Efficacy of ultrasound guidance for lumbar punctures: a systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Ultrasound guidance has been reported to facilitate the performance of lumbar punctures (LPs). However, the use of ultrasound guidance has not yet received consistent conclusions. We performed a systematic review and meta-analysis to determine the efficacy of ultrasound-guided LPs. PubMed, Embase and the Cochrane Library were searched for randomised controlled trials comparing ultrasound guidance with traditional palpation for LPs in adults. The primary outcome was risk of failed procedures. A random-effects Mantel-Haenzsel model or random-effects inverse variance model was used to calculate relative risks (RRs) or standardised mean differences (SMDs) with 95% CIs. Twenty-eight trials (N=2813) met the inclusion criteria. Ultrasound-guided LPs were associated with a reduced risk of failed procedures (RR=0.58, 95% CI 0.39 to 0.85, p=0.005). No significant heterogeneity was detected (I2=27%) among these trials. It further decreased first attempt to failure (RR=0.43, 95% CI 0.30 to 0.62, p<0.00001), mean attempts to success (SMD=−0.61, 95% CI −0.80 to −0.43, p=0.00001) and incidences of complications of headache and backache (RR=0.63, 95% CI 0.46 to 0.85, p=0.003). Ultrasound guidance is an effective technique for LPs in adults.

INTRODUCTION

Lumbar punctures (LPs) are commonly invasive procedures in various clinical settings, such as labour and delivery suite (LD), operating room (OR) and emergency department (ED).[1 2] Traditional procedures of LPs are performed by palpation base on the anatomical knowledge. However, the procedure can be often challenging in obese people and people with difficult anatomical landmarks,[3 4] even for experienced operators. Technical difficulty often leads to puncture failure and multiple needle attempts,[5] which consequently result in headache, back pain and haemorrhage.[6] Further adverse events included neurological complications, such as paresthesia, numbness[7] and radicular pain. To resolve this issue, ultrasound guidance has emerged as an alternative tool for LPs. It provides vertebral interspace level and optimal landmark for injection[8–10] in a visualisation situation. However, the use of ultrasound guidance for LPs remained controversial. Several randomised controlled trials (RCTs) reported conflicting conclusions,[11–14] and the results from latest meta-analysis[15] should be interpreted cautiously due to the underpowered evidence. Moreover, recent trials[16 17] with accumulating evidence have been published. Therefore, we conducted a meta-analysis of RCTs to evaluate the efficacy of ultrasound guidance for LPs in adults.

MATERIALS AND METHODS

Literature search

The present meta-analysis was performed in compliance with the statement of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[18] No protocol was registered for this meta-analysis.

Two authors (LPS and JH) independently searched PubMed, Embase and the Cochrane Library (from inception to December 2019) for RCTs that compared ultrasound guidance with conditional palpation technique for LPs. No language restriction was imposed. The searched terms were as follows: ('epidural puncture' OR 'subarachnoid puncture' OR 'spinal anesthesia' OR 'intraspinal puncture 'OR 'lumbar puncture') AND ('ultrasound' OR 'ultrasonography' OR 'ultrasonic'). We also scrutinised manually the reference lists of published reviews as well as identified studies for potentially eligible trials.

Selection criteria

Two of us (LPS and JH) separately carried out the initial records, removed the duplicative ones, screened the titles and abstracts, and reviewed detail in the full texts remained for identified eligibility.

The inclusive criteria were as follows: (1) population: adults required LP or epidural catheterisation (EC); (2) intervention: ultrasound guidance technique; (3) comparison: ultrasound guidance versus conditional palpation technique; (4) outcome: risk of failed procedures; (5) study design: RCT. Any discrepancies were resolved by discussion with coauthors.

Data extraction and outcome measures

We used a predefined standardised Excel (Microsoft Corporation) file to extract the following information: first author, publication year, country, number of patients, clinical setting, patient characteristics, procedure (LP or EC or a combination of the two), ultrasound equipment and operator experience. Mean and SD, number of events and total number of participants were extracted from the identified articles. As for some

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trials provided median and IQR rather than mean and SD, we judged median and IQR equivalent to mean and SD approximately as follows: the median was approximated to the mean, and the SD was estimated to be equal to the IQR divided by 1.35.[19] For trials that needed merging data of the mean and SD, we calculated it according to Cochrane handbook.[20] We contacted the corresponding authors to obtain some missing data if necessary.

The primary outcome was risk of failed procedures. Secondary outcomes included first attempt to failure, mean attempts to success and adverse events (neurological complications, headache and back pain). Any discrepancies were figured out by consensus.

Assessment for risk of bias

Assessment for risk of bias was conducted according to the Cochrane risk of bias tool.[21] Two authors subjectively reviewed all identified trials and classified each study as 'low', 'unclear' or 'high' risk of bias to the following seven domains: random sequence generation (selection bias); concealment of allocation sequence (selection bias); blindness of participants and related personnel (performance bias); blindness of outcomes (detection bias); incomplete outcome data (attrition bias); selective reporting (reporting bias); and other bias.[21] Any uncertainty arose were resolved through a consensus achieved.

Statistical analysis

Relative risks (RRs) for dichotomous data and standardised mean differences (SMDs) for continuous data were estimated. A random-effects Mantel-Haenzsel model or random-effects inverse variance model with 95% CI was selected regardless of heterogeneity. A p value <0.05 was considered significant statistic. For studies with zero-cell counts, RevMan will detect problematic zero cell counts and a fix value of 0.5 will be added when the problems occur.[20] Heterogeneity was quantified on the basis of I^2 statistic, and I^2>50% indicated significant heterogeneity.[22] The assessment of publication bias was assessed by Begg and Egger tests.[23 24] P values <0.05 were considered statistically significant. All statistical analyses were calculated using STATA (Stata Corp., USA) and RevMan 5.3 (Nordic Cochrane Centre, Cochrane Collaboration).

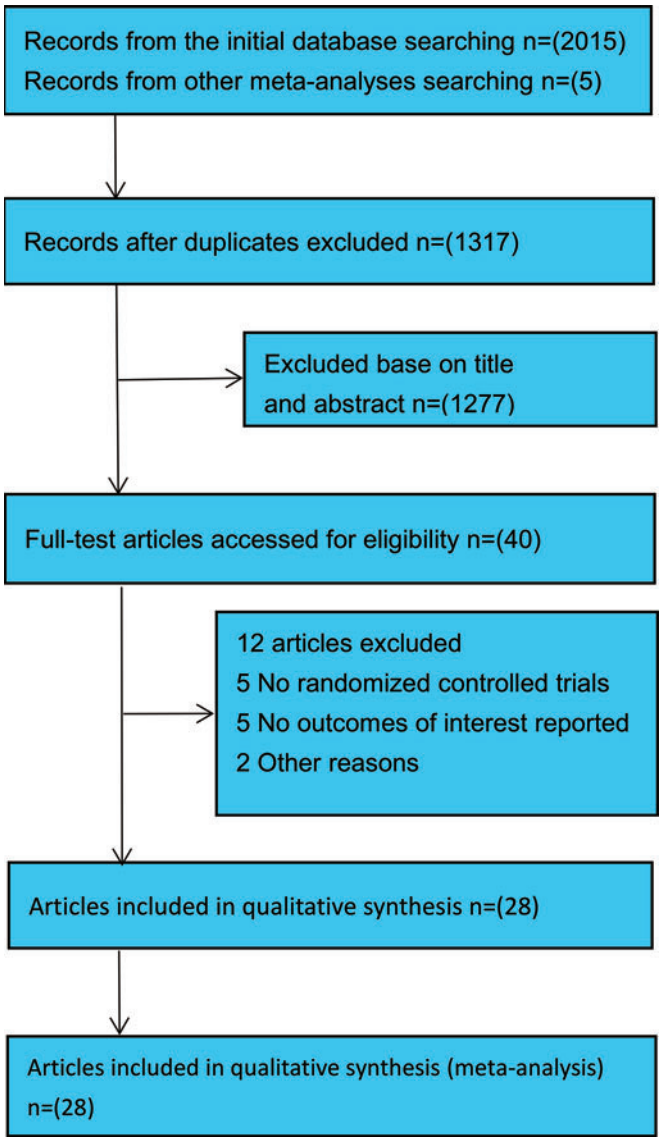

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart.

RESULTS

Study selection

Figure 1 shows the process of literature search. Of 2015 potential records yielded from the initial database search, 23 RCTs[11–14 16 17 25–33 40–47] were identified as eligible after full-text review, and 5 additional RCTs[34–38] were checked from the references of previous meta-analyses.[15 39 40] As a result, 28 RCTs were finally identified in the present meta-analysis.

Trials characteristics

The main characteristics of the identified RCTs are summarised in table 1. These trials were published between 2001 and 2019 with population size range from 20 to 370 (total 2813). Among the 28 included RCTs, 4 trials[32 37 41 42] enrolled obese people and 4 trials[14 25 32 43] enrolled people with difficult anatomy landmark. Two studies[29 30] were published in Korean, and the others were published in English. Except for Lahham *et al*[13] study, ultrasound-guided LPs were conducted by a combination of the transversal and longitudinal planes in most trials.

Risk of bias assessment

Figure 2 shows the details of risk of bias assessment. Except for studies performed by Chin *et al*,[43] Li *et al*,[42] Nomura *et al*[28] and Auyong[38] *et al*, which were categorised as being unclear, other trials were judged as being at high risk of bias. Random sequence generation was adequate in 25 trials.[11 12 14 16 17 25–33 35–38 41–47] Allocation concealment was reported in eight trials.[11 17 28 32 38 44–46] No trial generated blinding of participants and personnel; however, blinding of the operators who performed the LPs was nearly impossible due to the nature of studies. Despite blinding of outcome assessment was seldom generated in all studies, it was still classified as being at low risk of bias because outcome measurement was little probe to be changed by lacking blinding.

Primary outcome: risk of failed procedures

All the included trials[11–14 16 17 25–33 41 44 45] reported the primary outcome. Ultrasound-guided LPs were associated with a reduced

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Table 1 Main characteristics of randomised controlled trials in this meta-analysis of ultrasound-guided lumbar puncture and epidural catheterisation

Study	Year	Country	Patients (n)	Population	Setting	Procedure	Equipment	Operator experience
Grau[25]	2001	Germany	36/36	Parturients with presumed difficult puncture	LD	EC	NA	Not reported
Grau[26]	2002	Germany	150/150	Parturients scheduled for caesarean section or vaginal dilivery	LD	EC	Sonoace 6000, 5.0 MHz curved array probe (Kretz, Marl, Germany)	Not reported
Grau[27]	2004	Germany	20/10	Obstetric patients scheduled for caesarean section	LD	CSE	Logiq 400, 7.5 MHz linear array probe	Not reported
Pisupati[34]	2004	USA	14/19	Adults	ED	LP	Not reported	Not reported
Nomura[28]	2007	USA	24/22	Adults	ED	LP	SonoSite (Bothell, WA, USA), 5–10 MHz linear probe	Postgraduate year 2 residents who had fulfilled the ED
Lee[29]	2008	Korea	29/32	Adults	ED	LP	Sonosite MicroMaxx, 2–5 MHz curved probe	Not reported
Cho[30]	2009	Korea	30/30	Adults >60 years old	ED	LP	Sonosite MicroMaxx, 2–5 MHz curved probe	Not reported
Vallejo[31]	2010	Canada	189/181	Laboring parturients	LD	EC	The Sonosite MicroMaxx ultrasound system (Sonosite), 2–5 MHz curved probe	Residents had no more than five epidural placement attempts
Chin[32]	2011	Canada	60/60	Adults with difficult surface anatomic landmark	OR	LP	NA	Anesthetists with more than 5 years of clinical experience in regional anaesthesia or consultant
Mofid[33]	2011	Iran	40/40	Adults	ED	LP	NA	Not reported
Kawaguchi[35]	2011	Japan	12/12	Adults scheduled scheduled to undergo total replacement of a hip joint	OR	EC	Logiq Book XP with 3 C-RS 2–5 MHz convex probe	Not reported
Wang[41]	2012	China	30/30	Obese parturients scheduled for caesarean section	LD	CSE	A. Turbo with a 5–10 MHz, convex probe, Sonosite	Anaesthetist with more than 10 years of experience in obstetric anaesthesia
Abdelhamid[36]	2013	Egypt	45/45	Adults	A block room	LP	Sonosite S-Nerve (Sonosite) ultrasound machine, a low-frequency (2–5 MHz)	Not reported
Sahin[37]	2013	Germany	50/50	Parturients scheduled for caesarean section	LD	LP	A Esaote Mylab 30 (Florence, Italy, convex transducer of 2–5 MHz)	Operator who with extensive experience
Nassar[44]	2014	Egypt	55/55	Parturients scheduled for vaginal dilivery	LD	CSE	2–5 MHz, Sonosite MicroMaxx Ultrasound System English, USA	Operator with more than 10 years of experience
Ansari[12]	2014	United Arab Emirates	75/75	Obstetric patients scheduled for caesarean section	LD	LP	(GE, Solingen, Germany), 4CRS 2–5.5 MHz broadband multifrequency probe	Anesthetists with experience in ultra sound-guided neuraxial block (each had performed between 200 and 300 ultrasound-guided neuraxial blocks)
Peterson[14]	2014	USA	50/50	Adults	ED	LP	Aloka SSD 1400 US machin(Aloka, Wallingfod, CT), 3.5 MHz convex array or a 7.5 MHz linear array probe	Operators performed at least 10 previous successful LPs by their own report
Lim[45]	2014	Singapore	85/85	Adults	OR	LP	A. Turbo ultrasound machine (SonoSite, Fujifilm, Bothell, WA, USA), low frequency (2–5 MHz) curvi-linear probe	Anaesthetists experienced in ultrasound-assisted neuraxial block
Mrcpi[46]	2015	Ireland	50/50	Adults scheduled for elective total joint replacements	OR	LP	Ultrasound unit (SonixTablet, Peabody, MA) with a curved 2–5 MHz probe	Anaesthesiologists had performed >75 neuraxial ultrasound scans before the study
Creaney[11]	2016	Ireland	10/10	Obstetric patients scheduled for caesarean section	LD	LP	Sonosite NanoMaxx C60, 2–5 MHz	Anaesthetists had completed 10 LPs with ultrasound guidance
Lahham[13]	2016	USA	71/87	Adults	ED	LP	Sonosite Fujifilm, 10–5 MHz linear array probe	Resident physician
Perna[47]	2017	Italy	30/28	Obstetric patients scheduled for vaginal or caesarean dilivery	LD	EC	Sonosite NanoMaxx, 5-2 MHz C60n Convex probe	Anaesthetist with experience of more than 150 epidural procedures yearly

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Table 1 Continued

Study	Year	Country	Patients (n)	Population	Setting	Procedure	Equipment	Operator experience
Elsharkawy[43]	2017	USA	14/18	Adults with predicted difficult anatomy	OR	LP	GE Venue 40 (GE Healthcare, Waukesha, WI, USA) or Sonosite S-Nerve, low frequency (2–5 MHz) transducer	Anaesthesiologists experienced with previously performed at least 10 ultrasound-guided spinal anesthet ics prior to study initiation
Auyong[38]	2017	USA	33/37	Adults undergoing any thoracicor upper abdominal surgery	OR	EC	Not reported	Not reported
Abraham[39]	2018	Canada	20/20	Adults	Outpatient neuromuscular clinic.	LP	General Electric LOGIQ S7 Expert, Toronto, Canada, 5 MHz (ML2-5)	Not reported
Li[42]	2018	China	40/40	Obese parturients scheduled for caesarean section	LD	LP	M-Turbo ultrasound machine (GE, Solingen, Germany), a low-frequency (2–5 MHz) curvilinear probe.	Three anaesthesiologists with 3 years of clinical expe rience in spinal anaesthesia
Ghisi[16]	2019	Italy	47/52	Adults scheduled for lower limb surgery	OR	LP	Accuro, Rivanna Medical, Praesidia Medical Devices, via dei Lapidari 19, Bologna, Italy	Anaesthesiologists skilled in both tech niques with a 25 or 27 G needle
Rizk[17]	2019	USA	120/60	Adults scheduled for elective surgery	OR	LP	The Sonosite with a low frequency (2–5 MHz) curvilinear probe	Anaesthesiologist trained and experienced in ultrasound-assisted neuraxial block.

CSE, combined spinal-epidural anaesthesia; ED, emergency department; EC, epidural catheterisation; LD, labour and delivery suite; LP, lumbar puncture; NA; OR, operating room.

risk of failed procedures (RR=0.58, 95% CI 0.39 to 0.85, p=0.005). No significant heterogeneity was detected among these trials (I^2=27%).

Secondary outcomes

Ultrasound guidance for LPs decreased first attempt to failure (RR=0.43, 95% CI 0.30 to 0.62, p<0.00001), mean attempts to success (SMD=−0.61, 95% CI −0.80 to −0.43, p<0.00001) and incidences of complications of headache and backache (RR=0.63, 95% CI 0.46 to 0.85, p=0.003). Ultrasound guidance had no advantage on mean procedure time, which was defined as the time from skin puncture to complete block and neurological complications. Figure 3 represents the pool estimate of dichotomous variable data, including risk of failed procedures, first attempt to failure and incidences of complications of headache and backache.

Figure 4 represents the pool estimate of continuous variable data, including mean attempts to success and mean procedure time.

Details of primary and secondary outcomes are presented in table 2.

Publication bias

There was no evidence of publication bias by formal statistical Begg's test (p=0.624) but Egger's test (p=0.01) (figure 5); we then conducted trim-and-fill analysis[48] and no additional data was detected. Therefore, publication bias cannot be ruled out with respect.

DISCUSSION

Principal finding

Our meta-analysis is a further systematic review and meta-analysis of RCTs to assess the utility of ultrasound guidance for LPs. The present study demonstrated that (1) ultrasound guidance was associated with decreased risk of failed procedures and (2) ultrasound guidance further decreased first attempt to failure, mean attempts to success, and incidences of complications of headache and backache.

Notably, studies conducted by Nassar *et al*[44] and Ansari *et al*[12] got about a 20% failure rate of LPs. There are several possible explanations for the results, one of which is that both studies involved pregnant females, who often developed oedema of lumbar tissue and narrowing of intervertebral spaces, which make LPs difficult.[49] Another plausible explanation could be that both studies were performed from Africa, where economic development and healthcare systems were relatively poor. Besides, L3–4 or L4–5 were chosen for LPs in these two studies; however, one observational study conducted by Keplinger *et al*[50] demonstrated that L2–3 was the most appropriate puncture site for LPs among pregnant females, because of the greater length of the visible intervertebral posterior dura mater and least depth of the posterior dura mater to the skin at L2–3 level when ultrsound scans were used.[50] Last, obese people and people with difficult anatomical landmarks were not excluded in Nassar *et al*,[44] which may limit the success rate of LPs.

Interestingly, the study conducted by Lahham *et al*[13] got a different result and was completely out of range compared to the others. The negative result may be explained by (1) operator experience: as the Lahham *et al*[13] described, ultrasound guidance for LP was conducted by a resident physician who was under training and had limited experience, but in the other studies, operators were experienced or had completed at least 10 successful LPs; (2) ultrasound technique: in this study, the probe was placed

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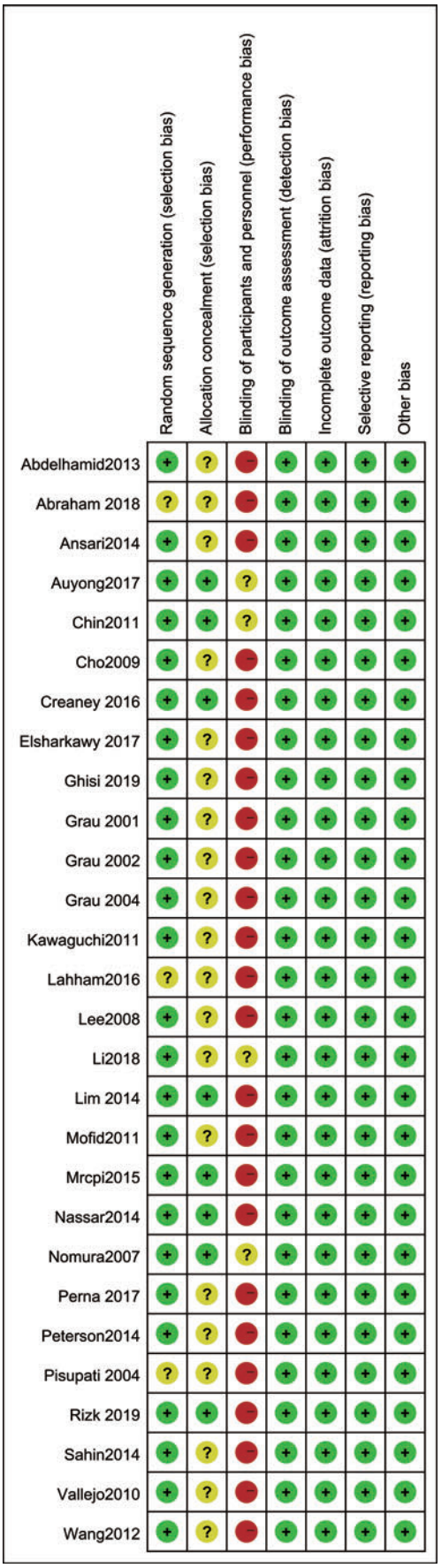

Figure 2 Risk of bias summary. −=Low risk; ?=Uncertain risk, and +=High risk.

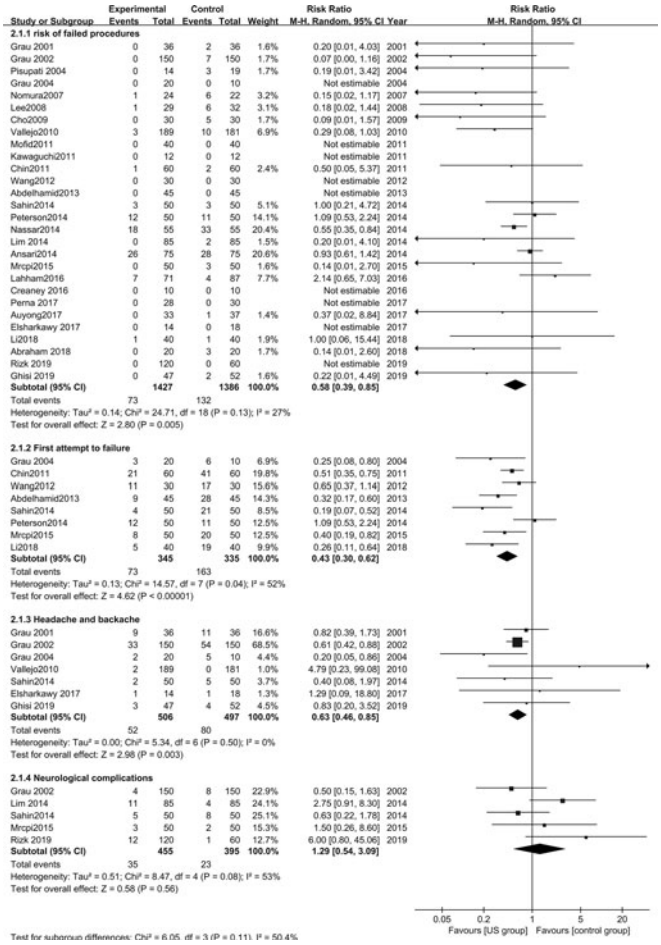

Figure 3 Forest plot of risk of failed procedures, first attempt to failure, headache and backache, and neurological complications.

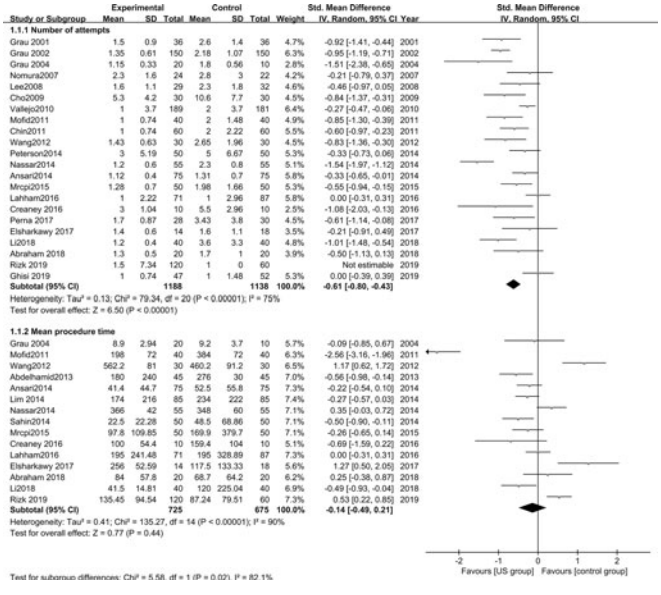

Figure 4 Forest plot of risk of mean attempts to success and mean procedure time.

in a transverse plane to identify the needle insertion site. However, in other trials, ultrasound guidance for LP was performed by a combination of the transversal and longitudinal planes.

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Table 2 Outcomes of RCTs in this meta-analysis

	Patients (n)	Studies (n)	RR or SMD (95% CI)	P value	I^2 (%)
Primary outcome					
Risk of failed procedures	2813	28	0.58 (0.39 to 0.85)	0.005	27
Secondary outcomes					
First attempt to failure	680	8	0.43 (0.30 to 0.62)	<0.00001	52
Mean attempts to success	2326	22	−0.61 (−0.80 to −0.43)	<0.00001	75
Headache and backache	1003	7	0.63 (0.46 to 0.85)	0.03	0
Mean procedure time	1400	15	−0.14 (−0.49 to 0.21)	0.04	90
Neurological complications	850	5	1.29 (0.54 to 3.09)	0.56	53

RCT, randomised control trial; RR, relative risks; SMD, standardised mean difference.

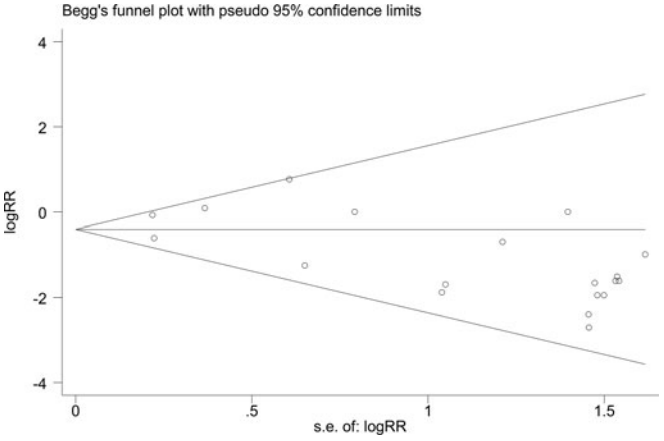

Figure 5 Begg's test for evaluating publication bias. RR, relative risks.

Comparison with other meta-analyses

There have been three meta-analyses on this topic published.[15 39 40] Our primary outcome was in line with these meta-analyses; however, several important differences between current meta-analysis and previous ones should be noted. First, evidence from our meta-analysis was more robust by including more than 10 additional RCTs, with expanding sample size of at least 1000 cases; this meta-analysis was the most recent and powerful one which generally confirms and reinforces the findings of the earlier ones. Second, analysis performed by Gottlieb *et al*[15] enrolled both adults and paediatrics. Paediatrics were more challenged than adults in terms of performing LPs, which may lead to a deviation of overall effect size of the result. The study conducted by Perlas *et al*[40] enrolled RCTs as well as observation studies that were highly subject to selection bias and limited the ability to control for confounding. In addition, we assessed the effect of ultrasound-guided LPs on first attempt to failure, neurological complications, and complications of headache and back pain compared with traditional palpation.

Implications for clinical practice

In obese people and people with difficult landmark, LPs can be challenging. Previous studies[3 10] reported favourable benefits of ultrasound guidance among these people; however, the determined conclusion cannot be drawn due to the small sample size. Further large-scale and high-methodological quality researches' focus on these people is warranted.

Although ultrasound guidance facilitated LPs, operator experience should be considered when interpreting the results. The operator experience that varied from primary level to proficiency is undoubtedly an important factor contributing to heterogeneity and has an impact on risk of failed procedures as well as other clinical end points. Subgroup analyses in our meta-analysis indicated that risk of failed procedures decreased only in experienced but not inexperienced operators. The learning curve of ultrasound-guided LPs may also affect clinical end points because ultrasound technique is relatively new and complex, particularly for those who did not receive formal training. Simulation-based practice has proved a good way to resolve this issue.[51]

Both ultrasound-guided pre-puncture site marking[26 28 34] and real-time ultrasound guidance[52–54] were reported to be feasible and beneficial; however, pre-puncture ultrasound imaging appeared to be more popular, because only a few studies[27 31 43] in this meta-analysis reported the use of real-time ultrasound guidance for LPs. Difficulty in obtaining needle tip and maintaining visualisation during the process of real-time ultrasonic guidance[55] may explain this. In addition, published trials that directly compared ultrasound-guided site marking with real-time ultrasound guidance is scarce. Therefore, a definitive conclusion about which ultrasound assistant approach was more superior cannot be drawn due to the limit evidence. Future researches should compare the efficacy of ultrasound-guided site marking versus real-time ultrasound guidance in LPs.

Strengths and limitations

For the primary outcome, our evidence was powerful with accumulating data. In addition, most RCTs included in this meta-analysis randomised for sequence generation appropriately and reported allocation concealed.

Our meta-analysis also had some limitations. Although no heterogeneity was detected in risk of failed procedures, patient characteristics (obese people and people with difficult landmark), clinical setting (ED, OR and LD), frequency of probes (range from 2 to 10 MHz) and operator experience differ among the identified trials, which may have a potential effect on the pool estimate of the results. Next, protocol was not registered prospectively, which may increase the risk of reporting bias. Furthermore, we cannot evaluate the effect of ultrasound-guided LPs on other clinical outcomes such as haematoma, maximum pain scores due to the sparse data.

CONCLUSION

This systemic review and meta-analysis demonstrated that ultrasound guidance for LPs is an effective technique. The sue of ultrasound guidance for LPs decreased risk of failed procedures, first attempt to failed, mean attempts to success and incidences of complications of headache and backache.

Main messages

- Ultrasound guidance has emerged as an alternative tool for lumbar puncture (LPs)
- There is no consensus on the effectiveness of ultrasound guidance for LPs
- This systematic review and meta-analysis estimates the efficacy of ultrasound guidance for LPs in adults

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Current research questions

- Traditional procedures of LPs can be often challenging in obesity and people with difficult anatomical landmarks
- ultrasound guidance provides vertebral interspace level and optimal landmark for injection in a visualization situation.
- The effect of ultrasound guidance for LPs does not form a unified opinion

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Self-assessment questions

1. Which intervertebral space is commonly used as the puncture point in lumbar puncture?
   A. L1–2
   B. L2–3
   C. L3–4
   D. L4–5
2. Is subgroup analysis necessary for a meta-analysis when the heterogeneity is non-significant?
   A. Yes
   B. No
3. The highest level of clinical research evidence is
   A. Systematic review of RCT (SR)
   B. Randomised controlled study (RCTS)
   C. Cohort study
   D. Case–control study
4. Lumbar puncture fails on which kind of patient easily?
   A. Normal anatomy
   B. Obesity
   C. Abnormal anatomy
   D. B+C
5. Which of the following is the most common complication of lunbar puncture?
   A. Headache
   B. Urinary retention
   C. Radicular pain
   D. Myelitis

Contributors LPS and JH participated in the entire procedure including the design and coordination of the study, the literature search, data extraction, performed the statistical analysis, drafted the manuscript and revised submitted the manuscript. All authors read and approved the final manuscript. JCL made substantial contributions to the conception and design of the work; revised it critically for important intellectual content; approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Answers

1. C
2. B
3. A
4. D
5. A

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