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Comparison of 2-point and 3-point point-of-care ultrasound techniques for deep vein thrombosis at the emergency department

A meta-analysis

Ju Hyung Lee, MD[a], Sun Hwa Lee, MD, PhD[b], Seong Jong Yun, MD, PhD[c,*]

Abstract

Background: To our knowledge, so far, no studies have comprehensively examined the performance of 2-point and 3-point point-of-care compression ultrasound (POCUS) in the diagnosis of lower extremity deep vein thrombosis (DVT). The aim of this meta-analysis was to compare the performance of 2-point and 3-point POCUS techniques for the diagnosis of DVT and evaluate the false-negative rate of each POCUS method.

Methods: A computerized search of the PubMed, EMBASE, and Cochrane library databases was performed to identify relevant original articles. Bivariate modeling and hierarchical summary receiver operating characteristic modeling were performed to compare the diagnostic performance of 2-point and 3-point POCUS. The pooled proportions of the false-negative rate for each POCUS method were assessed using a DerSimonian–Laird random-effects model. Meta-regression analyses were performed according to the patient and study characteristics.

Results: Seventeen studies from 16 original articles were included (2-point, 1337 patients in 9 studies; 3-point, 1035 patients in 8 studies). Overall, 2-point POCUS had similar pooled sensitivity [0.91; 95% confidence interval (95% CI), 0.68–0.98; $P=.86$) and specificity (0.98; 95% CI, 0.96–0.99; $P=.60$) as 3-point POCUS (sensitivity, 0.90; 95% CI, 0.83–0.95 and specificity, 0.95; 95% CI, 0.83–0.99). The false-negative rates of 2-point (4.0%) and 3-point POCUS (4.1%) were almost similar. Meta-regression analysis showed that high sensitivity and specificity tended to be associated with an initial POCUS performer (including attending emergency physician > only resident) and separate POCUS training for DVT (trained > not reported), respectively.

Conclusion: Both 2-point and 3-point POCUS techniques showed excellent performance for the diagnosis of DVT. We recommend that POCUS-trained attending emergency physicians perform the initial 2-point POCUS to effectively and accurately diagnose DVT.

Abbreviations: CFV = common femoral vein, CI = confidence interval, DVT = deep vein thrombosis, ED = emergency department, HSROC = hierarchical summary receiver operating characteristics, POCUS = point-of-care compression ultrasound, PV = popliteal vein, QUADAS-2 = Quality Assessment of Diagnostic Accuracy Studies-2.

Keywords: deep vein thrombosis, emergency physician, lower extremity, meta-analysis, point-of-care ultrasound

1. Introduction

Lower extremity deep venous thrombosis (DVT) is a life-threatening vascular condition that affects adults of all ages and has an annual incidence of 0.1%.[1] Accurate and fast diagnosis of the DVT in the emergency department (ED) is crucial because one-third of untreated DVTs may clinically progress to significant pulmonary embolism.[2] As DVT is difficult to diagnose clinically, imaging is required for its diagnosis.[3]

Although the gold standard for the diagnosis of DVT is contrast venography, point-of-care compression ultrasound (POCUS) is increasingly used in the ED for evaluation of lower extremity DVT.[4,5] POCUS is listed as one of the core emergency ultrasonographic applications in the most-recent emergency ultrasonographic guidelines of the American College of Emergency Physicians.[6] In addition, previous meta-analyses reported excellent diagnostic performance of POCUS for the diagnosis of DVT.[4,5]

Thus far, 2 kinds of POCUS techniques have been used for the diagnosis of DVT. The 2-point POCUS technique, which tests the compressibility of the common femoral vein (CFV) and the popliteal vein (PV), has been commonly used.[7–10] The other

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JHL and SHL contributed equally to this work.

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[a] Department of Medical Service, 8311 unit, the Republic of Korea Air Force, Chungcheongnam-do, [b] Department of Emergency Medicine, Sanggye Paik Hospital, Inje University College of Medicine, [c] Department of Radiology, Kyung Hee University Hospital at Gangdong, Kyung Hee University School of Medicine, Seoul, Republic of Korea.

[*] Correspondence: Seong Jong Yun, Department of Radiology, Kyung Hee University Hospital at Gangdong, Kyung Hee University School of Medicine, 892 Dongnam-ro, Gangdong-gu, Seoul 05278, Republic of Korea (e-mail: zoomknight@naver.com).

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technique is 3-point POCUS, which tests the compressibility of the CFV, superficial femoral vein (SFV), and PV, as well as detects isolated SFV thrombosis of lower extremity DVT.[11,12]

However, to our knowledge, so far, no studies have comprehensively examined the performance of 2-point and 3-point POCUS in the diagnosis of lower extremity DVT. In addition, the data regarding the diagnostic performance of the 2-point and 3-point POCUS techniques have revealed broad ranges of sensitivity and specificity, making it important to thoroughly analyze and compare the currently available data on the diagnostic performance of these techniques for DVT. Such high-level evidence would be particularly interesting to critical care physicians including emergency physicians and radiologists, as the study characteristics and methodological settings differed widely among previous studies.

This meta-analysis aimed to assess the pooled performance, compare the performance, and evaluate and compare the false-negative rates of the 2-point and 3-point POCUS techniques for the diagnosis of DVT.

2. Methods

This meta-analysis followed the revised guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Accuracy Studies (PRISMA-DTA) statement.[13] Institutional review board approval was waived because the nature of our study was a systemic review and meta-analysis.

2.1. Data sources

The PubMed and EMBASE databases were searched up to September 1, 2018, to identify English-language studies on 2-point and 3-point POCUS for diagnosing DVT. And then, the Cochrane library database was searched for additional articles that did not exist in PubMed and EMBASE databases. The search terms “lower extremity,” “deep vein thrombosis,” or “ultrasound” were combined with “diagnosis,” “sensitivity,” “specificity,” or “receiver operating characteristic” as follows: ((“lower extremity”) OR (“lower limb”) OR (leg)) AND ((“deep vein thrombosis”) OR (“DVT”)) AND ((ultrasound) OR (ultrasonography) OR (sonography)) AND ((compression) OR (“point-of-care”) OR (“point of care”) OR (“POCUS”) OR (bedside)) AND ((diagnosis) OR (sensitivity) OR (specificity) OR (receiver operating characteristic) OR (ROC curve)). The bibliographies of the identified articles were screened to identify additional relevant studies. Two investigators screened the titles and abstracts for potential eligibility, and any disagreements were resolved through discussion.

2.2. Study selection

We included studies that fulfilled the following criteria: patients with suspected DVT; 2-point (CFV and PV) or 3-point (CFV, SFV, and PV) POCUS performed by an emergency physician as the index test; use of contrast venography, follow-up, or additional US performed by a radiologist as the reference standard for DVT; availability of sufficient information to reconstruct 2×2 contingency tables regarding sensitivity and specificity; and original research article as the publication type.

The exclusion criteria were as follows: case report or case series; review articles, guidelines, consensus statements, letters, editorials, clinical trials, and conference abstracts; studies not pertaining to the field of interest; studies using duplex US as the index test; POCUS not performed by an emergency physician; and studies with different definitions of the 3-point POCUS (e.g., CFV, PV, and greater saphenous vein).

2.3. Data extraction and quality assessment

Two investigators independently extracted data on the patient and study characteristics. The same investigators evaluated the methodological quality using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool.[14] Any disagreement between the reviewers was resolved through discussion.

A standardized form was used to extract data on patient characteristics (number of patients, DVT proportion, mean age, age range, and sex), study characteristics (study location, publication year, study design, reference standard, and blinding to the reference standard), and POCUS characteristics (technical parameters and interpretive characteristics). The study outcomes were extracted to create the 2×2 tables (i.e., true-positive, true-negative, false-positive, and false-negative results). The 2×2 tables were obtained using the Bayesian method (data were back-calculated based on prevalence and sample size) if only sensitivity and specificity were presented in an eligible study. If 2 or more reviewers independently assessed the diagnostic accuracy, the result with the highest accuracy was extracted.

2.4. Data synthesis and analysis of the diagnostic performance

The patient demographic characteristics and extracted covariates were summarized using standard descriptive statistics. If available, the studies were stratified using vertebral compression fracture analysis. Continuous variables were expressed as means and 95% confidence intervals (95% CIs), whereas categorical variables were expressed as frequencies or percentages, unless stated otherwise.

We used a bivariate random-effects model for analyzing and pooling the diagnostic performance (sensitivity and specificity) measurements across studies. To derive summary estimates of the diagnostic performance, we plotted estimates of the observed sensitivities and specificities for each test in forest plots and hierarchical summary receiver operating characteristics (HSROC) curves derived from individual study results.[15–17] These results were plotted using HSROC curves with 95% confidence and prediction regions.

Heterogeneity was determined using Cochran Q test ($P < .05$ indicated the presence of heterogeneity) and the I^2 test (0–40%, possibly no heterogeneity; 30–60%, moderate heterogeneity; 50–90%, substantial heterogeneity; and 75–100%, considerable heterogeneity).[18] When heterogeneity was noted, heterogeneity according to a “threshold effect” was analyzed by visual assessment of the coupled forest plots of sensitivity and specificity. A meta-analysis of diagnostic test accuracy studies simultaneously evaluates a pair of outcomes (i.e., sensitivity and specificity). Sensitivity and specificity are commonly inversely correlated and influenced by the threshold (cut-off) value.[15–17] In addition, Spearman correlation coefficient between the sensitivity and false-positive rate was calculated to determine any threshold effect; a coefficient >0.6 was considered to indicate a considerable threshold effect.[19] We omitted Deeks funnel

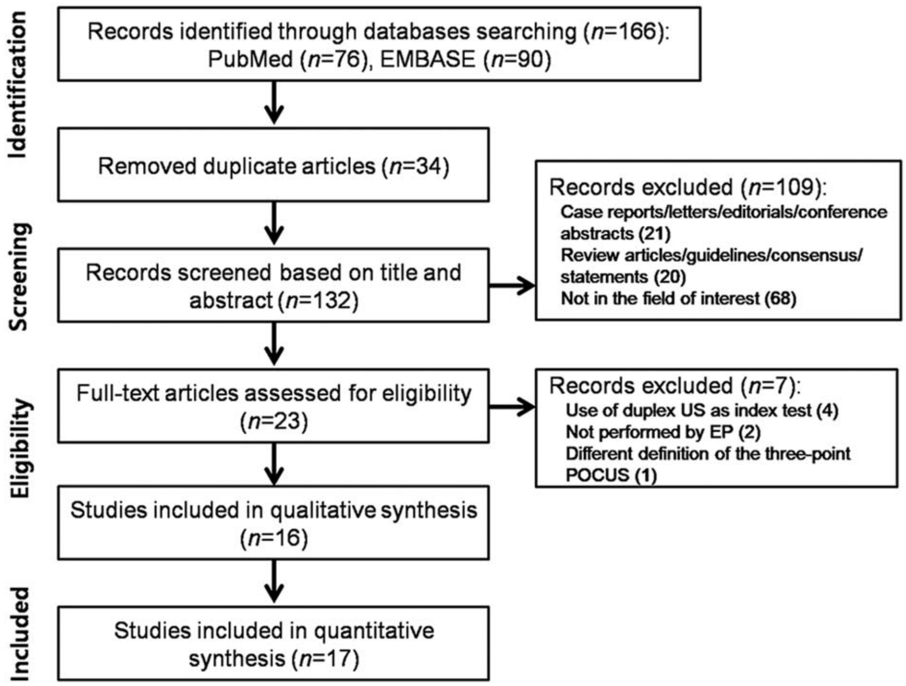

Figure 1. The study selection process for the meta-analysis. EP = emergency physician, POCUS = point-of-care ultrasound, US = ultrasound.

plot[20] of individual studies to test for publication bias according to the PRISMA-DTA.

2.5. Analysis of the false-negative rate

For analyzing the false-negative rate, the meta-analytic pooling was based on the inverse variance method for calculating weights, and the unadjusted pooled proportions and their 95% CIs were determined using the DerSimonian–Laird random-effect model.[15–17] Publication bias-adjusted pooled estimates (i.e., adjusted pooled proportions) were calculated using the trim-and-fill method.[21] If there was agreement between the unadjusted and adjusted pooled proportions, we considered the results to be robust against publication bias.

2.6. Meta-regression analysis

Meta-regression analyses using several covariates were performed to explore the potential causes of heterogeneity: study location (United States vs other countries), total patients (≥100 vs

Table 1

The included patients' demographic characteristics.

Author	No. of patients	No. of DVT	DVT (%)	Mean age	Age range	No. of male	No. of female	Male (%)
Two-point POCUS								
Crisp et al[29]	199	45	22.6	NR	NR	NR	NR	NA
Farahmand et al[8]	74	35	47.3	55.2	19-88	41	33	55.4
Frazee et al[30]	76	18	23.7	49	NR	48	28	63.2
Poley et al[33]	184	24	13.0	56	SD, 18	90	137	48.9
Pujol et al[34]	56	16	28.6	73	59-84	23	33	41.1
Theodoro et al[10]	156	32	20.5	NR	NR	NR	NR	NA
Zitek et al[37]	288	28	9.7	Median, 48	18-85	146	142	50.7
Zuker-Herman et al[38]	183	48	26.2	66.1	SD, 16.7	77	118	42.1
Jacoby et al[9]	121	27	22.3	NR	NR	NR	NR	NA
Three-point POCUS								
Abbasi et al[28]	81	58	71.6	47.2	SD, 18.6	46	35	56.8
Jang et al[11]	72	23	31.9	54	NR	24	48	33.3
Kim et al[31]	296	55	18.6	50	IQR, 37–60	147	149	49.7
Kline et al[12]	183	27	14.8	51.6	SD, 16.1	74	109	40.4
Pedraza Garcia et al[32]	109	59	54.1	68	22–89	49	60	45.0
Zuker-Herman R, et al[38]	183	48	26.2	66.1	SD, 16.7	77	118	42.1
Seyedhosseini et al[35]	50	21	42.0	55.4	NR	29	21	58.0
Shiver et al[36]	61	6	9.8	43	NR	20	41	32.8

DVT = deep vein thrombosis, IQR = interquartile range, No. = number, NR = not reported, POCUS = point-of-care ultrasound, SD = standard deviation.

Table 2

Characteristics of the included studies.

Ref.	Year	Locale	Study period	Study design	Reference standard for DVT	Blinding
Two-point POCUS						
Crisp et al[29]	2010	United States	2006.6–2007.7	Prospective, consecutive	Radiologist Duplex US	Blinding
Farahmand et al[8]	2011	Iran	NR	Prospective, consecutive	Radiologist Duplex US	Blinding
Frazee et al[30]	2001	United States	1997.2–1998.8	Prospective, consecutive	Radiologist Duplex US	Blinding
Poley et al[33]	2014	Canada	2009.11–2010.12	Prospective, consecutive	Radiologist Duplex US	Blinding
Pujol et al[34]	2018	France	2015.4–2017.2	Prospective, consecutive	Radiologist Duplex US	Blinding
Theodoro et al[10]	2004	United States	NR	Prospective, consecutive	Radiologist US	Blinding
Zitek et al[37]	2016	United States	2013.5–2014.7	Prospective, consecutive	Radiologist US	Blinding
Zuker-Herman et al[38]	2018	Israel	2015.7–2016.6	Prospective, consecutive	Radiologist Duplex US	Blinding
Jacoby et al[9]	2007	United States	NR	Prospective, consecutive	Radiologist Duplex US	Blinding
Three-point POCUS						
Abbasi et al[28]	2012	United States	2011.8–2013.11	Prospective, consecutive	Radiologist Duplex US	Blinding
Jang et al[11]	2004	United States	2009.8–2012.5	Prospective, consecutive	Radiologist Duplex US or contrast venography	Blinding
Kim et al[31]	2016	Republic of Djibouti	2010.11–2011.1	Prospective, consecutive	Radiologist Duplex US	Blinding
Kline et al[12]	2008	Turkey	2015.1–2015.3	Prospective, consecutive	Radiologist Duplex US	Blinding
Pedraza Garcia et al[32]	2018	Hong Kong	2004.1–2006.6	Prospective, consecutive	Radiologist Duplex US	Blinding
Zuker-Herman R, et al[38]	2018	United States	2011.5–2012.10	Prospective, consecutive	Radiologist Duplex US	Blinding
Seyedhosseini et al[35]	2017	Taiwan	2004.12–2006.6	Prospective, consecutive	Radiologist US	Blinding
Shiver et al[36]	2010	United States	2009.6–2010.6	Prospective, consecutive	Contrast venography	Blinding

DVT = deep vein thrombosis, No. = number, NR = not reported, POCUS = point-of-care ultrasound, US = ultrasound.

<100), proportion of DVT (≥25% vs <25%), proportion of male patients (≥50% vs <50%), initial POCUS performer (including attending emergency physician vs only resident), and separate POCUS training for DVT (trained vs not reported)

All statistical analyses were performed by 1 author with 3 years of experience performing systematic reviews and meta-analyses. The statistical analyses were performed using the "midas" and "metandi" modules in Stata software (version 10.0; StataCorp LP, College Station, TX) and the "mada" ad "metafor" packages in R software (version 3.4.1; R Foundation for Statistical Computing, Vienna, Austria). Results were considered statistically significant at a P value < .05.

3. Results

3.1. Literature

Figure 1 shows a flow diagram summarizing the literature search. During the initial search, 166 studies were identified. Additional articles were not found in Cochrane library database. After removing 34 duplicates, we reviewed 132 titles and abstracts and excluded 109 studies for the following reasons: case reports, letters, editorials, and conference abstracts (n = 21); review articles, guidelines, and consensus statements (n = 20); and not in the field of interest (n = 68). After reviewing the full text of 23 eligible articles, we excluded 7

Table 3

Technical parameters and interpretative characteristics of the included studies.

	Technical parameters			Interpretation	
Author	Vendor	Model	Frequency, MHz	Initial POCUS performer	Separate POCUS training
Two-point POCUS					
Crisp et al[29]	Bard	Bard Site-Rite IV	7.5	EM resident, attending EP	Yes
Farahmand et al[8]	Fukuda Denshi	FF Sonic UF-4300R	7.5	EM resident	Yes
Frazee et al[30]	Aloka	SSD-650 CL	3.5, 7.5	EM resident, attending EP	Yes
Poley et al[33]	Esaote	MyLab 5,	10, 12.5	EM resident, attending EP	Yes
Pujol et al[34]	GE	V-Scan Dualprobe	3.4–8	NR	Yes
Theodoro et al[10]	Agilent/SonoSite	Linear Point Hx/SonoSite 180	10	EM resident, attending EP	NR
Zitek et al[37]	Mindray	M7	7.5	EM resident	Yes
Zuker-Herman et al[38]	Philips	NR	7.5	EM resident, attending EP	Yes
Jacoby et al[9]	Philips	ATL 5000	7.5	EM resident	Yes
Three-point POCUS					
Abbasi et al[28]	Honda	HS-2000	NR	EM resident	NR
Jang et al[11]	Aloka	SSD-1400	7.5	EM resident	Yes
Kim et al[31]	Toshiba/Philips/GE	SSH-140A/ATL Ultramark 400C/Logiq E	7.5	EM resident, attending EP	NR
Kline et al[12]	Ultrasonix	Sonix CEP	14.5	EM resident, attending EP	Yes
Pedraza Garcia et al[32]	Esaote	MyLab 25	7.5	Attending EP	Yes
Zuker-Herman et al[38]	Philips	NR	7.5	EM resident, attending EP	Yes
Seyedhosseini et al[35]	Medison	Sonoace X8	NR	EM resident	Yes
Shiver et al[36]	Phillips/SonoSite	HDI 4000/MicroMaxx	12	EM resident	Yes

EM = emergency medicine, EP = emergency physician, NR = not reported, POCUS = point-of-care ultrasound.

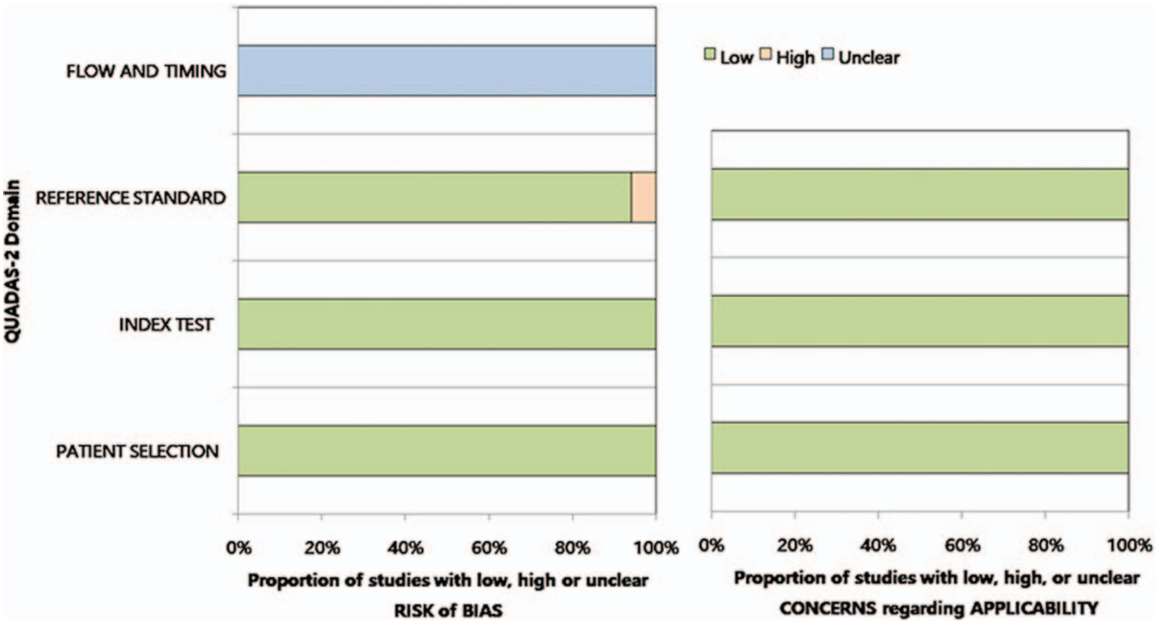

Figure 2. Grouped bar charts showing the risk of bias (left) and applicability concerns (right) for the 17 included studies, using the Quality Assessment of Diagnostic Accuracy Studies-2 domains.

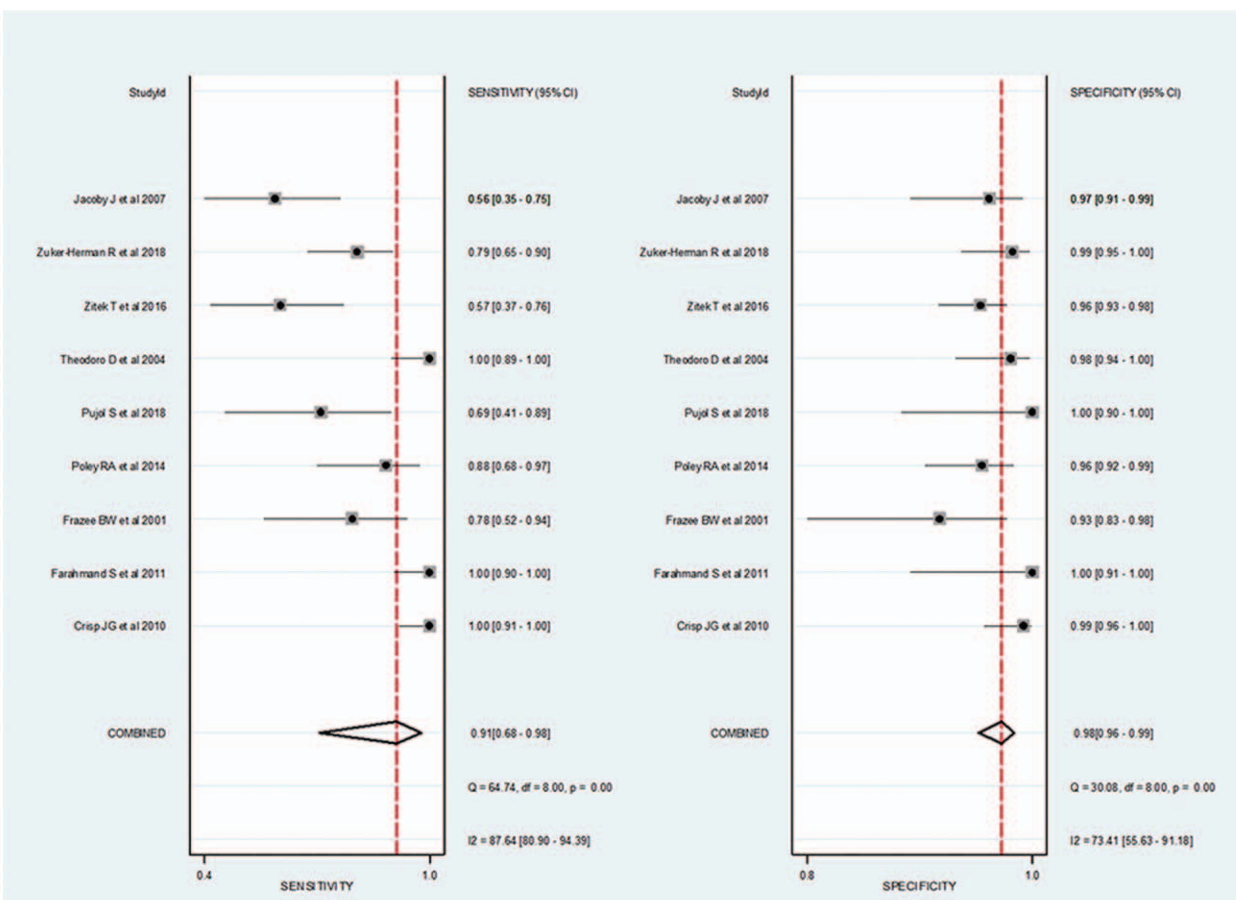

Figure 3. Coupled forest plots for the pooled sensitivity and specificity of 2-point point-of-care ultrasound for the diagnosis of deep vein thrombosis. Dots in squares represent sensitivity and specificity. Horizontal lines represent the 95% confidence interval (CI) for each included study. The combined estimate ("Summary") is based on the random-effects model and is indicated using diamonds. Corresponding heterogeneities (I^2) with 95% CIs are provided in the bottom right corners: $I^2 = 100\% \times (Q - \mathrm{df})/Q$, where Q is Cochran heterogeneity statistic and df is the degrees of freedom.

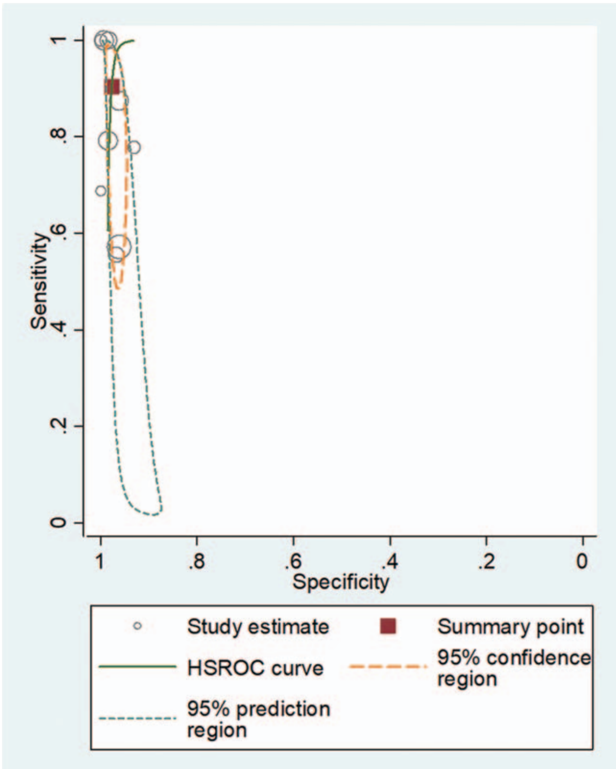

Figure 4. Hierarchical summary receiver operating characteristic (HSROC) curve for using 2-point point-of-care ultrasound for the diagnosis of deep vein thrombosis. The summary point (red box) indicates that the summary sensitivity was 0.84 (95% CI: 0.72–0.92) and the summary specificity was 0.91 (95% CI: 0.85–0.95). The 95% confidence region represents the 95% CIs of summary sensitivity and specificity, and the 95% prediction region represents the 95% CIs of sensitivity and specificity for each included study. The study estimates indicate the sensitivity and specificity estimated using the data from each study. The size of the marker is scaled according to the total number of patients in each study.

studies for the following reasons: use of duplex US as index test (n=4),[7,22–24] POCUS not performed by an emergency physician (n=2),[25,26] and different definition of the 3-point POCUS (n=1).[27] Ultimately, 16 original research articles,[8–12,28–38] including a total of 2372 patients, were included in the meta-analysis. One of them[38] evaluated the diagnostic performance of 2-point and 3-point POCUS using different 2 cohorts (2 diagnostic performance studies in 1 article); thus, we evaluated 17 studies from the final 16 original research articles. Among them, 9 studies[8–10,29, 30,33,34,37,38] evaluated the performance of the 2-point POCUS for diagnosing DVT, and 8 studies[11,12,28,31,32,35,36,38] evaluated the performance of the 3-point POCUS for diagnosing DVT.

3.2. Characteristics of the studies

The patient characteristics are summarized in Table 1. The patient number in all studies ranged from 50 to 296 (mean age, 33–63.6 years). The mean proportion of men was 43% to 73%. The study and POCUS characteristics are summarized in Tables 2 and 3, respectively. All studies were prospectively designed with blinding from reference standards and performed consecutive patient recruitment. All studies, except one, were single-centered.[31] Fifteen studies from 14 articles[8–10,12,28–35,37,38] used follow-up or additional US by radiologists as the reference standard, whereas 2 studies[11,36] used contrast venography as the reference standard.

In all studies, DVT was defined as noncompressible or no visualized veins at one or more target points. Absence of DVT was defined as visualization of the complete (anterior-to-posterior) obliteration of the veins.

3.3. Quality assessment

Figure 2 shows the risk of bias and applicability concerns for the 17 included studies. Overall, no studies were considered to be seriously flawed according to the QUADAS-2 tool. All the studies satisfied ≥4 of the 7 items.

Regarding the patient selection and index test domains, all studies were considered to have a low risk of bias. One study[11] was considered to have a high risk of bias about the reference standard because it used 2 modalities for reference standard (US or contrast venography). Regarding the flow and timing domains, all studies had an unclear risk of bias because the mean interval between POCUS and the reference standard was not reported. All studies exhibited low applicability to our research question in the patient selection, index test, and reference standard domains.

3.4. Performance of 2-point and 3-point POCUS for the diagnosis of DVT

For 2-point POCUS, the pooled sensitivity and specificity were 0.91 (95% CI, 0.68–0.98) and 0.98 (95% CI, 0.96–0.99), respectively. The Q test revealed significant heterogeneity (Q = 8.369, P = .008). Sensitivity (I^2 = 87.64%) and specificity (I^2 = 73.41%) indicated considerable and substantial heterogeneity, respectively. A threshold effect was shown by visual analysis of the coupled forest plot of sensitivity and specificity (Fig. 3) as well as a corresponding correlation coefficient of 0.103 (95% CI, –0.342 to 0.456) between sensitivity and the false-positive rate. The area under the HSROC curve was 0.99 (95% CI, 0.97–0.99; Fig. 4).

For 3-point POCUS, the pooled sensitivity and specificity were 0.90 (95% CI, 0.83–0.95) and 0.95 (95% CI, 0.83–0.99), respectively. The Q test revealed significant heterogeneity (Q = 18.264, P < .01). Sensitivity (I^2 = 77.21%) and specificity (I^2 = 94.19%) indicated substantial and considerable heterogeneity, respectively. A threshold effect was shown by visual analysis of the coupled forest plot of sensitivity and specificity (Fig. 5) as well as by a corresponding correlation coefficient of 0.091 (95% CI, –0.648 to 0.656) between sensitivity and false-positive rate. The area under the HSROC curve was 0.96 (95% CI, 0.94–0.97; Fig. 6).

3.5. Comparison of the diagnostic performance of 2-point and 3-point POCUS techniques

In a comparison of the overall diagnostic performance between 2-point and 3-point POCUS, the sensitivity (P = .86) and specificity (P = .60) were not significantly different.

3.6. False-negative rate of the 2-point and 3-point POCUS techniques

The forest plots for the false-negative rates of the 2-point POCUS demonstrated a pooled proportion of 4.0% (95% CI, 2.3–5.9;

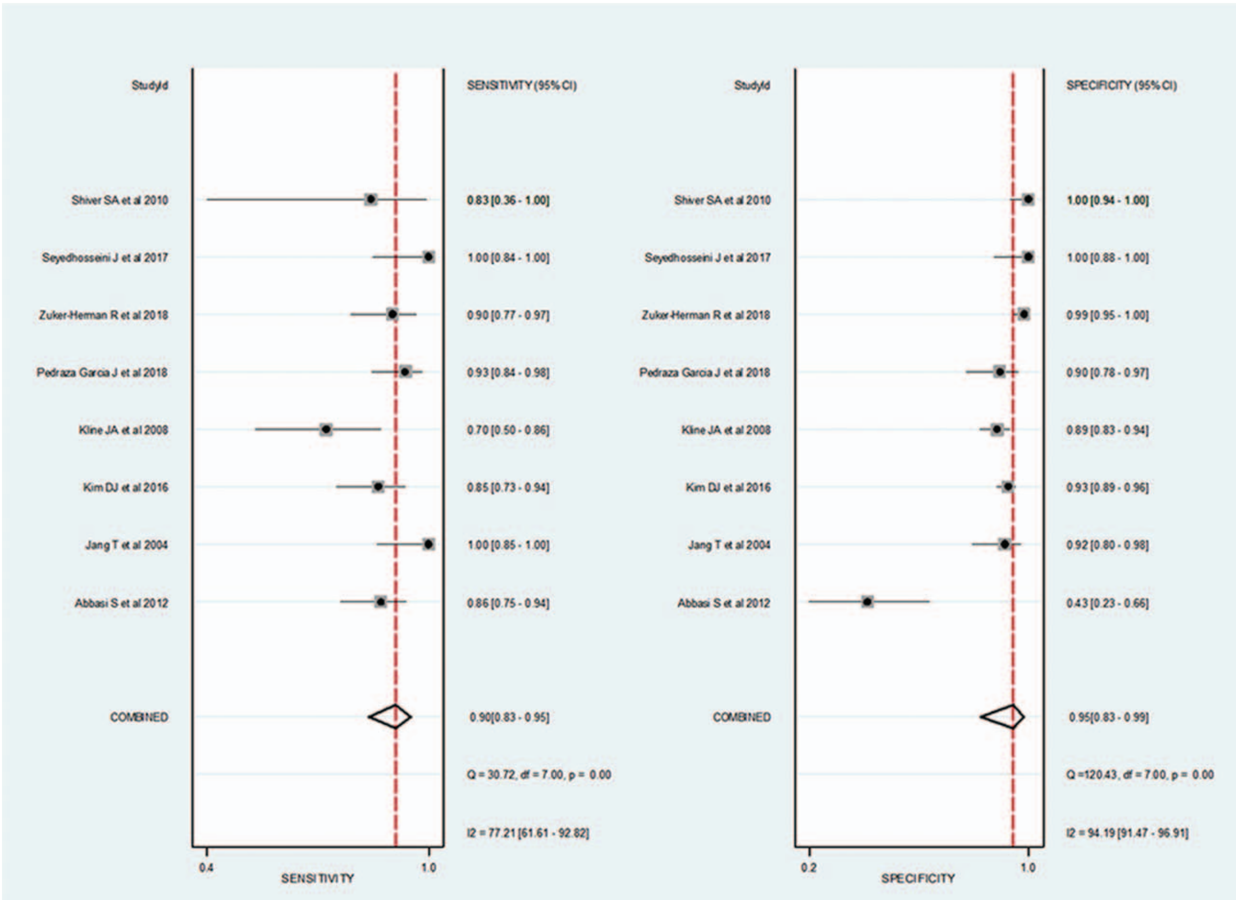

Figure 5. Coupled forest plots of pooled sensitivity and specificity of 3-point point-of-care ultrasound for the diagnosis of deep vein thrombosis. Dots in squares represent sensitivity and specificity. Horizontal lines represent the 95% confidence interval (CI) for each included study. The combined estimate ("Summary") is based on the random-effects model and is indicated using diamonds. Corresponding heterogeneities (I^2) with 95% CIs are provided in the bottom right corners.

Fig. 7). After adjusting for publication bias using the trim-and-fill approach, the adjusted pooled proportion was 4.2% (95% CI, 2.7–6.7), which was in perfect agreement with the unadjusted pooled estimates.

The forest plots for false-negative rates of the 3-point POCUS demonstrated a pooled proportion of 4.1% (95% CI, 2.3–7.0; Fig. 8). After adjusting for publication bias using the trim-and-fill approach, the adjusted pooled proportion was 4.4% (95% CI, 3.0–7.7), which was in perfect agreement with the unadjusted pooled estimates.

3.7. Meta-regression analysis results

The results of the meta-regression analyses showed that the only significant source of heterogeneity in sensitivity was the initial POCUS performer (2-point, $P=.01$; 3-point, $P=.04$), with higher sensitivity reported in studies with an attending emergency physician and resident than in those with only a resident (Table 4). The significant sources of heterogeneity in specificity were the presence of the separate POCUS training (3-point, $P=.02$), with higher specificity reported in studies with a definite description of the POCUS training than in those without such a description. Other factors, including study locale, total patient number, proportion of DVT, and proportion of male were not significantly different (2-point, $P=.15$–.86; 3-point, $P=.07$–.95).

4. Discussion

The present meta-analysis revealed that 2-point POCUS (sensitivity: 91%, specificity: 98%) and 3-point POCUS (sensitivity: 90%, specificity: 95%) were excellent methods for the diagnosis of DVT. There was no significant difference in the diagnostic performance between the 2 methods. Moreover, the pooled proportions of the false-negative rate of the 2-point POCUS (4.0%) and 3-point POCUS (4.1%) were almost similar.

The present study focused on the diagnostic performance of POCUS. The most-recent emergency US guidelines of the American College of Emergency Physicians[6] demonstrated that the POCUS is the core technique for diagnosing DVT in clinical practice. Comparison of the 2 POCUS techniques is important because of the uncertainty regarding which POCUS method is more accurate and effective in the ED. Generally, 2-point POCUS is less time-consuming than 3-point POCUS; thus, we believe that the 2-point POCUS is more useful for diagnosing DVT. We also evaluated the pooled proportion of the false-negative rate of each POCUS method. Due to the high mortality rate of DVT, the false-negative rate is as important as the accuracy. In our meta-

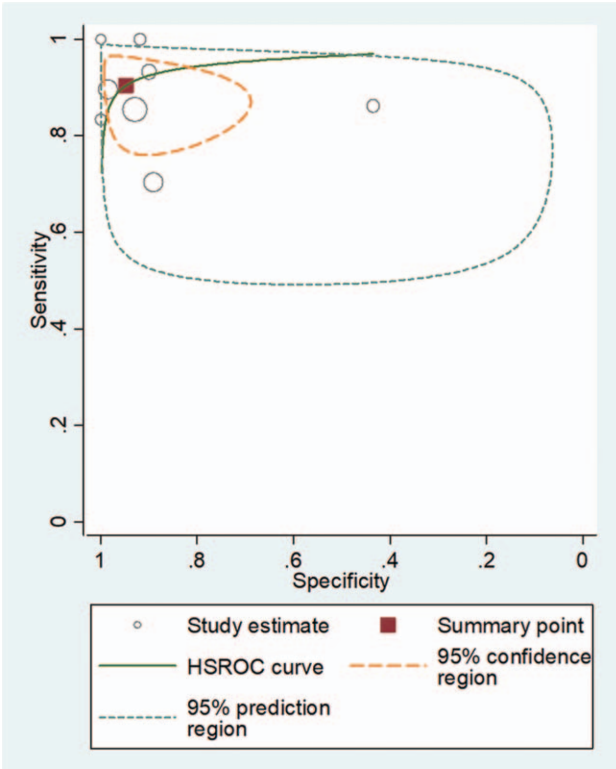

Figure 6. Hierarchical summary receiver operating characteristic (HSROC) curve for using 3-point point-of-care ultrasound for the diagnosis of deep vein thrombosis. The summary point (red box) indicates that the summary sensitivity was 0.95 (95% CI: 0.75–0.99) and the summary specificity was 0.95 (95% CI: 0.85–0.98). The 95% confidence region represents the 95% CIs of summary sensitivity and specificity, and the 95% prediction region represents the 95% CI of sensitivity and specificity for each included study.

analysis, the false-negative rates of the 2 POCUS methods were almost the same (approximately 4%). We believe the effect of the isolated SFV thrombosis in 2-point POCUS was minimal. In addition, we evaluated the meta-regression analysis. It is possible that the POCUS-trained emergency physician's awareness of the specific point of tenderness provided better sensitivity and specificity.

The current meta-analysis differs from the previous meta-analyses on POCUS in many aspects. Although the 2 previous meta-analyses[4,5] evaluated the diagnostic performance of US for DVT, they had several limitations. First, although they[4,5] evaluated the diagnostic performance of the heterogenous US methods (2-point POCUS, 3-point POCUS, and extended CUS, etc, with or without color Doppler), the studies were not divided and compared. Second, the studies did not perform a thorough analysis of the potential sources of heterogeneity, as they did not distinguish between sensitivity and specificity for the covariates' effects, which precluded any recommendations regarding methods to increase the diagnostic performance of POCUS for DVT. Third, one of the previous studies[4] did not use a hierarchical model (e.g., the bivariate model and the HSROC model), which is a recommended statistical tool for the meta-analysis of studies on diagnostic accuracy. Finally, the 2×2 table evaluation when 2 or more reviewers independently assess the diagnostic accuracy remains unclear. In our meta-analysis, the result with the highest accuracy was extracted.

Our meta-regression analysis revealed that the initial POCUS performer and receipt of separate POCUS training before the study were sources of heterogeneity. In particular, the pooled sensitivity was higher in studies including the attending emergency physician than in studies including only the resident. In addition, the pooled specificity was higher in studies that included POCUS training for DVT before the study. Thus, we recommend that POCUS-trained attending emergency physicians perform the initial US for accurate diagnosis of DVT.

The present study has several limitations. First, we included a relatively small number of included studies. Nevertheless, we were able to draw several important conclusions regarding the diagnostic performance of 2-point and 3-point POCUS and related factors, which we believe provides a useful overview owing to the broad search terms used and inclusion of only easily accessible studies (published in English and available in the PubMed and EMBASE databases). Second, all included studies revealed positive results, which could be attributed to a publication bias; however, such a bias cannot be quantified. Although we omitted Deeks funnel plots according to the

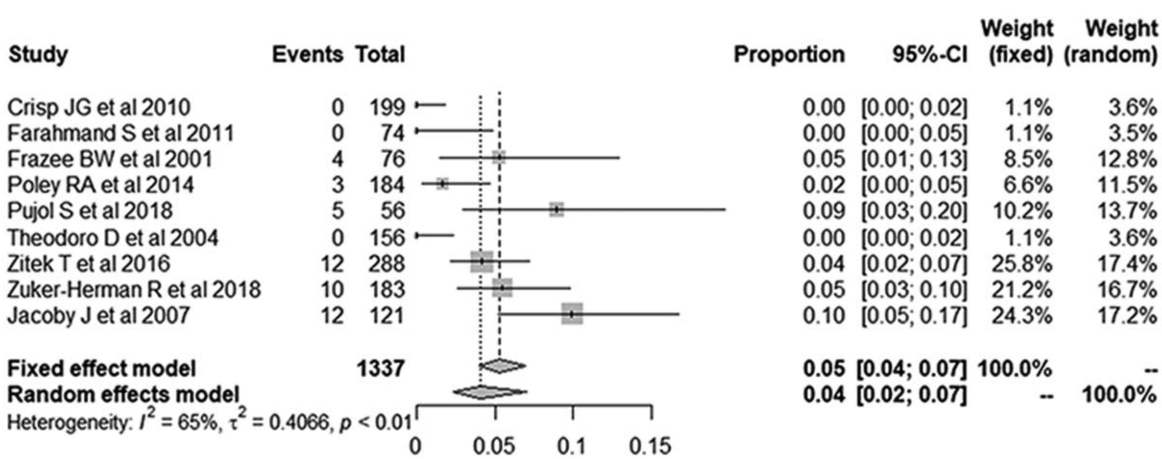

Figure 7. Forest plots of the false-negative rate of the 2-point point-of-care ultrasound for the diagnosis of deep vein thrombosis. Numbers are pooled estimates with 95% confidence intervals (95% CIs) in parentheses. Horizontal lines indicate 95% CIs, and the black box on each line indicates the standardized mean difference for each study. The black diamond at the bottom of the plot indicates the average effect size of the included studies.

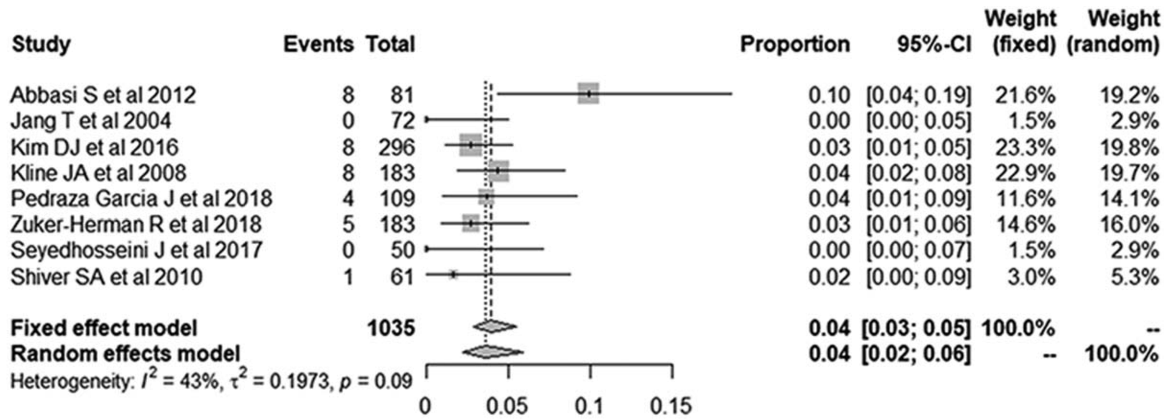

Figure 8. Forest plots of the false-negative rate of the 3-point point-of-care ultrasound for the diagnosis of deep vein thrombosis. Numbers are pooled estimates with 95% confidence intervals (95% CIs) in parentheses. Horizontal lines indicate 95% CIs, and the black box on each line indicates the standardized mean difference for each study. The black diamond at the bottom of the plot indicates the average effect size of the included studies.

Table 4

Meta-regression analyses for potential source of the heterogeneity.

Covariate	No. of studies	Sensitivity (95% CI)	*P*	Specificity (95% CI)	*P*
Two-point POCUS (n=9)					
Locale			.86		.21
United States	5	0.87 (0.70–1.00)		0.97 (0.96–0.99)	
Countries other than United States	4	0.90 (0.73–1.00)		0.98 (0.96–1.00)	
No. of patients			.85		.15
≥100	6	0.87 (0.72–1.00)		0.98 (0.96–0.99)	
<100	3	0.91 (0.73–1.00)		0.97 (0.94–1.00)	
DVT (%)			.46		.61
≥25%	3	0.90 (0.72–1.00)		0.99 (0.98–1.00)	
<25%	6	0.88 (0.72–1.00)		0.97 (0.96–0.99)	
Male (%)			.80		.50
≥50%	3	0.85 (0.67–1.00)		0.96 (0.94–0.99)	
<50%	3	0.80 (0.60–1.00)		0.98 (0.96 - 0.99)	
Initial POCUS performer			**.01**		.80
Including attending EP	5	0.94 (0.84–1.00)		0.98 (0.96–1.00)	
Only EM resident	4	0.80 (0.53–1.00)		0.98 (0.96–1.00)	
Separate POCUS training			.84		.41
Yes	8	0.86 (0.72–1.00)		0.98 (0.96–0.99)	
NR	1	0.98 (0.90–1.00)		0.98 (0.96–1.00)	
Three-point POCUS (n=8)					
Locale			.07		.24
United States	3	0.87 (0.74–0.99)		0.96 (0.89–1.00)	
Countries other than United States	5	0.91 (0.85–0.97)		0.94 (0.84–1.00)	
No. of patients			.07		.61
≥100	4	0.89 (0.78–0.96)		0.94 (0.86–1.00)	
<100	4	0.95 (0.91–1.00)		0.95 (0.85–1.00)	
DVT (%)			.33		.95
≥25%	5	0.92 (0.88–0.96)		0.93 (0.84–1.00)	
<25%	3	0.82 (0.73–0.92)		0.96 (0.89–1.00)	
Male (%)			.50		.52
≥50%	2	0.95 (0.87–1.00)		0.86 (0.59–1.00)	
<50%	6	0.89 (0.82–0.97)		0.96 (0.91–1.00)	
Initial POCUS performer			**.04**		.61
Including attending EP	4	0.96 (0.91–1.00)		0.95 (0.85–1.00)	
Only EM resident	4	0.87 (0.78–0.96)		0.94 (0.86–1.00)	
Separate POCUS training			.58		**.02**
Yes	6	0.91 (0.85–0.98)		0.97 (0.93–1.00)	
NR	2	0.86 (0.75–0.98)		0.77 (0.47–1.00)	

Boldface type indicates statistical significance ($P<.05$). CI=confidence interval, DVT=deep vein thrombosis, EM=emergency medicine, EP=emergency physician, No.=number, NR=not reported, POCUS=point-of-care ultrasound.

PRISMA-DTA guidelines, we observed a low probability of publication bias (2-point, $P=.38$; 3-point, $P=.77$), which suggests that this factor did not undermine our results. Third, there were methodological differences between the included studies, and the extensive meta-regression analysis revealed that these variables were significant sources of heterogeneity. This methodological diversity might affect the pooled estimates, especially as the POCUS technical parameters were not assessed in the meta-regression analysis because not all studies reported the values for gain, dynamic range, and mechanical index. Fourth, we only examined studies wherein the diagnostic performance of the 2-point and 3-point POCUS techniques was based on conclusive cases, as the eligible studies did not include cases with equivocal or inconclusive findings. Fifth, almost studies using 2-point and 3-point POCUS emphasized its diagnostic performance alone and did not compare it to other modalities. Thus, a future comprehensive study with a larger sample size that includes equivocal and inconclusive cases and more advanced methodology (e.g., comparison to computed tomography venography or magnetic resonance venography) may be needed to confirm the usefulness of 2-point and 3-point POCUS techniques as initial diagnostic tools in routine clinical practice and determine the optimal parameters for POCUS.

In summary, the present meta-analysis revealed that both 2-point and 3-point POCUS showed excellent performance for the diagnosis of DVT. The effect of the isolated SFV thrombosis in 2-point POCUS was minimal. We recommend that POCUS-trained attending emergency physicians perform the initial 2-point POCUS to effectively and accurately diagnose DVT.

Author contributions

Conceptualization: Sun Hwa Lee, Seong Jong Yun.
Data curation: Sun Hwa Lee, Seong Jong Yun.
Formal analysis: Sun Hwa Lee, Seong Jong Yun.
Methodology: Ju Hyung Lee, Seong Jong Yun.
Validation: Seong Jong Yun.
Writing – original draft: Sun Hwa Lee.
Writing – review & editing: Ju Hyung Lee, Seong Jong Yun.

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