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Diagnostic Performance of Two-Bed SPECT/CT versus Planar Bone Scan for Detection of Osseous Metastases in Urogenital Malignancies.

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ABSTRACT:

Objective: to assess the diagnostic performance of Planar Bone Scan (PBS) and Single Photon Emission Computed Tomography/Computed Tomography (SPECT/CT) of the chest, abdomen, and pelvis in patients with urogenital malignancies. **Methods:** Seventy-four patients with equivocal or negative PBS results were included. A two-bed SPECT/CT (SCT) was conducted after PBS. The examined body regions were divided into five regions (pectoral girdle, thoracic cage, pelvis, spine, and extremities). A four-base classification code was applied (0 = Free, 1 = Benign lesion(s), 2 = Equivocal lesion(s), and 3 = Malignant lesion(s)). Other imaging, clinical data, tumor markers, and follow-up PBS established the final diagnosis. The diagnostic performance of SCT and PBS was evaluated for each patient and each site. **Results:** Thirteen patients were proven to have bone metastases, whereas 61 patients did not prove to have bone metastases. SCT showed significantly higher sensitivity, specificity, and accuracy than PBS (p=0.014, 0.001, and 0.010, respectively). SCT showed substantially higher specificity and accuracy in the spine than PBS (p =

<0.001, 0.049, respectively). However, there was no significant difference regarding sensitivity (p= 0.059). SPECT/CT of the pelvis showed significantly higher sensitivity and accuracy than PBS (p=0.010, 0.049, respectively). However, there was no significant difference in specificity (p= 0.406). There was no statistically significant difference in sensitivity, specificity, or accuracy between SPECT/CT and PBS in the extremities (p = 0.113, 0.822, 0.251, respectively) and thoracic cage (p = 0.126, 0.823, 0.216, respectively). Diagnostic performance was not applicable for the pectoral girdle due to the few patients with positive findings in this region (only two).

Conclusion: SCT demonstrated relatively higher diagnostic performance than PBS in urogenital malignancies in the spine and pelvic region.

Keywords: Total body SPECT/CT, Planar Bone Scan, Urogenital Cancer, sensitivity, and specificity.

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INTRODUCION:

Bone metastasis (BM) is a common malignancy complication[1]. Prostate carcinoma prostatic Ca., renal cell carcinoma (RCC), and urinary bladder carcinoma are among the genitourinary cancers that frequently develop skeletal metastases[2]. BM has a substantial impact on patient quality of life and survival; thus, a precise diagnosis of BM is essential [3]. A conventional bone scan using Tc99m MDP is considered the most commonly used imaging modality for skeletal metastasis detection [4]. Planar bone scan (PBS) provides low cost, availability, and

sufficient sensitivity. However, it exhibits low specificity in the spine [5,6]. The widespread availability of SPECT/CT enables improvement in sensitivity and specificity of Tc 99-m PBS in the detection of BM, enabling better anatomical localization and a higher contrast between lesion and background [7]. Recent technological advancements allow the integration of two or more bed positions in SPECT/CT devices to produce trunk or full-body images [8]. In this study, we aimed to investigate the performance of PBS and SPECT/CT (SCT) site and patient-based analyses in urogenital malignancies.

PATIENTS and METHODS:

Following ethical approval from Assiut University (IRB No: 04-2022-200019), this prospective study was performed at South Egypt Cancer Institute, which is in Assiut University, Egypt. Informed consent from the patients was obtained to participate. We enrolled adult patients with genitourinary malignancies referred to our nuclear medicine unit to do bone scintigraphy for metastatic workup between October 2022 and November 2024. Patients with negative or equivocal PBS findings were recruited in this study. Patients with definite metastatic osseous lesion(s) at PBS or with lesions outside the field of SCT were excluded. Initially, 82 patients were enrolled. Eight patients were excluded from the study due to missing follow-up data, leaving a valid cohort for subsequent analysis of 74 patients.

The final diagnosis was obtained by correlating with other radiological modalities (CT and/or MRI), repeated bone scans, clinical and/or laboratory data, and tumor markers.

Imaging protocol:

The whole-body PBS was obtained using a dual-head gamma camera (Symbia) two to three hours after intravenous injection of 20–25mCi (740–925 MBq) Tc 99-m-labeled methylene diphosphonate (MDP). Anterior and posterior views of the

skeleton were obtained from the vertex to toes at a speed of 12 cm/min with a matrix size of 1024 x 256. The energy window was centered ± 15% around 140 keV. SCT was obtained over a 360°-arc, using 32 frames at 15 seconds per frame. Two-bed SCT images covering from the cervical spine to the mid-thigh were acquired using a 128 x 128 matrix with an iterative protocol "4 iterations, four subsets, and Gaussian filter 8". Then the CT part was obtained at a slice step of 1 mm, a current of 80 mA, and a voltage of 130 kV. The SCT acquisition time was about 25 minutes.

Images Interpretation

Two nuclear medicine physicians interpreted both PBS and SCT in different sessions. The clinical data, other than cancer type, were masked from readers. To ensure simplicity and alignment between modality findings, we divided the examined skeleton into five regions, including the pectoral girdle (clavicles and scapulae), thoracic cage (sternum and ribs), spine, pelvis (iliac bones and sacrum), and extremities (humeri up to the elbow and femora till mid-thigh). Four-based code, ranging from zero to three, was applied (0 = Free, 1= Benign lesion(s), 2 = Equivocal lesion(s), and 3 = Malignant lesion(s)). When judgments between readers did not match, another more experienced nuclear medicine physician evaluated each study and chose the appropriate classification.

Statistical analysis:

Data analysis was done using SPSS version 26. The categorical data was displayed in the form of frequencies and percentages. The mean and standard deviation represented numerical data, such as age. We consider codes 0 and 1 negative, whereas codes 2 and 3 positive. The diagnostic performance of SCT and PBS was calculated using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy. The **McNemar** test

evaluated the statistical significance of the differences in sensitivity and specificity between PBS and SPECT/CT. The receiver operating characteristic curve (ROC curve) was used to identify the overall accuracy and calculate the area under the curve (AUC) in PBS and SCT. **Medcalc** software was used to calculate the statistical significance between each of the two reader AUCs for pairwise comparison, and it has an online calculator that compares the diagnostic performance between both modalities.

RESULTS

Table 1: Patients Characteristics (74 patients).

Gender	
Male	66 (89.2%)
Female	8 (10.8 %)
Cancer types	
Prostate	44 (59.5 %)
Urinary Bladder	25 (33.8%)
Renal	5 (6.7%)
Final diagnosis	
Positive	61 (82.4 %)
Negative	13 (17.6 %)

A total of 74 patients were finally included in this study. The mean age was 66.4 ±11.15 (range: 21:87) years. Males represented 89.2% (66 patients) of the study population, whereas females were 10.8 % (8 patients). Prostatic cancer (PCa) accounted for 59.5 % (44 cases) of the study participants, followed by urinary bladder cancer (BC) (25 cases representing 33.8 %) and Renal Cell

Carcinoma (RCC) (5 cases representing 6.7 %). Thirteen patients (17.6%) were proven to have bone metastases, whereas 61 patients (82.4%) did not prove to have metastatic osseous metastases, as demonstrated in **Table 1**.

Interpretation of PBS and SCT:

Table 2 demonstrates the distribution of lesion interpretation in PBS and SCT. Sixteen patients were interpreted equivocal in PBS, whereas two in SCT. Twelve patients were falsely interpreted as positive in PBS; they showed benign lesions or degenerative changes confirmed by follow-up, tumor markers, or other imaging modalities. Two patients were falsely diagnosed as positive in both PBS and SCT, one of them with prostatic carcinoma had advanced arthritic changes of the right hip which falsely interperted postiive at both PBS and SCT whereas based on the follow-up bone scan, tumor markers and ^{18}F-Prostatic specific membranous antigen (PSMA) scan it was proved to be arthritis as shown in **Figure 1**. Another patient was falsely interpreted as positive at PBS and SCT; however, based on follow-up, tumor markers, and diagnostic CT, it was proven to have a benign traumatic nature. Five patients were falsely interpreted as negative in PBS; three of them were falsely interpreted as having benign degenerative spine lesions, one had multiple lytic bone lesions from renal cell carcinoma, and another patient was falsely interpreted as having a benign traumatic rib lesion. All of these five patients were interpreted as truly positive in SCT, one of them is illustrated in **Figure 2**.

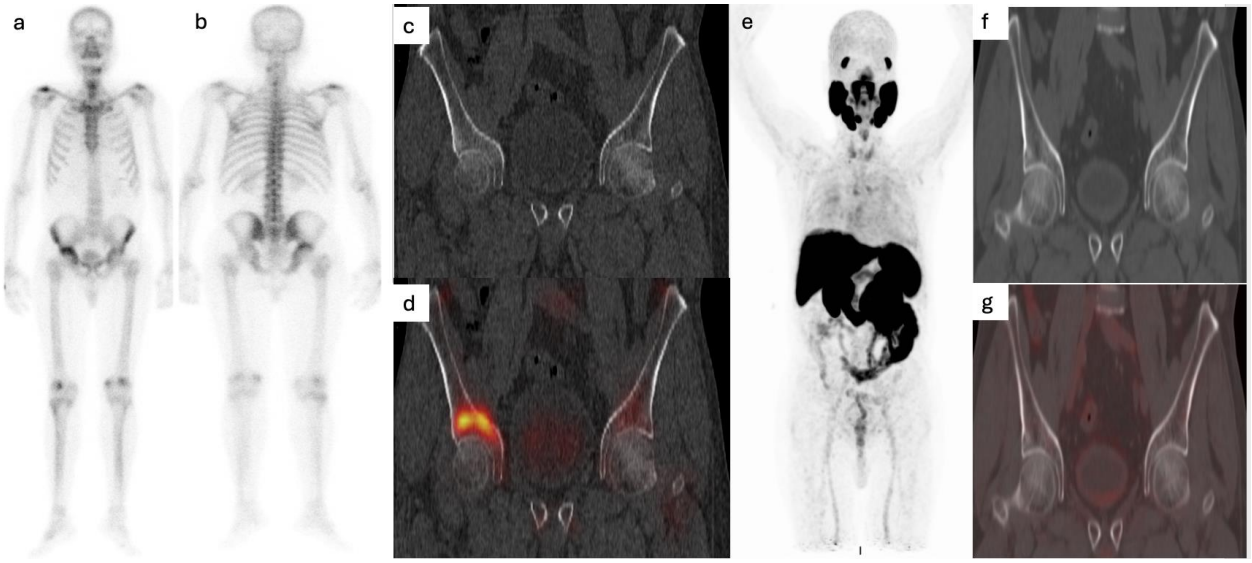

Figure 1: A 63-year-old male patient has a history of Prostate Ca., referred for metastatic workup. **A, B** images illustrated anterior, and posterior views of PBS which revealed equivocal osseous lesion at the right acetabulum, score 2. C, D, images illustrated CT and SPECT/CT coronal views of the pelvis equivocal osseous lesion at the right acetabulum, score 2. **E** Maximum intensity projection (MIP) image illustrated 18-F PSMA PET/CT study which revealed no active bone deposits. **F, G** images illustrated CT and PET/CT coronal views of the 18-F PSMA PET/CT with no active osseous lesion at the right acetabulum. Further correlation with MRI confirmed the absence of metastatic osseous deposits at the pelvis. Final impression of this case (after correlation with clinical data) was negative with arthritic changes of the right hip joint.

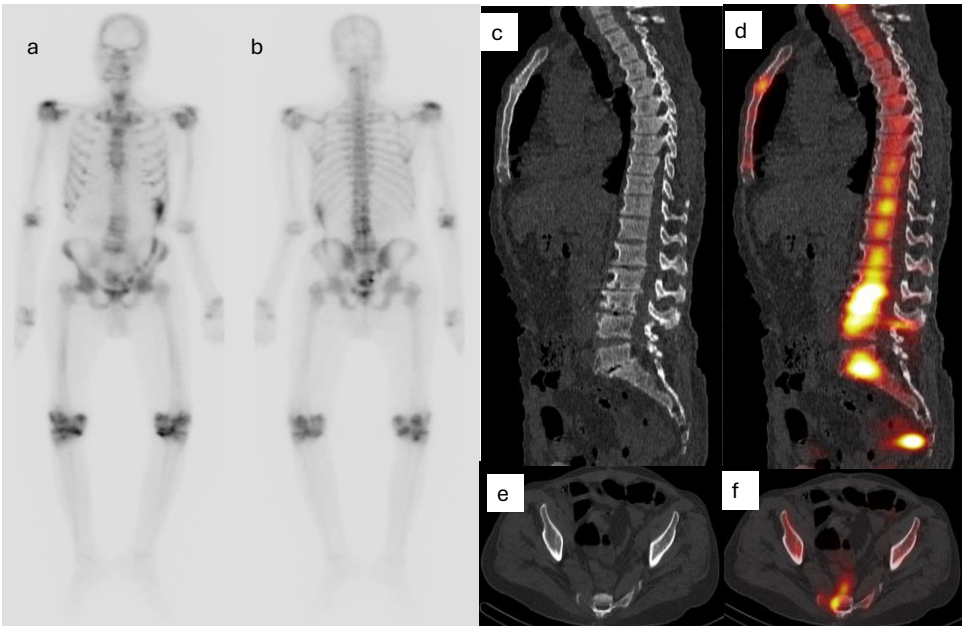

Figure 2: A 69-year of Protest Ca, referred for metastatic workup.

A, B images illustrated anterior, and posterior views of PBS which revealed benign lesions in ribs, and spine, score 1 **C, D**, images illustrated SPECT/CT, and CT sagittal views of the spine revealed degenerative changes more pronounced at the lumbar spine, score 1. E, F images illustrated SPECT/CT, and CT axial view of the pelvis revealed an active osseous lesion at the sacrum associated with lytic lesion and soft tissue component, score 3. Further correlation with MRI confirmed the presence of metastatic deposit at the sacrum.

SCT allowed upstaging, increasing the probability of metastatic nature of the bone lesions in 9 patients (12.2 %), who were falsely diagnosed as negative in PBS. SCT also allowed downstaging, reducing the probability of metastatic nature of the bone lesions in 12 patients (16.2 %), which were falsely interpreted as positive in PBS. In contrast, no changes in diagnosis occurred in the rest of the study participants **Table 2**.

Table 2: Interpretation of PBS, and SCT in all patients, and prostate Cancer patients.

	All patients (N =74)		Prostate Cancer (N = 44)	
	PBS	SCT	PBS	SCT
Scan interpretation				
1- Negative	14	17	8	8
2- Benign	38	42	23	26
3- Equivocal	16	2	8	2
4- Malignant	6	13	5	8
Final diagnosis regarding presence of absence of metastatic lesions				
5- TP	8	13	6	8
6- FP	14	2	7	2
7- TN	47	59	29	34
8- FN	5	0	2	0

Diagnostic performance of PBS and SCT

SCT showed significantly higher sensitivity, specificity, PPV, NPV, and accuracy compared to PBS (100% versus 61.54%, 96.7% versus 77.05%, 86.67% versus 36.36%, 100.00% versus 90.38% and 97.03% versus 74.03%; p = 0.014, 0.001, 0.002, 0.014, and 0.010 respectively) as illustrated in **Table 3, and Figure 3**.Regarding the most frequent cancer type (PCa), SCT showed higher sensitivity, specificity, PPV, NPV, and accuracy compared to PBS (100 % versus 75%, 94.44 % versus 80.56 %, 80 % versus 46.15%, 100% versus 93.55, and 95.45 % versus 79.55, respectively). However, these differences did not reach significant levels (p = 0.143, 0.077, 0.113, 0,149, and 0.251), as shown in **Table 3 and Figure 3.**

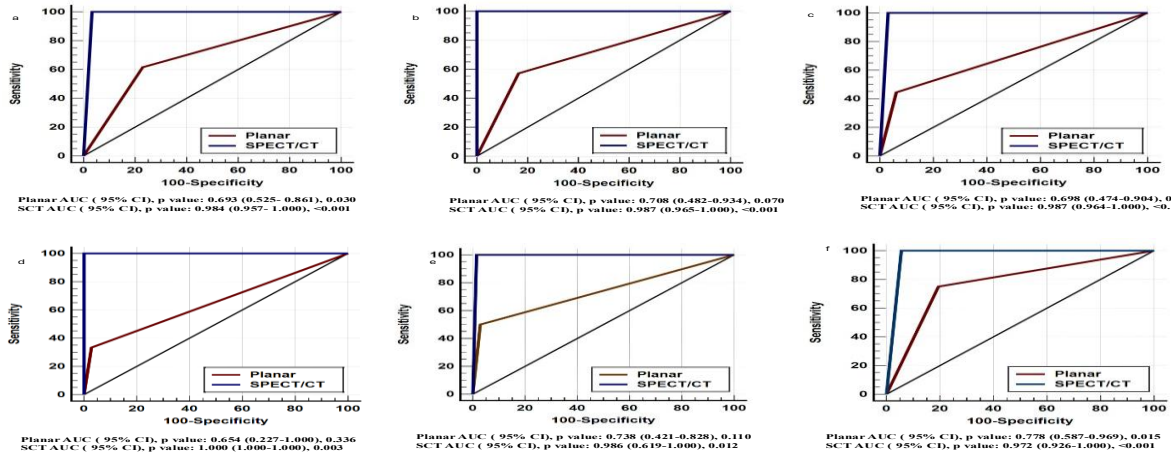

Figure 3: Roc curve for PBS in comparison to SPECT/CT in all cancer types (a), spine (b), pelvis (c), extremities (d), thoracic cage (e), and Prostate Ca. (f)

Table 3: Diagnostic performance of PBS and SCT in all patients, and in Prostatic carcinoma

	Total cases (N =74)		*P value*	Prostate Cancer (N=44)		*P value*
	PBS	SCT		PBS	SCT	
Sensitivity (95% CI)	61.54% (31.58% - 86.14%)	100.00% (75.29% - 100.00%)	**0.014**	75.00% (34.91% - 96.81%)	100.00% (63.06% - 100.00%)	0.143
Specificity (95% CI)	77.05% (64.50% - 86.85%)	96.72% (88.65% - 99.60%)	**0.001**	80.56% (63.98% - 91.81%)	94.44% (81.34% - 99.32%)	0.077
PPV (95% CI)	36.36% (23.34% - 51.74%)	86.67% (62.45% - 96.21%)	**0.002**	46.15% (28.29% - 65.06%)	80.00% (50.99% - 93.90%)	0.113
NPV (95% CI)	90.38% (82.34% - 94.99%)	100.00% (93.94% - 100.00%)	**0.014**	93.55% (81.20% - 97.99%)	100.00% (89.72% - 100.00%)	0.149
Accuracy (95% CI)	74.32% (62.84% - 83.78%)	97.30% (90.58% - 99.67%)	**0.010**	79.55% (64.70% - 90.20%)	95.45% (84.53% - 99.44%)	0.251

Site-based analysis:

SPECT/CT showed significantly higher specificity, PPV, and accuracy in the spine than PBS (100% versus 83.58%, 100% versus 26.67 %, 100% versus 81.08%, p = <0.001, 0.001, 0.049, respectively). SPECT/CT of the spine showed higher sensitivity and NPV but did not reach a significant level (100% versus 57.14%, and 100% versus 94.92 %; p = 0.059 and 0.062, respectively). SPECT/CT of the pelvis showed significantly higher sensitivity and accuracy than PBS (100% versus 44.44%, 97.30% versus 87.84 %, p = 0.010, 0.049, respectively). However, there was no significant difference in specificity, PPV, and NPV (p= 0.406, 0.151, 0.062, respectively). There was no statistically significant difference in the sensitivity, specificity, PPV, NPV, or accuracy between PBS and SPECT/CT in the extremities (33.33% versus 100.00%, 97.18% versus 100.00%, 33.33% versus 100.00%, 97.18% versus 100%, and 94.59% versus 100% in PBS and SPECT/CT, p = 0.113, 0.822, 0.113, 0.149, and 0.251, respectively) and thoracic cage (50% versus 100%, 97.14% versus 98.57%, 50% versus 80%, 97.14% versus 100%, and 94.59% versus 98.65% in PBS versus SPECT/CT, p=0.126, 0.077, 0.371, 0.155, and 0.216, respectively). In the pectoral girdle, since one patient had a confirmed positive lesion detected by SPECT/CT, not by PBS, the significance level between SPECT/CT and PBS could not be determined.

DISCUSSION:

BM often complicates genitourinary cancers, including prostate, urinary bladder, and renal carcinoma [(2)]. Diagnosis of BM is a requisite for staging, prognosis, and determining treatment plans that could lower morbidity and death [(9)]. The median survival time after detection of bone metastases varies by cancer type: 12-53 months in Prostate Ca., 12 months in RCC, and 6-9 months in

urinary bladder [10]. In clinical practice, PBS is a valuable method for diagnosing BM. Advances in SPECT/CT scanners enable the performance of more than one-bed position, improving the sensitivity and specificity of BPS, especially in the axial skeleton [8]. Spine, shoulders, and pelvic girdle are the most common sites of bone metastasis [11]. In the present study, we aimed to compare the diagnostic performance of PBS and SCT in detecting BM in urogenital cancers.

Additionally, we aimed to identify sites that SPECT/CT could better assess. We did not intend to count more metastatic lesions or sites; therefore, we included only patients with equivocal scan findings or no evidence of definite metastatic lesions in PBS. We interpreted both imaging modalities based on four classifications ranging from free to metastatic. Equivocal lesions were considered positive, as equivocal scan findings usually warrant greater attention and necessitate correlation with other diagnostic modalities. In our study, SCT showed higher sensitivity, specificity, and accuracy than PBS (100% versus 61.54%, 96.7% versus 77.05%, and 97.03% versus 74.03%; p = 0.014, 0.001, and 0.010, respectively). Our results also showed higher diagnostic performance in the pelvis and spine than in other examined regions. Many research studies investigated the performance of SCT, either as an additive to PBS or as a direct comparison to PBS [8,12].

Fleury et al. examined the additive benefit of SCT over PBS in breast cancer (BC) and Prostate Ca. In their analysis, PBS showed 67 equivocal results versus 6 in SCT; SCT allowed better characterization of indeterminate PBS findings [13]. Our results are in line with their conclusions; SCT showed a lower number of equivocal findings compared to PBS (2 versus 16, respectively). Another study by **Guezennec et al.** compared the diagnostic performance of adding SCT versus single-bed SPECT/CT; their analysis revealed that more lesions were detected in SCT. However, these findings did not impact the patient's diagnosis [16]. Moreover, a systematic review and meta-analysis concluded 11 research studies (1611 patients); their analyses revealed

that whole-body SPECT/CT (WB SPECT/CT) showed significantly higher sensitivity and specificity than PBS. However, there was no significant increase in specificity when considering negative PBS findings [14]. Our results globally support their finding that SCT showed higher performance compared to PBS. **Palmedo et al.** explored the added value of trunk SPECT/CT over PBS in 308 patients with Bladder Ca. and Prostate Ca. Their results demonstrated the significantly higher specificity of SPECT/CT than PBS in BC, but not in Prostate Ca. In the sub-analysis of Prostate Ca., SPECT/CT correctly excluded metastasis in 14/44 patients with suspicious lesions in PBS, while no upstaging was done by SPECT/CT [15]. Similarly, our results did not reveal significant differences in sensitivity, specificity, and accuracy in Prostate Ca. However, we have interesting findings in two cases falsely interpreted negatively at PBS (one of them is shown in Figure 2). Similar interesting findings were recently published in 2023; SEPCT/CT of the pelvis showed definite metastatic osseous lesions in the pelvis and lumbar regions, which cannot be caught in PBS [17]. Further studies focusing on prostatic cancer patients, including a larger sample size, would be encouraged. To our knowledge, no studies have analyzed in-depth the site-based performance of SPECT/CT over PBS in urogenital malignancies. Our results revealed the higher performance of SPECT/CT over PBS in the spine and pelvis; however, there was no significant difference regarding the extremities and thoracic cage. Finally, our findings come with multiple potential limitations. First, we included only patients with equivocal or negative PBS findings, which led to a small proportion of patients with bone lesions, which may affect the study's statistical power. Future research that enrolls patients irrespective of their PBS should be encouraged. Second, heterogeneity of study participants, including tumors with distinctive metastatic behavior; PBS has a low sensitivity in detecting osteolytic osseous lesions in renal cell carcinoma but high sensitivity in detecting sclerotic bone

lesions in prostatic carcinoma. Therefore, we encourage future studies focusing on a specific tumor type that could benefit from SPECT/CT. Third, the heterogeneous approach was used to establish the final diagnosis. Standardization of follow-up methods is encouraged in future research. Fourth, we included the patients regardless of their prior management, disease duration, and histopathological subtypes. Future research that recruits only patients at a particular time of diagnosis would strengthen the interpretation of findings.

CONCLUIONS:

SPECT/CT showed relatively higher diagnostic performance than PBS in urogenital malignancies in the spine and pelvic regions. However, other sites, including the pectoral girdle, extremities, and thoracic cage, SPECT/CT did not significantly detect bone metastases. We suggest omitting SPECT/CT for sites other than the pelvis and spine to save time and resources. However, these findings require larger sample sizes to accurately determine which site could benefit from adding SPECT/CT.

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