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Ultrasound-assisted Lumbar Punctures: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Lumbar punctures (LPs) are a common procedure in emergency medicine. However, studies have found that failed procedure rates can be as high as 50%. Ultrasound has been suggested to improve success rates by visually identifying the location and trajectory for the LP procedure. This systematic review and meta-analysis was performed to determine whether the use of ultrasound improved the rate of successful LP performance.

Methods: PubMed, CINAHL, Scopus, LILACS, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials, and bibliographies of selected articles were assessed for all randomized controlled trials comparing the success rates of ultrasound-assisted LP with landmark-based LP. Secondary outcomes included the rate of traumatic LPs, time to procedural success, number of needle passes, and patient pain score. Data were dual extracted into a predefined worksheet, and quality analysis was performed using the Cochrane Risk of Bias tool. Data were summarized and a meta-analysis was performed with subgroup analyses by pediatric versus adult patients and by operator training level.

Results: Twelve studies (n = 957 total patients) were identified. Ultrasound-assisted LP was successful in 90.0% of patients and landmark-based LP was successful in 81.4% of patients. The calculated risk difference (RD) was 8.9% (95% confidence interval [CI] = 1.2% to 16.7%) with an odds ratio (OR) of 2.22 (95% CI = 1.03 to 4.77) in favor of the ultrasound-assisted group. There were fewer traumatic LPs in the ultrasound-assisted group (10.7% vs. 26.5%; RD = -16.4%, 95% CI = -27.6% to -5.2%; OR = 0.28, 95% CI = 0.18 to 0.45). Ultrasound-assisted LP was also associated with a shorter time to successful LP (6.87 minutes vs. 7.97 minutes), fewer mean needle passes (2.07 vs. 2.66), and lower patient pain scores (3.75 vs. 6.31).

Conclusions: Ultrasound-assisted LPs were associated with higher success rates, fewer traumatic LPs, shorter time to successful LP, fewer needle passes, and lower patient pain scores. Ultrasound should be considered prior to performing all LPs, especially in patients with difficult anatomy. Further studies are recommended to determine whether this effect is consistent in both adult and pediatric subgroups, as well as the impact of transducer type and body habitus on this technique.

Lumbar punctures (LPs) are a common procedure in emergency medicine (EM). However, success rates can be suboptimal, especially in pediatric patients, where it has been found to be as low as 50% to 60% in some studies.^{1–3} Among adult patients, one large study found a 35% rate of traumatic or unsuccessful LPs.⁴ Unsuccessful LPs can lead to potential adverse events, including increased pain and prolonged immobilization or restraint, while traumatic LPs can be difficult to interpret, resulting in diagnostic uncertainty, prolonged hospital courses, additional procedures, and potential iatrogenic complications. $^{5-8}$

Ultrasound has been suggested to improve the success rates of LPs, but prior data were limited by small sample sizes.^{9–11} Recently, many studies have been published evaluating the use of ultrasound to facilitate LPs.^{12–20}

The primary goal of this study was to determine whether ultrasound-assisted LP would result in an

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improved success rate when compared with the traditional, landmark-based technique. Secondary outcomes included differences in the rates of traumatic LPs, time to procedural success, number of needle passes, and patient pain scores. Subgroup analyses were planned a priori between adult versus pediatric patients and resident versus attending physician sonographers.

METHODS

Our study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and was performed in accordance with best practice guidelines.²¹ In conjunction with a medical librarian, we conducted a search of PubMed, CINAHL, LILACS, Scopus, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials to include citations from inception to April 19, 2018. Details of the search strategy are included in Data Supplement S1, Appendix S1 (available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10. 1111/acem.13558/full). We reviewed the bibliographies of identified studies and review articles for potential missed articles. We also consulted with topic experts to help identify any further relevant studies.

Inclusion and Exclusion Criteria

Inclusion criteria consisted of all randomized controlled trials comparing the success rates of ultrasoundassisted LP with landmark-based LP. Adult and pediatric patients were included. Exclusion criteria included case reports, case series, retrospective studies, nonrandomized studies, cadaver studies, nonhuman studies, and conference abstracts. There were no language or date restrictions. Two investigators (MG, DH) independently assessed studies for eligibility based on the above criteria. All abstracts meeting initial criteria were reviewed as full manuscripts. Studies determined to meet the eligibility criteria on full-text review by both extractors were included in the final data analysis. Any discrepancies were resolved by consensus with the addition of a third reviewer (GDP) if needed.

Data Collection and Processing

Two investigators (MG, DH) independently extracted data from the included studies. The investigators underwent initial training and extracted data into a predesigned data collection form. The following information was abstracted: last name of the first author, publication year, study country, study population size, study location (e.g., emergency department [ED], operating room, intensive care unit), mean age of study patients, sex of study patients, mean body mass index (BMI), percentage of obese patients (defined as $BMI > 29 \text{ kg/m}^2$), type of ultrasound transducer used, ultrasound technique (i.e., preprocedure or realtime guidance), sonographer training, operator specialty, operator experience (i.e., attending or resident physician), total successful placements in each group, total number of patients in each group, number of traumatic LPs (as defined by the study authors), time to successful LP, number of needle passes, and patient pain score. When insufficient information was available, the authors were contacted a minimum of three times for additional data. Studies were independently assessed for quality by two separate investigators (MG, DH) utilizing the Cochrane Risk of Bias tool. Any discrepancies were resolved by consensus with inclusion of a third party if necessary (GDP).

Data Analysis

The effect of dichotomous variables was measured by both risk difference (RD) and odds ratio (OR) using the Mantel-Haenszel method. RD was chosen as the preferred measure for clinicians to interpret clinically meaningful absolute risk reductions, while OR was chosen to provide clinicians with a measure of association between exposure and outcomes. The effect of continuous variables was measured by mean difference using the inverse-variance method. All data were analyzed using 95% confidence intervals (CIs), and a twosided p-value of <0.05 was considered statistically significant. Chi-square and I² statistics were used to assess heterogeneity of included studies, with a p-value of <0.1 or I² greater than 50% considered significant for heterogeneity.²² In cases in which significant heterogeneity existed, adjusted data were analyzed with a random-effects model. In the absence of significant heterogeneity, a fixed-effects model was used. For the primary outcome, the fragility index was calculated using Fisher's exact test. Additionally, a post hoc sensitivity analysis was completed of the two largest trials of adult patients. A funnel plot and Egger's test with an alpha level of 0.05 were used to assess for publication bias for the primary outcome measure.²³ Statistical analyses were performed using RevMan (version 5.3, The Nordic Cochrane Centre) and StataMP (version

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13.0, StataCorp LP) was utilized to assess publication bias.

RESULTS

A total of 1,054 studies were identified. PubMed yielded 546 studies, Scopus identified 299 studies, CINAHL found 162 studies, LILACS discovered 14 studies, the Cochrane Database of Systematic Reviews yielded no studies, and the Cochrane Central Register of Controlled Trials identified 35 studies. After duplicates were removed, 698 abstracts were reviewed with 54 selected for full-text review (Figure 1). No additional papers were identified through bibliographic review.

Twelve studies, comprising 957 total patients, were selected for the final analysis (Table 1). Studies were published between 2007 and 2018 with individual population sizes ranging from 26 to 158 (Table 1). Seven studies were conducted in the United States,^{9,13–18} three were conducted in Korea,^{10–12} one study was conducted in Iran,¹⁹ and one study was conducted in Turkey.²⁰ All studies were performed in the ED setting, although two studies also included either pediatric floor patients¹⁴ or intensive care unit

patients.¹⁵ Six studies evaluated only adult patients⁹⁻ 11,13,17,19 and six studies evaluated only pediatric patients.^{12,14–16,18,20} Six studies used a linear transducer.^{9,13,14,16,17,19} three used a curvilinear transducer,^{10,11,20} and one allowed providers to use either transducer.¹⁵ The transducer type was not described in two studies.^{12,18} All 12 studies used ultrasound for preprocedural identification. No studies assessed dynamic ultrasound-guided LPs. Ultrasound was performed by an EM physician in 11 studies⁹⁻¹⁹ and by a radiologist in one study.²⁰ Ultrasound was performed by attending physicians in three studies^{14,18,20} and resident physicians in six studies.^{10-13,15,19} The remaining studies used a mix of providers or did not describe the sonographer experience level.^{9,16,17}

Overall, ultrasound-assisted LP was successful in 421 of 468 patients (90.0%) and landmark-based LP was successful in 397 of 488 patients (81.4%). The calculated RD was 8.9% (95% CI = 1.2% to 16.7%) with a number needed to ultrasound (NN_{US}) of 11 (95% CI = 6 to 83) to successfully perform one LP in a patient in whom a landmark-based approach would have failed (Figure 2A). The OR was 2.22 (95% CI = 1.03 to 4.77) in favor of the ultrasound-assisted group (Figure 2B). There was moderate statistical



Figure 1. PRISMA flow diagram.

es	Primary Study Patient Mean Male Mean Number (%) US Sonographer Country Location Population Patient Age Patients (%) Patient BMI BMI > 29 kg/m² Transducer Specialty Sonographer Experience	ted States ED Adults 36.9 years ND 26.5 12 (26.1%) Linear EM Resident and attending physicians	ea ED Adults 43.8 years 27 (44.3%) 22.8 ND Curvilinear EM Resident physician	ea ED Adults 70.2 years 23 (38.3%) 23.7 ND Curvilinear EM Resident physician	n ED Adults 42.3 years 32 (40%) ND 26 (32.5%) Linear EM Resident physician	ea ED Pediatrics 8.5 years 43 (67.2%) 18 ND ND EM Resident physician	ted States ED Adults 40.5 years 46 (46%) 27.6 ND Linear EM Resident physician	ted States ED and Pediatrics 24 days ND ND Linear EM Attending physician pediatric floor	ted States ED or ICU Adults 41.0 years 68 (43.3%) 26.3 45 (28.5%) Linear or EM Resident physician curvilinear	ted States ED Pediatrics 41.6 days 26 (60.5%) ND ND Linear EM ND	ted States ED Pediatrics 26.5 days 75 (58.6%) ND ND Linear EM Attending physician, resident physician, medical student	key ED Pediatrics 68 months 75 (67.6%) ND ND Curvilinear Radiology Attending physician	
	M %) Patie	26.5	%) 22.8	%) 23.7	ND	%) 18	27.6	ND	%) 26.3	MD (%	DN (%	MDN (%	
	Male Patients (9	QN	27 (44.39	23 (38.39	32 (40%)	43 (67.29	46 (46%)	QN	68 (43.3%	26 (60.59	75 (58.69	75 (67.69	
	Mean Patient Age	36.9 years	43.8 years	70.2 years	42.3 years	8.5 years	40.5 years	24 days	41.0 years	41.6 days	26.5 days	68 months	
	Primary Patient Population	Adults	Adults	Adults	Adults	Pediatrics	Adults	Pediatrics	Adults	Pediatrics	Pediatrics	Pediatrics	
	Study Location	ED	ED	ED	ED	ED	ED	ED and pediatric floor	ED or ICU	ED	ED	ED	
tudies	Country	United States	Korea	Korea	Iran	Korea	United States	United States	United States	United States	United States	Turkey	
Included S	Study opulation	9	1	0	0	4	00	9	58	3	28	11	
cs of the	<u>د</u>	07 ⁹ 4	9	Ō	19 8	Ó	014 ¹³ 1	015 ¹⁴ 2	16 ¹⁵ 1	6 4	1	017 ²⁰ 1	
racteristi	tudy	Jomura 20(.ee 2008 ¹⁰	cho 2009 ¹¹	Aofidi 2013	(im 2014 ¹²	eterson 20	am and Lambert 2(ahham 20	3orn 2017 ¹	Jeal 2017 ¹)zdamar 2(

Table 1

BMI = body mass index; ED = emergency department; EM = emergency medicine; ICU = intensive care unit; ND = not described; US = ultrasound.

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(A)	Ultraso	und	Landmark-b	based		Risk Difference		Risk Difference
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Nomura 2007	23	24	16	22	6.7%	0.23 [0.03, 0.43]	2007	
Lee 2008	28	29	26	32	8.3%	0.15 [0.00, 0.30]	2008	
Cho 2009	30	30	25	30	8.7%	0.17 [0.03, 0.31]	2009	
Mofidi 2013	40	40	40	40	11.6%	0.00 [-0.05, 0.05]	2013	+
Kim 2014	30	33	20	31	6.9%	0.26 [0.07, 0.46]	2014	
Peterson 2014	38	50	39	50	7.9%	-0.02 [-0.18, 0.14]	2014	
Lam 2015	7	11	12	15	3.5%	-0.16 [-0.51, 0.19]	2015	
Gorn 2016	20	21	15	22	6.3%	0.27 [0.06, 0.49]	2016	
Lahham 2016	64	71	83	87	10.7%	-0.05 [-0.13, 0.03]	2016	
Neal 2017	48	63	29	64	8.0%	0.31 [0.15, 0.47]	2017	
Ozdamar 2017	56	56	55	55	11.9%	0.00 [-0.03, 0.03]	2017	+
Kessler 2018	37	40	37	40	9.6%	0.00 [-0.12, 0.12]	2018	
Total (95% CI)		468		488	100.0%	0.09 [0.01, 0.17]		◆
Total events	421		397					
Heterogeneity: Tau ² =	0.01; Chi ²	= 71.5	7, df = 11 (P <	< 0.0000	1); l ² = 85%	%	F	1 05 0 05
Test for overall effect:	Z = 2.26 (I	> = 0.02	2)					Favors [I andmark-based] Favors [I lltrasound]



Figure 2. Risk difference (A) and OR (B) for success rate for all studies.



Figure 3. Funnel plot of included studies

heterogeneity with $I^2 = 0.61$, and the fragility index was 22. Visual assessment for publication bias with a funnel plot revealed some asymmetry with studies clustered near the 95% confidence limits; however, statistical assessment with the use of Egger's test indicated no significant bias existed (p = 0.571; Figure 3). Among adult studies, ultrasound-assisted LP was successful in 223 of 244 patients (91.4%) and landmarkbased LP was successful in 229 of 261 patients (87.7%). The calculated RD was 5.8% (95% CI = -2.6% to 14.2%) with an OR of 2.10 (95% CI = 0.66to 7.44) in favor of the ultrasound group (Figure 4). A sensitivity analysis of the two largest trials^{13,15} among adult patients resulted in a RD of -4.0% (95% CI = -12.1% to 4.2%) and an OR of 0.69 (95% CI = 0.33) to 1.46). There was no statistical heterogeneity among trials in the sensitivity analysis ($I^2 = 0$). Among pediatric studies, ultrasound-assisted LP was successful in 198 of 224 patients (88.4%) and landmark-based LP was successful in 168 of 227 patients (74.0%). The calculated RD was 12.0% (95% CI = -9.8% to 33.7%) with an OR of 2.55 (95% CI = 0.99 to 6.52) in favor of the ultrasound group (Figure 5). There was no statistically significant difference in success rates between attending physician and resident physician studies with respect to success rates (Data Supplement S1, Supplemental Figures 1A, 1B, 2A, and 2B).

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(A)	Ultraso	und	Landmark-b	based		Risk Difference		Risk Di	fference	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Rand	lom, 95% Cl	
Nomura 2007	23	24	16	22	10.5%	0.23 [0.03, 0.43]	2007			
Lee 2008	28	29	26	32	14.5%	0.15 [0.00, 0.30]	2008			
Cho 2009	30	30	25	30	15.3%	0.17 [0.03, 0.31]	2009			
Mofidi 2013	40	40	40	40	24.9%	0.00 [-0.05, 0.05]	2013	-	+	
Peterson 2014	38	50	39	50	13.3%	-0.02 [-0.18, 0.14]	2014			
Lahham 2016	64	71	83	87	21.5%	-0.05 [-0.13, 0.03]	2016		t	
Total (95% CI)		244		261	100.0%	0.06 [-0.03, 0.14]		,	•	
Total events	223		229							
Heterogeneity: Tau ² =	0.01; Chi ²	= 16.6	5, df = 5 (P = 0	0.005); l ^a	² = 70%		F -	0.5		
Test for overall effect: 2	Z = 1.35 (F	P = 0.18	3)				-1	Favors [Landmark-based]	Favors [Ultrasour	nd]

(B)	Illtraco	und	Landmark	hased		Odde Patio				Odde Patio		
Charles Calendary	Giuaso	Tatal	Lanumark-	Tatal	W-lake	MU Desidere 05% O	V			Dandara 05	0/ OI	
Study or Subgroup	Events	Total	Events	Total	weight	M-H, Random, 95% C	rear		IVI-FI,	Random, 95	% CI	
Nomura 2007	23	24	16	22	16.7%	8.63 [0.95, 78.71]	2007					
Lee 2008	28	29	26	32	16.9%	6.46 [0.73, 57.35]	2008			-	•	
Cho 2009	30	30	25	30	12.0%	13.16 [0.69, 249.48]	2009				-	
Mofidi 2013	40	40	40	40		Not estimable	2013					
Peterson 2014	38	50	39	50	28.9%	0.89 [0.35, 2.27]	2014		с .			
Lahham 2016	64	71	83	87	25.5%	0.44 [0.12, 1.57]	2016					
Total (95% CI)		244		261	100.0%	2.10 [0.60, 7.44]						
Total events	223		229									
Heterogeneity: Tau ² =	1.21; Chi ²	= 11.04	4, df = 4 (P =	0.03); l ² :	= 64%				01	1	10	100
Test for overall effect:	Z = 1.15 (I	P = 0.23	5)					0.01	U.I	L		100

Figure 4. Risk difference (A) and OR (B) for success rate for adult studies.

(A)	Ultraso	und	Landmark-b	pased		Risk Difference		Risk Difference	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl	
Kim 2014	30	33	20	31	16.6%	0.26 [0.07, 0.46]	2014		
Lam 2015	7	11	12	15	12.8%	-0.16 [-0.51, 0.19]	2015		
Gorn 2016	20	21	15	22	16.1%	0.27 [0.06, 0.49]	2016		
Neal 2017	48	63	29	64	17.3%	0.31 [0.15, 0.47]	2017		
Ozdamar 2017	56	56	55	55	19.0%	0.00 [-0.03, 0.03]	2017	+	
Kessler 2018	37	40	37	40	18.1%	0.00 [-0.12, 0.12]	2018	-+-	
Total (95% CI)		224		227	100.0%	0.12 [-0.10, 0.34]			
Total events	198		168						
Heterogeneity: Tau ² =	0.06; Chi ²	= 79.9	2, df = 5 (P < 0	0.00001)	; l² = 94%		F		-
Test for overall effect:	Z = 1.08 (I	P = 0.2	8)				-	Favors [Landmark-based] Favors [Ultrasound]	1

	(6)	Ultraso	und	Landmark-b	ased		Odds Ratio		Odds Ratio
_	Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	ar M-H, Random, 95% Cl
	Kim 2014	30	33	20	31	21.3%	5.50 [1.36, 22.22]	2014	4
	Lam 2015	7	11	12	15	16.6%	0.44 [0.08, 2.55]	2015	5
	Gorn 2016	20	21	15	22	12.6%	9.33 [1.03, 84.20]	2016	6
	Neal 2017	48	63	29	64	31.8%	3.86 [1.81, 8.26]	2017	7
	Ozdamar 2017	56	56	55	55		Not estimable	2017	7
	Kessler 2018	37	40	37	40	17.8%	1.00 [0.19, 5.28]	2018	8
	Total (95% CI)		224		227	100.0%	2.55 [0.99, 6.52]		
	Total events	198		168					
	Heterogeneity: Tau ² = 0	.57; Chi ²	= 8.42,	df = 4 (P = 0.0	08); I² =	53%			
	Test for overall effect: Z	= 1.95 (F	P = 0.05	5)					Eavors [Landmark-based] Eavors [Ultrasound]

Figure 5. Risk difference (A) and OR (B) for success rate for pediatric studies.

Overall, there were 35 traumatic LPs out of 327 total LPs (10.7%) in the ultrasound-assisted group and 78 traumatic LPs out of 294 total LPs (26.5%) in the landmark-based group. The calculated RD was – 16.4% (95% CI = -27.6% to -5.2%) with a NN_{US} of 6 (95% CI = 3 to 19) to successfully perform an LP without resulting in a traumatic tap (Figure 6A). The OR was 0.28 (95% CI = 0.18 to 0.45) in favor of

fewer traumatic LPs the ultrasound-assisted group (Figure 6B). Among adult studies, there were 12 traumatic LPs out of 159 total LPs (7.5%) in the ultrasound-assisted group and 31 traumatic LPs out of 146 total LPs (21.2%) in the landmark-based group. The calculated RD was -12.1% (95% CI = -27.3% to 3.1%) with an OR of 0.28 (95% CI = 0.14 to 0.59) in favor of fewer traumatic LPs the ultrasound-assisted group

(A)	Ultraso	und	Landmark-b	based		Risk Difference	Risk Difference	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI Yea	M-H, Random, 95% Cl	
Nomura 2007	3	23	3	16	8.6%	-0.06 [-0.29, 0.18] 200	· · · · · · · · · · · · · · · · · · ·	
Lee 2008	1	28	3	26	11.3%	-0.08 [-0.22, 0.06] 2008		
Cho 2009	1	30	6	25	10.2%	-0.21 [-0.39, -0.03] 2009	,	
Mofidi 2013	5	40	18	40	10.0%	-0.33 [-0.51, -0.14] 2013	· · · ·	
Peterson 2014	2	38	1	39	12.7%	0.03 [-0.06, 0.11] 2014	 - -	
Lam 2015	0	7	3	12	7.1%	-0.25 [-0.54, 0.04] 2015	; • • • • •	
Gorn 2016	1	20	3	15	8.9%	-0.15 [-0.37, 0.07] 2016	· · · · · ·	
Ozdamar 2017	5	56	9	55	11.8%	-0.07 [-0.20, 0.05] 201		
Neal 2017	10	48	21	29	9.6%	-0.52 [-0.71, -0.32] 201		
Kessler 2018	7	37	11	37	9.8%	-0.11 [-0.30, 0.09] 2018	• •	
Total (95% CI)		327		294	100.0%	-0.16 [-0.28, -0.05]	•	
Total events	35		78					
Heterogeneity: Tau ² =	0.02; Chi ²	= 40.0	1, df = 9 (P < 0	0.00001)	; l ² = 78%			
Test for overall effect:	Z = 2.87 (F	> = 0.0	04)				Favors [Landmark-based] Favors [Ultrasound]	1

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	Ultraso	und	Landmark-ba	ased		Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year	M-H, Fixed, 95% CI	
Nomura 2007	3	23	3	16	4.2%	0.65 [0.11, 3.73]	2007	· · · · · · · · · · · · · · · · · · ·	
Lee 2008	1	28	3	26	4.1%	0.28 [0.03, 2.92]	2008	• • •	
Cho 2009	1	30	6	25	8.7%	0.11 [0.01, 0.98]	2009	,	
Mofidi 2013	5	40	18	40	21.6%	0.17 [0.06, 0.54]	2013	· · · · · ·	
Peterson 2014	2	38	1	39	1.3%	2.11 [0.18, 24.30]	2014		
Lam 2015	0	7	3	12	3.4%	0.18 [0.01, 4.07]	2015	; • • •	
Gorn 2016	1	20	3	15	4.5%	0.21 [0.02, 2.27]	2016	;	
Ozdamar 2017	5	56	9	55	11.4%	0.50 [0.16, 1.60]	2017	· · · · ·	
Neal 2017	10	48	21	29	28.5%	0.10 [0.03, 0.29]	2017	·	
Kessler 2018	7	37	11	37	12.3%	0.55 [0.19, 1.63]	2018		
Total (95% CI)		327		294	100.0%	0.28 [0.18, 0.45]		◆	
Total events	35		78						
Heterogeneity: Chi ² = 1	11.03, df =	9 (P =	0.27); l ² = 18%	, 0					-
Test for overall effect:	Z = 5.43 (F	> < 0.00	0001)					U.U1 U.1 1 10 10 Eavors [Landmark based] Eavors [Liltrasound]	U

Figure 6. Risk difference (A) and OR (B) demonstrating an increased rate of traumatic LP in all studies. LP = lumbar puncture.

(A)	Ultrasou	und	Landmark-ba	ased		Risk Difference		Risk Difference	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	I Year	M-H, Random, 95% Cl	
Nomura 2007	3	23	3	16	16.1%	-0.06 [-0.29, 0.18]	2007		
Lee 2008	1	28	3	26	21.5%	-0.08 [-0.22, 0.06]	2008		
Cho 2009	1	30	6	25	19.3%	-0.21 [-0.39, -0.03]	2009		
Mofidi 2013	5	40	18	40	18.9%	-0.33 [-0.51, -0.14]	2013		
Peterson 2014	2	38	1	39	24.2%	0.03 [-0.06, 0.11]	2014	-	
Total (95% CI)		159		146	100.0%	-0.12 [-0.27, 0.03]		•	
Total events	12		31						
Heterogeneity: Tau ² =	0.02; Chi ²	= 19.44	4, df = 4 (P = 0.	.0006);	l² = 79%				1
Test for overall effect:	Z = 1.56 (F	9 = 0.12	2)					Favors [Landmark-based] Favors [Ultrasound]	
(B)	1.114		l an durante la			Odda Datia		Odda Batia	
	Ultraso	una	Landmark-b	ased	Mainh4	Udds Ratio	Veee		
Study or Subgroup	Events	Total	Events	Total	weight	MI-H, FIXed, 95% CI	rear	M-H, Fixed, 95% CI	
Nomura 2007	3	23	3	16	10.6%	0.65 [0.11, 3.73]	2007		
Lee 2008	1	28	3	26	10.3%	0.28 [0.03, 2.92]	2008		
Cho 2009	1	30	6	25	21.8%	0.11 [0.01, 0.98]	2009		
Mofidi 2013	5	40	18	40	54.1%	0.17 [0.06, 0.54]	2013		
Peterson 2014	2	38	1	39	3.2%	2.11 [0.18, 24.30]	2014		
Total (95% CI)		159		146	100.0%	0.28 [0.14, 0.59]		•	
Total events	12		31						
Heterogeneity: Chi ² =	4.90, df = 4	4 (P =)	0.30); l ² = 18%						100
Test for overall effect:	Z = 3.41 (I	= 0.0	007)						100
	(-							Favors [Landmark-based] Favors [Ultrasound]	

Figure 7. Risk difference (A) and OR (B) demonstrating an increased rate of traumatic LP in adult studies.

(Figure 7). Among pediatric studies, there were 23 traumatic LPs out of 168 total LPs (13.7%) in the ultrasound-assisted group and 47 traumatic LPs out of 148 total LPs (31.8%) in the landmark-based group.

The calculated RD was -21.3% (95% CI = -38.2% to -4.3%) with an OR of 0.28 (95% CI = 0.16 to 0.51) in favor of fewer traumatic LPs in the ultrasound-assisted group (Figure 8). There was no

(A)	Ultraso	und	Landmark-	based		Risk Difference		Risk Diff	erence	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Rando	om, 95% Cl	
Lam 2015	0	7	3	12	15.3%	-0.25 [-0.54, 0.04]	2015			
Gorn 2016	1	20	3	15	19.0%	-0.15 [-0.37, 0.07]	2016		-	
Neal 2017	10	48	21	29	20.4%	-0.52 [-0.71, -0.32]	2017			
Ozdamar 2017	5	56	9	55	24.7%	-0.07 [-0.20, 0.05]	2017		-	
Kessler 2018	7	37	11	37	20.7%	-0.11 [-0.30, 0.09]	2018		_	
Total (95% CI)		168		148	100.0%	-0.21 [-0.38, -0.04]		-		
Total events	23		47							
Heterogeneity: Tau ² =	0.03; Chi ²	= 14.94	4, df = 4 (P =	0.005); l ^a	² = 73%		L.	1	0.5	
Test for overall effect: 2	Z = 2.46 (F	o = 0.0	1)				-1	-0.5 0 Favors [Landmark-based]	0.5 Favors [Ultrasound]	1





Ultrasound			nd	Landm	nark-ba	sed		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Year	IV, Random, 95% CI
Nomura 2007	20.4	14.7	21	17.7	10.6	15	3.9%	2.70 [-5.56, 10.96] 2007	· · · · · · · · · · · · · · · · · · ·
Lee 2008	8.2	6.4	28	8.6	8.4	26	11.5%	-0.40 [-4.41, 3.61] 2008	
Cho 2009	5.3	4.2	30	10.6	7.7	25	13.9%	-5.30 [-8.67, -1.93] 2009	
Mofidi 2013	3.3	1.2	40	6.4	1.2	40	27.5%	-3.10 [-3.63, -2.57] 2013	
Kim 2014	3.9	1.5	30	6.7	9.2	20	11.3%	-2.80 [-6.87, 1.27] 2014	
Lam 2015	3	2.6	7	2.4	2.4	12	18.8%	0.60 [-1.76, 2.96] 2015	
Lahham 2016	6.6	7.8	53	7.1	13.7	83	12.9%	-0.50 [-4.12, 3.12] 2016	
Total (95% CI)			209			221	100.0%	-1.80 [-3.57, -0.03]	◆
Heterogeneity: Tau ² =	2.89; Cł	$hi^2 = 1$	5.91, df	= 6 (P =	0.01); I	$^{2} = 62\%$)		-20 -10 0 10 20
Test for overall effect:	Z = 1.99	(P = (0.05)						Favors [Landmark-based] Favors [Ultrasound]



	Ultrasound			Landmark-based				Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI Year	IV, Random, 95% CI			
Nomura 2007	2.3	1.6	23	2.8	3	22	6.2%	-0.50 [-1.91, 0.91] 2007				
Lee 2008	1.6	1.1	29	2.3	1.8	32	15.3%	-0.70 [-1.44, 0.04] 2008				
Cho 2009	1.5	0.8	30	3.3	2.4	30	12.0%	-1.80 [-2.71, -0.89] 2009				
Kim 2014	1.45	0.56	33	1.68	0.95	31	25.8%	-0.23 [-0.62, 0.16] 2014				
Lam 2015	2	1.5	10	2.3	2.2	15	5.9%	-0.30 [-1.75, 1.15] 2015				
Lahham 2016	3.3	3.6	68	3.3	3.6	87	8.6%	0.00 [-1.14, 1.14] 2016				
Neal 2017	1.5	0.9	63	2.2	1.2	64	26.3%	-0.70 [-1.07, -0.33] 2017				
Total (95% CI)			256			281	100.0%	-0.61 [-1.00, -0.23]	◆			
Heterogeneity: Tau ² = 0.11; Chi ² = 11.77, df = 6 (P = 0.07); l ² = 49%												
Test for overall effect: Z = 3.11 (P = 0.002)									Favors [Landmark-based] Favors [Ultrasound]			

Figure 10. Mean number of needle passes among all studies demonstrating increased needle passes in the landmark group.

statistically significant difference in success rates between attending physician and resident physician studies with respect to success rates (Data Supplement S1, Supplemental Figures 3A, 3B, 4A, and 4B).

Overall, mean (\pm SD) time to perform a successful LP was 6.87 (\pm 6.77) minutes in the ultrasoundassisted group and 7.97 (\pm 10.11) minutes in the landmark-based group. The adjusted mean difference was -1.80 minutes (95% CI = -3.57 to -0.03) in favor of the ultrasound group (Figure 9). Among adult studies, mean time to perform a successful LP was 7.55 (\pm 7.41) minutes in the ultrasound-assisted group and 8.46 (\pm 10.48) minutes in the landmark-based group with an adjusted mean difference of -3.03 minutes (95% CI = -3.54 to -2.52) in favor of the ultrasound group. The reduced time to successful LP was also

Study	Random Sequence Generation	Allocation Concealment	Selective Reporting	Other Bias	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data		
Nomura 2007 ⁹	L	L	L	L	L	L	L		
Lee 2008 ¹⁰	L	L	L	L	L	L	L		
Cho 2009 ¹¹	L	L	L	L	L	L	U		
Mofidi 2013 ¹⁹	U	U	L	L	U	U	L		
Kim 2014 ¹²	U	U	L	L	L	L	L		
Peterson 2014 ¹³	L	L	L	L	L	L	L		
Lam and Lambert 2015 ¹⁴	L	U	L	L	L	L	L		
Lahham 2016 ¹⁵	Н	U	L	L	L	L	L		
Gorn 2017 ¹⁶	L	U	L	L	L	L	L		
Neal 2017 ¹⁷	L	L	L	L	L	L	L		
Ozdamar 2017 ²⁰	U	U	L	L	L	L	L		
Kessler 2018 ¹⁸	L	L	L	L	L	L	L		
H = high risk of bias; L = I identified in the atter was insufficient data t to successful LP amor cian studies (Data Su	ow risk of bias; U = ur ading physician su to perform meta-an og the pediatric or pplement S1, Sup	nclear risk of bias Ibgroup. The nalysis on tin resident phy- oplemental Fi	s. re (±2.1 ne (95% si- the u ig- Suppl	7). The CI = Iltrasour	e adjusted me –3.89 to –1.1 nd-assisted gro l Figure 13). '	an difference 7) in favor oup (Data S There were	e was –2.53/10 of less pain ir Supplement S1 insufficient data		
ures 5–8).		1	to per	to perform subgroup analyses on this outcome.					

Overall, there was a mean (\pm SD) of 2.07 (\pm 2.06) needle passes in the ultrasound-assisted group and 2.66 (\pm 2.53) in the landmark-based group. The adjusted mean difference was -0.61 (95% CI = -1.00to -0.23) in favor of fewer passes in the ultrasound group (Figure 10). Among adult studies, there was a mean (\pm SD) of 2.46 (\pm 2.59) needle passes in the ultrasound-assisted group and 3.05 (± 3.07) in the landmark-based group with an adjusted mean difference of -0.81 (95% CI = -1.57 to -0.05) in favor of fewer passes in the ultrasound group (Data Supplement S1, Supplemental Figure 9). Among pediatric studies, there was a mean (\pm SD) of 1.53 (\pm 0.88) needle passes in the ultrasound-assisted group and 2.07 (± 1.32) in the landmark-based group with an adjusted mean difference of -0.47 (95% CI = -0.73 to -0.21) in favor of fewer passes in the ultrasound group (Data Supplement S1, Supplemental Figure 10). The reduced number of needle passes was also identified in the attending physician subgroup (Data Supplement S1, Supplemental Figure 11). There was insufficient data to perform meta-analysis on number of needle passes in the resident physician subgroup (Data Supplement S1, Supplemental Figure 12).

The ultrasound-assisted LP had a mean (\pm SD) pain score of 3.75/10.0 (±1.80) and the landmark-based group had a mean (\pm SD) pain score of 6.31/10.0

Studies were at an overall low risk of bias for most criteria (Table 2). One study was at high risk for "random sequence generation" because they allowed patients to switch groups based on provider preference.¹⁵ No studies were at high risk for any of the other criteria. Three studies were at unclear risk for random sequence generation due to limited description of the specific randomization technique.^{12,19,20} Six studies were at unclear risk for "allocation concealment" due to limited description of how allocation was concealed.^{12,14–16,19,20} All studies were at low risk of "selective reporting" and "other bias." One study was at unclear risk of "blinding of participants and personnel" because the sonographers also performed the LP.¹⁹ One study was at unclear risk of "blinding of outcome assessors" because it did not explicitly describe who performed the outcome assessments.¹⁹ One study was at unclear risk of "incomplete outcome data" because four patients with missing information were excluded.¹¹

DISCUSSION

This systematic review and meta-analysis demonstrated that ultrasound-assisted LP had a significantly higher success rate when compared with the traditional, landmark-based technique. While both techniques had

relatively high success rates, the ultrasound technique was associated with a calculated RD of 8.9%, corresponding to a NN_{US} of 11. With an incidence of approximately 100,000 LPs performed annually and a calculated RD of 8.9%, the use of ultrasound guidance has the potential to increase the success rate among nearly 9,000 patients every year.²⁴

The ultrasound-assisted approach was also associated with a significantly reduced rate of traumatic LPs. Our study identified a 16.4% calculated RD, corresponding to a NN_{US} of 6. Importantly, traumatic LPs can lead to diagnostic uncertainty, prolonged hospital courses, additional procedures, increased health care costs, and potential iatrogenic complications.^{5–8} By using ultrasound guidance, it is possible that providers will be able to identify a more accurate trajectory to the interspinous space or use fewer needle passes, thereby reducing the risk of traumatic LPs as noted in this review.

Total time to LP completion was 2 minutes less in the ultrasound-assisted group. The clinical significance of this to the provider may be limited, but this could be a potential patient-relevant outcome, as it will reduce the time spent with a sharp needle in their skin. While the current data were limited with respect to procedure time among pediatric patients, this could be particularly important in this subgroup, as it could also reduce the time spent in a restricted position, which can affect both the patient and caregiver anxiety about the procedure. Further studies are needed to determine whether the time reduction is also present in the pediatric subgroup.

Ultrasound was also associated with reduced patient pain scores. The clinically significant threshold for pain reduction has been suggested to be 0.9 to 1.2 out of 10.^{25–27} Our study found that there was a reduction of 2.5 out of 10, which exceeds the threshold of both statistical and clinical significance. It is possible that the reduced number of needle passes or reduced time to procedure completion may have led to reduced pain for patients. However, regardless of the cause, this is an important patient-centered outcome that should also be considered in the decision to use ultrasound prior to LPs.

Subgroup analyses comparing adult with pediatric patients demonstrated a trend toward improved outcomes in both subgroups, but none reached statistical significance. Similarly, the attending and resident physician subgroups demonstrated a trend toward improved outcomes, but also did not reach statistical significance. Given the relatively wider CIs and consistent trends in both subgroups, it is likely that they were underpowered to identify a difference in these outcomes. More trials are needed to determine whether one subgroup is more significantly impacted than the other.

One previous systematic review and meta-analysis was performed by Shaikh and colleagues in 2012.28 The authors combined both epidural catheterizations and LPs performed in wide range of settings and demonstrated an improved success rate in the ultrasound group. However, the authors included predominantly epidural catheterizations, which require a significantly different skill set than LPs. They included only three published LP studies comprising a total of 167 patients. Our study identified nine additional publications, resulting in a fivefold increase in the number of patients. As a result, this study provides more robust data to support the potential benefit of ultrasound for LP performance. Additionally, our study is the first to report data on rates of traumatic LP, time to procedural success, number of needle passes, and patient pain scores. Finally, our study is the first to perform subgroup analyses of pediatric patients, adult patients, attending physician sonographers, and resident physician sonographers.

Importantly, ultrasound is a provider-dependent skill. Consequently, like other ultrasound applications, it is important that clinicians learn and practice this technique regularly to maintain proficiency. Potential barriers to training can include lack of comfort with this application, absence of a trained faculty member to educate on this technique, and insufficient time for training.²⁹ Of note, while the ideal training protocol has not been described, many of the included studies utilized a 2-hour training period with both didactic and hands-on components. Therefore, time may be less of a barrier for this technique than other ultrasound applications.

The primary outcome fragility index of 22 indicates a fairly robust finding. However, the lack of statistical significance in the subgroup analysis of adult and pediatric patients signals a need for more randomized controlled trials to determine whether these subgroups demonstrate improved success rates with ultrasound in isolation. Future studies should also assess the effect of transducer type, body habitus, and provider training level on ultrasound accuracy, as well as the ideal training protocol and associated costs with acquiring and maintaining proficiency with this application.

LIMITATIONS

It is important to consider several limitations with respect to the current review. First, there was moderate statistical and clinical heterogeneity with some studies assessing this technique in all patients requiring LP, while others selected patients who were anticipated to be difficult LP procedures. Additionally, we included both pediatric and adult patients in this analysis. Pediatric patients have different challenges than adult patients with respect to performing LPs. While both adult and pediatric studies demonstrated a trend toward improved success rates in the ultrasoundassisted group, neither was statistically significant in isolation. While it is possible that this may have occurred because both groups were underpowered when assessed independently, further studies would be beneficial to determine whether the effect is truly present in both groups. It is also unclear whether specific pediatric age groups (e.g., neonate, infant, child, teenager) would have different outcomes compared with other groups. Moreover, there was variation in ultrasound transducer selection, with some studies using a linear transducer, while others used a curvilinear transducer. It is unclear from our current data which transducer is more accurate for this procedure. However, one recent study found that the curvilinear transducer was more accurate than the linear transducer among obese patients.³⁰ Furthermore, most studies did not adequately describe the ultrasound training for the providers. Therefore, it is unclear what the ideal training model is for this technique and current data are limited with respect to learning curves for this procedure.³¹ Finally, all of the studies used ultrasound to identify the space prior to the procedure, so there are limited data on the use of ultrasound for dynamic guidance.³²

CONCLUSION

Ultrasound-assisted lumbar punctures were associated with higher success rates, fewer traumatic lumbar punctures, shorter time to successful lumbar puncture, fewer needle passes, and lower patient pain scores. Ultrasound should be considered prior to performing all lumbar punctures, especially in patients with difficult anatomy. Further studies are recommended to determine whether this effect is consistent in both adult and pediatric subgroups, as well as the impact of transducer type and body habitus on this technique. The authors thank Jennifer C. Westrick, MSLIS, for her assistance with the literature search.

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Supporting Information

The following supporting information is available in the online version of this paper available at http:// onlinelibrary.wiley.com/doi/10.1111/acem.13558/full **Data Supplement S1.** Supplemental material.



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