Clinical value of the threshold derived from bone single-photon emission computed tomography/computed tomography in differentiating sternoclavicular arthritis

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Abstract
Objective: With the recent improvements in the quantitative accuracy of single-photon emission computed tomography (SPECT)/computed tomography (CT), the value of using standardized uptake value (SUV) in bone SPECT/CT for quantitative assessment has been reported. We established a threshold for inflamed and normal areas of the sternoclavicular joint and examined the clinical value of bone SPECT/CT. **Subjects and Methods:** The threshold between the inflamed and normal areas of the sternoclavicular joint was initially calculated. The diagnostic performance of the calculated threshold was subsequently compared with the visual assessment of the whole-body image. The clinical value of the threshold was examined in cases of ambiguous visual assessment and a sub-analysis with pustuloticarthro-osteitis (PAO) patients was done. **Results:** The threshold between the inflamed and the normal area in the 93 sternoclavicular joints of 51 patients was 4.46. The area under the ROC curve (AUC), accuracy, sensitivity, and specificity of SUVmax for differentiating sternoclavicular arthritis were 0.92, 0.86, 0.88, and 0.85, respectively. Similarly, the AUC of visual assessment were 0.87, and the difference was not significant (P=0.11). In 25 patients with PAO, the AUC, accuracy, sensitivity, and specificity of SUVmax were 0.94, 0.90, 0.96, and 0.84, respectively with a significant higher AUC of visual assessment (0.82, P=0.032). Furthermore, for cases where there was ambiguous uptake upon visual assessment, the accuracy, sensitivity, and specificity of SUVmax were 0.84, 1.00, and 0.71, respectively, which was useful to judge regarding the initiation of treatment. **Conclusion:** Quantitative assessment using SUVmax and the threshold found using bone SPECT/CT for the presence of sternoclavicular arthritis is clinically useful and can be a useful tool for the initiation of treatment, especially in PAO patients.

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Introduction

Recent advances in the integration of computed tomography (CT) for attenuation correction together with a sophisticated reconstruction technique have enabled the use of single-photon emission computed tomography (SPECT)/CT for obtaining quantitative measurements suitable for derivation of the standardized uptake value (SUV) [1-3]. In fact, the usefulness of quantitative assessment using SUV in bone SPECT/CT has been reported [4-11].

We conducted a quantitative bone SPECT/CT examination for cases with arthritis in our institution. In this study, we focused on the sternoclavicular joint and established threshold values for inflamed and normal regions of the sternoclavicular joint. Pustuloticarthro-osteitis (PAO) is a disease that causes pain and inflammation of the anterior thoracic joint [12-14]. The sternoclavicular and sternocostal joints, pelvis, vertebra, hip, and long bones are typically affected. Treatment is initiated if inflammation is observed in any of these joints.

Bone scintigraphy (BS) is a common test used to determine the presence of arthritis throughout the whole body. However, the uptake of BS is visually ambiguous, resulting in difficulties in differentiating sternoclavicular arthritis and deciding whether to initiate treatment or not. We hypothesized that the threshold between inflamed and normal areas may be a criteria for differentiating sternoclavicular arthritis and initiating treatment in such cases, and we examined the clinical value of this threshold.

Subjects and Methods

Patients

A retrospective analysis of 51 patients (14 males, 37 females; aged, 52.6±13.8 years; body weight of 59.4±11.5kg [mean±standard deviation (SD)]) who underwent bone SPECT/CT examinations was performed. These patients were suspected with sternoclavicular joint inflammation due to anterior thoracic pain and (or) sternoclavicular arthritis and (or) elevated C-reactive protein. The study protocol received approval from the institutional review board of our hospital (no. 3144).

Gold standard as a rule

The gold standard rules were determined by an experienced rheumatologist based on information from the medical records, physical examination, and diagnostic imaging (magnetic resonance imaging). Cases with inflammation of the sternoclavicular joint were assigned 1 whereas those without inflammation were assigned 0. Cases in which the left and right sides were clinically distinguishable were judged separately, and cases in which the left and right sides were clinically indistinguishable were not.

Bone scintigraphy

Planar BS was performed 3-4h after intravenous administration of technetium-99m-hydroxymethylene diphosphonate (^{99m}Tc-HMDP) at a dose of 555MBq. Immediately after acquisition of a planar image of the whole body, quantitative SPECT/CT images were acquired using a hybrid system, Discovery NM/CT 670 (GE Healthcare, Pittsburgh, Pa). The collimator used was for low energy high resolution.

Computed tomography images were obtained first using the following parameters: tube voltage, 120kV; tube current, 40-80mA with "AutomA" function and noise level of 35; X-rays collimation, 20mm (16×1.25mm); table speed, 55mm/s; table feed, 27.5mm/rotation; tube rotation time, 0.5s; pitch, 1.375:1; and matrix, 512×512. Computed tomography images were reconstructed into 3.75-mm-thick sections using an adaptive statistical iterative reconstruction algorithm (ASiR; GE Healthcare). Single photon emission computed tomography images were acquired based on the following parameters: energy peak, 140.5KeV with a 7.5% window (130-151KeV); step-and-shot mode acquisition (15s/step, 60 steps/detector) with 6°angular increments, and a body contour scanning option. The extra window for scatter correction was set at 120KeV with a 5% window (114-126KeV). Single photon emission computed tomography images were reconstructed using an ordered subset expectation maximization iterative algorithm (ten iterations, ten subsets) with CTAC, scatter correction, and resolution recovery applied using the vendor-supplied software package (GENIE Xeleris; GE Healthcare). A post-reconstruction filter (Gaussian filter at full-width and half-maximum [11.05mm] along the x-, y-, and z-directions) was applied. Reconstructed images were set at a matrix of 128×128, with a section thickness of 4.42mm and zoom factor of 1.0.

Image analysis

Quantitative analysis software was delineated using the commercially available GI-BONE software package (AZE Co., Ltd., Tokyo, Japan) by an experienced radiologist [9, 11]. Figure 1 is a diagram of the volume of interest (VOI) set up using GI-BONE. Data were obtained using the manual VOI installation function of the GI-BONE. Uptake values were extracted by setting a threshold of 40% or greater of the SUVmax in the VOI at the bilateral sternoclavicular joint, then SUVmax was calculated. The maximum concentration in the target lesion (maximum radioactivity/voxel volume)/(injected radioactivity/body weight) was used to define SUVmax.

The whole-body image of the BS was subjected to a 5-point visual assessment scoring system by the same radiologist. The scoring method was as follows: 1, no obvious uptake; 2, probably no uptake; 3, ambiguous uptake; 4, probably with uptake; 5, obvious uptake.

Moreover, we evaluated the accuracy, sensitivity and specificity of the use of the threshold method on cases with a visual assessment score of 3 on whole-body images. The aim was to assess the clinical usefulness of the threshold in cases where thevisual assessment is ambiguous, i.e., where the decision to start treatment is difficult.

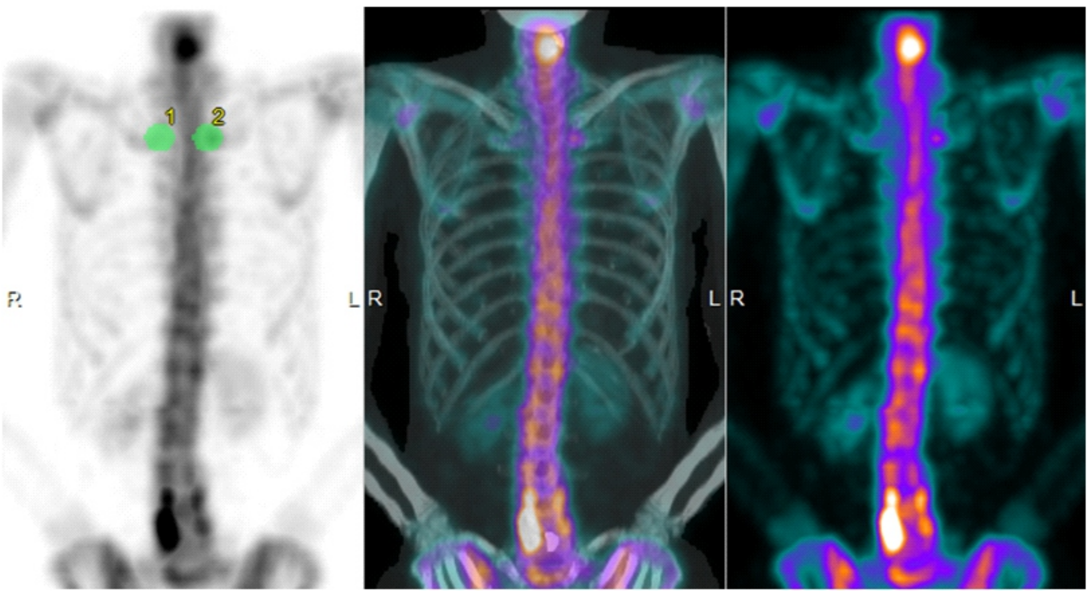

Figure 1. VOI setting method using GI-BONE. Nuclear medicine imaging (green indicates set VOI) (left). SPECT/CT fusion image (middle). Nuclear medicine image (right).

Statistical analysis

Maximum SUV of the two groups according to the rules of the gold standard were plotted as a sensitivity–specificity curve. The cut-off point was determined by the receiver operating characteristic (ROC) curve and the Youden index [15]. The visual assessment score and the calculated SUVmax for area under the ROC curve (AUC) were compared with the ROC curve. In cases where the left and right sides were indistinguishable, the region with the higher SUVmax was used. The JMP14 software package (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses.

Results

All subjects

The patients' characteristics are shown in Table 1. The total number of measurements was 93 (1; 34, 0; 59) since the left and right sides were clinically indistinguishable in 9 cases. The mean SUVmax of 34 inflamed and 59 normal sternoclavicular joints were 8.57±5.15 (range 2.61~28.38) and 3.61±1.14 (range 1.74~7.35), respectively. The ROC curve of SUVmax in 51 patients with and without sternoclavicular joint inflammation is shown in Figure 2. The threshold and the AUC were 4.46 and 0.92, respectively. Additionally, accuracy, sensitivity, and specificity were 0.86, 0.88, and 0.85, respectively. The ROC curve comparing SUVmax and visual assessment is shown in Figure 3. The AUC of SUVmax and the visual assessment were 0.92 and 0.87, respectively, with a difference that was not significant (0.05; P=0.11).

Visual assessment showed the numbers of score 1/2/3/4/5 were 17/13/29/17/17. Table 2 shows the results of the threshold diagnosis in 29 cases where the visual assessment score was 3. The mean SUVmax of 10 inflamed and 19 normal sternoclavicular joints were 5.33±1.39 (range 4.19~9.09) and 3.89±0.75 (range 2.49~5.39), respectively. The accuracy, sensitivity, and specificity of SUVmax for differentiating sternoclavicular arthritis using SUV threshold of 4.46 were 0.72, 0.70, and 0.73, respectively.

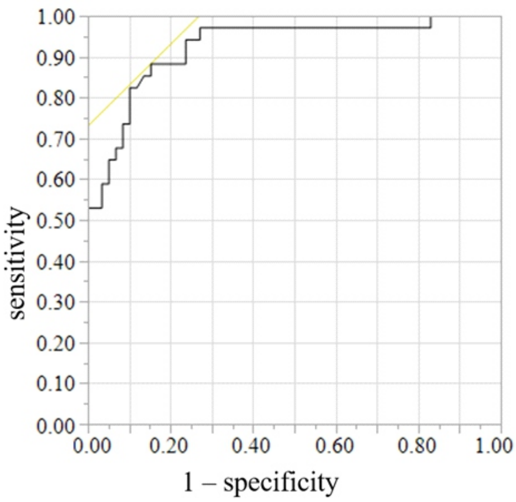

Figure 2. Receiver operating characteristic (ROC) curve of SUVmax in 51 patients with and without inflammation of the sternoclavicular joint.

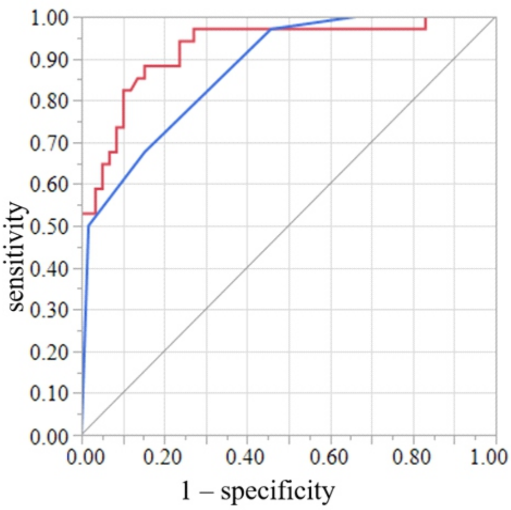

Figure 3. ROC curve comparing SUVmax and visual assessment on whole-body image in 51 patients. The red line is the curve of SUVmax. The blue line is the curve of the visual assessment score on whole-body image.

PAO patients

A subanalysis of 25 patients with PAO was done. The total number of measurements was 44 (1; 25, 0; 19) since the left and right sides were clinically indistinguishable in 6 cases. The mean SUVmax of 25 inflamed and 19 normal sternoclavicular joints were 9.19±5.68 (range 2.89~28.38) and 3.65± 0.60 (range 2.22~5.14), respectively. The ROC curve of SUVmax in patients with and without inflammation of the sternoclavicular joint is shown in Figure 4. The threshold and AUC were 4.19 and 0.94, respectively. Additionally, accuracy, sensitivity, and specificity were 0.90, 0.96, and 0.84, respectively. Similarly, the ROC curve comparing SUVmax and visual assessment on whole-body image is shown in Figure 5. AUC of SUVmax and visual assessment were 0.94 and 0.82, respectively, which had a significant difference of 0.12 (P=0.032).

Visual assessment showed the numbers of score 1/2/3/4/5 were 3/5/13/9/14. Table 3 shows the results of the threshold diagnosis in 13 cases where the visual assessment score was 3. The mean SUVmax of 6 inflamed and 7 normal sternoclavicular joints were 5.45±1.69 (range 4.19~9.09) and 3.94±0.64 (range 3.18~5.14), respectively. Accuracy, sensitivity, and specificity of SUVmax for differentiating sternoclavicular arthritisusing SUV threshold of 4.19 were 0.84, 1.00, and 0.71, respectively.

Table 1. *Patients' characteristics (n=51).*

Diagnosis	No (%)
PAO	25 (49)
Arthritis associated with IBD	3 (6)
CRMO	2 (4)
AS	2 (4)
BD	1 (2)
DISH	1 (2)
Unclassifiable arthritis	1 (2)
No abnormality	16 (31)

PAO; pustuloticarthro-osteitis, IBD; inflammatory bowel disease, CRMO; chronic recurrent multifocal osteomyelitis, AS; ankylosing spondylitis, BD; Behçet's disease, DISH; diffuse idiopathic skeletal hyperostosis

Table 2. *Diagnostic results using thresholds in cases with a visual assessment score of 3 (n=29).*

		Sternoclavicular arthritis	
		Positive	Negative
SUVmax	Positive	7	5
	Negative	3	14

SUVmax; maximum standardized uptake value

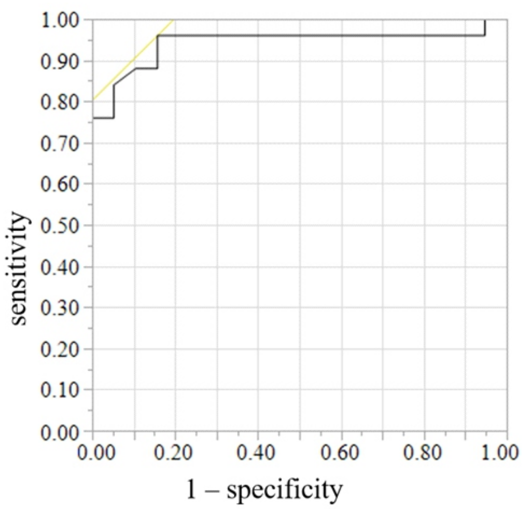

Figure 4. ROC curve of SUVmax in 25 PAO patients with and without inflammation of the sternoclavicular joint.

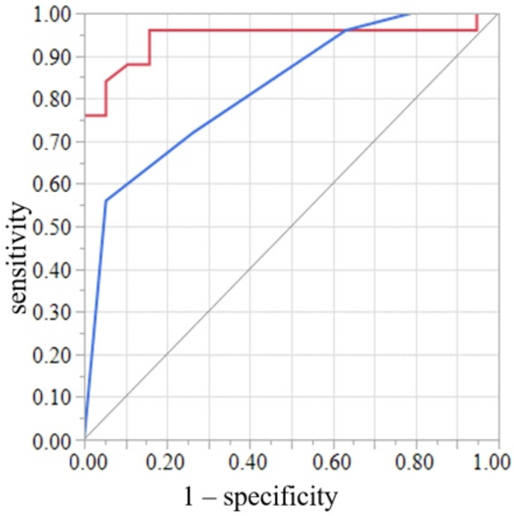

Figure 5. ROC curve comparing SUVmax and visual assessment on whole-body image in 25 PAO patients. The red line is the curve of SUVmax. The blue line is the curve of the visual assessment score on whole-body image.

Table 3. *Diagnostic results using thresholds in cases with a visual assessment score of 3 restricted to patients with PAO (n = 13).*

		Positive	Negative
SUVmax	Positive	6	2
	Negative	0	5

SUVmax; maximum standardized uptake value

Discussion

The present findings show the clinical usefulness of quantitative assessment using a SUVmax threshold in the presence of inflammation in the sternoclavicular joint using bone scintigraphy. Especially in patients with PAO, quantitative assessment using SUVmax showed significantly better diagnostic performance than the traditional visual assessment. In addition to the visual assessment of qualitative images, quantitative assessment using SUVmax allows a more accurate diagnosis. Although cases showing the equivocal visual assessment result in difficulties in deciding on the strategy for treatment in clinical setting, quantitative assessment using SUVmax may be useful to judge regarding the initiation of treatment.

Gamma camera imaging has been traditionally used in nuclear medicine for two-dimensional planar imaging, such as bone scintigraphy with ^{99m}Tc diphosphonates. Single photon emission computed tomography/CT generates imaging voxels, denoted as units of radioactivity per volume (i.e., kBq/mL), by using results of robust algorithms of CT-based three-dimensional attenuation correction, scatter correction, and resolution recovery. That is fundamentally different from planar scintigraphy, SPECT, and non-quantitative SPECT/CT, traditional nuclear imaging methods, which utilize counts per second for imaging units. Lesion radioactivity can be normalized for injected radioactivity with quantitative SPECT/CT, thus providing quantitative parameter values, such as percent injected dose and SUV [1-3]. In both phantom (error <3.6%) and patient (error <1.1%) studies, Zeintl et al. (2010) [1] reported that advanced SPECT/CT technology facilitated quantitative ^{99m}Tc SPECT imaging with excellent accuracy. Also, in a phantom study, Gnesin et al. (2016) [3] found that both absolute activity and activity concentration determined with quantitative ^{99m}Tc SPECT/CT were within 10% of expected values.

In the past, several groups have evaluated the threshold of SUVmax in differentiating bone metastases [5, 7, 8, 10]. Kuji et al. (2017) [5] evaluated normal vertebral body, skeletal degenerative change, and bone metastasis SUV obtained in analyses of 170 prostate cancer patients undergoing bone SPECT/CT with ^{99m}Tc-MDP. Their results showed SUVmax values of 7.58±2.42 for thoracic normal and 8.12±2.24 for lumbar normal vertebral bodies, and 16.73±6.74 for skeletal degenerative changes and 40.90±33.46 for bone metastasis. That for the bone metastasis group was significantly greater as compared to the other three groups (P<0.001). In ROC analyses performed to demonstrate the diagnostic accuracy of SUVmax for discrimination of bone metastasis from skeletal degenerative changes in hot foci, in patient-based mode the area under the ROC curve was 0.840, while that was 0.932 in lesion-based mode. Umeda et al. (2018) [7] established a threshold value between bone metastatic and non-bony metastatic lesions in 61 prostate cancer patients with bone metastases and 69 without bone metastases in order to calculate total bone uptake in nine prostate cancer patients undergoing radium-223 therapy and ROC analysis revealed the threshold of SUVmax was 7.0. Using quantitative skeletal SPECT/CT with ^{99m}Tc-DPD, Tabotta et al. (2019) [8] analyzed 264 areas of bone metastasis in 26 prostate cancer patients, as well as 24 spinal and pelvic osteoarthritic lesions in 13 patients without cancer and reported a mean SUVmax value of 34.6±24.6 for bone metastasis, as compared to 14.2±3.8 for spinal and pelvic osteoarthritic lesions, with the value for the osteoarthritic group significantly higher (P<0.0001). Using a SUVmax cut-off of 19.5 for prostate cancer bone metastases in the spine and pelvis, sensitivity and specificity were 87% and 92%, respectively. Rohani MFM et al. (2020) [10] evaluated SUVmax of normal vertebra, degenerative joint disease (DJD), and metastatic bone lesions in 34 prostate cancer patients. The mean SUVmax for normal vertebrae was 7.08±1.97, 12.59±9.01 for DJD and 36.64±24.84 for bone metastases. The cut-off SUVmax value ≥20 gave a sensitivity of 73.8% and specificity of 85.4% in differentiating bone metastases from DJD. To our knowledge, there have been no reports of evaluating the threshold of SUVmax in differentiating sternoclavicular arthritis.

This study has some limitations, including the small subject population. In addition, histological confirmation for sternoclavicular arthritis is lacking. However, it would have been unethical to investigate sternoclavicular arthritis using invasive procedures and that is not undertaken in the clinical setting.

In conclusion, quantitative assessment using SUVmax and threshold in bone SPECT/CT for the presence or absence of inflammation in the sternoclavicular joint is clinically useful and can be a helpful tool in making decisions regarding the initiation of treatment, especially in PAO patients.

The authors declare that they have no conflicts of interest.

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