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-Haenszel 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). 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. Even for experienced operators. Technical difficulty often leads to puncture failure and multiple needle attempts, which consequently result in headache, back pain and haemorrhage. Further adverse events included neurological complications, such as paresthesia, numbness 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 in a visualisation situation. However, the use of ultrasound guidance for LPs remained controversial. Several randomised controlled trials (RCTs) reported conflicting conclusions, and the results from latest meta-analysis should be interpreted cautiously due to the underpowered evidence. Moreover, recent trials 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). 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, screened 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 characteristis, 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
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. For trials that needed merging data of the mean and SD, we calculated it according to Cochrane handbook. 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. 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. 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-Haenszel 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. Heterogeneity was quantified on the basis of I² statistic, and I²>50% indicated significant heterogeneity.

RESULTS
Study selection
Figure 1 shows the process of literature search. Of 2015 potential records yielded from the initial database search, 23 RCTs were identified as eligible after full-text review, and 5 additional RCTs were checked from the references of previous meta-analyses. 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 enrolled obese people and 4 trials enrolled people with difficult anatomy landmark. Two studies were published in Korean, and the others were published in English. Except for Lahham et al 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, Li et al, Nomura et al and Auyong 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. Allocation concealment was reported in eight trials. 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 reported the primary outcome. Ultrasound-guided LPs were associated with a reduced
| Study   | Year  | Country       | Patients (n) | Population | Setting       | Procedure | Equipment                                      | Operator experience                                      |
|---------|-------|---------------|--------------|------------|---------------|-----------|------------------------------------------------|----------------------------------------------------------|
| Grau    | 2001  | Germany       | 36/36        | Parturients with presumed difficult puncture | LD           | EC        | NA                                             | Not reported                                              |
| Grau    | 2002  | Germany       | 150/150      | Parturients scheduled for caesarean section or vaginal delivery | LD           | EC        | Sonoace 6000, 5.0 MHz curved array probe (Kretz, Marl, Germany) | Not reported                                              |
| Grau    | 2004  | Germany       | 20/10        | Obstetric patients scheduled for caesarean section | LD           | CSE       | Logiq 400, 7.5 MHz linear array probe          | Not reported                                              |
| Pisupati| 2004  | USA           | 14/19        | Adults      | ED           | LP        | Not reported                                   | Not reported                                              |
| Nomura  | 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     | 2008  | Korea         | 29/32        | Adults      | ED           | LP        | SonoSite MicroMaxx, 2–5 MHz curved probe       | Not reported                                              |
| Cho     | 2009  | Korea         | 30/30        | Adults >60 years old | ED           | LP        | SonoSite MicroMaxx, 2–5 MHz curved probe       | Not reported                                              |
| Vallejo | 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 |
| Chint   | 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 |
| Mofidi  | 2011  | Iran          | 40/40        | Adults      | ED           | LP        | NA                                             | Not reported                                              |
| Kawaguch| 2011  | Japan         | 12/12        | Adults 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    | 2012  | China         | 30/30        | Obese parturients scheduled for caesarean section | LD           | CSE       | A. Turbo with a 5–10 MHz, convex probe, SonoSite | Anesthetist with more than 10 years of experience in obstetric anaesthesia |
| Abdelhamid | 2013  | Egypt         | 45/45        | Adults      | A block room | LP        | SonoSite S-Nerve (SonoSite) ultrasound machine, a low-frequency (2–5 MHz) | Not reported                                              |
| Sahin   | 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                    |
| Nasar   | 2014  | Egypt         | 55/55        | Parturients scheduled for vaginal delivery | LD           | CSE       | 2–5 MHz, SonoSite MicroMaxx Ultrasound System English, USA | Operator with more than 10 years of experience             |
| Ansari  | 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| 2014  | USA           | 50/50        | Adults      | ED           | LP        | Aloka SSD 1400 US machine (Aloka, Wallingford, 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     | 2014  | Singapore     | 85/85        | Adults      | OR           | LP        | A. Turbo ultrasound machine (SonoSite, Fujifilm, Bothell, WA, USA), low frequency (2–5 MHz) curvilinear probe | Anaesthetists experienced in ultrasound-assisted neuraxial block |
| Mrcpi   | 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 | 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  | 2016  | USA           | 71/87        | Adults      | ED           | LP        | SonoSite Fujifilm, 10–5 MHz linear array probe | Resident physician                                        |
| Perna   | 2017  | Italy         | 30/28        | Obstetric patients scheduled for vaginal or caesarean delivery | LD           | EC        | SonoSite NanoMaxx, 5–2 MHz C60n Convex probe | Anaesthetist with experience of more than 150 epidural procedures yearly |
## Study Year Country Patients (n) Population Setting Procedure Equipment Operator experience

| Study | Year | Country | Patients (n) | Population | Setting | Procedure | Equipment | Operator experience |
|-------|------|---------|--------------|------------|---------|-----------|------------|---------------------|
| Elsharkawy | 2017 | USA | 14/18 | Adults with predicted difficult anatomy | Outpatient neuraxial clinic | LP | General Electric LOGIQ S7 Expert, Toronto, Canada, Not reported | Anaesthesiologists experienced with previously performed at least 10 ultrasound-guided spinal anesthetics prior to study initiation |
| Auyong | 2017 | USA | 33/37 | Adults undergoing any thoracicor upper abdominal surgery | Outpatient neuraxial clinic | LP | General Electric LOGIQ S7 Expert, Toronto, Canada, Not reported | Anaesthesiologists experienced with previously performed at least 10 ultrasound-guided spinal anesthetics prior to study initiation |
| Li | 2018 | China | 40/40 | Obese parturients scheduled for caesarean section | In the labour and delivery suite | LP | Sonosite S-Nerve, low frequency (2–5 MHz) transducer | Anaesthesiologist trained and experienced in ultrasound-assisted neuraxial block |
| 12 | 2019 | Italy | 47/52 | Adults scheduled for elective surgery | Emergency department | LP | The Sonosite M-Turbo ultrasound machine (GE, Solingen, Germany), Not reported | Anaesthesiologist trained and experienced in ultrasound-assisted neuraxial block |

**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 a reduced 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. and Ansari et al. 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. 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. 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 ultrasound scans were used. Last, obese people and people with difficult anatomical landmarks were not excluded in Nassar et al., which may limit the success rate of LPs.

Interestingly, the study conducted by Lahham et al. 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. 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...
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.

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.
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 al15 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 al28 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 studies9 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.41

Both ultrasound-guided pre-puncture site marking26 28 34 and real-time ultrasound guidance52–54 were reported to be feasible and beneficial; however, pre-puncture ultrasound imaging appeared to be more popular, because only a few studies27 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 guidance55 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 included 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 use 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
The effect of ultrasound guidance for LPs does not form a uniform opinion. Ultrasound guidance provides vertebral interspace level and optimal landmark for injection in a visualization situation.
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