Ultrasound-Guided Regional Anesthesia and Patient Safety

An Evidence-Based Analysis

Joseph M. Neal, MD

Abstract: The role of ultrasound-guided regional anesthesia (UGRA) in reducing the frequency of regional anesthetic–related complications is difficult to ascertain from analyzing the limited literature on the topic. This evidence-based review critically evaluates the contributions of UGRA to improved patient safety, particularly as compared with standard nerve localization tools. Randomized controlled trials that compared UGRA with another form of neural localization and case series of more than 500 patients were used to compare safety parameters. The quality of studies and strength of evidence were graded. Of those randomized controlled trials identified by our search techniques, 22 compared the incidence of postoperative nerve symptoms, 17 assessed local anesthetic systemic toxicity parameters, and 3 studied hemidiaphragmatic paresis. Statistical proof for meaningful reduction in the frequency of extremely rare complications, such as permanent peripheral nerve injury, is likely unattainable. Although there is evidence for UGRA reducing the occurrence of vascular puncture and the frequency of hemidiaphragmatic paresis, as yet there is at best inconclusive scientific proof that these surrogate outcomes are linked to actual reduction of their associated complications, such as local anesthetic systemic toxicity or predictable diaphragmatic impairment in at-risk individuals. This evidence-based review thus strives to summarize both the power and the limitations of UGRA as a tool for improving patient safety.

(*Reg Anesth Pain Med* 2010;35: S59–S67)

Ultrasound-guided regional anesthesia (UGRA) is the latest in a series of tools designed to optimize localization of neural targets before the deposition of local anesthetic or other drugs. Because ultrasonography (US) 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. Furthermore, it can be challenging to determine precisely when US is directly responsible for safety improvements, that is, consequent to the visualization of target structures, versus indirectly beneficial, that is, by facilitating an altered needle approach that is inherently safer than a traditional approach, but not unique to UGRA. What follows is an analysis of the limited evidence for the role of UGRA in enhanced patient safety. The analysis focuses on 4 major complications—peripheral nerve injury, LAST, hemidiaphragmatic paresis (HDP), and pneumothorax. Also considered are potential mechanisms by which US might indirectly reduce the frequency of certain complications inherent to regional anesthetic practice.

From the Virginia Mason Medical Center, Seattle, WA.
Accepted for publication November 25, 2009.
Address correspondence to: Joseph M. Neal, MD, 1100 Ninth Avenue (B2-AN), Seattle, WA 98111 (e-mail: anejmn@vmmc.org).
No conflicts of interest.
No financial support was received for this study.
James P. Rathmell, MD, served as acting editor-in-chief for this article.

ISSN: 1098-7339
DOI: 10.1097/AAP.0b013e3181ccbc96

METHODS

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 these 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).[1] Strength of evidence (Table 3) was based on a recognized grading schema from the US Agency for Health Care Policy and Research.[2]

The literature search for this analysis was conducted for the 20-year period 1990 through September 2009 using standard search engines, including the National Library of Medicine's PubMed, the Cochrane Database for Systematic Reviews, Ovid, ScienceDirect, 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 abstracts translated into English were identified. The bibliographies of identified articles were perused for sources not procured through the search engines.

RESULTS

Twenty-two RCTs totaling 1863 subjects compared postoperative neurologic symptoms associated with UGRA (either UGRA alone or in combination with PNS) versus other techniques for nerve localization—PNS (18 studies), transarterial (2 studies), surface landmark (1 study), or fascial click (1 study). The median quality (Jadad score) of these studies was 3 (range, 2–5). These RCTs reported the incidence of immediate or transient paresthesia (<7 days) and/or the incidence of postoperative nerve injury (24 hrs to 2 months). Seven RCTs simply reported "none" for neurologic complications, whereas 15 RCTs reported actual incidence with or without statistical significance (Table 1). Four large case series reported incidences of postoperative neurologic symptoms from a combined total of 15,145 peripheral nerve blocks (Table 2).

TABLE 1. Randomized Controlled Trials of Ultrasound-Guidance Versus Other Nerve Localization Techniques

Reference (Year)	Jadad Score	Block	US, n	USNS, n	PNS, n	Vascular Puncture, n (%)	Paresthesia, n (%)	Nerve Injury, n (%)
Casati et al[39] (2007)	4	Femoral	30		30		0 US 0 PNS at 24 hrs	
Casati et al[47] (2007)	3	Axillary	30		29			None at 24 hrs
Chan et al[58] (2007)	5	Axillary	64	62	62	None	US 13 (20%) USNS 9 (15%) PNS 13 (21%) Transient (<5 d)	None
Danelli et al[59] (2009)	3	Popliteal sciatic	22		22	US 0 (0%) PNS 5 (22%)	US 0 (0%) PNS 5 (22%)	None at 24 hrs
Dingemans et al[60] (2007)	2	Infraclavicular	36	36		US 2 (6%) PNS 1 (3%)	US 1 (3%) Transient (<7 d)	
Domingo-Triado et al[61] (2007)	3	Midfemoral sciatic		30	31			PNS 1 neuropathic pain Resolved at 10 d
Dufour et al[62] (2008)	4	Popliteal sciatic		26	25			US 0 PNS 0
Fredrickson et al[63] (2009)	3	Continuous interscalene	41		40			US 1 (2%) PNS 4 (10%) Resolved 8 wk (NS)
Gurkan et al[64] (2008)	2	Lateral sagittal infraclavicular	40		40	US 0 (0%) PNS 3 (8%)		
Kapral et al[65] (2008)	2	Interscalene	80		80	None	None	None
Liu et al[66] (2005)	2	Axillary	60		30	US 0 (0%) PNS 3 (10%)	US 0 (0%) PNS 3 (10%)	
Liu et al[33] (2009)	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[67] (2008)	2	Median and ulnar nerves	30		30	None	None	None
Marhofer et al[68] (1997)	1	3-in-1	20		20	US 0 (0%) PNS 3 (15%)		

Marhofer et al[69] (1998)	2	3-in-1	20		40	US 0 (0%) PNS 4 (10%)		
Marhofer et al[70] (2004)	3	Infraclavicular	20		20	None		None
Mariano et al[71] (2009)	3	Continuous popliteal sciatic	20		20	US 0 (0%) PNS 2 (10%) (NS)		
Oberndorfer et al[72] (2007)	4	Femoral/sciatic	23		23	None	None	None
Perlas et al[73] (2008)	4	Popliteal sciatic	37		33	US 0 (0%) PNS 0 (0%)		US 0 (0%) PNS 0 (0%) At 7 d
Redborg et al[31] (2009)	5	Tibial nerve ankle	18		18			1 dysesthesia with US (improving after 2 mo)
Sauter et al[6] (2008)	3	Lateral sagittal infraclavicular	40		40	US 2 (5%) PNS 13 (33%) (*P* = 0.001)		
Sites et al[74] (2006)	3	Axillary	28		28*			None At 1–2 wk
Soeding et al[20] (2005)	1	Axillary and interscalene	20		20†	No seizure	US 1 (5%) Landmark 5 (25%) (*P* = 0.012)	None
Taboada et al[75] (2009)	3	Coracoid infraclavicular	35		35	US 1 (3%) PNS 1 (3%)		US 0 PNS 0 After block
Tedore et al[19] (2009)	3	US-infraclavicular	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[7] (2003)	2	Supraclavicular		40	40			US 2 (5%) PNS 1 (3%) Paresthesia resolved at 2 wk
Willschke et al[76] (2005)	3	Ilioinguinal/iliohypogastric	30		30§	None		None
Yu et al[77] (2007)	3	Axillary	40	40		US 0 (0%) PNS 16 (40%) (*P* < 0.001)		

*Transarterial.
†Landmark based.
‡Transarterial axillary.
§Fascial click.
LE indicates lower extremity; NS, not statistically significant; PONS, postoperative neurologic symptoms; TA, transarterial; US, ultrasound; USNS, ultrasound + nerve stimulation.

TABLE 2. Large Case Series of Ultrasound-Guided Regional Anesthesia With or Without Other Localization Techniques

Reference (Year)	Block	US, n (%)	USNS, n (%)	PNS, n (%)	Vascular Puncture, n (%)	LAST, n (%)	Nerve Injury, n (%)
Barrington et al[23] (2009)	Australasian collaboration 8189 Peripheral blocks (early complications)	1065 (13%)	4095 (50%)	2457 (30%)	Overall: 7.2/1000 (95% CI, 5.1–10.0/1000)	Overall: 0.98/1000 (95% CI, 0.42–1.9/1000)	30/7156 (0.42%) 27/30 not block related
	7156 Peripheral blocks (late complications)				US 5.1/1000 PNS 13.9/1000 ($P = 0.001$)	US vs PNS (NS)	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)
Fredrickson and Kilfoyle[28](2009)	1010 Single and continuous blocks Upper and lower extremity US +/− PNS						New, all-cause neurologic symptoms: Day 10—8.2% 1 mo—3.7% 6 mo—0.6%
Orebaugh et al[27] (2009)	Retrospective quality-assurance database (5436 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 EMG and NCS; 2 of 3 improving
Perlas et al[8] (2009)	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)

EMG indicates electromyogram; NCS, nerve conduction studies; LAST, local anesthetic systemic toxicity; UE, upper extremity; US, ultrasound; USNS, ultrasound + nerve stimulation.

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

Peripheral nerve injury (III)
- Proving statistical differences in nerve injury as a function of nerve localization technique is likely futile.
- Underpowered results from RCTs and large case series find no difference in surrogate markers of nerve injury, such as paresthesia during or immediately after block placement, or temporary postoperative neurologic symptoms.
- UGRA seems to be associated with perioperative nerve injury at an incidence similar to historical reports of nerve injury after PNS.

Local anesthetic systemic toxicity (Ia and III)
- Compared with PNS, UGRA lowers the risk of unintended vascular puncture, a surrogate outcome for LAST (Ia).
- The weight of conflicting evidence is that UGRA does not affect the incidence of local anesthetic–induced seizures (III).

HDP (Ia and IV)
- RCTs confirm the ability of low-volume UGRA to reduce (but not eliminate) the incidence and severity of HDP using the interscalene approach. The incidence of HDP is nearly 0% using the supraclavicular approach with ultrasound guidance (Ia).
- No RCTs or case reports address whether patients at risk for pulmonary compromise can undergo above-the-clavicle regional anesthetic block. Because HDP can still occur unpredictably, caution remains warranted in any patient unable to withstand a 30% diminution of pulmonary function (IV).

Pneumothorax (III)
- No adequately powered studies directly address the risk of pneumothorax with UGRA.
- Pneumothorax has occurred despite the use of UGRA (III).

HDP indicates hemidiaphagmatic paresis; LAST, local anesthetic systemic toxicity.

Seventeen RCTs totaling 1279 subjects recorded vascular puncture. Six of these studies simply reported vascular punctures as "none," whereas 11 provided actual incidence figures, with or without statistical significance. One study (40 patients) reported "no seizure." The median Jadad score of these studies was 3 (range, 1–5; Table 1). Two case series reported the frequency of vascular puncture and/or LAST in 13,625 peripheral nerve blocks (Table 2).

The effect of ultrasound guidance on the frequency and severity of HDP has been reported in 3 RCTs totaling 65 UGRA patients.[3–5] Jadad scores for these 3 studies were 2, 3, and 5. The absence of pneumothorax was mentioned in 3 RCTs totaling 110 UGRA patients[5–7] and 1 case series of 510 supraclavicular blocks.[8]

No RCTs were identified that directly addressed issues of patient safety using ultrasound-guided neuraxial techniques.

DISCUSSION

Peripheral Nerve Injury

Needle or catheter-induced disruption of a peripheral nerve's structural integrity, particularly the fascicles and their protective perineurium, is thought to contribute to peripheral nerve injury.[9] Ultrasonography may impact this potential injury mechanism by facilitating direct visualization of needle-to-nerve proximity. Ironically, UGRA research has furthered our understanding of more traditional forms of nerve localization such as PNS and paresthesia-seeking techniques and has confirmed previous research that demonstrates their low sensitivity for accurately identifying needle-to-nerve contact. Indeed in human axillary nerve block, US visualization demonstrates that paresthesia is only 38% sensitive and motor response only 75% sensitive in confirming needle-to-nerve contact.[10] This relatively low sensitivity of PNS has been confirmed in another study of human supraclavicular block, wherein a motor response at 0.2 mA or less was indicative of intraneural needle placement as confirmed by US, but a motor response of greater than 0.2 to 0.5 mA or less could not rule out intraneural needle placement.[11] Monitoring injection pressures may also aid in preventing intrafascicular injection, but this modality has been studied only in animals and, like other tools, is neither completely sensitive nor predictive of injury.[12,13] Conversely, ultrasound is a sensitive tool for demonstrating intraneural injection in porcine models, as manifested by consistent nerve expansion observed with 1-mL injectate or less.[13–15] However, although nerve expansion was correlated with histologic injury, concomitant functional injury was not observed.[15] Human correlation has been reported with axillary block, wherein no patient had a nerve injury despite clearly observed nerve expansion after the injection of 2 to 3 mL local anesthetic during UGRA.[16] Although these results suggest that PNS- or paresthesia-guided needles are likely placed within nerves much more frequently than previously realized, and that the usual absence of injury is likely explainable by the relative ease of placing needles into connective tissue rather than into a fascicle, in vitro studies of human sciatic nerve nevertheless demonstrate that sharp needles, in fact, enter fascicles 3.2% of the time, thereby potentially causing injury.[17] Moreover, as one proceeds proximal to distal, the amount of nonneural connective tissues present within the cross-sectional area of the brachial plexus increases,[18] suggesting that the interscalene area may be less forgiving of subepineurium needle placement compared with the axillary or supraclavicular areas. Thus, US is a more sensitive indicator of needle-to-nerve contact than either paresthesia or PNS, but it is unknown if this advantage translates to actual reduction of nerve injury. Adding balance to this observation is that current acoustic resolution limits our ability to consistently discern nerve microanatomy and that there are differences in technical skills between operators.

Of the 22 RCTs (Table 1) that compared UGRA, alone or in combination with PNS, with other forms of nerve localization, two found a statistically different incidence of paresthesia during block placement in dissimilar patient groups—26% in a US-infraclavicular group versus 40% in a transarterial axillary group ($P = 0.035$, 220 patients)[19] and 25% using landmarks versus 5% using UGRA in interscalene and axillary blocks ($P = 0.012$, 40 total patients).[20] The remaining 20 RCTs reported no difference in terms of transient paresthesia or short-lived postoperative neurologic symptoms, which is in agreement with a meta-analysis[21] and a qualitative systematic review.[22]

Several large case series (Table 2) confirm that serious nerve injury is rare. In the largest of these, Barrington et al[23] report a prospective audit of more than 7000 peripheral nerve blocks from the Australasian Regional Anaesthesia Collaboration. Unintended paresthesia during block placement (16.8/1000) and block-related late neurologic deficit (0.4/1000; 95% confidence interval [CI], 0.08–1.1 per 1000) did not differ between UGRA and PNS techniques. The incidence of late neurologic deficit (0.04%) was similar to that reported for PNS-guided peripheral nerve blocks by Auroy et al[24] (0.02%) and for continuous catheter blocks by Capdevila et al[25] (0.21%, all deficits resolved by 10 weeks). These comparisons suggest, but do not prove, that the incidence of late postoperative neurologic symptoms, that is, those lasting weeks to months after the block, has not been altered by the introduction of UGRA.[26] In a retrospective quality assurance review of 5436 peripheral nerve blocks performed with PNS or US with PNS, Orebaugh et al[27] noted 3 neurophysiologic study–documented nerve injuries, all in the PNS group (not statistically significant). Fredrickson and Kilfoyle[28] reported new neurologic symptoms (from any cause) in a cohort of 1010 patients undergoing single or continuous peripheral nerve blocks under UGRA with or without confirmatory PNS. The incidences of neurologic symptoms were 8.2% at 10 days and 3.7% at 1 month, which are similar to those reported by Borgeat et al[29] using PNS localization. The 0% to 0.1% (95% CI, 0%–0.56%) incidence of prolonged (>6 months) nerve injuries judged to be block related in the Fredrickson and Kilfoyle[28] study compared favorably with other reports of injury in continuous catheter patients.[28] Perlas et al[8] noted transient numbness (several weeks) after 510 UGRA supraclavicular blocks (0.4%; 95% CI, 0.1%–1.4%). To date, there are 2 reported cases of prolonged nerve injury associated with UGRA—a permanent brachial plexopathy in a patient with underlying multiple sclerosis and potential surgical causes of injury,[30] and a volunteer who had a dysesthesia of the tibial nerve, which was present but improving after 2 months (this subject is included in the RCTs).[31] In summary, limited literature and small patient numbers suggest 3 findings concerning peripheral nerve injury and UGRA: (1) block-related paresthesia, a surrogate outcome at best, was not reduced when similar block groups were compared; (2) RCTs and large case studies report no permanent neurologic injuries, nevertheless; and (3) peripheral nerve injury associated with, but arguably unrelated to, UGRA has been reported. Because the examined RCTs were not powered to assess nerve injury, the best data on this topic come from the large case series, thereby providing level III strength of evidence (Table 3).

It is important to understand that the relationship of nerve localization technique and peripheral nerve injury is unlikely to ever reach statistical resolution. For example, if one assumes a moderate incidence of early, nonpermanent peripheral nerve injury (3%),[32] a study would require 3000 patients per group to have 80% power (β) to prove a 50% reduction to 1.5%.[33] However, the number of subjects would expand exponentially if one intends to analyze long-term injury (6–12 months), which is estimated to occur in only 0 to 4 per 10,000 blocks.[23,24,26] Furthermore, recent analysis of block-related permanent nerve injury (>12 months) noted only one such injury reported in 65,092 blocks[32] (upper limit 95% CI, ~0.5/10,000).

Local Anesthetic Systemic Toxicity

Local anesthetic systemic toxicity (LAST) ranges from mild subjective symptoms to seizure and cardiac arrest. Ultrasound guidance has the potential to limit LAST by at least 3 mechanisms—identifying the absence of injectate spread around the target, visualizing turbulence or other intravascular anomaly during local anesthetic injection,[34] and facilitating reduced volume of injected local anesthetic. The 17 RCTs reviewed herein add credence to a meta-analysis that showed US can reduce the risk of aspiration-proven vascular puncture compared with other localization techniques (pooled risk ratio, 0.16; 95% CI, 0.05–0.47).[21] Although recognition of unintended vascular puncture is a necessary step toward eliminating LAST, it is only a surrogate outcome for seizure or cardiac arrest. Indeed, various case reports and correspondence document loss of consciousness, agitation, and cardiac arrest despite UGRA.[35–37] Barrington et al[23] found that although US significantly lowered the incidence of unintended vascular puncture as compared with PNS, the incidence of actual LAST (0.98/1000; 95% CI, 0.42–1.9 per 1000) did not differ as a function of localization technique. This incidence is very similar to the 0.8-per-1000 figure reported by Auroy et al[24] using PNS. Conversely, Orebaugh et al[27] reported more seizures ($P = 0.044$) in their upper-extremity blocks that involved PNS rather than UGRA. Thus, UGRA consistently reduces the likelihood of unintended vascular puncture, but case reports and most case series fail to link this advantage to an actual reduction in LAST. The strength of evidence for UGRA reducing the rate of vascular puncture as compared with PNS is level Ia, but only level III for its effect on the incidence of seizure.

The literature does not answer whether using less local anesthetic volume will reduce the frequency of LAST. Although 1 study showed no significant reduction in the volume of local anesthetic used for ultrasound-guided supraclavicular block,[38] several others have shown that UGRA reduces minimum effective local anesthetic volume (MEV) as compared with PNS. For instance, Casati et al[39] were able to lower the MEV using PNS-guided femoral nerve block from 26 to 15 mL using UGRA. However, the US MEV (15 mL; 95% CI, 7–23 mL) remains capable of causing LAST, particularly if injected intravascularly. Importantly, UGRA has been linked to faster absorption and higher maximum plasma concentrations of local anesthetic,[40] which suggests that lowering the local anesthetic volumes used during UGRA is not just possible, but perhaps well considered.

Hemidiaphragmatic Paresis

Hemidiaphragmatic paresis is a universal occurrence with landmark- and nerve stimulator-based interscalene blocks, becoming progressively less frequent as blocks are placed below the clavicle and farther distal along the brachial plexus. Particularly with the more proximal approaches, some patients may experience reduced spirometric measures of pulmonary function, and even fewer may suffer respiratory compromise. For these reasons, above the clavicle blocks are relatively contraindicated in patients unable to withstand a 25% decrease in pulmonary function.[9] Reducing the volume of injected local anesthetic to 20 mL does not limit the occurrence of HDP using traditional approaches, but because UGRA facilitates the use of even smaller local anesthetic volumes, 2 investigatory teams have examined whether this attribute could lower the incidence and severity of HDP without compromising anesthetic quality. One study[4] performed interscalene UGRA with 20 versus 5 mL ropivacaine 0.5% and lowered the incidence of HDP 1 hour after surgery to 90% and 33%, respectively, without compromising sleep or analgesia over the first 24 hrs. Another group[3] compared UGRA with PNS-guided interscalene block with 10 mL ropivacaine 0.75%, similarly lowering the incidence of complete or partial HDP to 13% and 93%, respectively, without affecting block success or early morphine requirements. The same group[5] then compared US- to PNS-guided supraclavicular block using 20 mL ropivacaine 0.75%. The incidence of HDP was 0% (95% CI, 0.00–0.14) versus 53% ($P < 0.0001$), respectively. Spirometric measures of pulmonary function were reduced 20%

or greater in the PNS patients with complete HDP (level Ia strength of evidence; Table 3). Despite the relative success of these UGRA/low-dose local anesthetic techniques, HDP continued to occur unpredictably in both interscalene studies, suggesting that this approach remains relatively contraindicated in those patients most at risk for pulmonary compromise (level IV strength of evidence). Although the supraclavicular study[5] suggests that the risk of HDP is very low using ultrasound guidance and 20 mL ropivacaine, the study was too small to detect a true incidence of HDP using this approach. A large series of UGRA supraclavicular blocks (n = 510) noted symptomatic HDP in 1% of patients (95% CI, 0.4%–2.3%) using 33 ± 8 mL local anesthetic.[8]

Pneumothorax

Ultrasonography enables the anesthesiologist to directly visualize the pleura and lung, which intuitively lessens the risk of pneumothorax. Three RCTs[5–7] and 1 case series[8] of patients undergoing the supraclavicular or lateral sagittal infraclavicular approaches report no pneumothorax in 575 patients (upper limit 95% CI, 0.5%). Nevertheless, a pneumothorax has been reported after UGRA lateral sagittal infraclavicular block[41] and an interscalene continuous catheter block,[42] plus an unreported pneumothorax complicated an attempted UGRA supraclavicular/infraclavicular approach at the author's institution (level III strength of evidence; Table 3).

Indirect Effects of UGRA on Patient Safety

If the incidence of a major complication can be reduced, the direct versus indirect association with UGRA might be seen as immaterial semantics. Yet, a critical review should attempt to differentiate between improved outcomes directly attributable to a unique trait of UGRA versus an indirect benefit that results from a change in technique facilitated by, but not unique to, UGRA. For instance, UGRA interscalene block changes the traditional needle-toward-midline technique of Winnie[43] to a more shallow posterior/lateral-to-anterior/medial needle trajectory that is superficial to the deep borders of the scalene muscles and that theoretically lessens the potential for unintended neuraxis contact. This approach, which should reduce the risk of direct neuraxial spread of local anesthetic and/or needle injury to the spinal cord, is not unique to UGRA; a modified lateral PNS-based approach has been described also by Borgeat et al.[29] Another example pertains to UGRA-facilitated reduction in local anesthetic volume, which may lessen the incidence of LAST. Whereas UGRA may instill the confidence to use smaller volumes of local anesthetic, the tendency for practitioners to use excessive local anesthetic doses for peripheral nerve blocks has been demonstrated by multiple studies,[9] including the ability to substantially reduce median effective volumes by using stimulating perineural catheters.[44] Another indirect (and unique) benefit of UGRA is preprocedural scan of the target area, which may reveal and thus avoid unanticipated findings such as vascular anomalies,[45] neurofibromatosis, or ventriculoperitoneal shunts.[46] Therefore, without diminishing the importance of improving patient safety by whatever tactic, future studies and critical assessments of UGRA should acknowledge both its direct and indirect benefits.

Limitations and Future Directions

Just as it may be important to differentiate direct from indirect benefits of UGRA, in the future it may be possible to link UGRA to patient safety issues that are not obvious from current data. For instance, several RCTs demonstrate fewer needle passes with UGRA versus PNS-guided techniques.[33,47] Although perhaps intuitive to link reduced needle passes to less nerve injury and vascular puncture, current data obtained from normal subjects cannot support this linkage. However, US may particularly improve nerve localization and perhaps reduce nerve injury in patients with diabetes mellitus, in whom PNS- or paresthesia-guided localization is insensitive, and whose nerves have an altered response to local anesthetics.[48,49] Fewer needle passes and vascular punctures may also limit hematoma formation in anticoagulated patients, in whom deeper peripheral nerve blocks are relatively contraindicated.[50] Finally, UGRA-facilitated reduction in local anesthetic volume may have a much greater benefit for the pediatric patient than the adult patient. Thus, future UGRA studies, if performed in patients at risk for specific complications, might reveal benefits not currently apparent in normal patients.

Just as the literature offers no proof that UGRA successfully improves patient safety with regard to rare devastating injuries, there is also no proof that UGRA indeed does not increase the likelihood of injury. Balancing the positive effects of UGRA is the recognition that characteristics of ultrasound machines vary,[51] acoustic resolution is limited, and that operator skill, training, and experience are an unquantifiable component of patient safety. Key to ultrasound safety is keeping the needle tip in view during advancement and injection, yet needle visualization can be challenging.[52] Furthermore, the most common mistakes made by novices include failure to identify the needle tip before injection and failure to recognize maldistribution of injected local anesthetic,[53,54] both of which negate the advantages of UGRA and conceivably lead to injury. Although difficult to quantify, it is likely that even the best ultrasound technology cannot improve safety without properly trained and skilled operators.[55–57] As investigators and everyday operators become well trained in UGRA, data regarding the impact of UGRA on patient safety should become more plentiful and reliable.

CONCLUSION

After a decade of critical appraisal, the science of UGRA remains in its infancy, particularly with regard to how it impacts patient safety. There are no RCT data that unequivocally support superior safety outcomes consequent to the use of UGRA. Statistical proof of improved outcomes for extremely rare events such as peripheral nerve injury is likely unattainable. Data from inadequately powered comparative studies show no differences in surrogate outcomes such as paresthesia during block placement or temporary neurologic symptoms. Improved surrogate safety outcomes such as vascular puncture or less frequent HDP are apparent with the use of UGRA, but there are no definitive data that confirm an actual reduction in true outcomes such as LAST or predictable elimination of HDP in normal patients. Case reports emphasize that absolute elimination of these serious complications has not occurred. Further research is necessary, particularly in those patients at increased risk for specific complications and for whom UGRA may be more likely linked to improved safety profiles.

REFERENCES

1. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials*. 1996;17:1–12.

2. US Department of Health and Human Services Agency for Health Care Policy and Research. Acute pain management: operative or medical procedures and trauma. Rockville, MD: AHCPR; 1993. AHCPR Clinical Practice Guideline No. 1; No. 92-0023-0107.

3. Renes SH, Rettig HC, Gielen MJ, Wilder-Smith OH, van Geffen GJ. Ultrasound-guided low-dose interscalene brachial plexus block reduces the incidence of hemidiaphragmatic paresis. *Reg Anesth Pain Med*. 2009;34:498–502.
4. Riazi S, Carmichael N, Awad I, Holtby RM, McCartney CJL. Effect of local anaesthetic volume (20 vs 5 mL) on the efficacy and respiratory consequences of ultrasound-guided interscalene brachial plexus block. *Br J Anaesth*. 2008;101:549–556.
5. Renes SH, Spoormans HH, Gielen MJ, Rettig HC, van Geffen GJ. Hemidiaphragmatic paresis can be avoided in ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:595–599.
6. Sauter AR, Dodgson MS, Stubhaug A, Halstensen AM, Klaastad O. Electrical nerve stimulation or ultrasound guidance for lateral sagittal infraclavicular blocks: a randomized, controlled, observer-blinded, comparative study. *Anesth Analg*. 2008;106:1910–1915.
7. Williams SR, Chouinard P, Arcand G, et al. Ultrasound guidance speeds execution and improves the quality of supraclavicular block. *Anesth Analg*. 2003;97:1518–1523.
8. Perlas A, Lobo G, Lo N, et al. Ultrasound-guided supraclavicular block. Outcome of 510 consecutive cases. *Reg Anesth Pain Med*. 2009;34:171–176.
9. Neal JM, Gerancher JC, Hebl JR, et al. Upper extremity regional anesthesia. Essentials of our current understanding, 2008. *Reg Anesth Pain Med*. 2009;34:134–170.
10. Perlas A, Niazi A, McCartney C, et al. The sensitivity of motor responses to nerve stimulation and paresthesia for nerve localization as evaluated by ultrasound. *Reg Anesth Pain Med*. 2006;31:445–450.
11. Bigeleisen PE, Moayeri N, Groen GJ. Extraneural versus intraneural stimulation thresholds during ultrasound-guided supraclavicular block. *Anesthesiology.* 2009;110:1235–1243.
12. Hadzic A, Dilberovic F, Shah S, et al. Combination of intraneural injection and high injection pressure leads to fascicular injury and neurologic deficits in dogs. *Reg Anesth Pain Med*. 2004;29:417–423.
13. Altermatt FR, Cummings TJ, Auten KM, et al. Ultrasonographic appearance of intraneural injections in the porcine model. *Reg Anesth Pain Med*. 2010;35:203–206.
14. Chan VW, Brull R, McCartney CJ, et al. An ultrasonic and histologic study of intraneural injection and electrical stimulation in pigs. *Anesth Analg*. 2007;104:1281–1284.
15. Lupu CM, Kiehl T-R, Chan VWS, et al. Nerve expansion seen on ultrasound predicts histological but not functional nerve injury following intraneural injection in pigs. *Reg Anesth Pain Med*. In press.
16. Bigeleisen PE. Nerve puncture and apparent intraneural injection during ultrasound-guided axillary block does not invariably result in neurologic injury. *Anesthesiology.* 2006;105:779–783.
17. Sala-Blanch X, Ribalta T, Rivas E, et al. Structural injury to the human sciatic nerve after intraneural needle insertion. *Reg Anesth Pain Med*. 2009;34:201–205.
18. Van Geffen GJ, Moayeri N, Bruhn J, et al. Correlation between ultrasound imaging, cross sectional anatomy, and histology of the brachial plexus: a review. *Reg Anesth Pain Med*. 2009;34:490–497.
19. Tedore TR, Ya Deau JT, Maalouf DB, et al. Comparison of the transarterial axillary block and the ultrasound-guided infraclavicular block for upper extremity surgery. A prospective randomized trial. *Reg Anesth Pain Med*. 2009;34:361–365.
20. Soeding PE, Sha S, Royse CE, et al. A randomized trial of ultrasound-guided brachial plexus anaesthesia in upper limb surgery. *Anaesth Intensive Care*. 2005;33:719–725.
21. Abrahams MS, Aziz MF, Fu RF, Horn J-L. Ultrasound guidance compared with electrical neurostimulation for peripheral nerve block: a systematic review and meta-analysis of randomized controlled trials. *Br J Anaesth*. 2009;102:408–417.
22. Liu SS, Ngeow JE, YaDeau JT. Ultrasound-guided regional anesthesia and analgesia. A quantitative systematic review. *Reg Anesth Pain Med*. 2009;34:47–59.
23. Barrington MJ, Watts SA, Gledhill SR, et al. Preliminary results of the Australasian Regional Anaesthesia Collaboration. A prospective audit of over 7000 peripheral nerve and plexus blocks for neurological and other complications. *Reg Anesth Pain Med*. 2009;34:534–541.
24. Auroy Y, Benhamou D, Bargues L, et al. Major complications of regional anesthesia in France. The SOS regional anesthesia hotline service. *Anesthesiology.* 2002;97:1274–1280.
25. Capdevila X, Pirat P, Bringuier S, et al. Continuous peripheral nerve blocks in hospital wards after orthopedic surgery. *Anesthesiology.* 2005;103:1035–1045.
26. Benhamou D, Auroy Y, Amalberti R. Safety during regional anesthesia: what do we know and how can we improve our practice [editorial]?. *Reg Anesth Pain Med*. 2010;35:1–3.
27. Orebaugh SL, Williams BA, Vallejo M, Kentor ML. Adverse outcomes associated with stimulator-based peripheral nerve blocks with versus without ultrasound visualization. *Reg Anesth Pain Med*. 2009;34:251–255.
28. Fredrickson MJ, Kilfoyle DH. Neurological complication analysis of 1000 ultrasound guided peripheral nerve blocks for elective orthopaedic surgery: a prospective study. *Anaesthesia*. 2009;64:836–844.
29. Borgeat A, Dullenkopf A, Ekatodramis G, Nagy L. Evaluation of the lateral modified approach for continuous interscalene block after shoulder surgery. *Anesthesiology.* 2003;99:436–442.
30. Koff MD, Cohen JA, McIntyre JJ, Carr CF, Sites BD. Severe brachial plexopathy after an ultrasound-guided single-injection nerve block for total shoulder arthroplasty in a patient with multiple sclerosis. *Anesthesiology.* 2008;108:325–328.
31. Redborg KE, Antonakakis JG, Beach ML, Chinn CD, Sites BD. Ultrasound improves the success rate of a tibial nerve block at the ankle. *Reg Anesth Pain Med*. 2009;34:256–260.
32. Brull R, McCartney CJL, Chan VWS, El-Beheiry H. Neurological complications after regional anesthesia: contemporary estimates of risk. *Anesth Analg*. 2007;104:965–974.
33. Liu SS, Zayas VM, Gordon MA, et al. A prospective, randomized, controlled trial comparing ultrasound versus nerve stimulator guidance for interscalene block for ambulatory shoulder surgery for postoperative neurological symptoms. *Anesth Analg*. 2009;109:265–271.
34. VadeBoncouer TR, Weinberg GL, Oswald S, Angelov F. Early detection of intravascular injection during ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2008;33:278–279.
35. Butterworth JF. Case reports: unstylish but useful sources of clinical information. *Reg Anesth Pain Med*. 2009;34:187–188.
36. Gnaho A, Eyrieux S, Gentili ME. Cardiac arrest during an ultrasound-guided sciatic nerve block combined with nerve stimulation. *Reg Anesth Pain Med*. 2009;34:278.
37. Zetlaoui RJ, Labbe J-P, Benhamou D. Ultrasound guidance for axillary plexus block does not prevent intravascular injection. *Anesthesiology.* 2008;108:761.
38. Duggan E, El Beheiry H, Perlas A, et al. Minimum effective volume of local anesthetic for ultrasound-guided supraclavicular brachial plexus block. *Reg Anesth Pain Med*. 2009;34:215–218.
39. Casati A, Baciarello M, Di Cianni S, et al. Effects of ultrasound guidance on the minimum effective anaesthetic volume required to block the femoral nerve. *Br J Anaesth*. 2007;98:823–827.
40. Weintraud M, Lundblad M, Kettner S, et al. Ultrasound versus landmark-based technique for ilioinguinal-iliohypogastric nerve blockade in children: the implications on plasma levels of ropivacaine. *Anesth Analg*. 2009;108:1488–1492.

41. Koscielniak-Nielsen Z, Rasmussen H, Hesselbjerg L. Pneumothorax after an ultrasound-guided lateral sagittal infraclavicular block. *Acta Anaesthesiol Scand*. 2008;52:1176.
42. Bryan NA, Swenson JD, Greis PE, Burks RT. Indwelling interscalene catheter use in an outpatient setting for shoulder surgery: technique, efficacy, and complications. *J Shoulder Elbow Surg*. 2007;16:388–395.
43. Winnie AP. Interscalene brachial plexus block. *Anesth Analg*. 1970;49:455–466.
44. Paqueron X, Narchi P, Mazoit JX, et al. A randomized, observer-blinded determination of the median effective volume of local anesthetic required to anesthetize the sciatic nerve in the popliteal fossa for stimulating and nonstimulating perineural catheters. *Reg Anesth Pain Med*. 2009;34:290–295.
45. Duggan E, Brull R, Lai J, Abbas S. Ultrasound-guided brachial plexus block in a patient with multiple glomangiomatosis. *Reg Anesth Pain Med*. 2008;33:70–73.
46. Manickam BP, Perlas A, Chan VWS, Brull R. The role of a preprocedure systematic sonographic survey in ultrasound-guided regional anesthesia. *Reg Anesth Pain Med*. 2008;33:566–570.
47. Casati A, Danelli G, Baciarello M, et al. A prospective, randomized comparison between ultrasound and nerve stimulation guidance for multiple injection axillary brachial plexus block. *Anesthesiology.* 2007;106:992–996.
48. Gebhard RE, Nielsen KC, Pietrobon R, Missair A, Williams BA. Diabetes mellitus, independent of body mass index, is associated with a “higher success” rate for supraclavicular brachial plexus blocks. *Reg Anesth Pain Med*. 2009;34:404–407.
49. Sites BD, Gallagher J, Sparks M. Ultrasound-guided popliteal block demonstrates an atypical motor response to nerve stimulation in 2 patients with diabetes mellitus. *Reg Anesth Pain Med*. 2003;28: 479–482.
50. Horlocker TT, Wedel DJ, Rowlingson JC, et al. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition). *Reg Anesth Pain Med*. 2010;35:64–101.
51. Wynd KP, Smith HM, Jacob AK, et al. Ultrasound machine comparison: an evaluation of ergonomic design, data management, ease of use, and image quality. *Reg Anesth Pain Med*. 2009;34:349–356.
52. Chin KJ, Brull R, Perlas A, Chan VWS. Needle visualization in ultrasound-guided regional anesthesia: challenges and solutions. *Reg Anesth Pain Med*. 2008;33:532–544.
53. Sites BD, Gallagher JD, Cravero J, Lundberg J, Blike G. The learning curve associated with a simulated ultrasound-guided interventional task by inexperienced anesthesia residents. *Reg Anesth Pain Med*. 2004;29:544–548.
54. Sites BD, Spence BC, Gallagher J, et al. Characterizing novice behavior associated with learning ultrasound-guided peripheral regional anesthesia. *Reg Anesth Pain Med*. 2007;32:107–115.
55. Smith HM, Kopp SL, Jacob AK, Torsher LC, Hebl JR. Designing and implementing a comprehensive learner-centered regional anesthesia curriculum. *Reg Anesth Pain Med*. 2009;34:88–94.
56. Ivani G, Ferrante FM. The American Society of Regional Anesthesia and Pain Medicine and the European Society of Regional Anaesthesia and Pain Therapy Joint Committee recommendations for education and training in ultrasound guided regional anesthesia: why do we need these guidelines? *Reg Anesth Pain Med*. 2009;34:8–9.
57. Sites BD, Chan VW, Neal JM, et al. The American Society of Regional Anesthesia and Pain Medicine (ASRA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA) Joint Committee recommendations for education and training in ultrasound guided regional anesthesia. *Reg Anesth Pain Med*. 2009;34:40–46.
58. Chan VW, Perlas A, McCartney J, et al. Ultrasound guidance improves success rate of axillary brachial plexus block. *Can J Anaesth*. 2007;54:176–182.
59. Danelli G, Fanelli A, Ghisi D, et al. Ultrasound vs nerve stimulation multiple injection technique for posterior popliteal sciatic nerve block. *Anaesthesia*. 2009;64:638–642.
60. Dingemans E, Williams SR, Arcand G, et al. Neurostimulation in ultrasound-guided infraclavicular block: a prospective randomized trial. *Anesth Analg*. 2007;104:1275–1280.
61. Domingo-Triado V, Selfa S, Martinez F, et al. Ultrasound guidance for lateral midfemoral sciatic nerve block: a prospective, comparative, randomized study. *Anesth Analg*. 2007;104:1270–1274.
62. Dufour E, Quennesson P, Van Robais AL, et al. Combined ultrasound and neurostimulation guidance for popliteal sciatic nerve block: a prospective, randomized, comparison with neurostimulation alone. *Anesth Analg*. 2008;106:1553–1558.
63. Fredrickson MJ, Ball CM, Dalgleish AJ, Stewart AW, Short TG. A prospective randomized comparison of ultrasound and neurostimulation as needle end points for interscalene catheter placement. *Anesth Analg*. 2009;108:1695–1700.
64. Gurkan Y, Acar S, Solak M, Toker K. Comparison of nerve stimulation vs. ultrasound-guided lateral sagittal infraclavicular block. *Acta Anaesthesiol Scand*. 2008;52:851–855.
65. Kapral S, Greher M, Huber G, et al. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. *Reg Anesth Pain Med*. 2008;33:253–258.
66. Liu FC, Liou JT, Tsai YF, et al. Efficacy of ultrasound-guided axillary brachial plexus block: a comparative study with nerve stimulator-guided method. *Chang Gung Med J*. 2005;28:396–402.
67. Macaire P, Singelyn F, Narchi P, Paqueron X. Ultrasound- or nerve stimulation-guided wrist blocks for carpal tunnel release: a randomized prospective comparative study. *Reg Anesth Pain Med*. 2008;33:363–368.
68. Marhofer P, Schrogendorfer K, Koinig H. Ultrasonographic guidance improves sensory block and onset time of three-in-one blocks. *Anesth Analg*. 1997;85:854–857.
69. Marhofer P, Schrogendorfer K, Wallner T, et al. Ultrasonographic guidance reduces the amount of local anesthetic for 3-in-1 blocks. *Reg Anesth Pain Med*. 1998;23:584–588.
70. Marhofer P, Sitzwohl C, Greher M, Kapral S. Ultrasound guidance for infraclavicular brachial plexus anaesthesia in children. *Anaesthesia*. 2004;59:642–646.
71. Mariano ER, Cheng GS, Choy LP, et al. Electrical stimulation versus ultrasound guidance for popliteal-sciatic perineural catheter insertion. A randomized controlled trial. *Reg Anesth Pain Med*. 2009;34:480–485.
72. Oberndorfer U, Marhofer P, Bosenberg A, et al. Ultrasonographic guidance for sciatic and femoral nerve blocks in children. *Br J Anaesth*. 2007;98:797–801.
73. Perlas A, Brull R, Chan VWS, et al. Ultrasound guidance improves the success of sciatic nerve block at the popliteal fossa. *Reg Anesth Pain Med*. 2008;33:259–265.
74. Sites BD, Beach ML, Spence BC, Wiley CW. Ultrasound guidance improves the success rate of a perivascular axillary plexus block. *Acta Anaesthesiol Scand*. 2006;50:678–684.
75. Taboada M, Rodriguez J, Amor M, et al. Is ultrasound guidance superior to conventional nerve stimulation for coracoid infraclavicular brachial plexus block? *Reg Anesth Pain Med*. 2009;34:357–360.
76. Willschke H, Marhofer P, Bosenberg A, et al. Ultrasonography for ilioinguinal/iliohypogastric nerve blocks in children. *Br J Anaesth*. 2005;95:226–230.
77. Yu WP, Xu XZ, Wu DZ, Guo XY, Huang PT. Efficacy of axillary approach brachial plexus blocking by ultrasound-guided four points via one-puncture technique. *Chung-Hua Hsueh Tsa Chih*. 2007;87: 740–745.

