Primary failure of thoracic epidural analgesia: revisited

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ABSTRACT

Primary failure of thoracic epidural analgesia (TEA) remains an important clinical problem, whose incidence can exceed 20% in teaching centers. Since loss-of-resistance (LOR) constitutes the most popular method to identify the thoracic epidural space, the etiology of primary TEA failure can often be attributed to LOR's low specificity. Interspinous ligamentous cysts, non-fused ligamenta flava, paravertebral muscles, intermuscular planes, and thoracic paravertebral spaces can all result in non-epidural LORs. Fluoroscopy, epidural waveform analysis, electrical stimulation, and ultrasonography have been proposed as confirmatory modalities for LOR.

The current evidence derived from randomized trials suggests that fluoroscopy, epidural waveform analysis, and possibly electrical stimulation, could decrease the primary TEA failure to 2%. In contrast, preprocedural ultrasound scanning provides no incremental benefit when compared with conventional LOR. In the hands of experienced operators, real-time ultrasound guidance of the epidural needle has been demonstrated to provide comparable efficacy and efficiency to fluoroscopy.

Further research is required to determine the most cost-effective confirmatory modality as well as the best adjuncts for novice operators and for patients with challenging anatomy. Moreover, future trials should elucidate if fluoroscopy and electrical stimulation could potentially decrease the secondary failure rate of TEA, and if a combination of confirmatory modalities could outperform individual ones.

Thoracic epidural analgesia (TEA) is commonly used to provide pain control for major thoracoabdominal surgery and rib fractures.[1–3] Compared with parenteral opioids, benefits include superior analgesia,[4] decreased incidence of pulmonary complications,[5] shorter postoperative ileus,[6] curtailed protein catabolism,[7] and improved patient satisfaction.[8] Unfortunately, primary failure of TEA, which can exceed 20%, remains a common occurrence.[9] In our two previous Daring Discourses (2015–2016), we explored reasons why primary failure is especially prevalent in teaching centers[9] as well as potential strategies to decrease its incidence.[10] Since 2016, the field has been fertile with research and has seen the publication of multiple randomized controlled trials (RCTs) investigating adjunctive modalities for TEA (ie, fluoroscopy, waveform analysis, electrical stimulation (ES), ultrasonography (US)).

In this updated Daring Discourse, we summarize the collective understanding regarding the incidence and etiology of primary TEA failure, traditional methods used to identify the thoracic epidural space and their attendant shortcomings, as well as confirmatory modalities for loss-of-resistance (LOR). We also discuss the evidence derived from recent RCTs (2016–2023) and identify areas requiring further research.

INCIDENCE OF PRIMARY TEA FAILURE

Historically (prior to 2016), the true incidence of primary TEA failure was difficult to ascertain, as most large audits indiscriminately combined thoracic and lumbar epidural blocks.[11–16] Moreover, the definition of success/failure was often ambiguous. For instance, in a large study (n=7548), Tanaka *et al*[17] reported a 2.5% primary failure rate. However, the latter, defined only as the inability to 'attain adequate analgesia,' was skewed by the epidural administration (and systemic redistribution) of morphine and buprenorphine. In our 2016 Daring Discourse,[9] based on the data collected by Ready[18] at the University of Washington Medical Center and assuming a mathematical worst-case scenario, we estimated that the primary TEA failure rate could reach 22% in teaching institutions.

Fortunately, since 2016, multiple RCTs have investigated technical adjuncts for TEA.[19–24] Because most studies employed clear definitions of success as well as blinded assessments of the latter, one can collate data from their control groups in order to obtain a more accurate assessment of TEA failure (table 1). In a combined 262 patients, the primary TEA failure rate ranged from 0% to 26% (weighted average=16.2%). Interestingly, subgroup analysis reveals that, when attending anesthesiologists performed ≥96% of the blocks, the failure rate (weighted average) was only 1.4%.[22 24] In contrast, when the operators included a higher proportion of trainees (fellows or residents), the primary TEA failure rate (weighted average) increased to 22.5%.[19–21 23] In an era where truncal blocks and alternatives abound, an unremedied failure rate exceeding 20% cannot justify the continued use of TEA even if the latter provides superior visceral analgesia (when functional).

ETIOLOGY OF PRIMARY TEA FAILURE

Failure of TEA can be broadly classified as primary or secondary. Primary TEA failure results from an incorrect placement of the epidural catheter (due to initial misidentification of the epidural space through the needle or a suboptimal physical position of the catheter tip). In contrast, secondary TEA failure can be attributed to an epidural catheter that was (originally) correctly positioned but that (subsequently) failed to provide satisfactory analgesia because of catheter dislodgment/migration or inadequate infusion regimens.[25] Discriminating between the two types of TEA failure is not only important from a conceptual standpoint, but it also becomes clinically paramount, as each etiology requires distinctive corrective measures (table 2). For instance, secondary failure due to catheter dislodgement or migration can be prevented with fixation devices,[26] tunneling,[27 28] and sutures.[29] Given the heterogeneity of patients, surgical dissections, and pain levels, all epidural catheters need to be aggressively managed postoperatively. This may include proactive changes in epidural solution rate, concentration, and bolus dose as well as replacing the epidural catheter if the block does not cover the appropriate dermatomes. Therefore, secondary failure due to suboptimal local anesthetic infusion regimens may be best remedied using a dedicated acute pain service (APS) and coordinated pathways between the APS, nursing staff and surgical team.[30] On the contrary, primary failure does not lend itself to simple or self-evident fixes: its solution requires the incorporation of novel technical adjuncts (table 1).

In theory, primary TEA failure can result from either misidentification of the epidural space or a misplacement of the catheter tip within the epidural

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Table 1 Primary failure rates of thoracic epidural blocks (using conventional loss-of-resistance) reported by recent randomized trials (2016–2023)

Study	N	Primary failure rate	Definition of success	Blinded assessment	Operators
Arnuntasupakul *et al*[19] (2016)	50	24%	Block to ice in at least 2 dermatomes bilaterally 15 min after the injection of epidural bolus (4 mL of lidocaine 2% with epinephrine 5 µg/mL)	Yes	22% expert 78% novice
Auyong *et al*[20] (2017)	37	21.6%	Dermatomal loss of temperature discrimination to ice with pain score of 5 or less (assessed postoperatively) Epidural catheter infused intraoperatively with 8 mL/hour of bupivacaine 0.05% with hydromorphone 0.01 mg/mL	Yes	56.8% attending 43.2% resident
Parra *et al*[21] (2017)	53	26%	Epidural catheter positioned inside the epidural space on epidurogram (5 mL Omnipaque 240)	Yes	Thoracic epidurals directly supervised or performed by 1 of 11 attendings.
Arzola *et al*[22] (2022)	24	0%	Not provided	Not provided	95.8% attending 4.2% Fellow
Dobson *et al*[23] (2022)	50	18%	Block to ice in at least two contiguous dermatomes bilaterally 15 min after the injection of epidural bolus (5 mL of lidocaine 1.5% with epinephrine 5 µg/mL)	Yes	100% senior resident or Fellow
Pakpirom *et al*[24] (2022)	48	2.1%	Sensory block after the test dose (3 mL of lidocaine 2% with epinephrine)	No	100% attending

space.[25] In a seminal imaging study (1999), Hogan has previously demonstrated that a variety of catheter tip locations (within the epidural space) could provide adequate analgesia thereby leading the author to conclude that "the epidural space is a forgiving system, and markedly different sites of catheter tips and spread of injected solution resulted are compatible with adequate anesthetic effect".[31] Thus, in clinical practice, primary TEA failure may result predominantly from the misidentification of the epidural space by the operator.[9 10] Consequently, a discussion of TEA failure inherently requires an understanding of the methods used to identify the thoracic epidural space as well as their attendant shortcomings (table 3).

METHODS TO IDENTIFY THE THORACIC EPIDURAL SPACE AND THEIR SHORTCOMINGS

Traditionally, the epidural space can be identified using one of three techniques, which incidentally rely on three different senses: tactile (ie, LOR), visual (ie, recognition of negative epidural pressure), and auditory (ie, acoustic fall in tonal pitch).[10] Despite the many devices aimed at detecting[32–37] or augmenting the negative epidural pressure,[38–40] few operators rely on the latter to identify the thoracic epidural space.[41] Furthermore, since the negative epidural pressure originates from the negative intrapleural pressure, this modality cannot be used as reliably for patients in the lateral decubitus position, patients undergoing positive pressure mechanical ventilation, or patients with decreased negative intrapleural pressure (eg, emphysematous patients).[42] Although works by Lechner *et al*[43–45] suggest that the acoustic fall in tonal pitch associated with needle transition from ligamentum flavum to epidural space could assist with catheter insertion, the equipment required (eg, pressure transducer, pressure amplifier, voltage-controlled oscillator, loudspeaker) limits its routine implementation. Consequently, because of its simplicity and familiarity, LOR, first described in 1921 by Sicard and Forestier,[46] remains the preferred method to this day.[47]

Despite its popularity, LOR is an imperfect technique. Though sensitive, it suffers from a notable lack of specificity. For example, age-related cysts can develop in interspinous ligaments and yield a non-epidural LOR.[48] Furthermore, cadaveric specimens have demonstrated frequent midline gaps in ligamentum flava in the upper thoracic (T1–3) and lower thoracic (T9–T12) spine.[49 50] The presence of such gaps invalidates midline LOR because the latter no longer represents the interface between ligamentum flavum and epidural space; instead, it simply detects the crossing point between interspinous ligament and ligamentum flavum. While it may be tempting to believe that a paramedian approach for TEA (in lieu of its midline counterpart) is foolproof because it circumvents all such midline ligamentous cysts and absences of flavum fusion, one should remember that the paramedian technique, in itself, is not immune to non-epidural LORs: if the epidural needle was to walk (too medially) off the spinous process (instead of the lamina), a false positive LOR could occur (figure 1).[51] Similarly, if the needle was to walk off the transverse process (into the thoracic paravertebral space), a non-epidural LOR could also be encountered.[52] These occurrences may explain the radically different success rates obtained by experienced and novice operators in RCTs published since 2016 (table 1). Compared with their seasoned counterparts, beginners will expectedly display a higher primary failure rate.[53] However, the latter can seldom be ascribed to the novice operator's inability to recognize LOR. Instead, because they are more adept at three-dimensional spatial configuration (midline and paramedian techniques) and interlaminar triangulation (paramedian technique), experienced epiduralists could position the needle tip in locations where the LOR is more likely to be the epidural space thereby increasing LOR's positive predictive value and, ultimately, the success of TEA.[53]

Table 2 Etiologies and possible solutions for failed thoracic epidural analgesia

Etiology	Possible solutions
Primary failure: Misidentification of the epidural space	Confirmation of loss-of-resistance with electrical stimulation, waveform analysis, ultrasonography, or fluoroscopy
Secondary failure: Catheter dislodgment/migration	Fixation device, tunneling, suture
Secondary failure: Inadequate infusion regimen	Coordinated clinical pathways between the Acute Pain Service, nursing staff and surgical team

Table 3 Traditional methods to identify the thoracic epidural space and their shortcomings

Method	Shortcomings
Loss-of-resistance	Lack of specificity (ligamentous cysts, paravertebral muscles, intermuscular planes, paravertebral spaces, and absent midline fusion of ligamenta flava can yield a non-epidural loss-of-resistance)
Negative pressure recognition	Cannot be used in patients undergoing positive pressure ventilation or patients with decreased negative intrapleural pressure (eg, emphysematous patients). Sitting position preferred over the lateral decubitus position: increased pulmonary functional residual capacity in the sitting position augments the negative intrapleural and thoracic epidural pressures.
Acoustic fall in tonal pitch	Sophisticated equipment required

CONFIRMATORY ADJUNCTS FOR LOR

To circumvent LOR's lack of specificity, one possible (and logical) solution consists in combining it with modalities that would confirm that the LOR identified by the operator is indeed the epidural space. To date, four such modalities have been investigated with RCTs: fluoroscopic guidance, epidural waveform analysis (EWA), ES, and US.

Fluoroscopic guidance

From a technical standpoint, fluoroscopic guidance provides the most complete confirmatory modality. Not only can it pinpoint the position of the epidural needle tip using epidurograms (thereby confirming that the LOR is indeed epidural space), it also enables the operator to efficiently navigate the needle between contiguous spinous processes or laminas.[54] Furthermore, it can help detect inadvertent epidural catheter placement inside the intrathecal space, subdural space, and blood vessels.[55] Parra *et al*[21] randomized 100 patients requiring TEA for thoracic surgery to conventional LOR versus LOR aided by fluoroscopic guidance. All blocks were performed by attending anesthesiologists or supervised trainees (proportions not specified). These authors found that the combination of modalities resulted indeed in a significantly higher primary success rate (98% vs 74%).

Epidural waveform analysis

EWA provides a simple confirmatory adjunct for LOR. When the needle (or catheter) is correctly positioned inside the epidural space, pressure measurement at its tip results in a pulsatile waveform synchronized with arterial pulsations.[56] Arnuntasupakul *et al*[19] randomized 100 patients requiring TEA to conventional LOR versus LOR confirmed with EWA through the needle. Most operators were novices. Arnuntasupakul *et al*[19] reported a lower primary failure rate (2% vs 24%; p=0.002) and a longer performance time (11.2±6.2 vs 8.0±4.6 min; p=0.006) with combined EWA-LOR. Interestingly, subgroup analysis revealed that EWA-LOR outperformed conventional LOR for novice (p=0.001) but not for expert operators. Subsequently, in 2019, the same team of researchers compared EWA through the needle versus EWA through the catheter in 104 patients undergoing thoracic or abdominal surgery.[57] No intergroup differences were found in terms of performance time, success rate, pain scores, local anesthetic requirement, and breakthrough opioid consumption.[57]

Electrical stimulation

ES for epidural catheters was pioneered in 1998 by Tsui *et al*.[58] By priming the epidural catheter with normal saline, these authors were able to elicit myotomal contractions using an average electrical current of 3.78 mA (pulse width=0.2 ms).[58] In addition to LOR confirmation, ES provides noteworthy side benefits. For instance, placement of a catheter in the intrathecal and subdural spaces or alongside a nerve root will yield stimulation at a current inferior to 1 mA.[59 60] Intravascular placement can also be detected by the failure of local anesthetic to abolish myotomal contractions.[59] More importantly, ES enables operators to position the epidural catheter tip at the desired spinal level, as evidenced by the contraction of corresponding myotomes. Dobson *et al*[23] randomized 100 patients requiring TEA for thoracic or abdominal surgery to conventional LOR versus LOR confirmed with ES. All operators were trainees (Fellows or senior residents). Using an intention-to-treat analysis, Dobson *et al*[23] reported no intergroup differences in overall success rates (82%–90%). These results could be explained by the fact that, in five epidural catheters that did not yield myotomal contraction (LOR-ES group), the operators did not reattempt epidural insertion. Instead, they disbelieved ES: in four out five instances, the operators were wrong, and the epidural block failed. When Dobson *et al*'s results were reanalyzed with a per-protocol strategy, LOR-ES resulted in a higher primary success rate than conventional LOR (98% vs 82%; p=0.017).[23]

Ultrasonography

US differs markedly from EWA and ES. While the latter modalities are implemented post hoc after the acquisition of

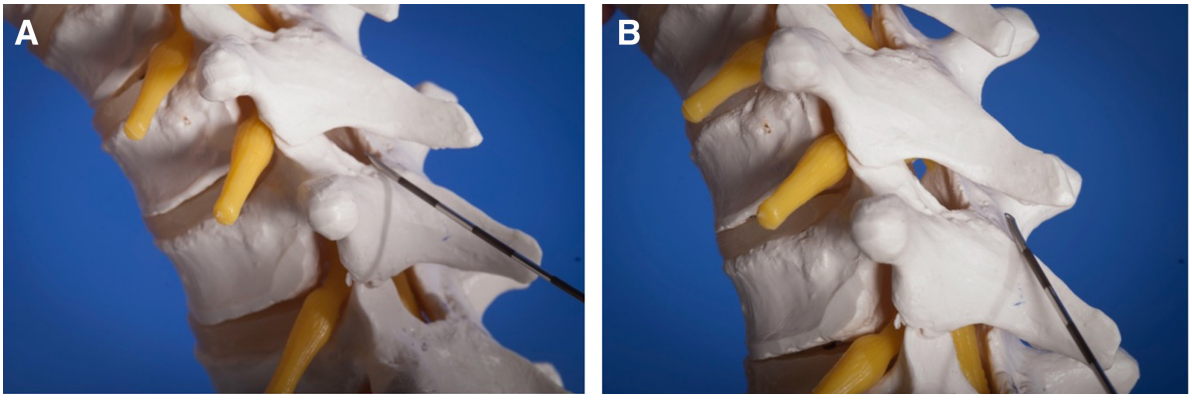

Figure 1 Paramedian thoracic epidural block. (A) Depiction of an epidural needle correctly 'walking off' the lamina during a paramedian thoracic epidural block. (B) Depiction of an epidural needle 'walking off' the spinous process (instead of the lamina) during a paramedian thoracic epidural block. A non-epidural loss-of-resistance may be encountered.

LOR (to confirm that the latter is truly epidural in nature), US is usually employed pre hoc, ie, before the search for LOR. In other words, US aims to place the needle tip in a position where, upon its advancement, the LOR obtained has the highest chance to be the epidural space. However, recent preliminary studies seem to suggest that pulsed wave Doppler US could also be used post hoc to detect catheters and local anesthetic boluses inside the thoracic epidural space.[61]

Currently, there exist two different US methods to aid with thoracic epidural catheter insertion: preprocedural US scanning (ie, US assistance) and real time US guidance.[10] With preprocedural scanning, an US examination is carried out to identify the relevant anatomy (eg, intervertebral level/spinous process/lamina), insonate the window between contiguous laminas, and determine the depth of the ligamentum flavum/dura complex.[62] Subsequently, the operator sets aside the US transducer and advances the epidural needle towards the interlaminar window while testing for LOR. To date, two RCTs have compared US assistance and conventional LOR for TEA. In the first trial (n=70), thoracic epidural blocks were carried out by a 57:43 mix of attending anesthesiologists and residents. Auyong *et al*[20] observed no intergroup differences in terms of primary failure rate (12.1%–21.6%), performance time and number of needle passes. In the second trial (n=47), thoracic epidural blocks were performed almost exclusively by attending anesthesiologists. Similarly to Auyong *et al*,[20] Arzola *et al*[22] found no intergroup difference in terms of success rate and number of needle redirections. Auyong *et al*[20] speculated that the absence of significant benefits associated with US assistance may stem from the fact that preprocedural US skin marking immediately loses its accuracy because of skin manipulation and movement during the procedure itself. More importantly, from a three-dimensional standpoint, it may be difficult for operators to infer the correct angle for epidural needle advancement by using two-dimensional skin markings.

With real-time US guidance, the anesthesiologist visualizes in real-time the sonographic advancement of the epidural needle toward the interlaminar window[63] thereby circumventing a major drawback associated with US assistance. Pakpirom *et al*[24] randomized 96 patients undergoing TEA for thoracic or abdominal surgery to US guided-LOR versus conventional LOR. For the former, using a parasagittal probe position, the US transducer was angled medially in order to identify the interlaminar window. Under direct vision, the epidural needle was inserted until its tip was adjacent to this window. Subsequently, the operator advanced the needle (without the US probe) until LOR was obtained. All conventional thoracic epidural blocks were carried out by attending anesthesiologists, and all US-guided epidural blocks were performed by one of three attending anesthesiologists with extensive experience in US-guided regional anesthesia. Pakpirom *et al*[24] observed similar success rates (100%) between the study groups. However, US-guided LOR resulted in improved efficiency (higher first-pass success, fewer skin punctures, and decreased number of attempts) despite requiring a longer performance time (15.5 (14, 20) vs 10 (7, 14) min; p<0.001). Kwon *et al*[64] randomized 132 patients undergoing thoracic or upper abdominal surgery to fluoroscopy-guided versus US-guided thoracic epidural blocks. Two investigators with extensive experience with both techniques performed all the blocks. Kwon *et al*[64] found no intergroup differences in overall success (98.5%–100%), first pass success (66.7%–68.2%), number of needle passes and number of skin punctures. However, US guidance was associated with a shorter performance time (39.5 (28–78) vs 112.5 (93–166) s; p<0.01).

ESSENTIALS OF OUR CURRENT UNDERSTANDING

In summary, primary TEA failure remains a vexing clinical problem, whose incidence can exceed 20% (especially in teaching centers). Since LOR constitutes the most popular method to identify the thoracic epidural space, the etiology of primary TEA failure can be attributed to LOR's low specificity. Interspinous ligamentous cysts, unfused ligamenta flava, paravertebral muscles, intermuscular planes, and thoracic paravertebral spaces can all result in false positive (ie, non-epidural) LORs. Novice operators, less adept at three-dimensional spatial configuration and interlaminar triangulation than their experienced counterparts, may be more prone to encounter one of these non-epidural LORs and mistake it for the epidural space. Fluoroscopy, EWA, ES, and US have been proposed as confirmatory modalities for LOR.

The current body of literature (derived from RCTs) suggests that, in teaching centers, fluoroscopy and EWA can decrease the primary failure rate of TEA from above 20% to 2%. ES could also provide valuable confirmation for LOR provided the operator believes the modality and reattempts epidural catheter insertion when myotomal contraction are not elicited. In contrast, preprocedural US scanning (ie, US assistance) provides no incremental benefit when compared with conventional LOR. This may stem from the difficulty to infer the correct three-dimensional angles for needle advancement by using the two-dimensional skin markings conferred by US assistance. Although two trials have reported improved procedural efficiency with US guidance when compared with conventional LOR, and similar efficacy and efficiency to fluoroscopy, these results should be interpreted with caution. In both studies, US-guided thoracic epidural blocks were performed solely by attending anesthesiologists with extensive experience.

FUTURE RESEARCH

Over the last 8 years, multiple RCTs have contributed to advance our collective understanding of primary TEA failure and its prevention. However, multiple research questions still demand answers (box 1).

Which confirmatory modality is simplest to use for trainees?

Since primary TEA failure is most prevalent in teaching centers, one should endeavor to find user-friendly confirmatory modalities for LOR. Thus, while US guidance was proven to be non-inferior to fluoroscopy in expert hands,[11] one wonders if EWA and ES, and to a certain extent fluoroscopy, would be easier for beginners to learn. In a recent RCT, Shin *et al*[65] have reported that, compared with the sitting position, US guidance with the patient in the prone position results in higher first pass success, shorter needling time as well as fewer skin punctures and skin

Box 1 Research questions requiring future investigation

- ⇒ Which confirmatory modality is simplest to use for trainees?
- ⇒ Which confirmatory modality is most cost-effective?
- ⇒ Which confirmatory modality is most useful in patients with challenging anatomy?
- ⇒ Which confirmatory modality can prevent secondary failure?
- ⇒ Does the combination of confirmatory modalities provide incremental benefits?

punctures. Consequently, though less intuitive, perhaps the prone position should be first employed when teaching US guidance to trainees.

Which confirmatory modality is most useful in patients with challenging anatomy?

To date, many RCTs investigating US assistance or US guidance have excluded patients with body mass indices superior to 35 kg/m^2.[22 24] Ironically, it is precisely in these difficult patients that technical adjuncts, such as US and fluoroscopy, become most needed. Thus, future research is required to compare these confirmatory modalities in patients with challenging anatomy.

Which confirmatory modality is most cost-effective?

Although fluoroscopic guidance provides the most complete confirmatory modality, it may be associated with the highest costs. To the initial expenses stemming from acquiring the C-Arm and reconfiguring the induction room for radiation safety, one must add the recurrent costs of manpower (ie, radiology technologist). In contrast, once the US machine has been paid in full, the costs of US guidance become minimal (ie, sterile sheath and gel, yearly maintenance/repair of US machine). The expenses related to EWA and ES may be even lower. In fact, for major surgery that requires invasive blood pressure monitoring with an arterial line, the costs of EWA would be nil: after LOR confirmation, the setup (ie, pressure transducer and rigid tubing) could be repurposed for the arterial line insertion.

Which confirmatory modality can prevent secondary failure?

Fluoroscopy and ES provide additional benefits that may impact secondary failure. Epidurograms and the peak level of myotomal contractions allow fluoroscopy and ES, respectively, to pinpoint the spinal level where the epidural catheter tip can be found. Thus, if one could position the catheter tip at a level that provides optimal analgesic coverage for the intended surgery, in theory, one would maximize the benefit of the local anesthetic regimen by allowing lower infusion rates and fewer boluses thereby decreasing the incidence of hypotension and (possibly) facilitating intravenous fluid restriction.

Do combined confirmatory modalities outperform individual ones?

In a 2005 observational study, de Medicis *et al*[11] reported that, compared with EWA or ES alone, combined EWA-ES resulted in improved sensitivity and negative predictive value. Therefore, future studies should investigate variable permutations of confirmatory modalities. Perhaps combining the more technically challenging US guidance with the more user-friendly EWA or ES could allow beginners to slowly gain proficiency and confidence with US.

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