Original Article

Ultrasonographic Classification of Subcutaneous Edema Caused by Infusion via Peripheral Intravenous Catheter

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Abstract
Background: Our aim in this study was to determine the ability of ultrasonography (US) to assess and classify the degree of subcutaneous edema caused by infusion via peripheral intravenous catheter, compared to assessment by the Infusion Nurses Society infiltration scale.
Methods: This prospective study included 64 adult patients who underwent infusion via peripheral intravenous catheter. All patients underwent US imaging of the subcutaneous tissue just after the insertion of indwelling catheters and just before catheter removal. The grade of swelling was then assessed using the infiltration scale. Subcutaneous edema and edema thickness were analyzed on transverse US images, and the edema was classified as normal, mild, or severe. The relationship between US-determined subcutaneous edema and that determined by the infiltration scale was evaluated.
Results: Among the 64 patients, US images of the subcutaneous edema were classified into three groups: normal in 15 patients, mild subcutaneous edema in 41 patients, and severe subcutaneous edema in eight patients. Thus, US classification of subcutaneous edema could provide more detailed information than the infiltration scale.
Conclusion: The results of the present study suggest that US imaging of subcutaneous tissue could help classify the degree of subcutaneous edema.

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Peripheral intravenous catheters (PIVCs) are widely used in clinical practice for the infusion of drugs and the administration of parenteral nutrition [1–3]. However, there are several recognized complications of PIVC placement such as thrombophlebitis, infiltration, and extravasation [4–6]. Healthcare providers must recognize the early signs of these complications (e.g., swelling, redness, and pain) to minimize tissue damage [7]. In particular, chemotherapeutic extravasation should be detected at an early stage because locally infiltrated solutions can cause skin necrosis and serious tissue damage [8]. Infiltration has been defined as swelling at the insertion site, based on the infiltration scale of the Infusion Nurses Society (INS) [3]. However, it is difficult to evaluate the initial changes at an early stage when using the infiltration scale [9].

Ultrasonography (US) is applied widely in the clinical field because of its safety, speed, absence of radiation exposure, and real-time observation [10,11]. In particular, US allows clear visualization of the peripheral veins for improved diagnostic imaging [12]. It can be used to observe tissues surrounding PIVCs in peripheral veins. US can also be used to measure subcutaneous fat thickness [13]. Thus, US can detect subcutaneous edema caused by intravenous infiltration [10]. However, there is little available information on the sonographic visualization of tissues surrounding the PIVC insertion sites.

Our aim in the present study was to examine the ability of US to assess and classify subcutaneous edema of tissues surrounding the PIVC placement site and to compare the US results with those of the INS infiltration scale, especially the initial changes.

Materials and Methods

Patients and setting

The participants in this study were patients who were admitted to the medical ward of a university hospital from January 2014 to June 2014 and who had been treated via PIVCs. Exclusion criteria were patients on chemotherapy, patients younger than 20 years, catheter insertion in veins other than those of the forearm, patients who had no approval from their attending physician, and patients with a low cognition level. All PIVCs had been inserted and maintained in accordance with the policies of the facility and clinically indicated catheter removal. Infusions were delivered via ethylene tetrafluoroethylene catheters (Surshields Surflo2; Terumo Corporation, Tokyo, Japan), which were typically inserted 19–32 mm in the forearm vein. The Research Ethics Committee of the Graduate School of Medicine and Faculty of Medicine at the University of Tokyo (Tokyo, Japan) approved the study protocol (approval number, 10348). Written informed consent to participate in the study was obtained from all patients or their families. All participants were free to retract their consent at any time and were encouraged to report any pain or discomfort during the US examination.

US scanning technique

All patients underwent real-time US imaging of the subcutaneous tissue just after the insertion of the indwelling catheter and just before catheter removal. US was performed without graded compression to obtain transverse scans when the clinical conditions allowed it. US imaging problems associated with vein disfiguration caused by pressure from the transducer can be improved by techniques such as soft placement of the transducer on the US gel (Aquasonic100; Parker Laboratories, Inc., Fairfield, NJ, USA) or the use of gel pads (Sonar Pad; Nippon BXI, Inc., Tokyo, Japan) on the arm. The positions of the PIVC tips were included as the anatomic landmarks to identify the starting point of US scanning.

US diagnostic equipment (Hitachi Aloka Medical, Ltd., Tokyo, Japan) was used with linear-array transducers (5–18 MHz). We performed US imaging with a focal range and image-depth thickness of 1.5–2 cm to determine the correct display range. The echo gain was set at 25 and the dynamic range at 65. Two researchers with sufficient US training performed all sonographic examinations in this study (1 of the 2 researchers performed the examination on each patient).

Data analysis

Just before catheter removal, the severity of swelling was classified according to the INS infiltration scale: 0, no swelling; 1, edema of < 1 inch; 2, edema of 1–6 inches; Grade 3, edema of > 6 inches [3]. The clinical presentation of subcutaneous edema on transverse US images was defined as follows: (1) normal (N) in which the superficial fascia was clearly confirmed with no thickened subcutaneous fat layer [14]; (2) mild subcutaneous edema (MSE) in which the superficial fascia was confirmed with an unclear layered structure and a thickened subcutaneous fat layer; and (3) severe subcutaneous edema (SSE) in which a thickened subcutaneous fat layer was confirmed by a homogeneous cobblestone appearance in the subcutaneous fat layer, caused by excessive fluid in the interstitium [15,16]. Patients who did not undergo US image evaluation or who had poor-quality images were excluded. A certified sonographer with > 20 years of experience assessed the US images. To ensure inter-rater reliability, a certified sonographer (who provided the reference value) and three independent sonographers evaluated the US images for image interpretation. All images were evaluated under blinded conditions.

Changes in subcutaneous edema thickness (SET) were defined as follows. The SET was first measured as the distance between the posterior echogenic border of the dermis and the anterior echogenic border of the muscular fascia on US images after the insertion of the PIVC and before catheter removal [17]. The difference in SET before catheter removal was then calculated from the SET after the insertion of the indwelling catheter. The US images were finally used to evaluate the relationship between the change in SET and the classification of subcutaneous edema. A single researcher determined the mean of three measurements that was used for calculation of the SET by...
using Image J software (National Institutes of Health free-ware; downloadable at http://imagej.nih.gov/ij/download.html; Figure 1). Test–retest reliability for measuring the depth thickness was investigated using intraclass correlation coefficients (ICCs). The mean ICCs and 95% confidence intervals were calculated from 10 random samplings of US images. The ICC1,1 was 0.95 (0.83–0.99). Thus, the test–retest reliability was nearly perfect.

**Statistical analysis**

The inter-rater reliability for classifying subcutaneous edema (i.e., N/MSE/SSE) using the nonparametric Kendall’s W test (i.e., Kendall’s coefficient of concordance) was assessed for establishing agreement between the certified sonographer and the three researchers. The change in SET was compared between the groups in terms of the subcutaneous edema classification using the Kruskal–Wallis one-way analysis of variance. We used Pearson’s correlation coefficient to evaluate the correlations between the change in SET and the classification of subcutaneous edema. Statistical analyses were performed with SPSS 22.0 software (IBM Corp., Armonk, NY, USA). A value of \( p < 0.05 \) indicated statistical significance.

**Results**

Among the 75 eligible patients, 11 patients were excluded because of insufficient image quality; thus the final analysis consisted of 64 patients (44 men, 20 women; mean age, 68 ± 13.4 years). The average duration for indwelling catheters was 52 hours. Table 1 shows the subcutaneous edema findings, based on the US images and classified by type. The US images of subcutaneous fat were classified as

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**Figure 1** The ultrasound images shows normal findings. (A) The transverse scan shows no subcutaneous edema in tissues surrounding the peripheral intravenous catheter (PIVC) (circle). The high-echo spots indicate the PIVC tip (arrow). (B) The transverse scan image, which is used to measure the depth from the posterior echogenic border of the dermis to the anterior echogenic border of the muscular fascia (double-headed arrow).
N in 15 patients, MSE in 41 patients (Figure 2), and SSE in eight patients (Figure 3).

The results obtained by three independent sonographers (A, B, C) were highly correlated with each other, based on the Kendall W test, which showed A, B, and C had findings of 0.95, 0.83, and 0.84, respectively. There was a slight correlation between the changes in SET and the classification of subcutaneous edema (Pearson’s $r = 0.31; p < 0.05$). Among the three subcutaneous edema groups, changes in SET differed significantly between the N and MSE groups, the N and SSE groups, and the MSE and SSE groups ($p < 0.01$, $p < 0.01$, and $p = 0.01$, respectively).

Table 2 shows the comparison of the INS infiltration scales and the US-classified subcutaneous edema. The INS infiltration scale was Grade 0 for all 15 patients in the N group. Among the 53 patients in the Grade 0 group, subcutaneous edema was identified as MSE in 35 patients and as SSE in two patients. Grades 3 and 4 were not detected in this study.

### Discussion

The present study classified subcutaneous edema as N, MSE, or SSE, based on US images. It also examined the correlation between the changes in SET and the classification of subcutaneous edema. Classification of subcutaneous edema

![Figure 2](image)

**Figure 2**  Mild subcutaneous edema in a 79-year-old man who was hospitalized for duodenal carcinoid. The nurse inserted an indwelling 22-gauge catheter into the peripheral vein. (A) After approximately 2 days without problems, the transverse scan shows the PIVC in the peripheral vein. The superficial fascia clearly indicates no thickening of the subcutaneous fat layer. The PIVC tip shows high-echo lines (arrow). (B) The transverse ultrasonography image of PIVC in the peripheral vein before catheter removal. The superficial fascia has an unclear, layered structure with localization of a thickened subcutaneous fat layer (circle). The PIVC tip shows high-echo lines with edema in the subcutaneous fat layer (arrow).
using US provided more detailed information than classification using the INS infiltration scale. We could classify the degree of subcutaneous edema and identify changes that were undetectable by the INS infiltration scale. For INS Grade 0, US detected SSE in two patients because the INS infiltration grading scale assessed only the size of the swelling.

Magnetic resonance imaging (MRI) can be used for visualizing skin and for detecting generalized subcutaneous edema [18]. However, slight changes in subcutaneous tissue (e.g., MSE) are difficult to detect by MRI [18]. In addition, MRI is unsuitable for frequent use because of its expense and its unsuitability for people with metallic implants such as pacemakers. Suehiro et al [15] reported that using US to classify three types of subcutaneous inflammation allowed them to observe significant changes in subcutaneous tissue because of the severity of extremity lymphedema such as leg edema. Our results indicated that US could precisely visualize subcutaneous edema in the forearm, despite there being only slight edema in surrounding tissues, compared to subcutaneous edema accompanying leg lymphedema.

Lymphedema morphologically increased the thickness of the skin and subcutaneous tissue. A previous study reported

**Table 2** Comparison of the Infusion Nurses Society infiltration scales and classification of the subcutaneous edema in ultrasonographic images (N = 64).

<table>
<thead>
<tr>
<th>Classification of the subcutaneous edema</th>
<th>INS Infiltration scales</th>
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<tr>
<td></td>
<td>Grade 0</td>
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<tr>
<td>Normality</td>
<td>15</td>
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<tr>
<td>Mild subcutaneous edema</td>
<td>35</td>
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<tr>
<td>Severe subcutaneous edema</td>
<td>3</td>
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<tr>
<td>Total</td>
<td>53</td>
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**Figure 3** Severe subcutaneous edema in a 65-year-old man who was hospitalized to undergo cholecystectomy for gastric cancer. The nurse inserted a 22-gauge indwelling catheter into the peripheral vein. (A) After ~2 days without problems, the transverse scan shows the PIVC in the peripheral vein. The superficial fascia has no thickened subcutaneous fat layer. The PIVC tip shows high-echo lines (arrow). (B) The transverse ultrasonography image shows the PIVC in the peripheral vein before its removal. A thickened subcutaneous fat layer is apparent, and fat lobules give a homogeneous cobblestone appearance in the subcutaneous fat layer (circle) with fluid collection in the echo-free space (arrowheads). The PIVC tip shows high-echo lines with edema of the subcutaneous fat layer (arrow).
measuring the subcutaneous tissue thickness by the distance between the posterior echogenic border of the dermis and the anterior echogenic border of the muscular fascia, which was used in the current study [17]. In the current study, US showed a clear significance between changes in the SET and the three subcutaneous edema groups. Thus, changes in SET could indicate initial changes at an early stage in the PIVC placement.

The INS infiltration scale is a widely accepted measurement of infiltration, although it is difficult to evaluate changes at an early stage using this scale [9]. Our results showed that US could detect initial changes in subcutaneous edema that were undetectable using the INS infiltration scale, and thus provide more detailed information. Classification of subcutaneous edema using US images may be an appropriate technique for determining the status of complications. Further studies are planned to investigate the role of US in preventing PIVC placement complications in chemotherapy patients and to determine the value of US as a routine assessment tool [19]. In conclusion, the results of the present study suggest that US imaging of subcutaneous tissue can be used to classify the degree of subcutaneous edema and to identify changes that are undetectable by the INS infiltration scale.

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