European Journal of Orthopaedic Surgery & Traumatology (2019) 29:1105–1113
https://doi.org/10.1007/s00590-019-02407-5

ORIGINAL ARTICLE • KNEE - ARTHROPLASTY

Three-phase Technetium-99m bone scanning in patients with pain in the knee region after cemented total knee arthroplasty

Daniel S. Hill[1] · **Denis Kinsella**[1] · **Andrew D. Toms**[1]

Received: 21 July 2018 / Accepted: 20 February 2019 / Published online: 19 March 2019

Abstract

Introduction Our aim was to question the usefulness of a three-phase bone scan in the evaluation of pain in the knee region after TKR. Our hypothesis was that an abnormal investigation had a poor association with the presence of infection or loosening, and did not provide any additional diagnostic information above that already available through other standard investigations.

Methods A retrospective study over a 24-month period was performed comprising 118 patients investigated with a TPBS. Investigations were summarised and analysed, and were classified as entirely normal, possibly abnormal, and definitely abnormal.

Results Thirty-three per cent (39/118) of TPBSs were reported as being entirely normal, 59% (69/118) as possibly abnormal, and 8% (10/118) as definitely abnormal. During the 24-month study period, 131 revision TKR procedures were performed at our institution; 9% (12/131) were investigated with TPBS and 91% (119/131) were not. No patient with an entirely normal pre-operative TPBS underwent revision TKR surgery. Eighty-five per cent (67/79) with an abnormal TPBS were managed conservatively. In our series, a TPBS had a positive predictive value of 2.53%, a negative predictive value of 100%, with an overall accuracy of 34.75% with 100% sensitivity (97.5% one-sided confidence interval 0–24.71%), and 33.62% specificity (95% confidence interval 53.29–72.37%), in the diagnosis of infection, or loosening with concurrent infection in determining the indication for revision surgery.

Conclusion A TPBS should only be considered following clinical evaluation, serological investigation, diagnostic imaging, and microbiological analysis of fluid obtained from arthrocentesis by a specialist revision arthroplasty surgeon. A TPBS may be useful in the situation where abnormal serology is present, but where repeated joint aspirations samples are inconclusive.

Keywords Pain in the knee region · Cemented total knee replacement · Three-phase Technetium-99m bone scan · Revision arthroplasty

Introduction

Continuing pain in the knee region following TKR surgery is uncommon, and although likely to improve prosthetic joint infection and component loosening must be excluded [1]. These are difficult to differentiate clinically and may coexist. A three-phase bone scan (TPBS) gives a highly sensitive indicator of bone turnover, but has a poor specificity [2–9]. Increased radionuclide uptake is seen in various circumstances including loosening, infection, stress fractures, tumours, pseudo-tumours, and metabolic bone disease. Post-surgical (physiological) increased radionuclide uptake may persist in the early phase images up to 1 year following the index surgical procedure, and indefinitely in the late phase images in both symptomatic and symptomatic patients [3, 4]. Serial scans may demonstrate component loosening [5], but are unlikely to differentiate between this and infection [10, 11]. If prosthetic loosening is evident on plain radiographs, a TPBS is unlikely to provide any additional information [12]. Our aim was to question the usefulness of a TPBS in

✉ Daniel S. Hill
drdanielhill@icloud.com

Denis Kinsella
denis.kinsella@nhs.net

Andrew D. Toms
andrewtoms@nhs.net

[1] Princess Elizabeth Orthopaedic Centre, Royal Devon and Exeter Foundation Trust, Barrack Road, Exeter EX2 5DW, UK

the evaluation of pain in the knee region after TKR. Our hypothesis was that an abnormal investigation had a poor association with the presence of infection or loosening, and did not provide any additional diagnostic information above that already available through other standard investigations.

Methods

A retrospective study of all cases investigated with a Technetium-99m (HDP) TPBS for pain in the knee region after primary cemented TKR at our institution during a 24-month period was performed. These consisted of referrals from consultant teams within our own institution and from a nearby referral unit. All patients were assessed using a standardised quadruple assessment (clinical evaluation, serological investigation, diagnostic imaging, and microbiological analysis) [13]. A TPBS was requested where the cause of pain in the knee region following TKR surgery remained unclear following evaluation [13]. This included both the absence of radiographic evidence of loosening on standard plain radiographic series and the absence of serological evidence of infection. Computerised tomographic (CT) scans were not utilised in the investigation of patients in this series.

Patients were scanned in the supine position, and images taken with a whole body digital gamma camera. Early flow phase images were taken immediately, and late flow phase images taken at two and a half hours after injection of with Tc99m HPD (haematoporphyrin derivative). All images were interpreted and reported by either one of two experienced consultant radiologists (each with over 15 years experience of reporting TPBS's) working independently of one another.

Following a TPBS, patients were reviewed with the results and followed up as required. Routine follow-up after primary TKR surgery at our institution occurs at 6 weeks in a physiotherapy lead clinic, then at 5-yearly intervals in a virtual clinic for routine cases. Full patient notes and clinical letters were reviewed to determine the date of primary arthroplasty surgery, and the period between this and investigation with a TPBS. The Clinical Radiological Information System (CRIS) was used to review scanned copies of hand written radiology request cards, the TPBS images, and the radiological reports. Serology and microbiology results of synovial fluid aspirates from arthrocentesis and intraoperative tissue cultures were reviewed using the hospital pathology system. Arthrocentesis was performed in laminar flow orthopaedic theatres with full sterile precautions. Synovial fluid aspirate was placed into a sterile microbiology pot and microscopic analysis performed for organisms on gram staining, cell counts, and differential counts. Synovial fluid aspirate was also placed into a blood culture bottle and incubated for a minimum of 48 h. Our criteria for a positive arthrocentesis for infection were a white cell count of > 1500 cells/μl. During revision surgery, a minimum of four peri-prosthetic tissue samples were sent for microbiological culture and histological analysis in order to reliably diagnose those patients with an infected arthroplasty.

We defined a prosthetic joint infection according to the Musculoskeletal Infection Society criteria [16]. Based on these criteria, definite prosthetic joint infection exists when:

1. There is a sinus tract communicating with the prosthesis; or
2. A pathogen is isolated by culture from at least two separate tissue or fluid samples obtained from the affected prosthetic joint; or
3. Four of the following six criteria exist:
    - Elevated serum erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) concentration,
    - Elevated synovial leucocyte count,
    - Elevated synovial neutrophil percentage (PMN%), presence of purulence in the affected joint, isolation of a microorganism in one culture of peri-prosthetic tissue or fluid, or
    - Greater than five neutrophils per high-power field in five high-power fields observed from histological analysis of peri-prosthetic tissue at 9400 magnification.

Cases investigated with a TPBS within 2 years of index joint replacement were excluded as a TPBS within this time is not clinically useful [3, 4]. Patients subsequently found to have a cause other than their TKR for their pain symptoms were also excluded. Patients were scanned in the supine position, and images taken with a whole body digital gamma camera. Early flow phase images were taken immediately, and late flow phase images taken at 2 h and 30 min after injection of with Tc99m HPD (haematoporphyrin derivative). All images were interpreted and reported by either one of two experienced consultant radiologists (each with over 15 years' experience of reporting TPBSs) working independently of one another. The written content of the radiologist's reports was scrutinised. Quantification of uptake by contralateral comparison was not attempted due to likely contralateral degenerative changes or arthroplasty. Performing an inter-observer analysis would not have altered the information available to the surgeon when determining the indication for intervention and so was not performed.

Reporting methodology

Written TPBS reports were utilised to classify the early and late flow scan phases as: normal, slightly increased, increased, or significantly increased. The overall content of

Table 1 Classification system—three-phase bone scan reports

Classification	Definition
Normal	Radionuclide uptake reported as being entirely within standard limits
Possibly abnormal	Minimal or questionable evidence of increased radionuclide uptake
Definitely abnormal	Significantly increased radionuclide uptake (in the early or late flow phases)

the TPBS reports was summarised as being either: normal, possibly abnormal, or definitely abnormal (Table 1). Clinical outcomes were determined through reviewing medical records and electronic data systems. The last TPBS was performed 24 months prior to writing, and clinical outcomes were accurate at this time. For those managed with surgical intervention, the final diagnosis was based upon intraoperative findings, microbiological and histological samples. Those that did not undergo surgical intervention were considered to have a non-infected TKR based on normal serology and the absence of any positive microbiology samples.

Statistical analysis

A statistician used the computer software "Stats Direct" to calculate the sensitivity and specificity of a TPBS in the detection of infection, or loosening with concurrent infection in the patients in our series with a pain in the knee region after TKR.

Results

A total of 127 patients with pain in the knee region after TKR surgery were referred for a TPBS. Nine were excluded, of which eight patients were investigated within 2 years of index joint replacement and one patient diagnosed with referred pain from an osteoarthritic hip. Mean joint replacement age at time of investigation was 4.5 years (range 2–20 years) (Fig. 1). Mean delay from requesting investigation to TPBS being performed was 33 days (range 2–80 days). Thirty-three per cent (39/118) of TPBSs were reported as being within entirely normal parameters, 59% (69/118) were reported as possibly abnormal, and 8% (10/118) as definitely abnormal. Degrees of radionuclide uptake in the early and late phases were determined (Fig. 2). Clinical outcomes are summarised in Fig. 3. Follow-up details were available in all cases. Revision TKR surgery was performed in 10% (12/118) of our cohort investigated with a TPBS. During the 24-month study period, 131 revision TKR procedures were performed at our institution; 9% (12/131) were investigated with TPBS, and 91% (119/131) were not. In our series, a TPBS had a positive predictive value of 2.53%, a negative predictive value of 100%, with an overall accuracy of 34.75% with 100% sensitivity (97.5% one-sided confidence interval 0–24.71%), and 33.62% specificity (95%

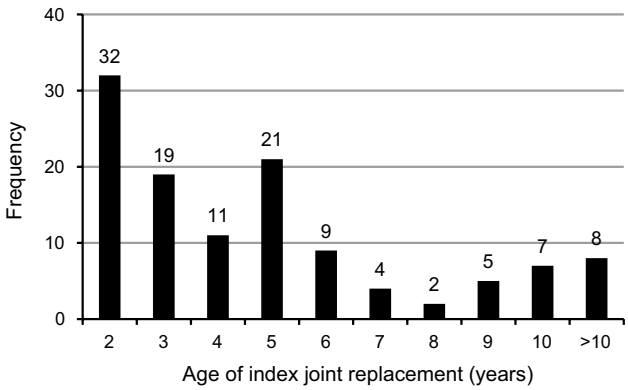

Fig. 1 Histogram illustrating age of index joint replacement (years) in 118 patients with pain in the knee region following cemented total knee replacement surgery, at the time of investigation with three-phase bone scan

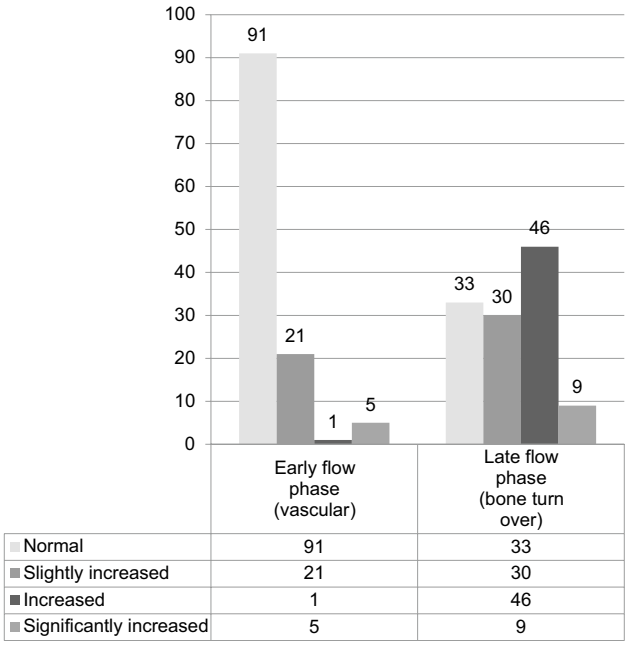

Fig. 2 Histogram demonstrating the degree of radionuclide uptake in the early and late phases of three-phase bone scan, as reported by a radiologist, in patients investigated for a painful total knee replacement

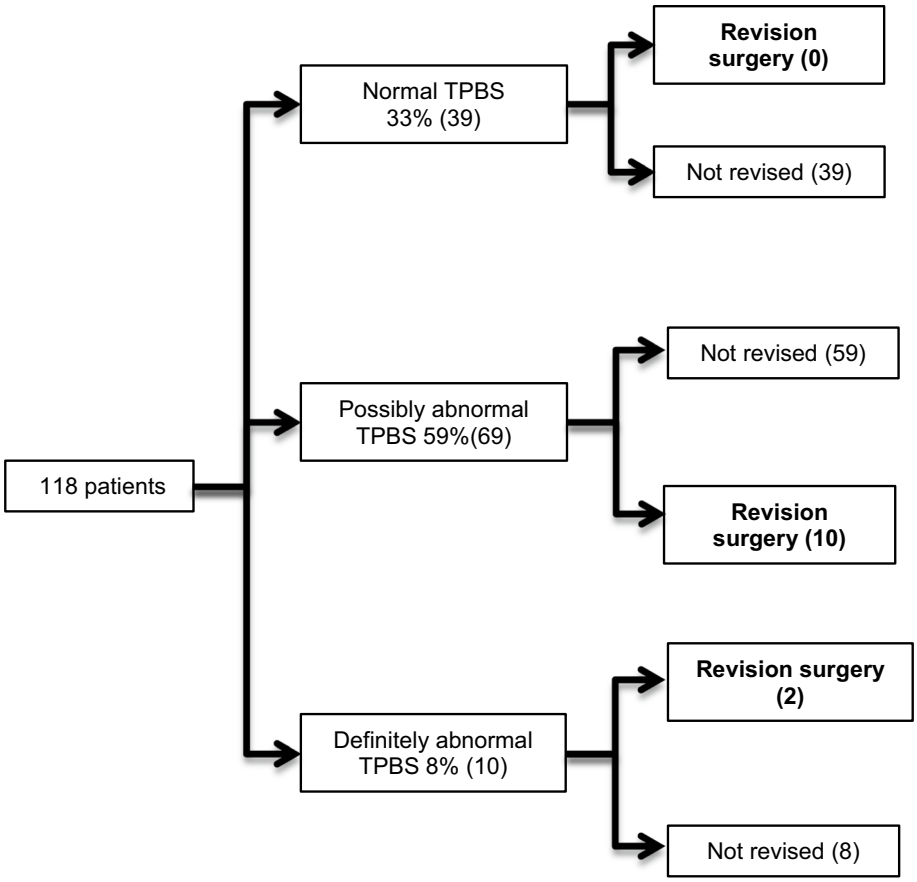

Fig. 3 Flow diagram depicting clinical management outcomes of patients with a painful total knee replacement ($N=118$) investigated with a three-phase bone scan. The findings are summarised as either normal, possibly abnormal, or definitely abnormal

confidence interval 53.29–72.37%), in the diagnosis of infection, or loosening with concurrent infection in determining the indication for revision surgery (Table 2).

Reported results

Definitely abnormal TPBS ($n=10$)

Two of the 10 patients with a definitely abnormal TPBS had a persistently elevated white cell count (WCC) in the presence of a normal CRP. Pre-operative arthrocentesis was negative for infection in both cases. Both underwent open debridement, synovectomy, and exchange of polyethylene insert on the basis of a presumed culture negative prosthetic joint infection. The femoral and tibial components were found not to be loose and were not revised. Intra-operative samples were negative for infection, and neither met the criteria for diagnosing a prosthetic joint infection [16]. In the cases with a definitely abnormal TPBS, the radiologists report stated that the appearances were "in keeping with prosthetic infection" (assumed false positive results in the presence of a CRP value ≤ 10 mg/l (in the eight cases managed non-operatively) and arthrocentesis negative for

Table 2 Diagnostic test analysis of TPBS in the evaluation of patients with pain in the knee region following cemented TKR surgery in the diagnosis of prosthetic joint infection, or component loosening with concurrent infection

True positive ($n=2$) Abnormal TPBS, with subsequent diagnosis of prosthetic joint infection, or component loosening with concurrent infection	False positive ($n=77$) Abnormal TPBS, with no subsequent diagnosis of prosthetic joint infection, or component loosening with concurrent infection
False negative ($n=0$) Normal TPBS, with subsequent diagnosis of prosthetic joint infection, or component loosening with concurrent infection	True negative ($n=39$) Normal TPBS, with no subsequent diagnosis of prosthetic joint infection, or component loosening with concurrent infection

N number of patients

infection in all patients in this subgroup. The possibility of a culture negative prosthetic joint infection does exist; however, all patients in this group were investigated at a relatively early stage following surgery (between 2 and 3 years). In addition, the eight cases managed non-operatively did not receive any antimicrobial therapy and were discharged with a pain-free TKR at the 24-month follow-up period (Table 3).

Possibly abnormal TPBS ($n = 69$)

Ten patients in this group underwent revision surgery. Open evaluation in one case revealed gross femoral component loosening (extracted with ease by hand). Prosthetic loosening was not diagnosed on the pre-operative TPBS (false-negative TPBS report for component loosening), but was, however, evident on serial pre-operative radiographs. The patient was discharged from follow-up with a pain-free TKR 24 months following revision of their femoral and tibial components. In another patient, massive metallosis delamination of the medial and lateral patella was evident upon open inspection of the knee joint. Pre-operative arthrocentesis and interoperative samples were all negative for infection. The TPBS reported "diffusely increased uptake in both the early and late flow phases makes the exclusion of both infection and loosening difficult". This patient responded well following revision TKR surgery and patella resurfacing surgery. The radiologist's reports for the other eight patients with a possibly abnormal TPBS who were managed with revision arthroplasty surgery indicated infection ($n = 5$), loosening ($n = 2$), and both infection and loosening ($n = 1$) as causes of increased radionuclide uptake. All were found to have well-fixed, non-infected TKR's during revision arthroplasty surgery. None met the diagnostic criteria for prosthetic joint infection [16], not had intra-operative evidence of component loosening.

In six patients, the indication for revision surgery was persistent pain in the knee region following TKR surgery, with a TPBS indicating the presence of peri-prosthetic infection. The TPBSs in this subgroup were all performed at least 5 years following the index arthroplasty surgery, and the increase in radionuclide uptake was deemed significant in the clinical context.

Fifty-nine patients with a possibly abnormal TPBS did not undergo surgical intervention. Serial plain radiographs were normal. Serology was within normal parameters, arthrocentesis was negative for infection (culture negative and SWCC $< 15{,}000$ cells/μl), and the diagnostic criteria for prosthetic joint infection were not met [16]. All patients received physical therapy, and nine were reviewed by the specialist pain management service. Again the possibility of a culture negative prosthetic joint infection does exist; however, all but six patients were discharged from follow-up 18–24 months after the investigation having received no antimicrobial therapy nor surgical intervention.

Normal TPBS ($n = 39$)

None of the patients with a normal TPBS underwent revision surgery. All had serology within normal parameters. None had arthrocentesis performed, and all had serial radiographs within normal parameters. Ten patients in this group remained under follow-up at 24 months following investigation with a TPBS, with all others being discharged with no clearly identifiable cause of pain in the knee region following TKR surgery.

Discussion

Evaluation of pain in the knee region after a cemented primary TKR represents a complex diagnostic challenge. Diagnosis in the presence of gross loosening or overt sepsis can be straight forward, but occasionally the diagnosis is not clear. TPBSs are reported to have a high sensitivity in detecting abnormality but a poor specificity. We question the existence of normal radionuclide uptake following TKR surgery and the timeframe following index joint replacement when this investigation might be considered useful. Our series indicates that a normal TPBS could be considered reassuring as an investigation of exclusion. This is in keeping with conclusions drawn by Henderson et al. [5] and Smith et al. [9] that a normal TPBS is reassuring and indicates a reduction in the probability of infection or loosening in the context of pain in the knee region following TKR surgery. Importantly, however, eight patients with a possibly abnormal TPBS and two patients with a definitely abnormal TPBS underwent revision surgery and were found to have no evidence of component loosening nor met the diagnostic criteria for prosthetic joint infection [16]. We report a poor association between an abnormal TPBS and the indication for revision surgery. A high incidence of increased radionuclide uptake (Fig. 3) in the context of a low revision rate brings the usefulness of an abnormal investigation into question. An abnormal TPBS was of very limited diagnostic value and did not provide any additional diagnostic information over that already available through other (more accurate) standard investigations. In our series, 86% (59/69) of patients with an abnormal TPBS reported where treated conservatively. This presents a difficult dilemma as the pain symptoms in the knee region could have been referred from a proximal cause (e.g., lumbar spine or hip joint), but equally could be attributed to the TKR and correlated with increased radionuclide uptake. An extensive meta-analysis performed by the American Academy of Orthopaedic Surgeons on the diagnosis of peri-prosthetic joint infections reported that

Table 3 Summary of details of patients who underwent revision total knee replacement surgery

Pre-operative TPBS summary	Pre-operative serology		Pre-operative radiographs	Pre-operative aspiration of synovial fluid	Intra-operative findings	Intra-operative cultures results	Intra-operative histology results	Diagnosis of peri-prosthetic joint infection [16]
	WCC (4.5–11.0 cells/μl)	CRP (< 4 mg/dl)						
Possibly abnormal	6.2	< 4	Lucency around femoral component	Culture negative SWCC < 15,000 cells/μl	Loose femoral component	Negative	5/5 negative tissue samples	Negative
Possibly abnormal	8.0	8	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Massive metallosis delimitation of the medial and lateral patella	Negative	6/6 negative tissue samples	Negative
Possibly abnormal	12.0	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	4/4 negative tissue samples	Negative
Possibly abnormal	9.8	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative
Possibly abnormal	7.2	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 tissue samples	Negative
Possibly abnormal	8.8	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	6/6 negative tissue samples	Negative
Possibly abnormal	9.4	< 4	Normal[a]	Culture negative. SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative
Possibly abnormal	5.6	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative
Possibly abnormal	6.6	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative
Possibly abnormal	8.4	< 4	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative

Table 3 (continued)

Pre-operative TPBS summary	Pre-operative serology		Pre-operative radiographs	Pre-operative aspiration of synovial fluid	Intra-operative findings	Intra-operative cultures results	Intra-operative histology results	Diagnosis of peri-prosthetic joint infection [16]
	WCC (4.5–11.0 cells/μl)	CRP (< 4 mg/dl)						
Definitely abnormal	14.0	6	Normal[a]	Culture negative SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative
Definitely abnormal	12.2	9	Normal[a]	Culture negative. SWCC < 15,000 cells/μl	Well-fixed prosthesis	Negative	5/5 negative tissue samples	Negative

[a]Normal radiographs imply appropriate limb alignment, appropriate component size and no overhang, correct component positioning, and absence of stress fractures, loosening, lucencies, osteolysis, wear of the polyethylene insert, heterotrophic ossification, overfilling of the patellofemoral joint, and anterior translation of the femoral component

TPBSs had a sensitivity of between 33 and 88% (95% CI) and a specificity of 76–90% (95% CI) [17]. This analysis concluded that TPBSs were an option in patients whom a diagnosis of prosthetic joint infection had not been established and were not scheduled for reoperation.

The large number of consultant teams referring patients for a TPBS made determining the threshold for requesting a TPBS in our series above that outlined in our methodology difficult. The resultant relatively heterogeneous study population is a limitation of this series. This has not been quantified or qualified in previous reports on TPBSs. We did not differentiate between non-specialised and specialised revision knee arthroplasty surgeons; however, consultants performing low volume numbers of revision TKR surgery made the majority of requests. Our series analysed the information available to the surgeon when assessing the patient. Therefore, retrospective evaluation for inter-observer error in TPBS reporting would not have changed the information available to the surgeon and therefore was not performed. Temmerman et al. [11] determined moderate inter-observer variability between two experienced radiologists in this context. Furthermore, the issue of limited clinical information supplied to the reporting radiologist on radiology request forms may be a significant factor in determining the specificity of the reporting terminology used by the reporting radiologist. An additional factor is the time between index joint replacement and investigation (Fig. 1). Increased radionuclide uptake has been reported at up to 2 years following uncomplicated TKR surgery, but the timeframe when this can be assumed to normalise has not been clearly defined. Hofmann et al. [3] reported that late phase radionuclide uptake gradually decreased to baseline 12 months following surgery. Duus et al. [18] reported persistent increase in radionuclide uptake in 20% of patients within one year following TKR, which was then lowered to 12.5% after 2 years. Other reports indicate that increased radionuclide uptake can persist in asymptomatic patients up to 12 years following TKR [19, 20], making the distinction between a normal and abnormal investigation almost impossible. These factors may explain the variation in reported accuracy, together with the impediment placed upon the radiologist by the near universal lack of good quality clinical information recorded upon the TPBS request cards. The need for surgeon education is evident, and surgeons should consider co-reporting TPBSs with the radiologist to allow for clinical correlation.

In our unit, the indication for revision TKR surgery in 91% of cases was determined without a TPBS being performed during our 24-month study period. This poses the difficult issue of what clinical question is the surgeon asking when requesting a TPBS? It is possible that junior surgeons, unaware of the poor diagnostic accuracy of a TPBS, are requesting TPBSs. We suspect that at least some TPBSs were performed on patients who despite a normal quadruple evaluation of pain in the knee region following TKR surgery request further investigation. The level of C-reactive protein (CRP) is a widely used serum marker for assessing bacterial infection in patients with a TKR. After joint replacement, the CRP level typically increases with an early peak at 2–3 days after surgery, returning to normal within the first 3 weeks post-operatively [14, 15]. A CRP value > 10 mg/l has been reported to have a 96% sensitivity, a 92% specificity, a 74% positive predictive value, and a 99% negative predictive value [12]. Consequently, we defined the absence of serological evidence of infection with a CRP value ≤ 10 mg/l. We acknowledge our inability to definitively exclude prosthetic loosening in the conservatively managed cohort, but highlight that during the 24-month follow-up period following investigation with a TPBS none had undergone further

intervention or revision surgery. We also acknowledge our inability to exclude low-grade infection in the conservatively managed cohort; however, we did not identify any subsequently positive joint aspirate cultures within the 24-month follow-up period, indicating no false negatives in the exclusion of peri-prosthetic infection.

Best outcomes in peri-prosthetic infection result from prompt diagnosis and timely intervention. Delays in obtaining investigation could delay diagnosis and treatment of infection. The associated radiation dose risk must also be considered. A single scan gives a typical radiation dose of 4 mSv. This is the equivalent of 200 chest or 400 knee radiographs and results in an additional lifetime cancer risk of 1:5000 (http://www.hpa.org.uk). Radionuclides also have a physical cost of £150 per scan in our centre, totalling £19,050 in our series. This does not include nuclear medicine staffing or radiologist reporting time. TPBS lacks sufficient specificity to differentiate between prosthetic failure and post-surgical bone remodelling. An additional shortcoming of this investigation in cemented implants is that the cement–implant interfaces cannot be analysed. Loosening at this interface will not create a bone reaction, and hence a TPBS will not detect this. Sterile inflammation or infection cannot be conclusively differentiated or excluded. If component loosening is present, a TPBS is unlikely to differentiate this from infection. Excluding infection is the primary task facing the surgeon; however, there is no reliable standard single radiological test for this. The significant radiation dose, delays in obtaining investigation, and subsequent follow-up make this investigation difficult to justify. The use of antibiotic and mono-clonal antibody labelled radioisotope scans to detect peri-prosthetic infection has been reported [19, 20], but have a variable accuracy and lack specificity. Positron emission tomography has been reported as showing potential [21]. Further studies are required to establish if these techniques have a role.

Conclusion

An abnormal TPBS has a limited diagnostic role, failed to provide any additional diagnostic information above that already available through other standard investigations, and had a high false positive value in the detection of infection. The indication to perform revision TKR surgery was determined in out unit in 91% of cases without a TPBS. A normal TPBS may be reassuring in that the TKR can be excluded as the cause of pain symptoms; however, better, cheaper, and more accurate methods of diagnosing peri-prosthetic infection exist. A TPBS should only be considered following assessment by a specialist revision knee arthroplasty surgeon; however, given its lack of specificity we no longer utilise this investigation in the evaluation of pain in the knee region following TKR surgery.

Acknowledgements We would like to acknowledge the support of our Statistical Advisor Dr. Roy J. Powell, B.Sc. (Hons), Ph.D., CBIOL, FSB, FHEA. Research Design Consultant, Research Design Service (RDS) South West.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The National Research Ethics Committee reviewed the protocol for this work and stated that formal ethical approval was not required.

References

1. Toms AD, Mandalia V, Haigh R, Hopwood B (2009) The management of patients with painful total knee replacement. J Bone Joint Surg Br 91(2):143–150
2. Math KRSF, Petchprapa C, Harwin SFZ, Math KR, Zaidi SF, Petchprapa C, Harwin SF (2006) Imaging of total knee arthroplasty. Semin Musculoskelet Radiol 10(1):47–63
3. Hofmann AA, Wyatt RW, Daniels AU, Armstrong L, Alazraki N, Taylor AJ (1990) Bone scans after total knee arthroplasty in asymptomatic patients. Cemented versus cementless. Clin Orthop Relat Res 251:183–188
4. Rosenthall L, Lepanto L, Raymond F (1987) Radiophosphate uptake in asymptomatic knee arthroplasty. J Nucl Med 28(10):1546–1549
5. Henderson JJ, Bamford DJ, Noble J, Brown JD (1996) The value of skeletal scintigraphy in predicting the need for revision surgery in total knee replacement. Orthopedics 19(4):295–299
6. Love C, Tomas MB, Marwin SE, Pugliese PV, Palestro CJ (2001) Role of nuclear medicine in diagnosis of the infected joint replacement. Radiographics 21(5):1229–1238
7. Wong MY, Beadsmoore C, Toms A, Smith T, Donell S (2012) Does 99mTc-MDP bone scintigraphy add to the investigation of patients with symptomatic unicompartmental knee replacement? Knee 19(5):592–596
8. Levitsky KA, Hozack WJ, Balderston RA, Rothman RH, Gluckman SJ, Maslack MM et al (1991) Evaluation of the painful prosthetic joint. Relative value of bone scan, sedimentation rate, and joint aspiration. J Arthroplasty 6(3):237–244
9. Smith SL, Wastie ML, Forster I (2001) Radionuclide bone scintigraphy in the detection of significant complications after total knee joint replacement. Clin Radiol 56(3):221–224
10. Temmerman OPP, Raijmakers PGHM, David EFL, Pijpers R, Molenaar MA, Hoekstra OS et al (2004) A comparison of radiographic and scintigraphic techniques to assess aseptic loosening of the acetabular component in a total hip replacement. J Bone Joint Surg Am 86–A(11):2456–2463
11. Lieberman JR, Huo MH, Schneider R, Salvati EA, Rodi S (1993) Evaluation of painful hip arthroplasties. Are technetium bone scans necessary? J Bone Joint Surg Br 75(3):475–478
12. Greidanus NV, Masri BA, Garbuz DS, Wilson SD, McAlinden MG, Xu M et al (2007) Use of erythrocyte sedimentation rate and C-reactive protein level to diagnose infection before revision total knee arthroplasty. A prospective evaluation. J Bone Joint Surg Am 89(7):1409–1416

13. Mandalia V, Eyres K, Schranz P, Toms AD (2008) Evaluation of patient with a painful total knee replacement. J Bone Joint Surg (British) 90-B(3):265–271
14. Spangehl MJ, Masri BA, O'Connell JX, Duncan CP (1999) Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. J Bone Joint Surg Am 81(5):672–683
15. Moreschini O, Greggi G, Giordano MC, Nocente M, Margheritini F (2001) Postoperative physiopathological analysis of inflammatory parameters in patients undergoing hip or knee arthroplasty. Int J Tissue React 23(4):151–154
16. Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ et al (2011) New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res 469(11):2992–2994
17. American Academy of orthopaedic surgeons. Guideline on the diagnosis of periprosthetic joint infections of the hip and knee
18. Duus BR, Stadeager C, Boeckstyns M (1990) The natural course of radionuclide bone scanning in the evaluation of total knee replacement. A two year perspective study. Clin Radiol 41(5):341–343
19. Rubello D, Caricasulo D, Borsato N, Chierichetti F, Zanco P, Ferlin G (1996) Three-phase bone scan pattern in asymptomatic uncemented total knee arthroplasty. Eur J Nucl Med 23(10):1400–1403
20. Verlooy H, Victor J, Renson L, Vandecruys A, Drent P, Mortelmans L et al (1993) Limitations of quantitative radionuclide bone scanning in the evaluation of total knee replacement. Clin Nucl Med 18(8):671–674
21. Reinartz P, Mumme T, Hermanns B, Cremerius U, Wirtz DC, Schaefer WM et al (2005) Radionuclide imaging of the painful hip arthroplasty: positron-emission tomography versus triple-phase bone scanning. J Bone Joint Surg Br 87(4):465–470