



Higher reliability of triple-phase bone scintigraphy in cementless total hip arthroplasty compared to cementless bipolar hemiarthroplasty



Burak Yoldas*, Deniz Cankaya, Kemal Andic, Enver Kilic, Olgun Bingol, Ali Tecirli, Ali Toprak, Yalçın Tabak

Department of Orthopaedic and Traumatology, Ankara Numune Training and Research Hospital, 06100 Altindag, Ankara, Turkey

HIGHLIGHTS

- Triple-phase bone scintigraphy is effective in ruling out infection with its higher sensitivity.
- Triple-phase bone scintigraphy has relatively low specificity compared to its high sensitivity.

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ABSTRACT

Purpose: Periprosthetic infection is one of the main reasons for revision surgery after hip arthroplasty. The purpose of the present study is to compare the reliability of triple-phase bone scintigraphy (TPBS) in the diagnosis of periprosthetic infection between cementless total hip arthroplasty (THA) and bipolar hemiarthroplasty (BHA).

Methods: In this retrospective study, 52 patients were analyzed; 33 of them were performed with THA and 19 of them were performed with BHA. The exclusion criteria were cementation in previous surgery, romatological joint disorders, periprosthetic fracture and malignancy history. C reactive protein (CRP) and erythrocyte sedimentation (ESR) rate results were recorded preoperatively. Tissue samples from the different areas periprosthetic tissue were obtained for histopathological examination and sample tissue culture.

Results: In the present study, the sensitivity, specificity and accuracy were 90.9%, 77.3% and 81.8%, respectively, for THA and 77.8%, 60.0% and 68.4%, respectively, for BHA. Positive predictive values for THA and BHA were 66.7% and 63.6%, and negative predictive values were 94.4% and 75.0%, respectively.

Conclusions: Due to the higher sensitivity, specificity and accuracy, TPBS has a more reliable diagnostic value for cementless THA in the diagnosis of periprosthetic infection compared to cementless BHA.

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1. Introduction

Hip arthroplasty is a successful orthopedic procedure in the treatment of patients with painful and diseased hips [1,2]. With the increasing number of hip arthroplasties, the number of failures due to septic loosening, infection, dislocation and fracture is also increasing with the necessity of revision surgery [2,3]. Differential diagnosis between aseptic loosening and infection is of great importance because the peri-prosthetic infection differs with the catastrophic complications, and the surgeon might choose two-stage revision surgery instead of one-stage definitive surgery in

the case of infection [1,4–6]. However, there is currently no single and reliable diagnostic method to differentiate between septic and aseptic loosening [1,7].

Although screening serum C reactive protein (CRP) and erythrocyte sedimentation (ESR) values can be used in the diagnosis of periprosthetic infections, they can be affected by other infectious and non-infectious diseases with poor specificity [1,8,9]. Recent studies examining the effectiveness of TPBS in hip arthroplasty exhibited a significantly heterogeneous study design regarding the etiology, cementation, surgical choice and presence of previous surgeries [5,7,10]. To the best of our knowledge, there was no study comparing the reliability of TPBS in the diagnosis of periprosthetic infection between cementless total hip arthroplasty (THA) and cementless bipolar hemiarthroplasty (BHA).

* Corresponding author.

E-mail address: yoldas_burak@hotmail.com (B. Yoldas).

In the present study, we investigated the effectiveness of TPBS in the diagnosis of periprosthetic infection in cementless hip arthroplasty patients. We asked whether there was a difference in the reliability of TPBS between cementless THA and BHA.

2. Methods

This retrospective study included 52 patients who underwent THA ($n = 33$) with primary hip osteoarthritis history and BHA ($n = 19$) with proximal femur fracture history according to the inclusion and exclusion criteria described below. The inclusion criteria were primary hip osteoarthritis for the THA group, proximal femur fracture for the BHA group and removal of the implant for both of the groups. The exclusion criteria were rheumatological joint diseases, previous hip surgery, cementation, shorter than two years duration after primary surgery and metabolic bone disease. None of the patients had any chronic hepatic or hematological disease and malignancy history. The age, sex distributions and durations from primary surgery of the groups are shown in [Table 1](#). Considering the demographic data and duration from the primary surgery, there were no significant differences between the groups.

Patients with a previous hip arthroplasty who had groin and thigh pain were suspected of septic or aseptic loosening of implants. In this situation, standard pelvic anteroposterior radiographs were obtained to evaluate the radiolucent lines and migration of components according to the Gruen zones for the femoral stem and the DeLee zones for the acetabular cup. Blood markers such as CRP, ESR and white blood cells (WBCs) were also screened. All patients underwent TPBS in the suspicion of loosening and infection. Because the bone scan may remain abnormal up to two years after implantation [[1,3](#)] patients who had primary surgery within the last two years were not included in this study.

Bone scintigraphy images were obtained after injecting technetium-99 m-labeled diphosphonate using an Infinia & Hawkeye 4 gamma camera of GE. The TPBS consists of three phases: blood flow phase, blood pool phase and late phase. The blood flow phase occurred immediately after infusion of technetium-99 m-labeled diphosphonate, the blood pool phase consisted of the acquisition of anterior and posterior static spot images of the hips between 3 and 5 min later, and the late phase reflected the same images of the blood pool phase 3–4 h after infusion. Images were obtained while the energy peak was set at 140 keV and a 20% window with an image matrix size of 256×256 pixels. After obtaining the TPBS images, the images were examined according to the density of area compared with the contralateral side using a digital viewing system. An increase in the radioisotope uptake in all three phases of TPBS was considered to be a peri-prosthetic infection. A true positive result of THA and false positive result of BHA are shown in [Figs. 1 and 2](#), respectively, with antero-posterior X-rays of the patients and typical TPBS images.

Due to the effect of the antibiotic treatment on the culture results [[1,3,4](#)] antimicrobial therapy was discontinued at least two weeks prior to the surgery in our routine clinical practice. After an

evaluation of the standard antero-posterior pelvic radiographies, screening of blood values and outcomes of TPBS, all operations were performed using the modified anterolateral (Watson Jones) approach by the same senior surgeon group in the supine position. Five samples close to the prosthesis, including the joint, proximal femur and acetabular ground, were obtained for microbiological examination. In addition, five samples from the area described above were obtained for histopathological examination.

We used criterias which were accepted by work group of the Musculoskeletal Infection Society (MSIS) for definitive diagnosing of periprosthetic infection [[11](#)]. We recorded ESR and CRP values preoperatively and evaluated intraoperative macroscopic appearance, report of the histopathological specimens, synovial leukocytes count and results of the sample cultures for diagnosing of periprosthetic infection. The intraoperative macroscopic appearance was defined and in the presence of purulence appearance recorded by a senior surgeon. In frozen and permanent histopathological examinations, five or more polynuclear leukocytes on a highly magnified view ($\times 400$) were considered positive. Besides this we investigated synovial leukocyte count and percentage of polymorphonuclear leukocytes (PMNL) for the infected hip arthroplasty [[11](#)]. The culture results were recorded by the same microbiology laboratory. According to the preoperative TPBS results and postoperative evaluation of infection according to the MSIS criteria, a false-positive result was assumed when the TPBS was positive instead of a negative post-operative result and a false-negative result was assumed when the TPBS was negative instead of a positive post-operative result.

This study was approved by the local ethics committee with ID number E-14-138. All data were calculated as the mean and standard deviation for the patient characteristics. The Chi-square test was used for statistical analysis of the patient data. A value of $p < 0.05$ was considered statistically significant. The sensitivity, specificity, accuracy, positive predictive value and negative predictive value for the TPBS in the diagnosis of infection were calculated. Intra-observer interclass correlation coefficients (ICC) and inter-observer ICC were assessed. Statistical calculations were performed using SPSS 13.0 (SPSS Inc., Chicago, IL, USA.).

3. Results

Among 52 patients, 32 hip arthroplasties underwent a revision THA after the diagnosis of aseptic loosening on the basis of intraoperative findings as well as histopathological results. Regarding the primary surgery, 22 patients had THA and 10 had BHA. In these patients, there was one infection (3.1%) after the revision THA. This patient was from the BHA group and had a reoperation one year after revision arthroplasty. Twenty hip arthroplasties underwent a removal of the implant and placement of antibiotic-impregnated cement spacers after the septic loosening diagnosis. Regarding the primary surgery, 11 patients had THA and 9 had BHA.

Regarding the results of the frozen and permanent histopathological specimens, there was no discordance. All of the samples that were negative for histopathology were also negative for the bacterial culture. Among 20 patients who had a positive histopathological result, six patients (30%) had positive culture results. MRSA was detected in two patients, staphylococcus epidermis was found in two patients, acinetobacter baumannii was observed in one patient, and pseudomonas aeruginosa was found in one patient. Regarding the TPBS measurement, the inter-observer ICC was 0.81 and the intraobserver ICC was 0.89. Intra-observer and interobserver agreements were good and reliable during the TPBS evaluations.

As the results were evaluated for all of the patients as hip arthroplasty, the sensitivity, specificity and accuracy were 85.0%,

Table 1
Demographic and clinical data of the patients.

	THA	BHA	P-value
Number of patients	33	19	
Age (years)	66.4 \pm 9.1	69.5 \pm 8.0	0.214
Sex (female/male)	21/12	14/5	0.548
Duration (years)	7.2 (2–14)	6.6 (2–12)	0.536

The values are expressed as the mean and number of patients with the standard deviation and range in parentheses. THA: total hip arthroplasty, BHA: bipolar hemiarthroplasty.

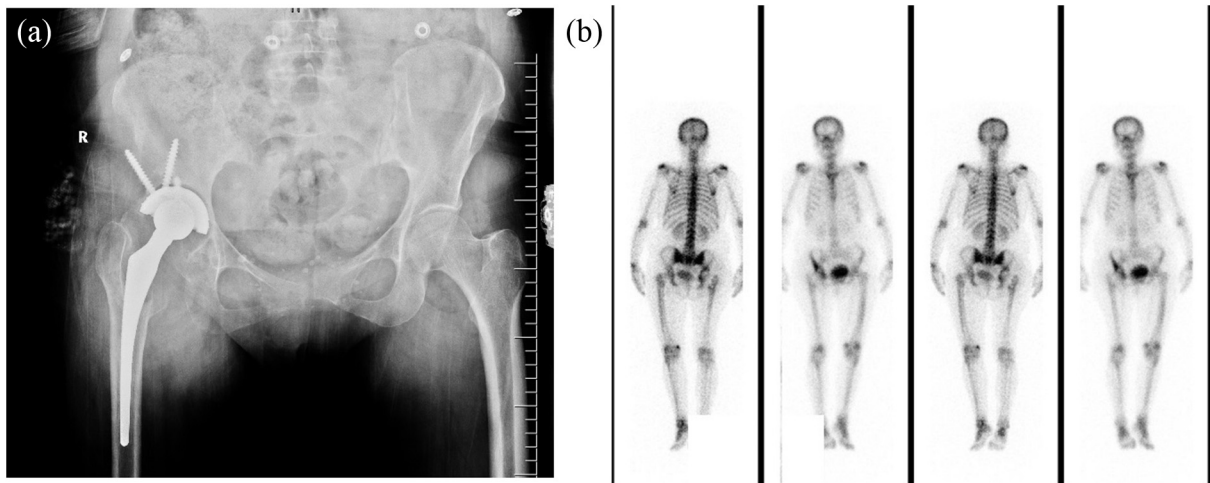


Fig. 1. Anteroposterior X-ray of the right hip of a 71-year-old female patient showing loosening seven years after primary cementless total hip arthroplasty (A); triple-phase bone scintigraphy was positive (B). Infection was reported in frozen and late histopathological results. *Staphylococcus epidermidis* was cultured from the periprosthetic tissue.

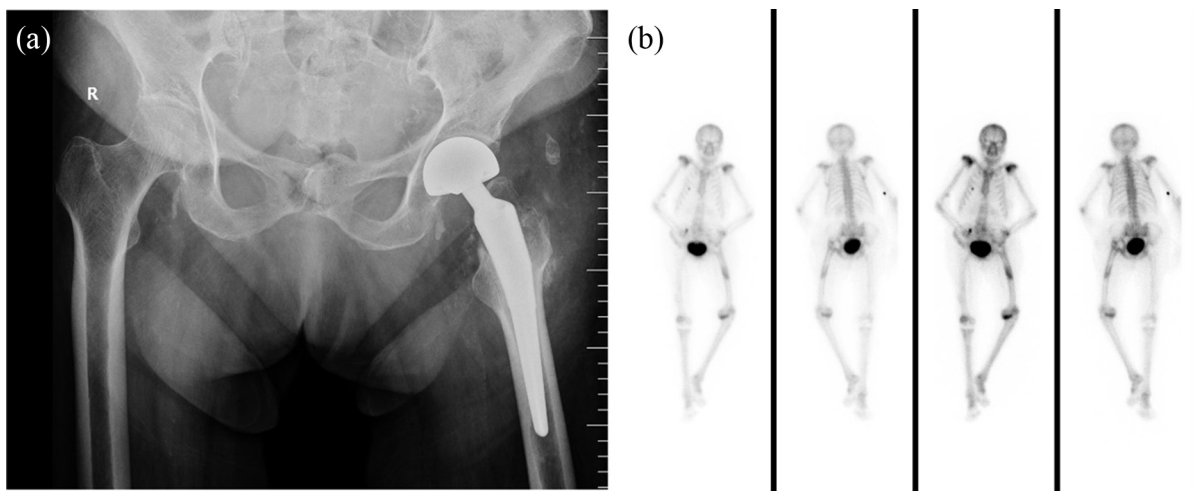


Fig. 2. Anteroposterior X-ray of the left hip of a 69-year-old male patient showed loosening five years after cementless bipolar hemiarthroplasty (A); triple-phase bone scintigraphy was positive (B). There was no infection reported in the frozen and late histopathological results. Culture results were negative.

71.9% and 76.9%, respectively. The positive predictive value was 65.4%, and the negative predictive value was 88.5%. In the THA group, the sensitivity, specificity and accuracy were 90.9%, 77.3% and 81.8%, respectively. The positive predictive value and negative predictive value were 66.7% and 94.4%, respectively. However, in the BHA group, the sensitivity, specificity and accuracy were 77.8%, 60.0% and 68.4%, respectively. The positive predictive value and negative predictive value were 63.6% and 75.0%, respectively. The number of true positive, false positive, true negative, and false negative records and the sensitivity, specificity, accuracy, positive predictive value and negative predictive value are shown in Table 2.

4. Discussion

As with any other surgical operation, serious complications in patients undergoing THA, such as aseptic loosening, dislocation and infection, are the main reasons for revision surgery [2,5,7,10,12,13]. Accurate and efficient diagnosis is needed for revision surgery, and it is essential to exclude septic causes to make the decision between one-stage and two-stage operation [1,5,7,10,13–16]. If an infection is detected preoperatively, then both the surgeon and patient are

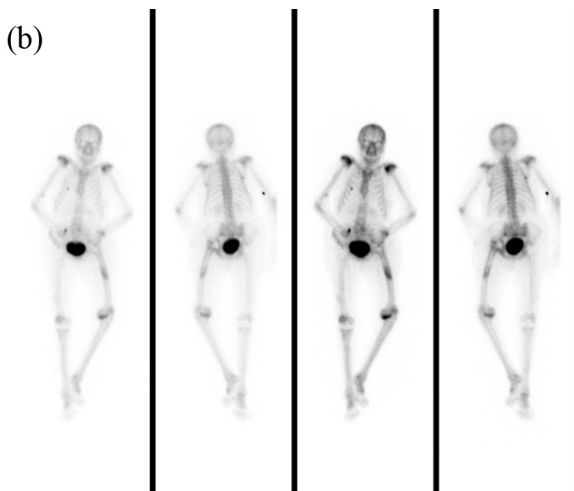


Table 2

The number of true positive, false positive, true negative, and false negative records and the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of the total hip arthroplasty (THA), bipolar hemiarthroplasty (BHA) and hip arthroplasty groups.

	THA	BHA	Hip arthroplasty
True positive	10	7	17
False positive	5	4	9
True negative	17	6	23
False negative	1	2	3
Total number of patients	33	19	52
Sensitivity (%)	91	78	85
Specificity (%)	77	60	72
Negative predictive value (%)	94	75	88
Positive predictive value (%)	67	64	65
Accuracy (%)	82	68	77

The values are expressed as the number of patients and percentage (%).

able to prepare for the operative procedure [1]. The aim of the present study was to compare the reliability of TPBS between cementless THA and BHA in diagnosing infection.

In clinical practice, plain radiography is the baseline imaging

technique in diagnosing the loosening of implants after hip arthroplasty with its acceptable sensitivity and specificity; however, it has no diagnostic value in diagnosing infection [1,2,10,16]. Serum ESR and CRP are known to be sensitive markers of periprosthetic infection with a relatively low specificity, but these markers have disadvantageous potential interactions with other infectious and non-infectious inflammatory diseases [1,9]. A recent prospective study with 100 patients reported relatively low sensitivity (64%) and specificity (75%) for serum CRP in diagnosing periprosthetic infection [5]. A persistent slight elevation of serum CRP is the most challenging diagnostic situation in the suspicion of infection, which highlights the need for a more reliable diagnostic method for the periprosthetic infection of hip arthroplasty [14].

There were several clinical studies and meta-analyses examining the reliability of TPBS in diagnosing septic and aseptic loosening [1,5,7,10,13,16–22]. Sensitivity values of 83%, 68%, 88% and 78% and specificity values of 79%, 76%, 90% and 70% were reported among these studies [1,5,7,10]. A relatively recent study with 35 patients reported differing result with 56% sensitivity and 88% specificity. The wide ranges of sensitivity and specificity reported in these studies elicit questions about the reasons for these variable results. On the basis of these studies, there has been no standardization regarding the surgical technique (not described), accompanying systemic and developmental disorders that affect the musculoskeletal system [1,5,7], the distribution of gender in which a five-fold higher number of male patients to female patients is present [1,5] and cementation [5,10]. These studies were also heterogeneous regarding the distributions of THA and BHA patients [7,10]. Male gender, avascular necrosis history, a longer duration from primary surgery and cementation have been shown to increase the risk for revision due to infection after hip arthroplasty [12]; in addition, study design and these patient characteristics might affect the results of the study described above. In the present study with the aforementioned restriction criteria, the sensitivity and specificity were 85.0% and 71.9% for overall cementless hip arthroplasty.

The present study is the first study to compare the reliability of TPBS in diagnosing periprosthetic infection between cementless THA and BHA, while there was no significant difference between these groups regarding gender, age and duration from primary surgery. In the case of cementless THA, TPBS has excellent sensitivity with a value of 91% and exhibits relatively good accuracy with a value of 82%. However, its relatively poor accuracy (68%) and specificity (60%) for the BHA group elicit questions regarding the reliability and use of TPBS in diagnosing infection for this patient group in routine clinical practice. These results support the rationale underlying the dramatic reliability differences of TPBS results between THA and BHA.

Regarding the false negative result, 16 of the 19 patients underwent BHA using bisphosphonate medication after hip fracture. This false negative finding might be due to a transient phenomenon of alendronate, a bisphosphonate cleared from the plasma by uptake into bone and renal excretion. 99 mTc-MDP is eliminated via the same pathways, and thus, competition may occur between the two substances [23]. In addition, relatively less metallic implants associated with bony structures due to the lack of an acetabular component in BHA might also result in higher false negative results in the BHA group. Regarding the relatively higher number of false positives of BHA, these patients had a previous fracture history and false positive outcome that could be continued due to the chronic process in the fracture region. A study reported lower specificity results for patients who had a fracture history compared to patients without a fracture history, although patients who had undergone hip arthroplasty operations more than two years earlier were isolated in that study [7]. The result of the above-mentioned study

supports our hypothesis of the potential reason for higher false positive results of the BHA group in the present study.

There are some limitations to this study. First, the results are only those of cementless hip arthroplasty. This study needs to be repeated with cemented hip arthroplasty to achieve a more generalized conclusion. Second, a larger number of patients in the THA and BHA groups is needed to corroborate our comparative results. Third, patients in the present study had primary hip osteoarthritis; cases of hip osteoarthritis secondary to other pathologies, such as rheumatological disorders, congenital or developmental deformities, were not evaluated. Finally, we did not categorize the types of implants used in previous THA and BHA surgeries. A variety of implant types might affect the results of TPBS measurements between these two groups.

5. Conclusion

TPBS is more reliable in ruling out infection with its relatively higher sensitivity. The main clinical relevance of the present study is that the TPBS has a more reliable diagnostic value for cementless THA in diagnosing periprosthetic infection compared to cementless BHA.

Ethical approval

The study was approved by the Local Ethics Committee of the tertiary referral hospital with the ID number of E-14-138.

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Author contribution

Burak Yoldas: writing, study design, final revisions.
Deniz Cankaya: study design, critical revisions.
Kemal Andic: writing, final revisions.
Enver Kilic: statistics.
Olgun Bingol: data collection.
Ali Tecirli: data analysis.
Ali Toprak: follow-up.
Yalcin Tabak: study design, critical revisions.

Conflict of interest

The authors declare that they have no conflict of interest.

Guarantor

Dr. Burak Yoldas.

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Declared none.

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