Role of point-of-care ultrasound (POCUS) in the diagnosis of an abscess in paediatric skin and soft tissue infections: a systematic review and meta-analysis

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Introduction

Skin and soft tissue infections (SSTI) are commonly encountered among children presenting to the paediatric emergency department (ED). Over the past 20 years, the number of visits for SSTI in outpatient and ED has substantially increased at more than 14 million patients per year in the United States [1,2]. For patients under 18 years old, the rate of SSTI-related outpatient visits, incision and drainage, and hospitalization has almost doubled from 1997 to 2005, higher than any other age group [2,3].

In the paediatric ED, it is highly important to distinguish cellulitis from an abscess, which can appear similar on history and physical examination (PE), but their treatment approaches are significantly different, with incision and drainage (I&D) recommended for an abscess and antibiotics alone for cellulitis in general. Misdiagnosis and inappropriate treatment of an abscess may result in prolonged symptoms or disease progression, such as local spread to deep tissue or bone, as well as systemic spread, leading to bacteraemia and septicaemia [2-4]. Medical history and physical examination are usually used only to determine whether antibiotics are suitable for the treatment of SSTI. However, in equivocal clinical cases, clinical assessment has a high rate of inaccuracy with regard to differentiating abscess from cellulitis [5,6].
In recent years, point-of-care ultrasound (POCUS) is increasingly being utilized to aid in differentiating an abscess from cellulitis in the ED. Several studies have described the application of POCUS in guiding diagnosis and management of SSTI in adults by the ED physicians, showing the superior sensitivity and specificity of POCUS compared with clinical assessment only and the positive role of POCUS in improving bedside decision-making in adults with SSTI [7-11]. The use of POCUS in the diagnosis of an abscess in children with SSTI is increasing in paediatric ED [12-18] and POCUS is frequently used as the initial imaging technology of choice for the evaluation of paediatric SSTI, as it is an effective, highly available, noninvasive, economical [19,20] and non-radiating imaging modality. However, prior studies in the field of POCUS use for paediatric SSTI include small sample size, single-centre studies and the lack of integration of findings into clinical decision-making. The diagnostic performance of POCUS was variable in these studies, with the sensitivity ranging from 0.65 to 0.97 and specificity from 0.68 to 1.0 [12,14].

To our knowledge, no meta-analysis of the diagnostic value of POCUS in the differentiation of abscess and cellulitis in paediatric patients with SSTI has been reported. Thus, we thought it is necessary and timely to summarize the currently available data to provide valuable information for clinical practice. The objective of this systematic review and meta-analysis was to evaluate the effect of POCUS for the diagnosis of abscess and to compare the diagnostic accuracy of POCUS and PE in paediatric patients with SSTI in the paediatric ED.

Material and methods

Meta-analysis principles
The present meta-analysis was designed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [21] and registered with International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLAY), and the registered number was INPLASY202110063.

Search strategy
A comprehensive literature search through PubMed, EMBASE, and Cochrane Library was performed from inception to November 2020, to identify English-language studies on POCUS for differentiating abscess and cellulitis in paediatric patients with SSTI. The search strategy was on account of the combination of the medical subject heading (MeSH) terms, keywords and word variants for ultrasound, skin and soft tissue infections, abscess, cellulitis, and paediatric. Reference lists of the included studies after the initial search were also manually screened to find additional relevant studies. Detailed search terms are provided in supplementary file 1.

Inclusion and exclusion criteria
Two investigators reviewed the titles and abstracts of the relevant studies independently. Before identifying the studies, the inclusion and exclusion criteria were established to increase validity and reproducibility. Any discrepancies between the investigators were resolved through discussion.

All potentially relevant studies meeting the following inclusion criteria were enrolled: (1) diagnostic studies were included; (2) studies evaluating the diagnostic accuracy of POCUS in differentiating abscess from cellulitis in paediatric patients with SSTI were included; and (3) reference standards were adopted to confirm abscess, such as incision and drainage or clinical follow-up.

The exclusion criteria were as follows: (1) case reports, consensus statements, and unpublished articles; (2) studies without sufficient data to construct diagnostic 2x2 tables; and (3) studies written in languages other than English.

Data extraction
Two investigators independently extracted the relevant data from the included studies using a standardized data extraction form. Any disagreements were resolved via discussion. For included studies, the following items were extracted: author, year of publication, country, study type, study setting, sample method, abscess prevalence, sonographer speciality, sonographer experience, diagnostic standard, blinding method, ultrasound equipment and probe, study period, study population, mean age, gender, reference standard, the time between POCUS and the reference standard, and the assessment of inter- or intra-observer agreement.

Study quality assessment
The quality of each enrolled study was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool as recommended by the Cochrane collaboration [22]. QUADAS-2 tool comprises two main categories including the risk of bias of four domains and the clinical applicability of three domains. Four domains include patient selection, index test, reference standard, and flow and timing. Every domain is assessed for risk of bias, and the first three domains are assessed for applicability. The quality assessment was performed using RevMan 5.3 software (Nordic Cochrane Centre, Copenhagen, Denmark).

Statistical analysis
From the included studies, the pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR)
with corresponding 95% confidence intervals were calculated using a bivariate effect model in this meta-analysis, which indicated the diagnostic accuracy of POCUS in the differentiating abscess from cellulitis in paediatric patients with SSTI. Furthermore, the best-fitting summary receiver operator curve (SROC) was constructed and this allowed us to calculate the area under the curve (AUC). An AUC close to 0.5 reveals a poor test, and an AUC close to 1.0 shows a perfect test [23]. The inconsistency index ($I^2$) and the Cochrane Q test were utilized to evaluate the degree of between-study heterogeneity with a p value <0.1 or $I^2$>50% indicating significant heterogeneity [24]. A random-effects model is used when there is significant heterogeneity across studies, otherwise, a fixed-effects model is used. The Deeks’ funnel plot asymmetry test was utilized to evaluate publication bias [25], through a p value >0.05 indicating no significant publication bias.

Meta-regression and subgroup analyses using several covariates were conducted to investigate the potential factors of heterogeneity: abscess prevalence (>60% versus <60%), year of publication (1997-2013 versus 2016-2019), and sample size (>100 versus <100). Subgroup analysis was also performed to investigate the differences in diagnostic accuracy between POCUS and physical assessment. All above the statistical analyses were conducted by StataSE 15 (Stata Corporation, College Station, Texas).

**Results**

**Study selection**

Though the three databases, our literature search initially yielded 2373 publications for consideration. PubMed identified 816 studies, EMBASE found 1514, and the Cochrane Library discovered 43. After removing 862 duplicate publications, there were 1511 studies remained. According to the inclusion criteria, 1480 studies were discarded after screening the titles and abstracts. Thirty-one studies were evaluated by reading the full text, of which 24 were further excluded. Finally, 7 studies were included in this meta-analysis [12-18]. No additional study was enrolled after screening the reference lists of included studies. Figure 1 reveals the detailed flow chart of the literature search.

**Characteristics of the included studies**

The included studies were published between 1997 and 2019 and written in English [12-18]. A total of 870 patients with 917 lesions were included. Six studies were performed in the United States [13-18] and one in Ireland [12]. All of the included studies were prospective. The study population ranged from 23 to 348 and the mean age ranged from 23.5 months to 9.5 years. The abscess prevalence ranged from 30% to 74% across different studies. Single blinding between the POCUS and the reference standard was found in 6 studies [12,14-18] and one study [13] did not depict a blinding method. The patients were consecutively enrolled in one study [12] and the other six studies enrolled patients with convenience sample method [13-18]. Table I and II epitomizes the data extracted from the enrolled studies. More details are showed in the additional file 2.

**Quality assessment**

The quality assessment results of each enrolled study based on QUADAS-2 tool were shown graphically in figure 2. Concerning the patient selection domain, 6 studies were considered as “unknown” [13-18], because they enrolled patients with convenience sample method. With respect to the index test domain, 2 studies [13,18] were considered as “unknown” because the blinded status of the reference standard was not explicitly reported. Concerning the reference standard domain, 6 studies [12-17] were considered as “unknown” because the blinded status of POCUS was not definitely depicted. With regard to the flow and timing domain, all studies were considered as “unknown” because they did not definitely report the precise duration between POCUS and the reference standard. Concerning applicability, for patient selection, index test, and reference standard domains, all studies were considered to have low concerns.
Table I. Primary data extracted from the included studies for meta-analysis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study type</th>
<th>Sample method</th>
<th>Study setting</th>
<th>Blinding method</th>
<th>Study population (lesion)</th>
<th>Male/ Female</th>
<th>Mean age (years)</th>
<th>Number of abscess</th>
<th>Abscess prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quraishi [12]</td>
<td>1997</td>
<td>Ireland</td>
<td>Pro</td>
<td>Consecutive sample</td>
<td>PED</td>
<td>Single blind</td>
<td>23</td>
<td>10/13</td>
<td>23.5 (months)</td>
<td>17</td>
<td>74</td>
</tr>
<tr>
<td>Adams [16]</td>
<td>2016</td>
<td>United States</td>
<td>Pro</td>
<td>Convenience sample</td>
<td>PED</td>
<td>Single blind</td>
<td>148 (151)</td>
<td>67/81</td>
<td>7 (median)</td>
<td>102</td>
<td>68</td>
</tr>
<tr>
<td>Levine [18]</td>
<td>2019</td>
<td>United States</td>
<td>Pro</td>
<td>Convenience sample</td>
<td>PED</td>
<td>Single blind</td>
<td>27</td>
<td>17/10</td>
<td>5.3</td>
<td>8</td>
<td>30</td>
</tr>
</tbody>
</table>

Pro, prospective; PED, paediatric emergency department; ED, emergency department; NR, not reported; POCUS, point-of-care ultrasound

Table II. Characteristics of the included studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Sonographer</th>
<th>Diagnostic standard</th>
<th>Reference standard</th>
<th>Time between reference standard and POCUS</th>
<th>Study period</th>
<th>US equipment and probe</th>
<th>Observer agreement</th>
<th>Sen (%)</th>
<th>Spe (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sivitz [13]</td>
<td>EM</td>
<td>Trained</td>
<td>A subcutaneous spherical or elliptical shaped hypoechoic area</td>
<td>I&amp;D or follow-up</td>
<td>2007.2-2007.12</td>
<td>A linear array 8-13 MHz transducer (SonoSite Inc., Micromaxx, Bothell, WA)</td>
<td>No</td>
<td>91</td>
<td>82</td>
</tr>
<tr>
<td>Iverson [14]</td>
<td>EM</td>
<td>Trained</td>
<td>A hypoechoic or an anechoic collection with variation in septation and debris</td>
<td>I&amp;D</td>
<td>NR</td>
<td>A Siemens Sonoline G60S with a linear array transducer</td>
<td>Yes</td>
<td>98</td>
<td>68</td>
</tr>
<tr>
<td>Marin [15]</td>
<td>EM</td>
<td>Trained</td>
<td>Hypoechoic, heterogeneously echogenic, irregularly shaped lesion with posterior acoustic enhancement</td>
<td>I&amp;D</td>
<td>2008.7-2010.4</td>
<td>A SonoSite MicroMaxx machine using a linear or curved array transducer</td>
<td>Yes</td>
<td>88</td>
<td>72</td>
</tr>
<tr>
<td>Adams [16]</td>
<td>PEM</td>
<td>Trained</td>
<td>A anechoic, or heterogeneous hypoechoic collection and lack of internal vascularity</td>
<td>I&amp;D or follow-up</td>
<td>2012.7-2014.2</td>
<td>A SonoSite Edge machine with a 13-6 MHz linear array transducer</td>
<td>Yes</td>
<td>96</td>
<td>87</td>
</tr>
<tr>
<td>Lam [17]</td>
<td>EM</td>
<td>Trained</td>
<td>NR</td>
<td>I&amp;D or follow-up</td>
<td>2014.3-2016.7</td>
<td>NR</td>
<td>No</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>Levine [18]</td>
<td>PEM</td>
<td>Trained</td>
<td>An irregular shape, variable degree of echogenicity of internal contents, and lobulated or septated appearance</td>
<td>Radiology department imaging</td>
<td>NR</td>
<td>Zonare Medical Systems, Mountain View, CA; a linear probe (L10-6 MHz)</td>
<td>No</td>
<td>75</td>
<td>89</td>
</tr>
</tbody>
</table>

NR, not reported; EM, emergency medicine; PEM, paediatric emergency medicine; I&D, incision and drainage; POCUS, point-of-care ultrasound; US, ultrasound; Sen, sensitivity; Spe, specificity
Data synthesis and publication bias

The summary estimates of diagnostic sensitivity and specificity of POCUS for differentiating an abscess from cellulitis were analysed by the random effects method on the basis of significant statistical heterogeneity ($I^2$=74.74% for sensitivity, p=0.00). No significant threshold effect was found (Spearman correlation coefficient =-0.29, p=0.09) in the Spearman rank correlation test. Overall, the pooled sensitivity and specificity of POCUS were 0.90 (95% confidence interval [CI]: 0.82-0.95) and 0.80 (95% CI, 0.72-0.86) (fig 3). The pooled PLR, NLR, and DOR of POCUS were 4.5 (95% CI, 3.1-6.4), 0.13 (95% CI, 0.07-0.23), and 36 (95% CI, 17-75), respectively.

The AUC under the SROC curve for the value of POCUS in the diagnosis of abscess was 0.89 (95% CI, 0.86-0.91) (fig 4).

The Deeks’ funnel plot was carried out to evaluate the publication bias of the eligible studies. As shown in figure 5, no significant publication bias existed (p=0.52).

Meta-regression and subgroup analyses

Due to the significant heterogeneity among studies, a meta-regression analysis was performed to explore potential sources of heterogeneity. The covariables included abscess prevalence (>60% versus <60%), year of publication (1997-2013 versus 2016-2019) and sample size (>100 versus <100). Among the various potential covariates, abscess prevalence, sample size, and year of
Four studies [13-16] provided data regarding the PE method. The pooled sensitivity, specificity and AUC of PE for abscess were 0.84 (95% CI, 0.80-0.88), 0.69 (95% CI, 0.62-0.76) and 0.85 (95% CI, 0.81-0.88) (fig 7, fig 8).

The subgroups concerning abscess prevalence, the sensitivity between >60% and <60% was similar (sensitivity, 0.91 versus 0.89, p=0.36), but the specificity of >60% was lower (specificity, 0.76 versus 0.82, p=0.00).

The subgroups about year of publication, the sensitivity between 1997-2013 and 2016-2019 was similar (sensitivity, 0.88 versus 0.92, p=0.48), but the specificity of 1997-2013 was lower (specificity, 0.74 versus 0.83, p=0.04). Finally, the subgroups with respect to sample size, the sensitivity between >100 and <100 was similar (sensitivity, 0.92 versus 0.87, p=0.57), but the specificity of >100 was lower (specificity, 0.79 versus 0.81, p=0.04) (Table III).

<table>
<thead>
<tr>
<th>Covariate</th>
<th>No. of Studies</th>
<th>Sensitivity % (95% CI)</th>
<th>p value</th>
<th>Specificity % (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abscess prevalence, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 60</td>
<td>4</td>
<td>91 (84 - 97)</td>
<td>0.36</td>
<td>76 (69 - 82)</td>
<td>0.00</td>
</tr>
<tr>
<td>&lt; 60</td>
<td>3</td>
<td>89 (79 - 99)</td>
<td></td>
<td>82 (75 - 89)</td>
<td></td>
</tr>
<tr>
<td>Year of publication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016-2019</td>
<td>3</td>
<td>92 (85 - 99)</td>
<td>0.48</td>
<td>83 (77 - 89)</td>
<td>0.04</td>
</tr>
<tr>
<td>1997-2013</td>
<td>4</td>
<td>88 (80 - 97)</td>
<td></td>
<td>74 (67 - 81)</td>
<td></td>
</tr>
<tr>
<td>Sample size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 100</td>
<td>3</td>
<td>92 (86 - 98)</td>
<td>0.57</td>
<td>79 (71 - 86)</td>
<td>0.04</td>
</tr>
<tr>
<td>&lt; 100</td>
<td>4</td>
<td>87 (76 - 97)</td>
<td></td>
<td>81 (70 - 93)</td>
<td></td>
</tr>
</tbody>
</table>

CI, confidence interval

Fig 6. The meta-regression and subgroup analyses

Fig 7. Forest plots of sensitivity and specificity of PE for abscess

Fig 8. Summary receiver operating characteristic curve of PE for abscess
**Discussion**

To our best knowledge, this is the first systematic review and meta-analysis to evaluate the effect of POCUS in the detection of an abscess in pediatric patients with SSTI. Our meta-analysis finds that POCUS has a pooled sensitivity of 0.90 (95% CI, 0.82-0.95), specificity of 0.80 (95% CI, 0.72-0.86), PLR of 4.5 (95% CI, 3.1-6.4), NLR of 0.13 (95% CI, 0.07-0.23) and DOR of 36 (95% CI, 17-75), respectively, with an SROC AUC of 0.89 (95% CI, 0.86-0.91). Comparing the diagnostic accuracy of POCUS and physical examination for the abscess, the pooled sensitivity, specificity and AUC of the POCUS were higher than that of the physical examination (sensitivity: 0.90 > 0.86; specificity: 0.80 > 0.69; AUC: 0.89 > 0.85). Based on the aforementioned findings, we consider that POCUS performs well in correctly differentiating an abscess from cellulitis in pediatric patients with SSTI and has superior test characteristics compared with physical examination alone.

A prior systematic review by Subramaniam et al [26] in 2016 assessed the role of POCUS in diagnosing an abscess, identifying 6 studies with a sensitivity of 0.97 and specificity of 0.83. The sensitivity and specificity of our pediatric-specific meta-analysis including 7 eligible studies were lower than the results of the above study with a mixed population of both children and adults. The lower accuracy of our study only including pediatric patients might be on account of several causes, such as a smaller abscess size of pediatric patients, pediatric patient cooperation or provider comfort with the POCUS examination. This might be also associated with differences in POCUS training between pediatric ED and general ED providers [27,28].

In 2017, a meta-analysis by Barbic et al [29] regarding the POCUS diagnosing abscess reported that the pooled sensitivity was 0.96 and specificity was 0.83 for a mixed population of both children and adults. In Barbic’s study, subgroup analysis of 5 studies [12-16] only including pediatric patients demonstrated a pooled sensitivity of 0.94 and specificity of 0.83, respectively. In our meta-analysis, we included the same 5 studies as Barbic et al and two additional studies [17,18]. This led to a change to both the sensitivity and specificity compared with the prior meta-analysis. The results of our meta-analysis yielded a pooled sensitivity and specificity that were lower than the study by Barbic et al. However, our meta-analysis included more recently objective studies that not only resulted in higher statistical power but also supported the clinical practice of POCUS for diagnosing an abscess in pediatric patients with SSTI.

Marin et al [15] reported that for lesions that were not clinically evident based on clinical examination in pediatric patients, the sensitivity and specificity of PE for abscess were 0.43 and 0.42, while POCU were 0.77 and 0.61. Study by Adams et al [16] demonstrated that POCUS in diagnosis of the abscess in pediatric patients outperformed physical examination in equivocal lesions (sensitivity: 0.95 > 0.78; specificity: 0.83 > 0.30). Lam et al [17] also found that POCUS was more useful in lesions of higher clinical uncertainty, improving sensitivity from 0.69 to 0.91. We observed that POCUS might be more useful in lesions that were not clinically evident when compared with PE. This might provide pediatric emergency physicians caring for children with an additional valuable tool to assess SSTI, particularly when there is a clinical uncertainty.

There was a significant heterogeneity observed across the eligible studies in this meta-analysis. No threshold effect was observed. Therefore, a meta-regression analysis was performed to explore the source of the heterogeneity. We found that abscess prevalence, year of publication and sample size might be the sources of the heterogeneity. However, other factors such as blinding method, ultrasonic equipment, sonographer experience and specialty might also play an important role in the heterogeneity. Further meta-regression analyses according to other factors referred above could not be performed due to the insufficient information in the eligible studies. In the subgroup analysis, studies with abscess prevalence <60% had a higher specificity than studies with abscess prevalence >60%. Also, the studies published between 2016 and 2019 had a higher specificity than studies published between 1997 and 2013. Furthermore, the studies with a sample size >100 had lower specificity than studies with a sample size <100. The other subgroups did not show significantly different sensitivities.

Given that ultrasound is operator-dependent, the lack of experience would lead to a misdiagnosis [30-32]. So, the diagnostic accuracy of POCUS for abscesses might not be generalizable because of different levels of sonographer experience with ultrasound for this application. The POCUS training protocols of the included studies were variable, ranging from 60-minute didactic and hands-on training in soft tissue US by a PED physician with US certification [14] to a 6-hour training program that included lectures and hands-on scanning practice [15]. Therefore, further prospective studies with larger sample sizes are required to identify a well-defined training protocol for POCUS in the diagnosis of abscess in pediatric patients with SSTI.

There are several limitations in the present study. First, the included studies were limited by language, as
articles in languages other than English were not enrolled. Second, the convenience sampling method was adopted in all of the studies except one by Quraishi et al [12]. Therefore, it might not reflect the full range of paediatric patients presenting to paediatric ED, due to the limitation of the sampling method. Further studies using consecutive sampling method are required to address the issue under investigation. Third, all of the included studies did not definitely report the precise duration between POCUS and the reference standard. It should be noted that abscess and cellulitis are not mutually exclusive. Cellulitis is thought to be an infection of inflammation of the skin and soft tissues without the presence of an abscess. However, the abscess has a focal purulent accumulation, which may have associated cellulitis changes [33,34]. When comparing POCUS with the reference standards, it is significant that both are performed within a narrow time frame to reduce performance bias. Fourth, only 3 studies [14-16] depicted intra- or inter-observer agreement. Operator dependency is one of the shortcomings often cited with respect to ultrasound technology. Therefore, more studies are required to evaluate the agreement. Finally, the majority of the included studies had methodological limitations, especially in domains like patient selection, reference standard, and flow and timing. Therefore, improvements in the future study design are needed to address the issue.

In conclusion, based on the findings of this meta-analysis, POCUS is useful in identifying an abscess in paediatric patients with SSTI in paediatric ED, especially when the physical examination is equivocal, and performs better than a physical examination alone. However, the conclusion of our study based on a small number of studies that met our specific inclusion criteria should be interpreted with caution. Large prospective international multicentre studies are still required to identify the present conclusion and to further develop the diagnostic application of POCUS in the abscess.

Conflict of interest: none

References