Ultrasound-Guided Regional Anesthesia and Patient Safety
Update of an Evidence-Based Analysis

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Abstract: In 2010, the American Society of Regional Anesthesia and Pain Medicine's evidence-based medicine assessment of ultrasound (US)-guided regional anesthesia (UGRA) analyzed the effect of this nerve localization technology on patient safety. That analysis focused on 4 important regional anesthesia complications: peripheral nerve injury, local anesthetic systemic toxicity (LAST), hemidiaphragmatic paresis (HDP), and pneumothorax. In the intervening 5 years, further research has allowed us to refine our original conclusions. This update reviews previous findings and critically evaluates new literature published since late 2009 that compares the patient safety attributes of UGRA with those of traditional nerve localization methods. As with the previous version of this exercise, analysis focused on randomized controlled trials that compared UGRA with an alternative neural localization method and case series of more than 500 patients. The Jadad score was used to grade individual study quality, and conclusions were graded as to strength of evidence. Of those randomized controlled trials identified by our search techniques, 28 compared the incidence of postoperative nerve symptoms, 27 assessed LAST parameters, 7 studied HDP, and 9 reported the incidence of pneumothorax. The current analysis strengthens our original conclusions that US guidance has no significant effect on the incidence of postoperative neurologic symptoms and that UGRA reduces the incidence and intensity of HDP but does so in an unpredictable manner. Conversely, emerging evidence supports the effectiveness of US guidance for reducing LAST across its clinical presentation continuum. The predicted frequency of pneumothorax has grown smaller in tandem with increased experience with US-guided supraclavicular block. This evidence-based review summarizes both the power and the limitations of UGRA as a tool for improving patient safety.

What's New: Since the original 2010 publication of this analysis, evidence has continued to support the concept that ultrasound (US) guidance does not meaningfully affect the incidence of peripheral nerve injury (PNI) associated with regional anesthesia. Similar confirmatory evidence attests to US guidance reducing the incidence and intensity of hemidiaphragmatic paresis (HDP) but not eliminating it. Literature published since late 2009 reports the effective role of US guidance in reducing the incidence of local anesthetic systemic toxicity and allows calculation of a lower predicted frequency of pneumothorax associated with US-guided supraclavicular blocks.

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As part of the 2010 American Society of Regional Anesthesia and Pain Medicine's Evidence-Based Assessment of Ultrasound-Guided Regional Anesthesia and Pain Medicine, a critical analysis was undertaken to evaluate the effect of ultrasound (US) guidance on patient safety. As stated in the introduction to that exercise[1]: "Ultrasound-guided regional anesthesia (UGRA) is the latest in a series of tools designed to optimize localization of neural targets prior to the deposition of local anesthetic or other drugs. Because ultrasound can provide direct visualization of the target nerve, surrounding tissues, and injectate spread—advantages not present with any other method of nerve localization—it is logical to assume that these traits may lead to improvements in patient safety in the form of decreased nerve injury, local anesthetic systemic toxicity (LAST), or other complications. Because serious regional anesthesia–related complications are infrequent, proving that UGRA is truly safer than peripheral nerve stimulation (PNS), paresthesia-seeking, fluoroscopy, or other localization methods is difficult." The current update builds on previous knowledge by analyzing literature published since 2009 to further clarify the capability of UGRA to enhance patient safety as it relates to 4 major regional anesthetic complications—postoperative neurologic symptoms (PONS), LAST, HDP, and pneumothorax. The term *peripheral nerve injury* has henceforth been replaced by PONS, which better reflects the rarity of long-term or permanent nerve injury as compared with the transient and relatively common neurologic symptoms that present during the short-term postoperative period.

METHODS

The methodology of the current update mirrors that used in 2010[1]: "Randomized controlled trials (RCTs) were sought that compared UGRA with another form of neural localization, such as PNS or transarterial techniques (Table 1); subsequent comparative analysis of UGRA safety was based only on those RCTs. Case series (>500 patients) were used to provide supplemental information regarding the frequency of complications (Table 2). Some complications are so rare as to have been described only in case reports or correspondence. This form of reporting was used to document the existence of complications but was not used to compare UGRA with other neural localization techniques. The relative quality of individual RCTs was graded using the Jadad score (0–5 points)."[51] Strength of evidence (Table 3) was based on the US Department of Health and Human Services Agency for Health Care Policy and Research Levels of Evidence construct.[52]

The updated literature search for this analysis was conducted for the 6-year period that encompassed 2009 through early 2015. As in 2010,[53] the search was conducted "using standard search engines, including the National Library of Medicine's PubMed, the Cochrane Database for Systematic Reviews, Ovid, Science Direct, and Google Search. Search terms included "ultrasound-guided regional anesthesia," "ultrasound + nerve injury," "ultrasound + local anesthetic toxicity," "ultrasound + diaphragmatic paresis," "ultrasound + pneumothorax," and "ultrasound + complications." English-language articles and articles with sufficiently detailed abstracts translated into English were identified. The bibliographies of identified articles were perused for sources not procured through the search engines."

RESULTS

Since the 2010 publication, 14 additional RCTs and 5 additional large case series have reported at least 1 aspect of patient safety fitting our inclusion criteria. Readers should recognize that

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TABLE 1. RCTs of US Guidance Versus Other Nerve Localization Techniques

Author, Year	Jadad Score	Block	No. US	No. USNS	No. PNS	Vascular Puncture, n (%)	Paresthesia, n (%)	Nerve Injury, n (%)
Antonakakis et al, 2010[2]	4	Deep peroneal	18		18*		US 3; LM 3; Resolved at 1 wk	
Aveline et al, 2010[3]	4	Femoral catheter		92	92			USNS 1 paresthesia; Resolved at 5 d
Bendtsen et al, 2011[4]	3	Popliteal sciatic	50		50	No hematoma	None	
Brull et al, 2009[5]	5	Infraclavicular	52		51	US 0 (0); PNS 4 (8); ($P = 0.11$)	US 3 (6); PNS 22 (45); ($P < 0.001$)	
Casati et al, 2007[6]	3	Axillary	30		29			None at 24 h
Casati et al, 2007[7]	4	Femoral	30		30		0 US; 0 PNS at 24 h	
Chan et al, 2007[8]	5	Axillary	64	62	62	None	US 13 (20); USNS 9 (15); PNS 13 (21); Transient (<5 d)	None
Danelli et al, 2009[9]	3	Popliteal sciatic	22		22	US 0 (0); PNS 5 (22)	US 0 (0); PNS 5 (22)	None at 24 h
Danelli et al, 2012[10]	2	Interscalene catheter	25		25	US 0 (0); PNS 3 (30); ($P = 0.04$)	No difference	
Dingemans et al, 2007[11]	2	Infraclavicular	36	36		US 2 (6); PNS 1 (3)	US 1 (3); Transient (<7 d)	
Domingo-Triado et al, 2007[12]	3	Midfemoral sciatic		30	31			PNS 1 neuropathic pain; Resolved by 10 d
Dufour et al, 2008[13]	4	Popliteal sciatic		26	25			US 0; PNS 0
Fredrickson et al, 2009[14]	3	Interscalene catheter	43		39			US 3; PNS 3; (ns); PONS; day 10
Fredrickson et al, 2009[15]	3	Femoral catheter	21		24	None		
Fredrickson et al, 2009[16]	3	Continuous interscalene	41		40			US 1 (2); PNS 4 (10); Resolved by 8 wk (ns)
Gurkan et al, 2008[17]	3	Lateral sagittal infraclavicular	40		40	US 0 (0); PNS 3 (8)		
Kapral et al, 2008[18]	2	Interscalene	80		80	None	None	None
Liu et al, 2005[19]	2	Axillary	60		30	US 0 (0); PNS 3 (10)	US 0 (0); PNS 3 (10)	
Liu et al, 2009[20]	3	Interscalene	111		108			Confirmed PONS; At 1 wk: PNS 12 (11); US 9 (8); (ns); At 4–6 wk: PNS 8 (7); US 7 (6); (ns)
Macaire et al, 2008[21]	2	Median and ulnar nerves	30		30	None	None	None
Manassero et al, 2012[22]	4	Obturator	25	25		None		
Marhofer et al, 1997[23]	1	3-in-1	20		20	US 0 (0); PNS 3 (15)		
Marhofer et al, 1998[24]	2	3-in-1	20		40	US 0 (0); PNS 4 (10)		
Marhofer et al, 2004[25]	3	Infraclavicular	20		20	None		None

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TABLE 1. *(Continued)*

Author, Year	Jadad Score	Block	No. US	No. USNS	No. PNS	Vascular Puncture, n (%)	Paresthesia, n (%)	Nerve Injury, n (%)
Mariano et al, 2009[26]	2	Infraclavicular catheter	20		20	US 0 (0); PNS 6 (30); ($P < 0.01$)		
Mariano et al, 2009[27]	2	Femoral catheter	20		20	US 0 (0); PNS 4 (20); ($P < 0.04$)		
Mariano et al, 2009[28]	3	Interscalene catheter	20		20	US 1 (5); PNS 5 (25); ($P < 0.18$)		
Mariano et al, 2009[29]	3	Continuous popliteal sciatic	20		20	US 0 (0); PNS 2 (10); (ns)		
Mariano et al, 2010[30]	3	Popliteal sciatic catheter	40		40	US 0 (0); PNS 5 (13); ($P = 0.02$)		
Oberndorfer et al, 2007[31]	4	Femoral/sciatic	23		23	None	None	None
Perlas et al, 2008[32]	4	Popliteal sciatic	37		33	US 0 (0); PNS 0 (0)		US 0 (0); PNS 0 (0); at 7 d
Redborg et al, 2009[33]	5	Tibial nerve ankle	18		18			1 Dysesthesia with US (improving after 2 mo)
Sauter et al, 2008[34]	3	Lateral sagittal infraclavicular	40		40	US 2 (5); PNS 13 (33); ($P = 0.001$)		
Sites et al, 2006[35]	3	Axillary	28		28†			None at 1–2 wk
Soeding et al, 2005[36]	1	Axillary and interscalene	20		20*	No seizure	US 1 (5); Landmark 5; (25); ($P = 0.012$)	None
Taboada et al, 2009[37]	3	Coracoid infraclavicular	35		35	US 1 (3); PNS 1 (3)		US 0; PNS 0; after block
Tedore et al, 2009[38]	3	US infraclavicular and transarterial axillary	111		109†		US 29 (26); TA 44 (40); ($P = 0.035$)	Dysesthesias at 10 d; US 2 (2); TA 3 (3); (ns)
Williams et al, 2003[39]	2	Supraclavicular		40	40			US 2 (5); PNS 1 (3); Paresthesia resolved at 2 wk
Willschke et al, 2005[40]	3	Ilioinguinal/ iliohypogastric	30		30‡	None		None
Yu et al, 2007[41]	3	Axillary	40	40		US 0 (0); PNS 16 (40); ($P < 0.001$)		

*Landmark based.

†Transarterial axillary.

‡Fascial click.

LE indicates lower extremity; ns, not significant; TA, transarterial; UE, upper extremity; USNS, ultrasound + nerve stimulation.

RCTs that address LAST and PONS include relatively few patients. Higher-level evidence from meta-analysis[54] or registry data[42,43,47,48,50] has better elucidated the effect of US on these specific complications.

Six new RCTs reported the occurrence of transient paresthesia or PONS (2 months' or less follow-up) as a secondary outcome. This brings to 28 the number of studies (2298 subjects) that compared PONS associated with UGRA (either UGRA alone or in combination with PNS) with other techniques for nerve localization—PNS (23 studies), transarterial (2 studies), surface landmark (2 studies), or fascial click (1 study). The median quality (Jadad score) of these studies was 3; range, 2 to 5. Nine RCTs reported "none" for neurologic complications, whereas 19 RCTs reported actual incidence with or without statistical significance (Table 1). Eight large case series (4 new since 2009) reported incidences of PONS from a combined total of at least 55,818 peripheral nerve blocks (PNBs) (Table 2).

Ten additional RCTs reported unintended vascular puncture as a secondary outcome, bringing the total to 27 RCTs (1867 subjects). Eight of these studies reported no observed vascular punctures; 18 provided actual incidence figures with or without statistical significance. One study each reported "no seizure" or "no hematoma." The median Jadad score of these studies was 3; range, 1 to 5 (Table 1). Seven case series of at least 500 subjects

TABLE 2. Large Case Series of UGRA With or Without Other Localization Techniques

Author, Year	Block	US, n (%)	USNS, n (%)	PNS, n (%)	Vascular Puncture, n (%)	LAST, n (%)	Nerve Injury, n (%)
Barrington et al, 2009[42]	Australasian Collaboration; 8189 peripheral blocks (early complications); 7156 peripheral blocks (late complications)	1065 (13)	4095 (50)	2457 (30)	Overall: 7.2/1000 (95% CI, 5.1–10.0/1000); US 5.1/1000 PNS 13.9/1000; ($P = 0.001$)	Overall: 0.98/1000; (95% CI, 0.42–1.9/1000); US vs PNS; (ns)	30/7156 (0.42); 27/30 not block related; 3/30 block related (<6, >6, <12 mo duration)—0.4/1000; (95% CI, 0.08–1.1/1000); PNS 2 injuries; USNS 1 injury; (ns)
Barrington and Kluger, 2013[43]	AURORA; 25,336 peripheral blocks; (includes a portion of 2009 data)		20,401 (81)	4745 (19)	Overall: 4.1/1000; USNS 83/20,401; 4.1/1000; (95% CI, 3.2–5.0); PNS 21/4745 4.4/1,000; (95% CI, 2.7–6.8); (ns)	Overall: 0.87/1000; (95% CI, 0.54–1.3); USNS 12/20,401; 0.59/1000; (95% CI, 0.30–1.03); PNS 10/4745; 2.1/1000 (95% CI, 1.0–3.9); ($P = 0.004$)	
Fredrickson and Kilfoyle, 2009[44]	1010; single and continuous blocks; Upper and lower extremity		1010				New, all-cause neurologic symptoms: Day 10, 8.2%; 1 mo, 3.7%; 6 mo, 0.6%
Lecours et al, 2013[45]	627; Single-injection infraclavicular blocks	627				2 (0.3); possible	Paresthesia 43/627 (7); Block-related PONS; 4/627; 0.8% (95% CI, 0%–2%)
Liu et al, 2010[46]	1169; Prospective registry of supraclavicular (654); and interscalene (515) blocks		1169				PONS; 5/1169 at 1 wk; 4/1000 (95% CI, 1–10); All resolved within 3 mo; 0% (95% CI, 0–0.3)
Orebaugh et al, 2009[47]	Retrospective Quality Assurance database; 5436 peripheral blocks		2146 (39)	3290 (61)		UE immediate seizures: USNS 0 vs PNS 4; ($P = 0.044$) LE immediate seizures: USNS 0 vs PNS 1 (ns); 5 seizures/5436 blocks = 0.09%	USNS 0 vs PNS 3; (ns); All documented with electromyography and nerve conduction studies; 2 of 3 improving
Orebaugh et al, 2012[48]	Retrospective Quality Assurance database; 14,498 peripheral blocks (includes 2009 data)		9062	5436		USNS 0/1000; (95% CI, 0.003–0.41); PNS 6/1000; (95% CI, 0.5–2.4); ($P = 0.006$)	6–12 mo; USNS 1/1000; (95% CI, 0.03–0.6); PNS 4/1000; (95% CI, 0.3–1.9); ($P = 0.13$); Over 12 mo USNS 0/1000; (95% CI, 0.003–0.41); PNS 3/1000; (95% CI, 0.2–1.6); ($P = 0.10$)
Perlas, 2009[49]	Supraclavicular (510 blocks)	510			2 (0.4); (95% CI, 0.1%–1.4%)		2 (0.4); (95% CI, (0.1%–1.4%); Transient numbness (several weeks)
Sites et al, 2012[50]	12,668 peripheral blocks	12,668			Venous; 0.6/1000; (95% CI, 0.2–1.2); Arterial 1.2/1000; (95% CI, 0.7–2.0)	Seizure; 0.08/1000; (95% CI, 0.0–0.3)	PONS more than 5 d; 1.8/1000 (95% CI, 1.1–2.7); PONS more than 6 mo; 0.9/1000; (95% CI, 0.5–1.7)

AURORA indicates Australian and New Zealand Registry of Regional Anesthesia; USNS, ultrasound + nerve stimulation.

TABLE 3. Strength of Evidence—The Effect of US Guidance on Patient Safety

Postoperative Neurologic Symptoms (III)
- Proving statistical differences in nerve injury as a function of nerve localization technique is likely futile
- Underpowered results from randomized controlled trials, registries, and large case series find no difference in surrogate markers of nerve injury, such as paresthesia during or immediately after block placement, or transient postoperative neurologic symptoms (Level III evidence)
- Ultrasound-guided regional anesthesia seems to be associated with postoperative neurologic symptoms at an incidence similar to historical reports of nerve injury associated with PNS (Level III evidence)

Local Anesthetic Systemic Toxicity (Ia and III)
- Compared with PNS, US guidance lowers the risk of unintended vascular puncture, a surrogate outcome for local anesthetic systemic toxicity (Level Ia evidence)
- Registry data provide strong support to the statement that US guidance reduces the incidence of local anesthetic systemic toxicity across its clinical continuum (Level III evidence)
- Ultrasound guidance does not completely eliminate the risk of local anesthetic systemic toxicity; therefore, practitioners should remain vigilant and use other preventive and/or diagnostic modalities as appropriate (Grade B recommendation)

Hemidiaphragmatic Paresis (Ib and IV)
- Randomized controlled trials confirm the ability of low-volume US guidance to reduce (but not eliminate) the incidence and severity of HDP using the interscalene approach. The incidence of HDP ranges from nearly 0% to 34% with the US-guided supraclavicular approach (Level Ib evidence)
- No randomized controlled trials or case reports address the role of US-guided brachial plexus blockade in patients at risk for pulmonary compromise from underlying severe pulmonary disease. Because HDP can still occur unpredictably, caution is warranted in any patient unable to withstand a 25% diminution of pulmonary function (Grade C recommendation)

Pneumothorax (III)
- No adequately powered studies directly address the risk of pneumothorax with US-guided regional anesthesia
- Registry data and case reports describe the occurrence of pneumothorax despite the use of UGRA (Level III evidence)

(4 new since 2009) reported the frequency of vascular puncture and/or LAST in at least 53,639 PNBs (Table 2).

The effect of US guidance on the frequency and severity of HDP was reported in 7 RCTs (4 new since 2009), totaling 239 UGRA patients.[55–61] The median Jadad score for these studies was 3.5. Absence of pneumothorax was mentioned in 7 studies of supraclavicular block (3 new since 2009)[34,39,46,49,50,57,62] and 1 new study of infraclavicular block[45] that together amassed 3466 patients. A large registry reported 1 pneumothorax in 2384 supraclavicular blocks.[63]

Since our previous report, a meta-analysis of technical failure associated with lumbar puncture and epidural catheter placement (secondary outcomes) reported that US guidance reduces the risk of traumatic procedures (risk ratio, 0.27; 95% confidence interval [95% CI], 0.11–0.67; $P = 0.005$).[64] A similar meta-analysis in this series[65] addresses the effect of US on neuraxial procedure safety.

DISCUSSION

Levels of evidence for each of the 4 major complications discussed in this review are presented in Table 3.

Postoperative Neurologic Symptoms

Of all the anticipated benefits of US guidance, perhaps the most optimistic was that it would reduce or eliminate PNI. Such an expectation was understandable because heretofore no nerve localization technique allowed the operator to directly observe the target tissue, its surrounding structures, and injectate spread. That US may be safer because it facilitates a needle-to-nerve relationship that ensures needle proximity without actual entry into the nerve is consistent with the then prevailing theory that the pathophysiology of PNI, at least in part, is associated with direct needle trauma. Although UGRA has not resulted in a meaningful reduction of PNI, nonetheless, it has revolutionized our understanding of the contribution of needle-to-nerve relationship to the pathophysiology of PNI.

Surrogate markers of PNI are often referred to as PONS to distinguish them from the true outcome of long-term or permanent nerve injury. One day after PNB procedures, neurologic symptoms such as paresthesia or residual blockade may be present in up to 19% of patients[66] and may persist in approximately 3% of patients during the first few months.[44,67] Long-term (6–12 months) PONS have an incidence of 2 to 4 per 10,000 PNBs[68,69] and are a common metric by which PONS is compared between US and other forms of nerve localization, most commonly PNS. Proving a statistically significant reduction of long-term nerve injury is unlikely to occur because it would require a controlled study of more than 70,000 subjects per group to demonstrate a 50% reduction from 4 to 2 injuries per 10,000 blocks ($\alpha = 0.05$, $\beta = 0.8$). Moreover, the rate of permanent injury (1 year or longer) is even lower, for example, only 1 permanent injury in 65,092 blocks was reported in the literature between 1995 and 2005.[67]

The 2010 version of this article concluded that US guidance does not reduce the incidence of PONS.[53] The primary support for this conclusion came from 2 large studies that reported no difference in the incidence of long-term PONS when US guidance (with or without supplemental PNS) was used to localize nerves versus PNS alone. The Australasian Collaboration[42] reported no differences in more than 7000 PNBs. Of the 30 instances of PNI, only 3 were judged anesthetic related after neurologic workup that included electrophysiologic testing—an incidence of 0.4 per 1000 PNBs (95% CI, 0.08–1.1). Similarly, the Pittsburgh quality assurance database of more than 5000 PNBs[47] found no difference in PNI as a function of nerve localization method. By adding 2 smaller studies of 510[49] and 1010[44] blocks each, our 2010 analysis was based on a combined 15,145 PNBs.[53] The calculated incidence of long-term PONS reported in these studies is similar to that reported in previous single-injection[69] and continuous perineural catheter[70] studies that used PNS as the primary nerve localization tool.

In the interim since 2010, additional registry data and case reports (Table 2) corroborate our initial interpretation that UGRA does not significantly reduce the incidence of PONS. A follow-up

report from the Pittsburgh quality assurance database once again found no difference in nerve injuries that lasted longer than 1 year when US was incorporated into nerve localization as compared with landmark/PNS techniques.[48] Two large registries and a case series reported varied incidences of long-term PONS. Higher than expected incidence was reported by the Dartmouth registry of 12,668 US-guided blocks (persistent at 6 months; 0.9/1000; 95% CI, 0.5–1.7)[50] and a case series of 627 US-guided infraclavicular blocks (short-term follow-up not specified; 8/1000; 95% CI, 0–20).[45] Conversely, the Hospital for Special Surgery registry of 1169 US-guided interscalene and supraclavicular blocks reported an incidence that was lower than expected (resolved by 3 months; 0/1000; 95% CI, 0–0.3).[46] Case reports of long-term and permanent nerve injury in the setting of US guidance have since emerged.[71–73]

In summary, the occurrence of PONS has been recorded from large registries and case series, totaling nearly 56,000 patients (Level III evidence). The use of US guidance for nerve localization has not reduced the incidence of PONS as compared with landmark/PNS guidance. Case reports and registry data report PNI despite US guidance. Indeed, if one were to analyze long-term nerve injuries from only the US groups of the 3 largest registries,[42,48,50] the 5/10,000 incidence is consistent with historic reports of long-term perioperative nerve injury when only PNS was used.[69]

Local Anesthetic Systemic Toxicity

The 2010 review[53] concluded that there was no firm evidence that UGRA reduced the incidence of LAST compared with other nerve localization methods. Although a meta-analysis[54] concluded that US reduced the incidence of unintended vascular puncture as compared with other methods, there was conflicting evidence whether or not this surrogate outcome resulted in fewer episodes of LAST. For instance, a 2009 publication by Barrington et al[42] found no difference in actual LAST as a function of localization technique. A quality assurance study by Orebaugh et al[47] noted a reduction in seizures after US-guided upper extremity procedures but no statistically significant difference compared with PNS techniques when all blocks were included. Both of these groups have subsequently published work that provides strong evidence that US guidance can indeed reduce the incidence of LAST (Table 2).

In a follow-up study by Orebaugh et al,[48] 6 of 5436 PNS/landmark blocks were associated with seizure, whereas no seizure occurred in 9062 US/PNS block patients ($P = 0.006$). In a follow-up study by Barrington and Kluger,[43] US guidance was associated with a reduced incidence of LAST throughout its clinical continuum from minor symptoms (n = 13) to seizure (n = 8) and cardiac arrest (n = 1). There were 12 LAST events in 20,401 US-guided techniques (0.59/1000; 95% CI, 0.30–1.03) versus 10 events in 4745 non-US techniques (2.1/1000; 95% CI, 1.0–3.9) ($P = 0.004$). When propensity analysis was used, the risk of LAST was reduced by more than 65% by the use of US guidance. Taken together, these 2 studies provide the strongest evidence to date that US improves patient safety as related to LAST prevention (Level III evidence).

If one were to analyze only those major LAST events (seizure or cardiac arrest) that occurred in the US groups of the 3 largest registries,[43,48,50] the resulting 2.6/10,000 incidence is less than historic norms.[74] Yet, LAST continues to be reported in isolation, including 2 patients with seizure after US-guided transversus abdominis plane blocks.[75] Practitioners are cautioned not to abandon vigilance when using potentially toxic doses of local anesthetics.[76]

Hemidiaphragmatic Paresis

Transient HDP is a universal side effect of non–US-guided interscalene approaches to the brachial plexus that typically use 20 mL or more local anesthetic.[66] The advent of UGRA not only facilitated more accurate deposition of local anesthetic but imparted increased practitioner confidence to use lower volumes.[43] The 2010 version of this article cited 3 studies of low-volume local anesthetic that aimed to reduce or eliminate HDP by limiting local anesthetic spread to the phrenic nerve during the interscalene and supraclavicular approaches. Those studies showed that reducing local anesthetic volumes to 5 to 10 mL indeed lowered the incidence and lessened the intensity of HDP associated with the interscalene approach and nearly eliminated it using the supraclavicular approach. However, these desirable effects are not predictable for an individual patient, which could be problematic for those patients who could most benefit from eliminating HDP, that is, those with severe pulmonary disease who require oxygen or long-term steroid therapy.[53]

In the interim 5 years, several new investigations of UGRA and HDP have been reported. These investigations both validate our previous conclusion and provide additional insight into the ability of low-volume local anesthetics to provide effective surgical blockade. Three new studies[58,59,77] report differing incidences of HDP during US-guided interscalene block. Sinha et al[60] reported the same incidence of HDP when 10 mL versus 20 mL ropivacaine 0.5% was deposited at the cricoid cartilage level. Using lower volumes, Lee et al[58] reported that 5 mL or 10 mL ropivacaine 0.75% produced equal analgesia, but that 5 mL reduced chest x-ray–diagnosed HDP from 60% to 33% ($P = 0.035$). Renes et al[59] further clarified the role of volume by determining the minimum effective volume (MEV) of ropivacaine 0.75% deposited adjacent to the C7 root: The MEV-50% was 2.9 mL, and the calculated MEV-95% was 3.6 mL. Importantly, there was no US-diagnosed HDP up to 2 hours after surgery, but ventilatory function and ipsilateral hemidiaphragmatic movement were reduced in all subjects after 24 hours of ropivacaine 0.2% at 6 mL/h.[59] These newer studies confirm previous observations that the incidence of HDP is most reduced when smaller volumes of less concentrated local anesthetic are deposited at more caudad cervical vertebral levels. Although others have confirmed observations that the brachial plexus can be anesthetized at the interscalene approach with remarkably low volumes of local anesthetic, there is also evidence that anesthetic block failure may increase at ropivacaine 0.75% volumes of 5 mL and less.[78,79]

A new RCT reported that 34% of 32 subjects who underwent US-guided supraclavicular blocks experienced at least 75% reduction in diaphragmatic excursion compared with 1 (3%) of 32 subjects ($P = 0.001$) in the US-guided infraclavicular group (both with 30 mL of 0.5% ropivacaine).[61] These results are consistent with previous landmark-based studies that demonstrate progressively fewer instances of HDP with more distal approaches to the brachial plexus[66] but still the potential for hemidiaphragmatic involvement. A case report documented HDP associated with infraclavicular block, even when a lateral approach was used.[80]

In summary, recent evidence corroborates our previous conclusion that low-volume (5–10 mL) local anesthetic upper extremity blockade indeed results in less frequent and less intense HDP but does so in an unpredictable manner (Level Ib evidence). There are no studies of low-volume upper extremity blockade in patients with chronic pulmonary disease who are the most likely to benefit, or be harmed, by these techniques. Importantly, even if HDP is absent or less intense immediately after surgery, practitioners are cautioned that, just as with landmark-based approaches,[81] HDP will likely occur when a postoperative infusion is used.[59]

Pneumothorax

As reported in 2010, there are no studies that specifically compared the incidence of pneumothorax from US guidance with

alternative localization methods. Historically, a supraclavicular block was associated with up to 6% incidence of pneumothorax, but these incidence data are from the original supraclavicular techniques[66,82] wherein the block needle, if it missed its neural target, was on a direct trajectory to the lung. Subsequent landmark-based techniques[83,84] likely reduced pneumothorax occurrence significantly, but data do not exist to confirm this clinical impression.

In our 2010 report, 1 large case series reported no pneumothorax after 510 US-guided supraclavicular blocks. This series plus 3 small RCTs allowed us to amass 575 reported US-guided supraclavicular blocks without a pneumothorax (calculated 5:1000 upper limit 95% CI).[53] In the interim, the International Registry of Regional Anesthesia reported 1 pneumothorax in 2384 US-guided supraclavicular blocks (point estimate, 0.4:1000; 95% CI, 0.01–2.3:1000).[63] This point estimate is comparable to an estimated 1:1000 upper 95% CI that results from combining "zero incidence data" from our 2010 report with 2 subsequent registries[46,50] and a small case series,[62] giving a total of 2839 blocks. In addition to supraclavicular block data, no pneumothorax was identified during an observational study of 627 US-guided infraclavicular blocks.[45]

Although the predicted incidence has decreased during the past 5 years, pneumothorax has been reported despite US guidance using the interscalene,[85] supraclavicular,[63,86] and infraclavicular[87] approaches. Although it seems that the incidence of pneumothorax associated with UGRA is substantially less than with the classic supraclavicular approaches, it is unclear if the incidence is less than that experienced during the 1980s and 1990s using landmark-based techniques that were developed to direct needle trajectory away from the lung. In summary, the incidence of pneumothorax associated with UGRA is low but may or may not be lower than with landmark-based techniques (Level III evidence).

Indirect Effects of UGRA on Patient Safety

Not all benefits of US are necessarily linked to direct visualization of target structures. The 2010 review[53] suggested that US may reduce some complications because the technique facilitates a different, perhaps safer, needle trajectory that might result in safety benefits unrelated to US per se. For example, the superficial posterolateral-to-anteromedial needle trajectory characteristic of the US-guided interscalene approach theoretically reduces the opportunity for unintended neuraxial deposition of local anesthetic, a complication that has been reported using the classic interscalene approach wherein the needle can be mistakenly directed toward the neuraxis. Several publications since 2009 refute this assumption. Two cases of epidural spread of local anesthetic—one delayed presentation associated with catheter use[88] and one presentation shortly after block placement[89]—have been reported with US-guided interscalene block. Furthermore, imaging or dissection of cadavers has shown that ultrasonically guided subepineurial needle placement and injection using the interscalene approach can result in epidural spread of dye.[89,90]

Limitations and Future Directions

The literature of UGRA has grown substantially since 2009, but its effect on our understanding with regard to patient safety has been variable. Despite a 4-fold increase in the number of patients for whom PONS has been reported, we are no closer to a statistically significant determination of whether or not UGRA results in fewer nerve injuries as compared with other localization techniques. Indeed, as detailed in our previous report,[1] the extreme rarity of long-term and permanent nerve injury associated with regional anesthesia makes statistical proof unlikely.[91] Conversely, the higher incidence of LAST (relative to PONS) combined with the power of large registry data has identified a positive role for US lowering the incidence of LAST. Nevertheless, the UGRA literature remains sparse with regard to those patient groups that are most at risk for complications and that might derive the most benefit from direct visualization of neural and surrounding tissues. These groups include patients at a higher risk for perioperative nerve injury (eg, diabetics or those with preexisting neurologic disease), LAST (small children or adults with cardiac comorbidities[92]), hematoma (anticoagulated patients), or postoperative pulmonary compromise (severe pulmonary disease).

Ultrasound guidance allows real-time visualization of the needle-to-nerve relationship, yet, as noted in 2010 and further elucidated in the interim,[93] practitioners must be aware of the technical limitations of US. For instance, US facilitates the early detection of a 0.5-mL intraneural injection into cadaveric sciatic nerve or supraclavicular plexus, as manifested by cross-sectional expansion of the nerve and echogenic changes.[94] However, although practitioners are excellent at recognizing extraneural injection, even experts fail to detect 1 in 6 intraneural injections,[95] a cadaveric finding that is similar to reported unintended intraneural injection in the clinical realm.[96–99] Furthermore, cadaveric studies of low-volume detection may not adequately mimic those clinical scenarios wherein nerve damage has likely occurred by the time a higher-volume injection has been detected.[100] Animal studies correlate worse functional outcome and more severe histologic damage with intrafascicular injection as compared with extrafascicular injection,[101–103] yet the resolution of current US machines is inadequate to detect intrafascicular needle placement.[104] Moreover, keeping the needle tip in full view during blocking procedures can be difficult based on artifact[105] and operator skill.[106] These points become relevant when one considers recent cadaver studies that describe how difficulty distinguishing deep cervical fascia from epineurium resulted in unintended subepineurial injection in 5 of 10 trials.[107] In addition to potential nerve injury, unintended intraneural injection in the interscalene region has been associated with cadaveric and human evidence of unintended epidural spread of injectate.[89,90] Recent clinical studies suggest that block effectiveness is not compromised by local anesthetic deposition a small distance from the nerve,[108,109] which argues that placing the needle as close as possible to the neural target may not always be beneficial, although these observations are likely to be block specific.

Previous and current analysis[1,110] has not found US to be inferior to more traditional nerve localization tools with regard to any reported outcome. During the past decade, US technology has become increasingly available throughout North America, and a generation of anesthesiology residents is now unfamiliar with alternative nerve localization methods. For 1 group of experienced investigators, the reported incidence of PONS seems to have decreased between studies, which suggests an adverse outcome reduction coincident with evolving skill and experience.[20,111] Nevertheless, the absence of US machines at all practice locations, the ongoing presence of anesthesiologists extremely experienced and proficient with non-US nerve localization techniques, and (with the possible exception of LAST) the absence of definitive scientific proof of US's superiority make it impossible to assert that US guidance has become the standard of care for nerve localization.

CONCLUSIONS

Since 2009, 19 additional RCTs or large case series that address issues of US guidance and patient safety have been published. These studies confirm and strengthen previous conclusions that UGRA does not have a meaningful impact on the incidence of PONS, and indeed permanent nerve injury has been reported despite its use. Similarly, the use of US reduces the incidence and severity of HDP, but its inability to do so consistently becomes problematic when considering interscalene brachial plexus blockade

in patients with severe pulmonary disease. The increased number of reported US-guided supraclavicular blocks has allowed calculation of a lower predicted incidence of pneumothorax overall, but the complication continues to be reported in individual patients. The greatest progress during the previous 5 years concerns LAST, where strong registry data show that US guidance can reduce the risk of LAST across its clinical presentation continuum by 65%.

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