Objective Epidural Space Identification Using Continuous Real-Time Pressure Sensing Technology: A Randomized Controlled Comparison With Fluoroscopy and Traditional Loss of Resistance

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BACKGROUND: Performance of epidural anesthesia and analgesia depends on successful identification of the epidural space (ES). While multiple investigations have described objective and alternative methodologies to identify the ES, traditional loss of resistance (LOR) and fluoroscopy (FC) are currently standard of care in labor and delivery (L&D) and chronic pain (CP) management, respectively. While FC is associated with high success, it exposes patients to radiation and requires appropriate radiological equipment. LOR is simple but subjective and consequently associated with higher failure rates. The purpose of this investigation was to compare continuous, quantitative, real-time, needle-tip pressure sensing using a novel computer-controlled ES identification technology to FC and LOR for lumbar ES identification.

METHODS: A total of 400 patients were enrolled in this prospective randomized controlled noninferiority trial. In the CP management arm, 240 patients scheduled to receive a lumbar epidural steroid injection had their ES identified either with FC or with needle-tip pressure measurement. In the L&D arm, 160 female patients undergoing lumbar epidural catheter placements were randomized to either LOR or needle-tip pressure measurement. Blinded observers determined successful ES identification in both arms. A modified intention-to-treat protocol was implemented, with patients not having the procedure for reasons preceding the intervention excluded. Noninferiority of needle-tip pressure measurement regarding the incidence of successful ES identification was claimed when the lower limit of the 97.27% confidence interval (CI) for the odds ratio (OR) was above 0.50 (50% less likely to identify the ES) and *P* value for noninferioirty <.023.

RESULTS: Demographics were similar between procedure groups, with a mild imbalance in relation to gender when evaluated through a standardized difference. Noninferiority of needle-tip pressure measurement was demonstrated in relation to FC where pain management patients presented a 100% success rate of ES identification with both methodologies (OR, 1.1; 97.27% CI, 0.52–8.74; *P* = .021 for noninferiority), and L&D patients experienced a noninferior success rate with the novel technology (97.1% vs 91%; OR, 3.3; 97.27% CI, 0.62–21.54; *P* = .019) using a a priori noninferiority delta of 0.50.

CONCLUSIONS: Objective lumbar ES identification using continuous, quantitative, real-time, needle-tip pressure measurement with the CompuFlo Epidural Computer Controlled Anesthesia System resulted in noninferior success rates when compared to FC and LOR for CP management and L&D, respectively. Benefits of this novel technology may include nonexposure of patients to radiation and contrast medium and consequently reduced health care costs. (Anesth Analg 2019;129:1319–27)

KEY POINTS

- **Question:** Is continuous quantitative real-time needle-tip pressure measurement noninferior to current standards of care (fluoroscopy and loss of resistance) for epidural space identification?
- **Findings:** Needle-tip pressure measurement using a novel computer-controlled pressure sensing technology was found to be noninferior to fluoroscopy and loss of resistance regarding success rates, procedural times, and complications.
- **Meaning:** Needle-tip pressure sensing is a potential alternative to current standards of care and may avoid exposure to radiation when compared to fluoroscopy and offer greater accuracy when compared to loss of resistance.

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Successful and safe performance of epidural anesthesia/analgesia in the perioperative setting or for labor and delivery (L&D), as well as epidural injections for chronic pain (CP) management, relies on correct identification of the epidural space (ES) by the operator. Multiple methods for objective and more or less simple identification of the ES have been proposed such as waveform analysis,[1] nerve stimulation,[2] fiber optical or ultrasound (US) guidance,[3,4] and acoustic signal assistance.[5]

However, none of these suggested techniques is currently standard of care (SC), and most anesthesiologists and/or pain physicians still use either the subjective manual feeling of a loss of resistance (LOR) or objective but relatively invasive radiological confirmation via fluoroscopy (FC), if available and indicated.[6] Consequently, reported epidural failure rates using LOR for ES identification vary greatly and can range for instance for labor epidural analgesia from 1.5% up to 23%, if a standardized definition of epidural failure is applied.[7,8] Failure rates for epidural analgesia for postoperative pain management after major surgery are even higher and can reach up to 27% for lumbar and 32% for thoracic epidurals.[9]

For the purpose of epidural steroid injection, inability of the LOR technique to correctly identify the ES with subsequent requirement of FC has been described at a frequency of 26%.[10]

In addition, complications such as accidental dural puncture (ADP) are not infrequent and carry the potential need for further treatment and interventions such as epidural blood patches.[8]

Pressure measurement at the tip of the epidural needle and real-time graphic, numeric, and audible display of such pressures via a computerized pressure sensing instrument (CompuFlo Epidural Computer Controlled Anesthesia System [CEI]; Milestone Scientific, Livingston, NJ) has previously been demonstrated to successfully identify the ES with high sensitivity.[11] The aim of this randomized, controlled, clinical trial was to investigate this simple, objective, noninvasive technology in 2 common clinical scenarios (accessing the lumbar ES for L&D analgesia and accessing the lumbar ES for CP management injections), and to evaluate it prospectively for noninferiority (NI) and safety when compared to current SC for ES identification (LOR and FC) in these 2 scenarios.

METHODS

After institutional review board approval, US Food and Drug Administration Investigational Device Exemption, clinical trial registration (NCT02378727, ClinicalTrials.gov, March 4, 2015), and written patient informed consent, a total of 400 patients scheduled to receive epidural needle placement, as part of their medical management, were enrolled until June 2016 in this prospective, controlled, randomized multicenter trial at 6 different clinical sites in the United States. Sites consisted of 2 CP clinics (both located in California) and 4 academic hospital–based L&D suites (located in Texas, California, and Illinois). The study is described by the Consolidated Standards of Reporting Trials statement and its NI extension and was conducted in 2 arms: CP management and L&D.

Inclusion Criteria

Patients between 18 and 90 years of age, who were scheduled to undergo lumbar ES identification for either epidural steroid injection or insertion of an epidural catheter for labor pain, were included in this investigation.

Exclusion Criteria

Patients who presented with contraindication for lumbar epidural anesthesia or injection, as well as patients with signs of systemic infection and patients with neurological deficits that potentially could interfere with dermatome assessment, were excluded from this trial. In addition, previous lumbar back surgery, participation in another clinical trial within the previous 4 weeks, presentation for emergency cesarean delivery or other emergency conditions, and presence of a coexisting severe or terminal disease were also considered exclusion criteria.

Randomization

A master confidential randomization list specific to each investigation site was created by the selected Contract Research Organization responsible for overseeing the study. The randomization code list was generated by a dynamic algorithm, and each randomization code was placed in a sealed envelope on which the subject identification was later written. The master randomization list was then sealed and kept by either the local institutional review board or by the principal investigator in a secured area to be breached only in the case of an emergency. The screening process commenced once the device was delivered to the site, and the site was approved to enroll subjects. On verifying the subject's eligibility to the study, the principal investigator opened an envelope corresponding with the subject's identification for the 5-digit randomization code, which was then written down in the source documents and on the appropriate case report form. All sites received initially blocks that would allow for enrollment of up to 100 subjects per site. Additional randomization blocks were distributed to high enrolling sites. Sites were unaware of the size of the randomization blocks.

Blinding

Only individuals assessing patients or correct dye spread in the ES were blinded to the intervention allocation.

CP Management Arm

Two hundred forty patients undergoing lumbar epidural injections for CP management were randomized to either have their ES identified by using continuous real-time pressure measurement at the epidural needle tip via the CEI (study group of CP patients in whom CEI was used for ES identification [CEI–CP] group) or by SC methods using FC (study group of CP patients in whom FC was used for ES identification [SC–CP] group). Anesthesiologists, who were board certified in pain medicine and who had previously received training in the use of the CEI technology, performed all procedures. Study procedures were performed in the following manner:

Group CEI–CP. Patients were positioned prone and after American Society of Anesthesiologists standard monitors were applied. After disinfection and draping, skin and subcutaneous tissue were infiltrated with 1% lidocaine at the chosen level of the lumbar spine. A sterile set containing

a 20-mL normal saline syringe with an in-line pressure transducer and an extension tubing was then assembled on the sterile field. An 18G Tuohy needle was introduced to a depth of 3 cm. The normal saline syringe was then handed to an assistant and loaded into the CEI. The pressure transducer was connected to the CEI, and the distal end of the extension tubing remained with the operator. The system was then zeroed at the level of the skin to allow for accurate pressure readings at the needle tip. After removal of the stylet, the extension tubing was connected to the Tuohy needle. The CEI was set to set to deliver normal saline at a rate of 0.050 mL/s with an exit-pressure limit not to exceed 130 mm/Hg, and thus allowing for a pressure-controlled infusion during the measurements. The Tuohy needle was then slowly advanced until the pressure readings and the graphic display on the CEI indicated correct position in the ES as previously described[11] and defined by a decrease in pressure readings to <20 mm Hg lasting ≥5 seconds (low pressure plateau). A typical CEI screen display of positive and objective ES identification is demonstrated in Figure 1.

If the correct position of the Tuohy needle in the ES (as indicated by the readings on the CEI) could not be obtained, the epidural Tuohy needle was withdrawn or redirected and a new attempt of epidural Tuohy needle insertion and identification of the ES began. Alternatively, the operator could choose to completely remove the epidural Tuohy needle and insert at a new puncture site, which also counted as a new attempt. After a maximum of 3 failed attempts, ES identification was considered unsuccessful and the patient was converted to FC.

After successful ES identification according to criteria above, the CEI was disconnected and dye was injected into the ES under FC observation. At both investigational sites, a board-certified pain management physician, independent and blinded to the treatment group, determined whether dye spread in the ES space indicated correct ES identification.

Group SC–CP. Patients in group SC–CP were prepared in similar fashion. After the Tuohy needle was introduced to 3 cm at the skin, the stylet was removed and a LOR syringe filled with normal saline was attached. The Tuohy needle was then advanced under FC guidance into the ES, and correct position was confirmed with LOR. If the correct position of the Tuohy needle in the ES could not be obtained or dye injection indicated incorrect position, the operator was allowed to make adjustments up to 3 failed attempts as described under group CEI–CP. Definition of failure and evaluation of correct dye spread in the ES were the same as in group CEI–CP.

L&D Arm

One hundred sixty patients undergoing lumbar epidural catheter insertions for L&D were randomized to either have their ES identified with the CEI technology as described above (study group of L&D patients in whom CEI was used for ES identification [group CEI–L&D]) or by SC with the conventional LOR technique (study group of L&D patients in whom LOR was used for ES identification [group SC–L&D]). Procedures were performed by fellows in obstetric anesthesia or senior anesthesia residents (postgraduate year 4) under direct supervision of an anesthesiologist, after all anesthesia team members received training in CEI technology. Study procedures were conducted in the following manner:

Group CEI–L&D. ES identification was performed in the same fashion as in group CEI–CP except that patients were positioned sitting. Operators were as well allowed up to 3 attempts as defined above. Inability to advance an epidural catheter despite successful ES identification (as per criteria defined for group CEI–CP), and subsequent repositioning or reinsertion of the Tuohy needle also counted as a failed attempt. After a maximum of 3 failed attempts, ES identification was considered unsuccessful and the patient was converted to other noninvasive forms of labor analgesia. After successful ES identification, an epidural catheter was advanced 3–5 cm into the ES and a 3 mL test dose (lidocaine 15 mg/mL with epinephrine 5 µg/mL) was injected via the catheter to rule out intrathecal or intravascular placement. The catheter was then dosed by the operator with a local anesthetic/medication and volume of their choice. Successful ES identification was defined as a loss of sensation to cold in ≥2 symmetrical dermatomes bilaterally as judged by an attending anesthesiologist blinded to the treatment group, 30 minutes after the initial dosing. In the case of a unilateral block, the operator was permitted to manipulate the catheter at their discretion (eg, withdraw the catheter) and redose the catheter. In such case, another assessment of loss of sensation to cold as described above was permitted 30 minutes after catheter redosing to assess whether ES identification was successful (same criteria as above). If loss of sensation to cold in ≥2 dermatomes bilateral could not be established, ES identification was considered unsuccessful, and patients were converted to other noninvasive forms of labor analgesia. Adequate pain relief as expressed by the subjects at 45 minutes after final dosing of the epidural catheter was also evaluated.

Group SC–L&D. Patients were prepared in similar fashion as in group CEI–L&D. ES identification was performed using a traditional LOR to normal saline technique. Definitions of number of attempts and failure or success of ES identification were the same as described under group CEI–L&D, and patients were also evaluated and managed identically.

Statistical Methods

Balance between randomization arms was evaluated through a standardized difference, that is, the difference in means or proportions divided by the pooled standard deviation.

Primary Outcomes. The protocol defined a successful ES identification as the primary outcome for the trial. NI was evaluated in relation to epidural procedures performed with the intervention CEI device (CEI–CP, CEI–L&D) compared with control defined as the current SC (LOR and FC). The assessment was performed regarding the proportion of successful performance (yes/no) of lumbar ES identification using a logistic regression model in which we adjusted

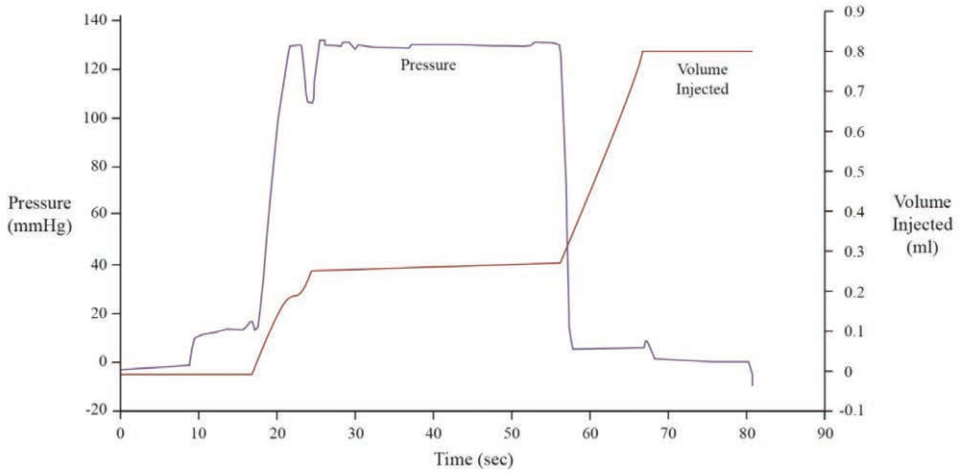

Figure 1. Typical pressure and volume display observed on the CompuFlo Epidural Computer Controlled Anesthesia System during epidural space identification. A sudden drop in pressure followed by formation of a low-pressure plateau indicates that the epidural space has been reached. Injection of normal saline halts when the preset pressure limit (130 mm Hg) is reached.

for confounding by including unbalanced variables.[12] For events occurring with a frequency of zero, logistic regression with a Cauchy prior was used.[13] The NI threshold was set as an odds ratio (OR) of 0.50 (50% less likely to identify the ES), representing an absolute difference of approximately 0.05 (intervention) versus 0.1 (control) in ES identification. This NI margin was chosen a priori because no previous reliable studies had adequately established a minimal clinically important difference for this outcome. NI was claimed if the lower limit of the 97.27% confidence interval (CI) for the OR was above 0.50. One-tailed statistical tests reported with 97.27% confidence intervals and an α of .023 (ie, using alpha spending for 1 interim analysis, see section on sample size calculation) in the direction of interest were used. Analyses were performed following a modified intention-to-treat protocol, which allowed for the exclusion of subjects who did not undergo the procedure. These subjects were later replaced by other randomized subjects until the final sample size was reached.

Secondary Outcomes. Secondary outcomes included the performance of the procedure using a single attempt, the absence of ADP, adequate pain relief reported by the subjects 45 minutes after dosing of the epidural catheter (EAPR 45), and the duration of the ES identification procedure (in minutes). Because the performance of the procedure of a single attempt, EAPR 45, and the absence of ADP were categorical outcomes with the same direction displayed (ie, a positive response on these variables is a clinically desirable outcome), the assessment followed the exact same strategy and assumptions used for the primary outcome. Regarding the duration of the ES identification, separate linear regression models were used to estimate the effect of the CEI device versus the current SC (LOR and FC) on the duration of the ES identification procedure (in minutes). Using the estimated effect from the regression models, we assessed the NI of CEI to the SC on procedure time with 1-tailed NI tests with an a priori NI ratio of means of 1.1, which represents a 10% difference in mean times.[12,14] A ratio was chosen because this metric is independent from the original unit of the outcome measure, although its interpretation differs from the interpretation of evaluations using a mean difference in NI trials.[15] Thus, the alternative hypothesis was that the mean for the CEI device was no >10% greater than that of the SC regarding procedure time. Results derived from this design were interpreted as noninferior for the duration of the ES identification if the upper limit of the 97.27% CI was below 1.1. Because the time to perform the procedure presented a normal distribution, analyses were conducted using values in their original rather than in a log-transformed format, and also because log and other types of transformations might distort results of NI trials.[15] Because secondary outcomes were deemed exploratory, we did not adjust for multiple measurements.[16]

Subgroup analyses were part of our initial protocol, and therefore were conducted without an omnibus or interaction test.[16] These included subgroup analyses conducted for the CP arm and the L&D arm.

Comparisons for the analysis to evaluate balance between randomization arms were conducted through a standardized difference in mean (for numeric variables) and proportion (for categorical variables) to evaluate residual imbalances between randomization groups using a 0.10 threshold.

Sample Size Justification

The sample size calculation for a 1-sided NI was calculated under the following assumptions: the primary study end point was defined as successful performance (yes/no) of lumbar ES identification. Using a NI margin (delta) of 0.1, different scenarios regarding statistical power (0.8–0.9, with a final choice of 0.8), proportions of failures in SC control group (0.08, 0.10, 0.12, 0.14, with a final choice of 0.10), and proportion of failures in the CEI group (0.1, 0.2, with a final choice of 0.1) were investigated. Estimates indicated that a sample size of 150 subjects per randomization group would result in power of 80% or greater, provided that the failure rates were within the estimated ranges. The total sample size was then inflated to account

for the effects of the interim analysis. Although one could argue that with these preliminary expected rates of failures, it would have been possible to design a study to determine that the new intervention would be superior to LOR, at the time of the design there was uncertainty regarding the role of a potential learning curve that would decrease the comparative effectiveness of the intervention. Consequently a more conservative approach with a NI trial was chosen. A preplanned interim analysis for efficacy was conducted after accumulating 200 evaluable subjects. Enrollment continued to a total of 400 subjects for randomization.

Per protocol, a Lan-DeMets spending function with O'Brien-Flemming boundaries were used to preserve the 1-sided type I error rate. It was established that a single interim analysis would occur when half of all subjects had completed their protocol. This point in time occurs on the same day of recruitment and therefore at a point when approximately half of the information is obtained (time fraction = 0.5). After this protocol, the α at the interim analysis was set as α (.5) = .025, while the α at the end of the trial was set at α (1) = .023.[17]

RESULTS

Out of a total of 400 enrolled subjects in this clinical trial, 195 individuals received treatment with the CEI technology, while 193 subjects were allocated to the control group. Participant flow is presented in Figure 2.

Study Sample and Randomization Effectiveness

Table 1 reports information on the total study sample and randomization effectiveness regarding imbalances between intervention groups evaluated through standardized difference in means and proportions. The average age of the total sample was 48.8 years of age, with 71.4% of them being women. Most of the patients were overweight with a mean body mass index (BMI) of 29.9 ± 6.62. Using a 0.10 standardized difference threshold for baseline variable imbalance, gender was mildly imbalanced. In the CP management arm, mean age was 58.4 years with 54.2% of participants being women. Balance was achieved for all variables except gender (standardized difference, 0.18). The mean age in the L&D arm was 33.7 years, with an average BMI of 30.4 ± 5.46. Both age and BMI were imbalanced in the L&D arm, with a standardized difference of 0.28 and 0.13, respectively.

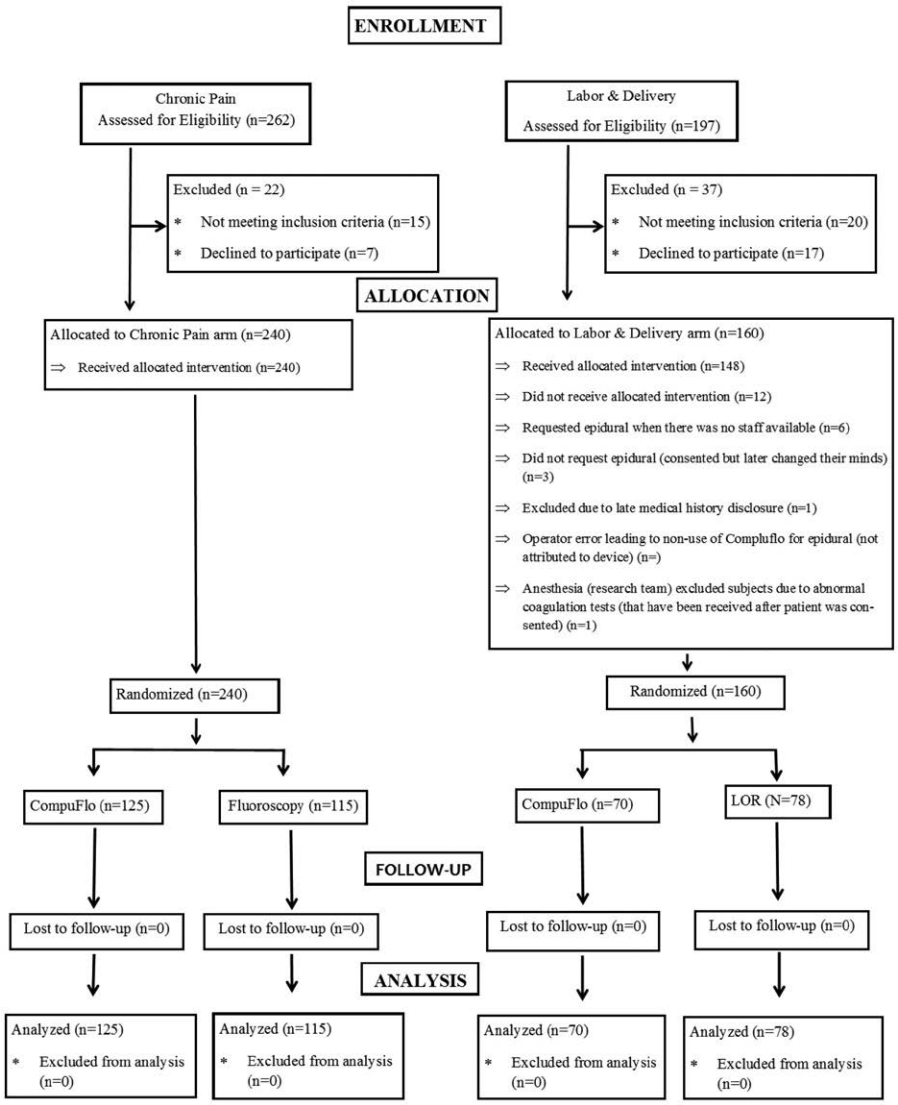

Figure 2. Study enrollment. LOR indicates loss of resistance.

Table 1. Total Study Sample Stratified by Intervention

	Total Study			
Variable	**Total (388)**	**CEI (N = 195)**	**SC (N = 193)**	**Standardized Difference**
Age	48.8 (16.3)	49.5 (15.8)	48.2 (16.8)	0.077
Female	277 (71.4%)	133 (68.2%)	144 (74.6%)	0.16
Body mass index	29.9 (6.62)	29.8 (6.32)	30.1 (6.93)	0.035
Chronic pain management arm				
Variable	**Total (240)**	**CEI–CP (N = 125)**	**SC–CP (N = 115)**	**Standardized Difference**
Age	58.4 (12.8)	57.9 (12.3)	59 (13.3)	0.083
Female	130 (54.2%)	63 (50.4%)	67 (58.3%)	0.18
Body mass index	29.7 (7.26)	29.7 (6.92)	29.6 (7.64)	0.016
Labor and delivery arm				
Variable	**Total (148)**	**CEI–L&D (N = 70)**	**SC–L&D (N = 78)**	**Standardized Difference**
Age	33.7 (7.12)	34.7 (8.54)	32.7 (5.43)	0.28
Body mass index	30.4 (5.46)	30 (5.13)	30.7 (5.75)	0.13

Data are mean (SD) and n (%).

Abbreviations: CEI, CompuFlo Epidural Computer Controlled Anesthesia System; CEI–CP, study group of CP patients for whom CEI was used for ES identification; CEI–L&D, study group of L&D patients for whom CEI was used for ES identification; SC, standard of care; SC–CP, study group of CP patients in whom FC was used for ES identification; SC–L&D, study group of L&D patients for whom LOR was used for ES identification.

Table 2. Outcome Data for Both Study Arms

	CEI (N = 195)	SC (N = 193)	NI *P* Value	Effect Estimate (97.27% CI) Odds Ratio	NI Criteria for Effect Estimate
Primary outcome: ES identification success	193 (99%)	186 (96.4%)	.006	4.73 (0.93–22.82)	Lower CI above 0.50
Success at first attempt	176 (90.3%)	169 (87.6%)	.009	1.3 (0.52–2.78)	Lower CI above 0.50
Absence of ADP	195(100%)	189 (97.9 %)	.022	9.28 (0.63–53.84)	Lower CI above 0.50
				Mean Ratio	
Procedure time (min)	6.03 (4.96)	6.07 (4.79)	.006	1.0 (0.93–1.18)	Upper CI below 1.1
Normal saline injected (mL)	1.9 (8.42)	N/A	N/A	N/A	N/A
Pressure (mm Hg)	9.34 (22.1)	N/A	N/A	N/A	N/A

Data are mean (SD) and n (%).

Abbreviations: ADP, accidental dural puncture; CEI, CompuFlo Epidural Computer Controlled Anesthesia System; CI, confidence interval; ES, epidural space; N/A, not applicable; NI, noninferiority; SC, standard of care; SD, standard deviation.

Table 3. Outcomes in the Chronic Pain Management Arm

	CEI–CP (N = 125)	SC–CP (N = 115)	NI *P* Value	Effect Estimate (97.27% CI) Odds Ratio	NI Criteria for Effect Estimate
Primary outcome: ES identification success	125 (100%)	115 (100%)	.021	1.1 (0.52–8.74)	Lower CI above 0.50
Success at first attempt	120 (96%)	112 (97.4%)	.022	0.64 (0.51–3.1)	Lower CI above 0.50
				Mean Ratio	
Procedure time (min)	7.11 (5.6)	6.46 (4.65)	.072	1.1 (0.9–1.2)	Upper CI below 1.1
Normal saline injected (mL)	0.99 (3.59)	N/A	N/A	N/A	N/A
Pressure (mm Hg)	5.28 (19.6)	N/A	N/A	N/A	N/A

Data are mean (SD) and n (%).

Abbreviations: CEI–CP, study group of CP patients in whom CEI was used for ES identification; CI, confidence interval; ES, epidural space; NI, noninferiority; SC–CP, study group of CP patients in whom FC was used for ES identification; SD, standard deviation.

Combined Results for the CP Management and L&D Arms

Table 2 reports the NI of the CEI technology to the current SC evaluated through 1-tailed statistical tests and reported with 97.27% confidence intervals and a 0.023 α. Results were interpreted as noninferior if the lower limit of the 97.27% CI for the OR was above 0.50 for categorical variables and the upper limit of the 97.27% CI was below 1.1 for continuous variables along with a *P* value < 0.023. Overall, objective ES identification with the CEI technology was noninferior in relation to SC (99% vs 96.4%; OR, 4.73; 97.27% CI, 0.93–22.82; *P* = .006 for NI) with a NI delta of 0.50. Using a NI delta of 0.50 for each outcome, CEI was found noninferior to the SC on respectively: success rate at the first attempt (90.3% vs 87.6%; OR, 1.3; 97.27% CI, 0.52–2.78; NI *P* = .009), and absence of ADP (100% vs 97.9%; OR, 9.28; 97.27% CI, 0.63–53.84; *P* = .022). Procedure time for the CEI device was also found noninferior in relation to the SC (6.03 vs 6.07 minutes; mean ratio, 1; 97.27% CI, 0.93–1.18; *P* = .006) with a NI delta of 1.1.

CP Management Arm. In this arm of the investigation, 125 individuals had their ES identified with the CEI technology, while 105 subjects received SC. Using a NI delta of 0.50, the CEI technology was noninferior (not worse) to the current SC in identifying the ES as indicated by similar success rates (OR, 1.1; 97.27% CI, 0.52–8.74; *P* = .021 for NI) and successful at first attempt (OR, 0.64; 97.27% CI, 0.51–3.1; *P* = .022; Table 3).

The procedural time for CEI technology was 7.11 and 6.46 minutes for the SC. The CEI technology was thus not found to be noninferior compared to the current SC on procedural time (mean ratio, 1.1; 97.27% CI, 0.9–1.2; $P = .072$) using the a priori NI ratio of means of 1.1. No ADP was observed in this study arm.

L&D Arm

In L&D, 70 cases of ES identification were performed using CEI, and SC with LOR in 78 patients. NI of the CEI technology in relation to SC was observed using a priori NI delta of 0.50 for ES identification success rates (OR, 3.3; 97.27% CI, 0.62–21.54; $P = .019$) as well as for success rate at the first attempt (OR, 1.47; 97.27% CI, 0.69–3.65; $P = .013$), effective pain relief at 45 minutes (OR, 0.21; 97.27% CI, 0.75–33.84; $P = .001$), and absence of ADP (OR, 8.51; 97.27% CI, 0.78–85.30; $P = .002$; Table 4). There were also noninferior procedural times (ratio mean, 0.79; 97.27% CI, 0.53–0.91; $P = .019$) in the CEI–L&D group using a priori NI ratio of means of 1.1. In addition, NI of the CEI methodology regarding success rate was not observed when stratified for obesity (BMI >30) (OR, 1.00; 97.27% CI, 0.38–14.34; $P = .34$). Out of the 2 failures that were observed in group CEI–L&D, one was caused by accidental placement of an epidural catheter into a blood vessel, and the other one by exceeding the number of allowed attempts before ES identification. In group SC–L&D, 5 failures were contributed to false-positive LORs resulting in misplaced epidural catheters, while 2 failures were due to the inability of obtain LOR within 3 attempts.

DISCUSSION

This randomized controlled prospective trail evaluated continuous, quantitative, real-time pressure measurement at the epidural needle tip for lumbar ES identification in CP management and L&D patients. Our data suggest that this technology results in noninferior success rate and noninferior patient safety when compared to the current SC. To our knowledge, this is the first report of a methodology that achieves NI to FC for this indication. In contrast to FC, this simple, compact, and mobile technology may have the potential to avoid exposure of the patient to radiation and also allow for greater flexibility and cost savings.

When performing epidural anesthesia in settings that rely on ES identification with LOR such as L&D, one must first navigate the bony structures of the spine and then correctly identify false-positive LOR. False-positive LOR occurs due to changes in tissue compliance (eg, cysts) which are manually perceived as sudden decreases in pressure at the plunger of the LOR syringe, resulting in low specificity of the traditional LOR technique.[18] The incidence of false-positive LOR can be as frequent as 17%.[19]

Preprocedural US examination has been shown to reduce the number of redirections and attempts by visualizing the exact location of the intervertebral space.[20] However, with exception of the pediatric patient population, real-time US guidance to verify an epidural needle actually correctly entering the ES is rarely used. When compared to US, CEI has the disadvantage of not offering any information regarding intervertebral space or other bony obstacles. However, it does have the potential to differentiate between "true" LOR and false-positive LOR and objectively identify the ES, because the pressure patterns and pressure values observed with these 2 entities are distinctively different, as described previously.[11]

Consequently, combining preprocedural US assessment with such an objective method to identify the ES may prove potentially advantageous, rather than relying on the subjective manual perception of the operator to feel LOR. Carvalho et al[21] recently evaluated the superiority of objective ES identification to LOR in a meta-analysis. They conclude that moderate-quality evidence supports better efficacy with less commonly used but objective modalities than with traditional LOR. In another clinical trial, a device that relies on simple pressure change (Epidrum; Exmoor, Somerset, United Kingdom) to identify the ES was compared to LOR for cervical ES injections.[22] Both methods had high rates of false-positive LOR (63% and 75%, respectively), emphasizing the shortcomings of relying just on qualitative pressure change for ES identification. In contrast, the technology

Table 4. Outcomes in the Labor and Delivery Arm

	CEI–L&D (N = 70)	SC–L&D (N = 78)	NI *P* Value	Effect Estimate (97.27% CI) Odds Ratio	NI Criteria for Effect Estimate
Primary outcome: ES identification success	68 (97.1%)	71 (91%)	.019	3.3 (0.62–21.54)	Lower CI above 0.50
Successful at first attempt	56 (80%)	57 (73.1%)	.013	1.47 (0.69–3.65)	Lower CI above 0.50
Absence of ADP	70 (100%)	74 (94.9%)	.002	8.51 (0.78–85.30)	Lower CI above 0.50
EAPR 45	69 (98.6%)	73 (93.6%)	.001	0.21 (0.75–33.48)	Lower CI above 0.50
				Mean Ratio	
Procedure time (min)	4.16 (2.88)	5.26 (4.67)	.019	0.79 (0.53–0.91)	Upper CI below 1.1
Normal saline injected (mL)	3.42 (12.8)	N/A	N/A	N/A	N/A
Pressure (mm Hg)	15.2 (24.8)	N/A	N/A	N/A	N/A
	CEI–L&D, BMI >30 (N = 27)	**SC–L&D, BMI >30 (N = 30)**	**NI *P* Value**	**Effect Estimate (97.27% CI) Odds Ratio**	**NI Criteria for Effect Estimate**
Primary outcome: ES identification success	26 (96.3%)	25 (83.3%)	.34	1.00 (0.38–14.34)	Lower CI above 0.50

Data are mean (SD) and n (%).

Abbreviations: ADP, accidental dural puncture; BMI, body mass index; CEI–L&D, study group of L&D patients for whom CEI was used for ES identification; CI, confidence interval; EAPR 45, adequate pain relief reported by the subjects 45 min after dosing of the epidural catheter; ES, epidural space; N/A, not applicable; NI, noninferiority; SC–L&D, study group of L&D patients for whom LOR was used for ES identification; SD, standard deviation.

investigated in our investigation provides clear quantitative criteria for this purpose, which are displayed to the operator in real time. Furthermore, unlike most devices that measure qualitative pressure change at the proximal end of the Tuohy needle, the quantitative measurements are actually obtained at the needle tip with the CEI technology.

ADP, while performing lumbar ES identification with FC for CP management purposes, occurs in 0.8% of procedures[23] and is reported with a varying incidence of 0.2%–6.6%[24,25] for L&D patients. While the use of liquid in the LOR syringe has been associated with reduced risk for this complication in lower quality studies,[26] no methodology, including use of US or Epidrum, appears to have a positive effect.[27,28] A high percentage of patients that experience ADP develop postdural puncture headache, which results in need for treatment and prolonged hospital stay.[23] Consequently, it would be highly desirable to reduce ADP in the first place and avoid any sequelae. While ADP occurred only in the SC–L&D group of this investigation, the only conclusion that can be drawn based on the study design is that the CEI technology is noninferior to SC regarding the incidence of this complication.

This study was solely designed to evaluate the capability of CEI technology to correctly identify needle-tip position within the ES. Because successful performance of epidural anesthesia/injections depends on many factors (eg, correct placement of the epidural catheter and amount of local anesthetic used), no statements can be made regarding the impact of this novel technology on the overall success of epidural anesthesia or epidural injections. However, correct identification of needle-tip placement within the ES is the one prerequisite that must be fulfilled before further management can potentially determine the eventual success or failure of epidural anesthesia/injections. Another limitation of this investigation is that we did not specifically evaluate the CEI technology for ES identification under more challenging scenarios, such as ES identification in patients suffering from extreme obesity (BMI, >40), or when performing thoracic or cervical epidural anesthesia. Consequently, no conclusions can be drawn whether CEI is noninferior to SC for ES identification in such settings.

Introducing new technology for ES identification carries the theoretical risks for increased infection rates. While this was not an outcome specifically investigated by this trial, no such complication was observed. To maintain sterility of the procedure, all needed disposables to connect the CEI to the Tuohy needle are provided in a sterile kit. The instrument itself can be cleaned in between patient use in similar fashion as any currently commercially available injection or infusion pump.

In summary, our results suggest that this objective ES identification technology is a feasible alternative to traditional SC methodologies. The NI to FC is especially encouraging, while the lower rate of ADP when compared to LOR warrants further investigation.

Future research is needed to specifically investigate the potential synergistic effects of combining the CEI technology with US, the impact of real-time pressure measurement at the Tuohy needle tip on the incidence of ADP, as well as potential superiority regarding success rate when compared to traditional LOR.

DISCLOSURES

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