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ORIGINAL ARTICLE

Ultrasound features of purulent skin and soft tissue infection without abscess

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Abstract

Purpose Ultrasound (US) aids clinical management of skin and soft tissue infection (SSTI) by differentiating non-purulent cellulitis from abscess. However, purulent SSTI may be present without abscess. Guidelines recommend incision and drainage (I & D) for purulent SSTI, but US descriptions of purulent SSTI without abscess are lacking.

Methods We retrospectively reviewed pediatric emergency department patients with US of the buttock read as negative for abscess. We identified US features of SSTI with adequate interobserver agreement (kappa > 0.45). Six independent observers then ranked presence or absence of these features on US exams. We studied association between US features and positive wound culture using logistic regression models (significance at $p < 0.05$).

Results Of 217 children, 35 patients (16%) had cultures positive for pathogens by 8 h after US and 61 patients (32%) had cultures positive by 48 h after US. We found kappa > 0.45 for focal collection > 1.0 cm ($\kappa = 0.57$), hyperemia ($\kappa = 0.57$), swirling with compression ($\kappa = 0.52$), posterior acoustic enhancement ($\kappa = 0.47$), and cobblestoning or branching interstitial fluid ($\kappa = 0.45$). Only cobblestoning or interstitial fluid was associated with positive wound cultures in logistic regression models at 8 and 48 h.

Conclusions Cobblestoning or interstitial fluid on US may indicate presence of culture-positive, purulent SSTI in patients without US appearance of abscess. Although our study has limitations due to its retrospective design, this US appearance should alert imagers that the patient may benefit from early I & D.

Keywords Ultrasound · Abscess · Skin and soft tissue infection · MRSA · Pediatric emergency care

Introduction

Skin and soft tissue infections (SSTIs) are on the rise and nearly tripled between 1996 and 2005. Between 2000 and 2004, the hospitalization rate for these infections rose by 29% [1]. SSTIs are frequently encountered in the emergency department (ED), where clinicians must differentiate simple non-purulent cellulitis from purulent collections. This distinction is important because purulent and non-purulent infections are treated differently, with incision and drainage (I & D) recommended for purulent collections [2, 3]. Failure to diagnose and appropriately treat a purulent infection may lead to prolonged duration of symptoms or progression of disease, including local spread to deep tissues or bone and systemic spread, leading to bacteremia and sepsis.

Ultrasound (US) is frequently performed to help evaluate SSTI [4]. The sonographic appearance of SSTI varies and has been described as proceeding through several stages, including tissue thickening without pus, tissue disarray without pus, tissue disarray with pus, and tissue disarray with formed abscess [5, 6]. The classical sonographic appearance of soft tissue abscess is widely recognized as a well-circumscribed, hypoechoic fluid collection with peripheral hyperemia [7, 8]. However, a more varied sonographic appearance of SSTI has

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also been described, including isoechoic collections and irregular borders [9]. There is evidence that community-acquired MSRA (CA-MRSA), currently the most prevalent cause of SSTI, may form collections that vary from the classic abscess appearance. CA-MRSA appears more likely to form small, irregular collections [10, 11]. The importance of these collections may be overlooked by physicians and sonographers searching for a well-defined focal fluid collection.

At our institution, we have noticed a number of cases without sonographic findings of abscess, but which are frankly purulent or produce positive cultures upon attempted manual expression or I & D in the ED. We hypothesized that these collections may lack the classical abscess appearance, but may show other signs of purulence that are not commonly recognized as significant. By identifying US features associated with culture-positive SSTI in the absence of classical abscess appearance, we hope to improve detection and treatment of these cases in the ED.

Methods

Our institutional review board (IRB) approved this retrospective cohort study. We included children < 18 years old presenting to our tertiary care pediatric ED with SSTI of the buttock or perineum and US report negative for abscess. We studied only infection of buttocks and perineum because these are the common locations for SSTI in children [11], and it is less prone to other common reasons for US assessment of soft tissue, such as trauma, retained foreign body, or palpable mass. We queried the radiology information system (RIS) using Illuminate® (Softek, Overland Park, KS) for radiology-performed US exams of buttocks or perineum performed between 1/1/2011 and 12/31/2015. Enrolled patients met the following inclusion criteria: age < 18 years, patient location in the ED, and final interpretation negative for abscess. Interpretation was considered negative for abscess if the impression or findings section of the report stated at least one of the following terms: normal, no abscess, cellulitis only, phlegmon, or fluid collection ≤ 1 cm. We defined fluid ≤ 1 cm as negative for abscess because our ED practice is to attempt drainage only if abscess is > 1 cm. We excluded exams performed for indications other than SSTI or if history revealed underlying abnormality. Exclusions were defined as any of the following terms in the exam history or report: trauma, hemophilia, evaluation of genitourinary anomalies, pilonidal cyst or sinus tract, Crohn disease, foreign body, Bartholin gland cyst, recent surgery to the area, follow-up of previously treated abscess, mass, multi-focal abnormalities with at least one site meeting exclusion criteria, and non-diagnostic due to patient agitation. An index case known to most authors was also excluded. Images were not reviewed during inclusion/exclusion process.

Clinical data were collected by chart review and have been previously described [12]. A patient was considered to have a purulent SSTI if a culture collected after US, as defined by time stamps for US completion and culture collection in the electronic medical record (EMR), grew a pathogenic organism. We studied association between US appearance and positive cultures at 8 and 48 h after US. Cultures collected within 8 h are likely to represent SSTI at the time of US, while cultures within 48 h are of interest in the clinical realm, representing cases that may have benefitted from earlier intervention in a developing SSTI. Patients were considered negative for purulent SSTI if one of the following was true: (1) no culture was sent; (2) culture was sent but grew no organisms; (3) culture was sent but grew only commensal skin flora; and (4) culture was sent prior to US (presumably resulting in US in which a collection had already been drained). Reason for attempted incision and/or drainage of a soft tissue infection without sonographic signs of abscess was made by individual ED providers at the time of clinical contact. These reasons were not routinely stated in the clinical notes, but it is likely that induration or fluctuance on physical exam raised sufficient concern to attempt drainage. Volume and method of collection were not routinely recorded in the EMR and could not be included in statistical analysis, but were noted for descriptive purposes when available. We recorded which organism(s) grew in positive cultures.

In this retrospective study, diagnostic US exams had been performed using routine clinical protocol, utilizing high-frequency linear probes and curved probes manufactured by Philips (Philips Ultrasound, Philips Healthcare, Bothell, WA) and GE (GE Ultrasound, Wauwatosa, WI). Multi-planar static and cine images with and without color and spectral Doppler were reviewed. Five board-certified pediatric radiologists (R.D.B., > 20 years of pediatric radiology experience; D.M.B., 7 years; V.M.H.-F., 7 years; M.L.F., 2 years; S.L.K., 3 years) and one point-of-care US (POCUS)-trained pediatric emergency medicine (PEM) physician (A.E.C., 6 years of pediatric POCUS experience, 11 years of PEM experience) assessed the images. Radiology raters viewed images on a diagnostic digital picture archiving and communications system (PACS) (Philips IntelliSpace, Philips Healthcare, Eindhoven, The Netherlands), while the PEM rater viewed images on an enterprise viewer (EasyViz, Karos Health, Ontario, Canada) integrated with the electronic medical record (EMR) system. All raters were blinded to presence of culture sample and its results.

First, we assessed interobserver agreement using Fleiss' kappa for presence or absence of 12 sonographic features associated with SSTI, but without appearance of classic abscess (Table 1), on a subset of approximately 10% ($N = 24$) of our sample size. A single representative example of each imaging feature was circulated to all raters. We did not attempt more intensive training of the raters in order to better simulate how these features may be understood and applied at point of image interpretation during routine clinical practice. Each

Table 1 Interobserver agreement for US features associated with soft tissue infection

US appearance	Fleiss' kappa
Focal collection > 1 cm	0.57
Hyperemia	0.57
Swirling with compression[a]	0.52
Posterior acoustic enhancement	0.47
Cobblestoning or branching interstitial fluid[b]	0.45
Effaced tissue planes	0.42
Focal collection ≤ 1 cm	0.41
Superficial striations	0.35
Tract to surface	0.31
Echogenicity of fluid	
Hypoechoic	0.31
Isoechoic	0.20
Anechoic	0.14
Bone or cartilage visualized deep to the area	0.24
Normal tissue visualized deep to the area	0.15

[a] Compression and swirling was rated by five radiologists only due to limitations on evaluating cine clips in the enterprise imaging viewer used by pediatric emergency medicine rater

[b] Cobblestoning and branching interstitial fluid were intended to be separate categories, but we combined them after multiple comments from raters that the difference between the two was not clear

rater independently reviewed each study, assessing presence or absence of each feature. Fleiss' kappa ≥ 0.45 was considered adequate agreement for > 2 observers evaluating categorical data [13, 14]. All raters were included in the kappa analysis, with the exception of assessing for compression and swirling. The PEM rater was not able to effectively view these cine clips in the enterprise viewer, so agreement for this feature was assessed only among the five radiologists.

We then assessed imaging features with adequate interobserver agreement in the total sample. Five of the raters reviewed 25 exams each (R.D.B., D.M.B, V.M.H.-F., M.L.F., and A.E.C.); one of the raters reviewed 68 exams (S.L.K.). To ensure that assessment was not biased by one rater reviewing more studies than the others, we performed a sub-analysis including only the 25 most recent exams from rater S.L.K., matching the number evaluated by all other raters. The 24 exams assessed during interobserver agreement were included in the assessment of soft tissue infection to increase statistical power. For these 24 exams, we assigned the mode among all raters as the central tendency for each US feature. If there was no mode, we assigned the rating given by the most experienced reviewer. To ensure that assessment was not biased by inclusion of these interobserver agreement exams, we also ran a sub-analysis omitting these 24 exams. If the two sub-analyses did not change the direction or relevance of the results, we included them in the whole analysis for greater statistical power.

After identifying US features of SSTI with adequate interobserver agreement, we assessed association between these features and presence of positive wound culture using univariate logistic regression models. For statistical power and to model clinical decision-making, exams were considered negative for purulent SSTI if cultures were negative or grew commensural flora, if culture was obtained before ultrasound, or if culture was not sent. To control for confounding variables, we applied a multivariate logistic regression model with a forward stepwise model selection strategy. Variables with $p < 0.20$ in the univariate analysis were considered to be included in the multivariate model. p value < 0.05 was used as statistical significance threshold. Statistical analysis was performed using STATA version 14 (College Station, TX).

Results

We identified 217 US examinations that met our inclusion criteria but not exclusion criteria (Fig. 1). Demographics and clinical characteristics of this cohort have been reported separately [12]. Of the 217 exams sonographically negative for abscess, 41 cases (19% of exams) were sent for culture within 8 h of ultrasound. At this time point, 35 cases (16% of all exams) grew pathogenic organisms (83% MRSA; 17% methicillin-sensitive *Staphylococcus aureus* (MSSA)), and 6 had no growth or grew only commensural flora. By 48 h, a total of 69 cases (32% of exams) had been cultured. At 48 h, 61 cases (28% of exams) grew pathogens (81% MRSA; 19% MSSA), while 8 had no growth or grew only commensural flora. The volume of the material collected was recorded

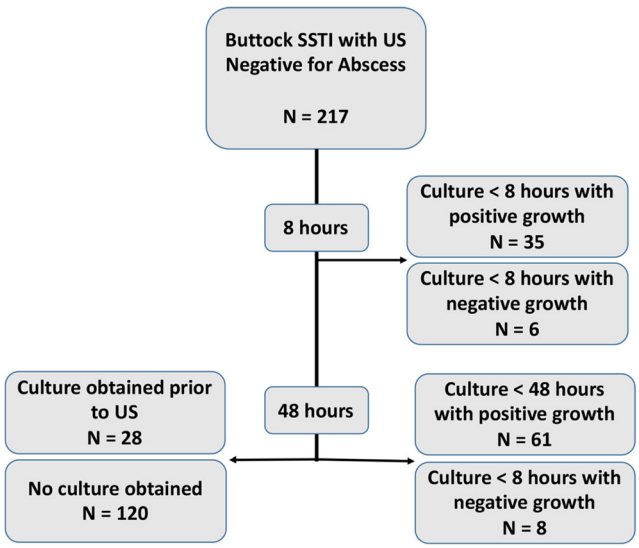

Fig. 1 Flow chart illustrates number of cases sampled and number of positive cultures within 8 h of ultrasound (US) and within 48 h of US. At both time points, 28 exams were considered to be negative for signs of undetected purulent SSTI because material had already been expressed and sent for culture before the patient came to US

during the ED visit in 13 cases (6% of exams), ranging from 0.3 to 15 mL (mean 4 mL, median 2 mL).

Interobserver agreement between the five radiologists and one PEM physician was adequate ($\kappa > 0.45$) for the following five US features: presence of focal collection > 1 cm ($\kappa = 0.57$); hyperemia ($\kappa = 0.57$); swirling with compression ($\kappa = 0.52$); posterior acoustic enhancement ($\kappa = 0.47$); and cobblestoning or branching interstitial fluid ($\kappa = 0.45$) (Table 1, Fig. 2). Three of the US features had only poor agreement: presence of isoechoic fluid ($\kappa = 0.20$); presence of anechoic fluid ($\kappa = 0.14$); and normal tissue visualized deep to the area ($\kappa = 0.15$).

In our cohort of 217 exams, 62% ($N = 135$) had posterior acoustic enhancement, 58% ($N = 126$) had cobblestoning or branching interstitial fluid, 58% ($N = 126$) had swirling with compression, 45% ($N = 98$) had hyperemia, and 30% ($N = 66$) had focal collection > 1 cm. For exams with cultures obtained within 8 h after the exam, cobblestoning or interstitial fluid was associated with positive cultures (OR 2.83, $p = 0.01$) (Table 2), compared to exams with negative cultures, pre-US cultures, or no cultures sent. No other US features correlated with positive cultures in the 8-h univariate analysis, so a multivariate regression was not performed. At 48 h, US features associated with culture-positive SSTI in univariate analysis included presence of posterior acoustic enhancement (OR 1.66, $p = 0.11$) and cobblestoning or branching interstitial fluid (OR 2.91, $p < 0.01$) (Table 2). In multivariate regression, only presence of cobblestoning/interstitial fluid was independently associated with purulent infection (OR 2.73, $p < 0.01$).

Table 2 Correlation between US features and positive cultures

	OR (95% CI)[a]	*p* value
48 h, univariate regression		
Focal collection > 1 cm	0.75 (0.39–1.46)	0.40
Hyperemia	0.89 (0.51–1.57)	0.69
Swirling with compression	0.94 (0.42–2.07)	0.87
Posterior acoustic enhancement	*1.66 (0.88–3.14)*	*0.11*
Cobblestoning or branching interstitial fluid	*2.91 (1.50–5.65)*	*< 0.01*
48 h, multivariate regression		
Posterior acoustic enhancement	1.25 (0.64–2.46)	0.51
Cobblestoning or branching interstitial fluid	2.73 (1.38–5.44)	< 0.01
8 h, univariate regression		
Focal collection > 1 cm	0.90 (0.41–2.00)	0.79
Hyperemia	0.85 (0.42–1.71)	0.65
Swirling with compression	1.56 (0.65–3.78)	0.33
Posterior acoustic enhancement	1.40 (0.64–3.02)	0.39
Cobblestoning or branching interstitial fluid	*2.83 (1.22–6.56)*	*0.01*

Italics denote US features with significant p-values in univariate and multivariate regression analyses

[a] *OR*, odds ratio; *CI*, confidence interval

Presence of interstitial fluid or cobblestoning remained independently associated with positive cultures in multivariate regression at 48 h when sub-analysis considered the equal number of exams for all raters (OR 2.34, $p < 0.05$) or omitted the 24 exams used for interobserver agreement (OR 3.09, $p < 0.01$) (Appendix Table 3). This sub-analysis was not

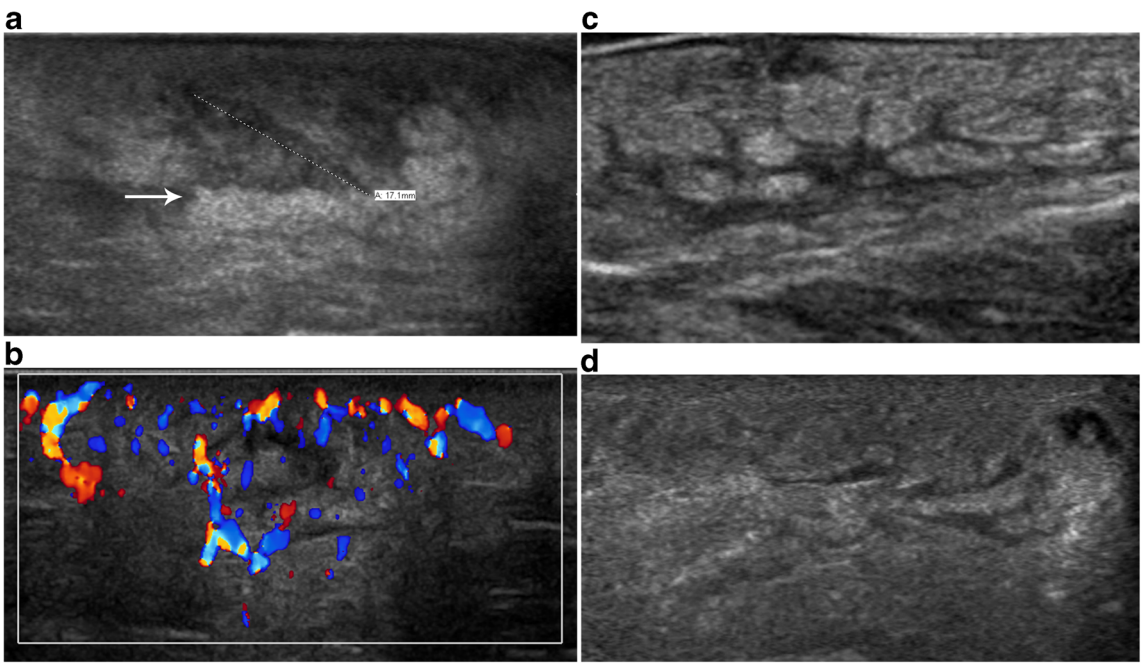

Fig. 2 Focal collection > 1 cm and posterior acoustic enhancement (arrow) in a 15-year-old female (**a**), hyperemia in an 11-month-old female (**b**), cobblestoning in an 8-year-old male (**c**), and interstitial fluid in a 13-month-old female (**d**). Cobblestoning and interstitial fluid exist on a spectrum and may be indistinguishable or coexistent, so the presence of either was treated as one entity, called "cobblestoning or interstitial fluid"

performed for the 8-h positive culture exams due to limitations imposed by smaller sample size.

Discussion

Our study shows that one in six (16%) soft tissue infections without US findings of abscess by US may grow pathogenic organisms from fluid cultured within 8 h after US. One in three (32%) may go on to develop positive cultures within 48 h. Over 80% of cultures grew MRSA at both time points, in keeping with the high prevalence of MRSA in SSTI. The only sonographic feature significantly associated with culture-positive SSTI at both time points was cobblestoning or branching interstitial fluid, a feature that overlaps with classical descriptions of cellulitis. For SSTI sampled within 48 h of US, posterior acoustic enhancement also showed a weak association with positive cultures, meeting the threshold for univariate analysis, but not significant for independent association on multivariate analysis. Only 5 of the 12 US features of SSTI showed a strong enough interobserver agreement to serve as the basis for evaluating signs of culture-positive SSTI.

Exams enrolled in our study were interpreted as negative for abscess, but these patients nonetheless appear to have a form of purulent SSTI which may benefit from an earlier incision and drainage. Clinical treatment guidelines from the Infectious Disease Society of America (IDSA) rely on the sonographic differentiation of soft tissue infections as purulent or non-purulent. Purulent SSTI are classified as abscess, carbuncle, and furuncle. US appearance of abscess is widely recognized, but there is little guidance on identifying US appearance of the other purulent SSTIs. IDSA recommends incision and drainage for purulent SSTI in the ED, but more conservative treatment for non-purulent cellulitis [3]. In outpatients, IDSA guidelines recommend treating purulent SSTI in which no abscess is suspected with coverage for CA-MRSA, while non-purulent cellulitis should be treated for β-hemolytic streptococci [15]. Our results show that SSTI may contain as much as 15 mL of pus in the absence of a formed abscess. In the era of CA-MRSA, imagers may need to consider a broader definition for sonographic appearance of purulent collection in patients with clinical concern for abscess.

Some common US findings associated with SSTI did not have statistically significant association with culture-positive, purulent SSTI. All five criteria evaluated, including posterior acoustic enhancement, cobblestoning or branching fluid, swirling with compression, hyperemia, and focal collection > 1 cm, were present in 30–62% of exams. However, only cobblestoning or branching interstitial fluid associated with cases in which an ED provider decided to obtain culture material from the SSTI and the fluid grew positive cultures. Clinical reasoning for collecting material after an US negative for abscess was not consistently documented, and we are unable to draw conclusions about the clinical scenario that raised persistent concern for purulent SSTI. In our experience, fluctuance and induration on physical exam often leads to a higher suspicion of purulence. It may be that cobblestoning and branching interstitial fluid are associated with purulent induration and fluctuance on physical exam. Cases that did not go to I & D or other fluid sampling methods may have lacked these physical exam findings. In our study, 28 patients (13%) had culture material sent prior to US, and these exams may have displayed more of the classical US signs of SSTI and abscess prior to drainage. Although we excluded exams with focal fluid collection > 1 cm by report, upon image review, we found that 30% of our exams did have a fluid collection > 1 cm. Where fluid volume was recorded, as much as 15 mL of pus was collected from SSTI without sonographic findings of abscess. Interestingly, we found no association between positive cultures and the presence of collection > 1 cm. In most cases, these fluid collections were irregular and asymmetric and did not measure > 1 cm in three orthogonal planes. Small, irregular, ill-defined collections have shown an association with CA-MRSA infections [10, 11], and this pathogen grew in the majority of our cultures. Although previous publications describe a stepwise progression in the sonographic appearance of soft tissue infection from tissue thickening, to tissue disarray, to purulence, or to abscess, it is not clear that CA-MRSA infections follow this course. Many core papers describing US appearance of soft tissue infections predate the spread of CA-MRSA, first documented in the later 1990s. CA-MRSA owes much of its virulence to immune-modulating factors that interfere with immune system containment [16], and these factors may interfere with development of a walled-off abscess in some cases. In the era of CA-MRSA, imagers may need to consider a broader definition for sonographic appearance of purulent SSTI in patients with clinical concern for abscess. Because the vast majority of our positive cultures grew MRSA, our results do represent appearance of MRSA infections, but our study was not designed to identify features specific to MRSA.

Our study demonstrates some of the limitations of US criteria for diagnosis. US is known to be operator dependent and prone to differences in interpretation, especially when images are not viewed real-time. We found adequate interobserver agreement for only 5 of the 12 SSTI criteria we evaluated. We asked raters to evaluate some of the more subtle findings of SSTI, rather than obvious abscess, so differences in interpretation are expected. Our interobserver agreement is similar to that of other studies on radiologist agreement for US criteria. For example, diagnostic US criteria for thyroid imaging reporting and data system (TI-RADS) endorsed by the American College of Radiology showed interobserver agreement ranging from kappa 0.25 to 0.58 for all but two of the TI-RADS criteria [17]. Interobserver agreement rating as fair (0.41–0.60) is adequate as the basis for evaluating diagnostic criteria on US.

Interpretations of our results have some limitations inherent to the retrospective design. About half of the patients in our study did not have cultures sent, and our analysis assumes that these patients were adequately treated, likely for non-purulent cellulitis. Our study also does not capture any positive culture results that could have occurred if there was subsequent purulent drainage at home or during follow-up in an outside outpatient setting or ED. Follow-up at an outside hospital is unlikely given the size of our institution in the region. Given these limitations, it is reasonable to consider that the incidence of purulent soft tissue infections on patients with US negative for abscess may be larger than our data suggest.

Other limitations and considerations arise from our study design. We studied infections of the buttock and perineum, because these are most common in children and have fewer other reasons for US, such as foreign body, trauma, or mass. However, SSTIs in different regions of the body generally have similar clinical presentations, and it is reasonable to expect that our findings may also apply to other body parts. We designed our image review methods to mimic the likely setting in which these findings would be used clinically: by a single imager estimating presence or absence of findings based on a single representative image from the literature. Had we designed image review methods to maximize interobserver agreement, we may have identified additional associations, but we could not be confident that these US features could be consistently identified and recommendations appropriately applied in the clinical setting. It is important to note that we describe association, not specificity or predictive value. Cobblestoning or branching interstitial fluid could also be linked with trauma or third-spacing in the absence of infection.

Our study design also assumes that any positive culture indicates a purulent SSTI. Purulence denotes the presence of white blood cells and bacteria in a sample; it is reasonable to assume that positive cultures correspond to a purulent collection, whether frankly purulent material is visible or not. It is not routine practice to send samples for growth and culture in the absence of fluid, so it is also reasonable to assume that the patients with positive cultures had fluid expressed, though the volume of that fluid was not recorded in most cases. Our findings support the hypothesis that US findings other than classic appearance of focal fluid or walled-off abscess may represent purulent SSTI. Imagers should exercise caution when interpreting US for SSTI and should refrain from commenting on whether any visible fluid is drainable. Additional studies should be performed to better correlate US appearance with the appropriate pathways for clinical management.

Conclusion

Imagers should be aware that cobblestoning and branching interstitial fluid may be associated with purulent SSTI, and that these patients may benefit from early I & D in accordance with management pathways established by the Infectious Diseases Society of America. Further studies are needed to better define the sensitivity, specificity, and predictive value of sonographic criteria associated with purulent SSTI in the absence of classical appearance of abscess.

Compliance with ethical standards

Our institutional review board (IRB) approved this retrospective cohort study.

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

Appendix

Table 3 Bias testing for methods in correlation between US features and positive cultures

	OR (95% CI)[a]	*p* value
Equal number of exams per rater[b], univariate regression		
Focal collection > 1 cm	*0.55 (0.23–1.32)*	*0.16*
Hyperemia	0.97 (0.49–1.94)	0.94
Swirling with compression[a]	1.00 (0.39–2.61)	0.92
Posterior acoustic enhancement	1.05 (0.94–4.57)	0.89
Cobblestoning or branching interstitial fluid[b]	*2.07 (0.94–4.57)*	*0.06*
Equal number of exams per rater, multivariate regression		
Focal collection > 1 cm	0.47 (0.19–1.15)	0.10
Cobblestoning or branching interstitial fluid[b]	*2.73 (1.38–5.44)*	*< 0.05*
Omitting 24 kappa test exams[c], univariate regression		
Focal collection > 1 cm	0.76 (0.39–1.50)	0.43
Hyperemia	0.91 (0.50–1.65)	0.75
Swirling with compression[a]	1.10 (0.48–2.50)	0.82
Posterior acoustic enhancement	*1.54 (0.80–2.95)*	*0.19*
Cobblestoning or branching interstitial fluid[b]	*3.12 (1.57–6.21)*	*< 0.01*
Omitting 24 kappa test exams, multivariate regression		
Posterior acoustic enhancement	1.02 (0.50–2.10)	0.94
Cobblestoning or branching interstitial fluid[b]	*3.09 (1.48–6.46)*	*< 0.01*

Italics denote US features with significant p-values in univariate and multivariate regression analyses

[a] *OR*, odds ratio; *CI*, confidence interval

[b] Equal number of exams per rater: one of the authors (S.L.K.) reviewed 68 exams, while the other authors reviewed 25 exams each. To evaluate any bias arising from unequal number of exams per rater, we performed a sub-analysis running univariate and multivariate logistic regression including only 25 most recent exams from this rater along with the other raters' exams

[c] Omitting 24 kappa test exams: to increase statistical power for the study, we included into our correlation analysis the 24 exams assessed for interobserver agreement kappa values. Because these exams had six answers for each US features (one from each rater), we assigned the mode of the six answers as the value for that US feature, as described in "Methods" section. Because this technique was different than the evaluation method for the rest of the exams, we ran the univariate and multivariate logistic regression without these 24 exams to test for any effects of this different assessment on outcome

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