h) time points [11,12]. Uptake at the prosthesis interfaces at the blood pool and late time points suggests PJI. A limitation of this technique is the lack of specificity.

Asymptomatic patients frequently have uptake detected by delayed-phase imaging in the first year or two after implantation [13]. Given that many PJI occur within this time period, this lack of specificity, reportedly as low as 18%, is a limitation for the use of this technology. However, three-phase bone scintigraphy may be more useful for PJI occurring late after arthroplasty.

A study of 92 patients undergoing evaluation for revision of hip arthroplasty at mean of 9 years after implantation found that increased uptake at both the second and third phases provided sensitivity and specificity for making an accurate diagnosis of 68% and 76%, respectively [14]. The fact that only a minority of these patients underwent revision limits comparison to a true diagnostic gold standard. Another study reported a sensitivity of 88% and a specificity of 90% for detecting PJI in 46 patients at a mean of 8.5 years after hip arthroplasty [15].

Other imaging modalities may be performed in conjunction with bone scintigraphy in an effort to increase specificity. Radioactive Indium (In111) is used to label autologous leukocytes, which are then re-injected with images being obtained 24 hours later. A positive scan is typically considered when there is uptake on the labeled leukocyte image, with absent or decreased uptake at the same location on the late-phase bone scan [16]. A late-phase bone scan combined with a 111In leukocyte scan was 64% sensitive and 70% specific for detection of PJI in 166 revision knee or hip arthroplasties at a median of 7 years after implantation [17].

Indium In 111-labeled white blood cell (WBC) scan has been regarded as the gold standard technique for diagnosis of infectious conditions that involve local accumulation of leukocytes (usually pyogenic organisms) [18]; however, the accuracy for PSJI is reported to be poor. In a study of 17 patients with verified PSJI, Strickland et al. [19] reported that 111In-labeled WBC count scan was obtained in eight shoulders and all scans were negative. Variable and often poor sensitivity and specificity of nuclear imaging in diagnosis of PSJI make the interpretation of the findings difficult [20].

Other studies using slightly different technologies have reported somewhat higher accuracies, with sensitivities ranging from 77 to 100% and specificities ranging from 86 to 91% [16,21,22]. Fluoro-2-deoxyglucose [¹⁸F-FDG] positron emission tomography (FDG-PET) is widely used in cancer care and treatment and has emerged as a diagnostic modality for PJI. A meta-analysis of 11 studies involving 635 prosthetic hip and knee arthroplasties found that FDG-PET had pooled sensitivity and specificity values of 82.1% and 86.6%, respectively, for the diagnosis of PJI [23–27].

While several nuclear imaging techniques [28] have been used to diagnosis PJI, the most accurate and cost-effective technique has yet to be elucidated. Furthermore, with the high cost of performing and analyzing nuclear imaging, its role in the workup for PJI should be limited. As such, there is rare utility for nuclear imaging with the multitude of more cost-effective measures.

REFERENCES

- [1] Tigges S, Stiles RG, Roberson JR. Appearance of septic hip prostheses on plain radiographs. *AJR Am J Roentgenol*. 1994;163:377–380. doi:10.2214/ajr.163.2.8037035.
- [2] Cyteval C, Hamm V, Sarabère MP, Lopez FM, Maury P, Taourel P. Painful infection at the site of hip prosthesis: CT imaging. *Radiology*. 2002;224:477–483. doi:10.1148/radiol.224.2.10989.
- [3] Pottinger P, Butler-Wu S, Neradilek MB, Merritt A, Bertelsen A, Jette JL, et al. Prognostic factors for bacterial cultures positive for *Propionibacterium* acnes and other organisms in a large series of revision shoulder arthroplasties performed for stiffness, pain, or loosening. *J Bone Joint Surg Am*. 2012;94:2075–2083. doi:10.2106/JBJS.K.00861.
- [4] Vavken P, Sadoghi P, von Keudell A, Rosso C, Valderrabano V, Müller AM. Rates of radiolucency and loosening after total shoulder arthroplasty with pegged or keeled glenoid components. *J Bone Joint Surg Am*. 2013;95:215–221. doi:10.2106/JBJS.L.00286.
- [5] Klepps S, Chiang AS, Miller S, Jiang CY, Hazrati Y, Flatow EL. Incidence of early radiolucent glenoid lines in patients having total shoulder replacements. *Clin Orthop Relat Res*. 2005;118–125.
- [6] Lazarus MD, Jensen KL, Southworth C, Matsen FA. The radiographic evaluation of keeled and pegged glenoid component insertion. *J Bone Joint Surg Am*. 2002;84-A:1174–1182.
- [7] Olsen RV, Munk PL, Lee MJ, Janzen DL, MacKay AL, Xiang QS, et al. Metal artifact reduction sequence: early clinical applications. *Radiographics*. 2000;20:699–712. doi:10.1148/radiographics.20.3.g00ma10699.
- [8] Lohmann CH, Rampal S, Lohrengel M, Singh G. Imaging in peri-prosthetic assessment: an orthopaedic perspective. *EFORT Open Rev*. 2017;2:117–125. doi:10.1302/2058-5241.2.160058.
- [9] Love C, Marwin SE, Palestro CJ. Nuclear medicine and the infected joint replacement. *Semin Nucl Med*. 2009;39:66–78. doi:10.1053/j.semnuclmed.2008.08.007.
- [10] Zmistowski B, Della Valle C, Bauer TW, Malizos KN, Alavi A, Bedair H, et al. Diagnosis of periprosthetic joint infection. *J Orthop Res*. 2014;32 Suppl 1:S98–S107. doi:10.1002/jor.22553.
- [11] Glaudemans AWJM, Galli F, Pacilio M, Signore A. Leukocyte and bacteria imaging in prosthetic joint infection. *Eur Cell Mater*. 2013;25:61–77.
- [12] Erba PA, Glaudemans AWJM, Veltman NC, Sollini M, Pacilio M, Galli F, et al. Image acquisition and interpretation criteria for 99mTc-HMPAO-labelled white blood cell scintigraphy: results of a multicentre study. *Eur J Nucl Med Mol Imaging*. 2014;41:615–623. doi:10.1007/s00259-013-2631-4.
- [13] Rosenthal L, Lepanto L, Raymond F. Radiophosphate uptake in asymptomatic knee arthroplasty. *J Nucl Med*. 1987;28:1546–1549.
- [14] Reinartz P, Mumme T, Hermanns B, Cremerius U, Wirtz DC, Schaefer WM, et al. Radionuclide imaging of the painful hip arthroplasty: positron-emission tomography versus triple-phase bone scanning. *J Bone Joint Surg Br*. 2005;87:465–470. doi:10.1302/0301-620X.87B4.14954.
- [15] Nagoya S, Kaya M, Sasaki M, Tateda K, Yamashita T. Diagnosis of peri-prosthetic infection at the hip using triple-phase bone scintigraphy. *J Bone Joint Surg Br*. 2008;90:140–144. doi:10.1302/0301-620X.90B2.19436.
- [16] Love C, Marwin SE, Tomas MB, Krauss ES, Tronco GG, Bhargava KK, et al. Diagnosing infection in the failed joint replacement: a comparison of coincidence detection 18F-FDG and 111In-labeled leukocyte/99mTc-sulfur colloid marrow imaging. *J Nucl Med*. 2004;45:1864–1871.
- [17] Teller RE, Christie MJ, Martin W, Nance EP, Haas DW. Sequential indium-labeled leukocyte and bone scans to diagnose prosthetic joint infection. *Clin Orthop Relat Res*. 2000;241–247.
- [18] Gemmel F, Van den Wyngaert H, Love C, Welling MM, Gemmel P, Palestro CJ. Prosthetic joint infections: radionuclide state-of-the-art imaging. *Eur J Nucl Med Mol Imaging*. 2012;39:892–909. doi:10.1007/s00259-012-2062-7.
- [19] Strickland JP, Sperling JW, Cofield RH. The results of two-stage re-implantation for infected shoulder replacement. *J Bone Joint Surg Br*. 2008;90:460–465. doi:10.1302/0301-620X.90B4.20002.
- [20] Saltzman MD, Marecek GS, Edwards SL, Kalainov DM. Infection after shoulder surgery. *J Am Acad Orthop Surg*. 2011;19:208–218.
- [21] Love C, Tomas MB, Marwin SE, Pugliese PV, Palestro CJ. Role of nuclear medicine in diagnosis of the infected joint replacement. *Radiographics*. 2001;21:1229–1238. doi:10.1148/radiographics.21.5.g01se191229.
- [22] Scher DM, Pak K, Lonner JH, Finkel JE, Zuckerman JD, Di Cesare PE. The predictive value of indium-111 leukocyte scans in the diagnosis of infected total hip, knee, or resection arthroplasties. *J Arthroplasty*. 2000;15:295–300.
- [23] Kwee TC, Kwee RM, Alavi A. FDG-PET for diagnosing prosthetic joint infection: systematic review and metaanalysis. *Eur J Nucl Med Mol Imaging*. 2008;35:2122–2132. doi:10.1007/s00259-008-0887-x.
- [24] Kwee TC, Basu S, Torigian DA, Zhuang H, Alavi A. FDG PET imaging for diagnosing prosthetic joint infection: discussing the facts, rectifying the unsupported claims and call for evidence-based and scientific approach. *Eur J Nucl Med Mol Imaging*. 2013;40:464–466. doi:10.1007/s00259-012-2319-1.
- [25] Kwee TC, Basu S, Alavi A. Should the nuclear medicine community continue to underestimate the potential of 18F-FDG-PET/CT with present generation scanners for the diagnosis of prosthetic joint infection? *Nucl Med Commun*. 2015;36:756–757. doi:10.1097/MNM.0000000000000318.
- [26] Kwee TC, Basu S, Alavi A. The ongoing misperception that labeled leukocyte imaging is superior to 18F-FDG PET for diagnosing prosthetic joint infection. *J Nucl Med*. 2017;58:182. doi:10.2967/jnumed.116.181461.
- [27] Palestro CJ. Radionuclide imaging of musculoskeletal infection: a review. *J Nucl Med*. 2016;57:1406–1412. doi:10.2967/jnumed.115.157297.
- [28] Gyltopoulos S, Rosenberg ZS, Roberts CC, Bencardino JT, Appel M, Baccei SJ, et al. ACR appropriateness criteria imaging after shoulder arthroplasty. *J Am Coll Radiol*. 2016;13:1324–1336. doi:10.1016/j.jacr.2016.07.028.