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Point of Care Ultrasound in the Emergency Department: An Umbrella Review of Systematic Reviews of Diagnostic Test Accuracy

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 September 2024 and was last updated on 7 September 2024.

INTRODUCTION

Review question / Objective In response to these gaps, we plan to conduct an umbrella review with three objectives: i) to summarize the existing evidence for various specific conditions, ii) to provide a grading of the reported sensitivity and specificity of POCUS for these conditions in comparison to the respective reference standard, enabling clinicians to confidently use POCUS among adults or mixed population in emergency settings, and iii) to offer a qualitative synthesis where multiple MA exist for the same condition, ensuring that the best available evidence is accessible and clearly presented to guide clinical practice.

Rationale Emergency departments (EDs) face significant challenges due to overcrowding, which can lead to prolonged waiting times, increased patient discomfort, and potentially adverse outcomes due to diagnostic errors. Therefore, faster and particularly safer diagnostic procedures are needed. Diagnostic errors occur frequently, leading to longer hospital stays and higher in-hospital mortality rates for affected patients, making them a leading cause of death in hospitals. In this high-pressure environment of the ED, clinicians must rely on diagnostic tools that not only expedite patient care but also maintain a low rate of diagnostic errors to ensure patient safety and effective treatment.

Point-of-care ultrasound (POCUS), defined as ultrasound brought to the patient and performed by the provider in real time, emerges as a powerful tool that fulfils these critical needs in the ED. POCUS offers real-time imaging possibilities that can rapidly assist in the diagnosis and management of various conditions, reducing the reliance on more time-consuming and resource-intensive imaging modalities. Its advantages include portability, immediacy of results, and the ability to perform bedside evaluations, which can significantly improve patient flow and outcomes in the ED.

A substantial body of systematic reviews (SR) and meta-analyses (MA) exists on the use of POCUS across a variety of diseases and conditions. However, a critical issue is that estimates of diagnostic accuracy, particularly regarding sensitivity and specificity of POCUS, often lack a clear evidence rating, leaving clinicians uncertain about its reliability for safely ruling in or ruling out specific conditions. Additionally, for several conditions, multiple MA have been conducted, yet to our knowledge no comprehensive synthesis has been conducted to consolidate these findings.

Condition being studied Diagnostic test accuracy (DTA-SR) including a MA with a specific research question related to the DTA of a POCUS examination in ED settings; all studies that are no SRs of DTA for an ultrasound examination applicable as a POCUS in an ED setting or which have not conducted a MA will be excluded.

METHODS

Search strategy A systematic literature search will be performed on the databases Ovid (Medline) and Embase. The detailed search algorithm has been developed and validated in collaboration with an information specialist (Tanya Karrer, University of Bern) and content experts in POCUS (Beat Lehmann and Martin Müller).

Ovid MEDLINE(R) ALL
1 exp "sensitivity and specificity"/
2 false negative reactions/ or false positive reactions/
3 (sensitivity or specificity).ti,ab.
4 (predicitve adj value$1).ti,ab.
5 (likelihood adj ratio$1).ti,ab.
6 (false adj (negative$1 or positive$1)).ti,ab.
7 (randomized controlled trial or controlled clinical trial).pt.
8 double blind method/ or single blind method/
9 practice guideline.pt.
10 consensus development conference.pt.
11 random$.ti,ab.
12 random allocation/
13 (single blind$3 or double blind$3 or triple blind$3).ti,ab.
14 (review or review academic).pt.
15 meta analysis.pt.
16 (systematic adj review$).ti,ab.
17 or/1-14
18 17 and (15 or 16)
19 (pocus or (point*-of-care* adj3 (ultrasound* or ultra-sound* or sonograph*)) or ultrasound* or sonograph* or (focused cardiac ultras* or cardiac ultras* or ((transthoracic or trans-thoracic) and echocardiogra*) or tte)).ti,ab,kw.
20 exp "Sensitivity and Specificity"/ or sensitivity.tw. or specificity.tw. or ((pre-test or pretest) adj probability).tw. or post-test probability.tw. or predictive value$.tw. or likelihood ratio$.tw. or diagnos* test*1 accurac*.ti,ab,kw.
21 19 and 20
22 18 and 21

Embase
1 exp "Sensitivity and Specificity"/
2 false negative result/ or false positive result/
3 (sensitivity or specificity).ti,ab.
4 (predicitve adj value$1).ti,ab.
5 (likelihood adj ratio$1).ti,ab.
6 (false adj (negative$1 or positive$1)).ti,ab.
7 (randomized controlled trial* or controlled clinical trial* or rct).ti,ab.
8 double blind procedure/ or single blind procedure/
9 practice guideline.ti,ab.
10 random$.ti,ab.
11 randomization/
12 (single blind$3 or double blind$3 or triple blind$3).ti,ab.
13 or/1-12
14 meta-analys*.ti,ab,kw. or exp meta analysis/
15 (systematic adj review$).ti,ab,kw. or exp "systematic review"/
16 13 and (14 or 15)
17 (pocus or (point*-of-care* adj3 (ultrasound* or ultra-sound* or sonograph*)) or ultrasound* or sonograph* or (focused cardiac ultras* or cardiac ultras* or ((transthoracic or trans-thoracic) and echocardiogra*)) or tte).ti,ab,kw.
18 exp "Sensitivity and Specificity"/ or sensitivity.tw. or specificity.tw. or ((pre-test or pretest) adj probability).tw. or post-test probability.tw. or predictive value$.tw. or likelihood ratio$.tw. or diagnos* test*1 accurac*.ti,ab,kw.
19 17 and 18
20 19 and 16.

Participant or population We will include adult populations (16 years or older) or mixed populations (adults and children) with an emergency medicine relevant condition and/or acute intervention in which ultrasound was used as a diagnostic tool. Studies on patients with chronic conditions without acute exacerbation, on cancer diagnostics, or focusing on children, will be excluded.

Intervention We will evaluate any ultrasound examination with (potential) applicability as a POCUS examination in an acute care setting as the index text. Only DTA-SR focusing on the use of conventional ultrasound (B-Mode, color doppler)

and/or contrast enhanced ultrasound (CEUS) will be included. SR focusing on specialized ultrasound such as transvaginal, transrectal, or endosonographic ultrasound as well as elastography will be excluded.

Comparator We will include studies that compared ultrasound to an accepted reference standard of the respective complaint/region of interest. If the authors of a DTA-SR combined different reference standards in a metanalytic approach, both reference standards will be considered accepted. If the authors stratify their meta-analytic approach only according to different reference standards, the most accepted reference standard will be determined by our research team and will be preferred for study reporting especially in the GRADE approach (see below).

Study designs to be included We will include all SR of diagnostic test accuracy (DTA-SR) with MA that addressed specific research questions related to the diagnostic accuracy of ultrasound examinations with applicability as a POCUS examination in an ED.

Eligibility criteria A review has to fulfil the criteria suggested by Krnic Martinic et al. (2019) to be defined as an SR and included in this umbrella review:
i. Specific research question
ii. A reproducible search strategy (naming of databases, naming of search platforms/engines, search date and complete search strategy)
iii. Reporting of inclusion and exclusion criteria
iv. Presentation of selection/screening methods
v. Critically appraisal and report of the quality/risk of bias of the included studies
vi. Information about data analysis and synthesis that allows the reproducibility of the results.

Information sources Databases Ovid (Medline) and Embase.

Main outcome(s) Pooled sensitivity & specificity for the studied condition. If no pooled sensitivity or specificity is presented graphically or numerically, e.g., a SROC curve without a summary estimate due to high heterogeneity, the study will be excluded.

Additional outcome(s) None.

Data management The titles and abstracts will be independently assessed by four reviewers using a two-step approach. Initially, two reviewers will conduct a sensitive screening of all DTA-SR with MA. Subsequently, the titles and abstracts of these reviews will further be evaluated by two senior emergency physicians for their applicability as a POCUS examination in an ED setting. The reviews deemed applicable will then be selected as the preliminary eligible publications for full-text evaluation.
Any discrepancies between researcher screening decisions will be discussed, and, where no consensus is achieved, rectified by an ED and ultrasound expert. The full texts of the potentially eligible reviews will be obtained. Two reviewers will independently review each full text for inclusion, involving a third researcher in case of discrepancies. Studies excluded during full-text review will be presented.
Data extraction from the eligible articles will be independently performed by two reviewers, with discrepancies solved through discussion with a senior emergency physician: general study characteristics (first author, publication year, study design); the condition or disease being studied, categorized into a main group (Cardiovascular, Eye, Ear/Nose/Throat, Gastrointestinal, Genitourinary, Musculokeletal/rheumatoloigcal, Neurological, Respiratory, Trauma, Further), subgroup (e.g. Aortic disease, Endocarditis, Venous thromboembolism, Shock related, Heart disease, Arterial disease for Cardiovascular), and detailed description of the condition; details on the index test and reference standard; information about funding, information to assess the risk of bias of the DTA-SR and a summary statement of the risk of bias of the included studies; and DTA measures, including the selected (see Data synthesis) pooled sensitivity and specificity with 95% confidence interval (CI) or standard error (SE) and a summary statement about all reported diagnostic accuracies. For each condition, the number of studies and participants in each study for the DTA measure, prevalence of the condition, and information for GRADE for sensitivity/specificity will be extracted. If a study conducted a subgroup analysis, these DTA will be as well extracted. When a study presented different index tests to evaluate the conditions, all the tests with their information will be extracted.

Quality assessment / Risk of bias analysis To assess the methodological quality of the included DTA-SR, we adapted the AMSTAR-2 checklist for quality assessment for SR. Included articles will be independently categorized by two reviewers as “critically low”, “low”, “moderate”, or “high” quality based on the identified critical and non-critical weaknesses. Discrepancies will be solved by discussion with a third researcher.
The risk of bias including the potential impact of risk of bias on the results of the MA of primary

studies will also be evaluated with the adapted AMSTAR-2 checklist (items 12 and 13).
The quality of evidence for each specific condition and for each pooled diagnostic accuracy measure, i.e., pooled sensitivity and specificity, as described in Data synthesis, will be independently assessed by two reviewers using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. With GRADE, the following domains will be assessed: the i) risk of bias, ii) indirectness, iii) inconsistency and iv) imprecision (see below). As the impact of publication bias in DTA-SR is not well understood and the evaluation as well as the reporting of publication bias in DTA-SR is not adequate, publication bias assessment was only used indirectly for downgrading of the evidence through risk of bias evaluation (adapted Amstar-2 tool).
Detailed explanation on how the grading will be performed:
The pooled sensitivity and specificity, along with their 95% confidence intervals, will initially be rated as high-quality evidence. The evidence will be downgraded (to moderate, low, or very low) based on the following GRADE criteria:
Risk of Bias: If the AMSTAR-2 rating is moderate or low, the evidence may be downgraded. A critically low rating will automatically result in downgrading.
Inconsistency: If high heterogeneity is observed in the results of the DTA studies, the evidence will be downgraded. This will be assessed through visual inspection of the forest plot, the I^2 statistic, and the Chi^2 test. Lack of data for assessing inconsistency will also lead to downgrading.
Indirectness: Evidence will be downgraded if the studies are not directly applicable to the umbrella review's research question, such as when studies are conducted in specialized settings or require extensive experience for interpretation.
Imprecision: Evidence will be downgraded if the confidence interval of the pooled measure is wide (greater than 0.10) or includes clinically relevant thresholds for diagnostic accuracy (below 0.70).

Strategy of data synthesis The included DTA-SR will be grouped according to the conditions studied (one DTA-SR could be listed several times if multiple conditions were studied): i) cardiovascular, ii) ear/nose/throat, iii) eye, iv) further clinical assessment, v) gastrointestinal, vi) genitourinary, vii) intervention-related, vii) musculoskeletal/rheumatological, viii) neurological, ix) respiratory, x) trauma conditions, xi) other. Each main group will be further subdivided into subgroups and/or followed by the detailed specific condition, mostly the suspected disease.
Each DTA-SR that fulfils our inclusion criteria will be summarized for each examined condition with the following framework: clinical context, index test(s), reference standard, included study characteristics, methodological quality (of the DTA-SR), diagnostic accuracy, quality of evidence, conclusion of study authors. Multiple fact sheets may exist for one specific condition if there are multiple (overlapping/not overlapping) DTA with MA on that specific condition. For each condition, a narrative synthesis will be conducted based on all fact sheets for that condition, integrating all available DTA-SR for the specific condition. As there is anticipated overlap in the included studies, a meta-analytic approach is waived. For each fact sheet, one pair of pooled sensitivity and specificity will be selected, graded (see: quality assessment) and shown in a forest plot with other DTA-SR for that condition. If multiple pooled pairs of sensitivities and specificities are presented on a fact sheet, the pair that will be used for grading is identified in a hierarchical evaluation process: 1.) DTA-SR that most focused on ED/POCUS, 2.) Multi-organ POCUS was preferred over single organ US for complex conditions such as pulmonary embolism, 3.) the largest number of studies. If this pair is not unique, all pairs with the highest sensitivity and/or specificity with the narrowest CI will be graded.

Subgroup analysis None planned.

Sensitivity analysis None planned.

Language restriction English.

Country(ies) involved Switzerland.

Other relevant information Adapted Amstar-2 rating tool
Only adapted icons are listed. The changes of the tools are highlighted through bold (added criteria) or in brackets (not assessed criteria). An asterixis indicates a critical domain. Additionally, we classified domains 2 and 15 as non-critical.
1. Did the research questions and inclusion criteria for the review include PICO components?
Population, Index test (Intervention), Reference standard (Comparator), and Outcome are considered.
(3. Did the authors explain study design selection for inclusion?)
4.* Did the authors use a comprehensive literature search strategy?
Partial Yes: Searched at least 2 databases, provided keywords and/or search strategy, justified publication restrictions.
Yes: Searched bibliographies, conducted search within 24 months of completion of the review, and

consulted experts. (searched trial/study registries, searched for grey literature)
8. Did authors describe included studies in detail?
Partial Yes: Described populations, index test (interventions), reference standard (comparators), outcomes, and research designs.
Yes: Also included study settings and follow-up timeframes.
9.* Did authors use a satisfactory technique to assess risk of bias (RoB)?
Partial Yes: Assessed RoB from patient selection, index test, reference standard, (confounding and selection bias).
Yes: Also assessed timing (methods for exposures, outcomes, and flow).
11.* If meta-analysis was performed, did authors use appropriate methods for statistical combination of results?
Justified combining the data in a meta-analysis and used appropriate weighted technique to combine study results, adjusting for heterogeneity.
(Combined data using weighted techniques and reported separate summary estimates for RCTs and NRSI).
12 If meta-analysis was performed, did authors assess RoB impact on results?
Included only low RoB DTA studies (RCTs) or analyses for RoB impact.
13.* Did authors account for RoB in interpreting results?
Included only low RoB DTA studies (RCTs) or discussed RoB impact if moderate or high RoB studies were included.

Keywords POCUS; Point-of-care ultrasound; diagnostic test accuracy; sonography; sensitivity; sepecificity; echocardiography; ultrasound; emergency medicine.

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