propofol. We have subset the original dataset to the 2,210 patients who received one of those regimens and report a regression-based analysis as well as a propensity-matching analysis. Table 3 shows the comparison between regimens midazolam plus etomidate and midazolam plus propofol among the subset of patients who received one of the regimens using the suggested propensity-matching approach and a regression modeling approach. In neither case would we conclude any difference between the treatments.

Finally, Sanders *et al.* suggested that we adjust for hypertension as a potential confounder for the observed angiotensin-converting enzyme inhibitor effect seen in figure 3 of the original article. We agree that if interest was in angiotensin-converting enzyme inhibitor effects, controlling for hypertension would certainly be warranted. That said, even though we were explicit about showing all modeling results, our interest in including covariates was to control for confounding of etomidate effects. We are aware that one could always improve modeling approaches; however, ours was a prespecified model that we thought would be adequate (not perfect) in its capacity to control for confounding of etomidate associations with outcomes.

Competing Interests

The authors declare no competing interests.

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Total Local Anesthetic Administered Is Integral to the Syndrome of Local Anesthetic Systemic Toxicity

To the Editor:

We read with interest the report of local anesthetic systemic toxicity in the recent issue of Anesthesiology.[1] The authors deserve credit for their review of the subject and detailed analysis of factors culminating in the death of their patient. The transparency required to present such a case is of benefit to all anesthesiologists, who can apply the principles described to improve safety for patients undergoing regional anesthesia techniques.

However, we were concerned that one integral factor contributing to the poor outcome in this case was not discussed, and that is the total dose of local anesthetic (LA) administered. We believe that a relative overdose of LA was administered and subsequent systemic absorption was likely a factor in the toxicity observed.

Total doses of LA used include 30 ml of mepivacaine 1.5% without epinephrine (450 mg) plus 10 ml of bupivacaine 0.25% with epinephrine 1:200,000 (25 mg). The dose of mepivacaine exceeds the manufacturer's recommended maximum dose of 400 mg for an adult.[2] Of note, the manufacturer's product information inserts for mepivacaine and bupivacaine additionally caution that the dose should be reduced for elderly or debilitated patients.*†

Further to this point, maximum adult doses for LAs cited in textbooks often assume a adult patient of 70 kg.[2] When treating a patient less than the assumed weight, 45 kg in this case, the dose must be reduced. Lastly, an elderly, American Society of Anesthesiologists physical status 4 patient is presumed to have impaired hepatic and renal function, as well as increased susceptibility to toxicity because of cardiovascular disease and reduced serum protein binding capacity.[3] All these factors conspire to put such a patient at risk of local anesthetic systemic toxicity from seemingly "normal" doses of LA.

When a regional technique is chosen, LA dosing must take into account patient factors predisposing to local anesthetic systemic toxicity, and doses of LA must be reduced accordingly.

Competing Interests

The authors declare no competing interests.

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Did Preoperative Fixation on Choice of Anesthetic Confound Assessment of Alternative Techniques?

To the Editor:

We commend Vadi *et al.*[1] for their valuable case report of local anesthetic systemic toxicity (LAST) and for highlighting human factors that likely contributed to the poor outcome. At the risk of displaying outcome or hindsight bias, we would like to highlight two further educational aspects of the case. One possible scenario is that in deciding on technique the anesthesiologist was fixated on using a peripheral nerve block and discounted the relative merits of alternative techniques. It should be emphasized that for this patient, there were no contraindications to general or neuraxial anesthesia. The blocks necessitated a relatively large total dose of local anesthetic. Moreover, low body weight and site of injection are recognized, independent risk factors for LAST[2]; notably, that site of injection is associated with high serum levels[3] of local anesthetic and increased risk of LAST.[4]

The authors' indicated that they thought the presentation of LAST was atypical. However, the presentation and onset of LAST are extremely variable. Loss of consciousness is a known symptom of LAST and may or may not be preceded by prodromal features.[5] Recognizing such clinical variability can aid in the prompt diagnosis and management of LAST.

The incorporation and discussion of human factors in the case scenario is particularly welcome. The value of such nontechnical skills are important components of anesthesiology practice and particularly pivotal in crisis resource management (CRM).[6] Lack of implementation of CRM might have contributed to the delay in calling for help and secondarily to the poor outcome. For instance, as a first step in CRM, calling for aid and engaging helpers in a dialogue assists in critical decision making and might have included saying something like: "*I think this patient may have local anesthetic toxicity, but I am unsure; it is unusual, she has many medical problems, what do you think?*" This would encourage a structured discussion of the differential diagnosis and treatment priorities. One important by-product of CRM is that all clinicians should feel empowered to make critical treatment decisions. CRM applies to many scenarios in anesthesiology and should be considered important universally, especially in crisis management scenarios like LAST.

In sum, we believe attention to systems issues including consideration of all management options and timely use of CRM can reduce the risk of LAST specifically and regional anesthesia in general.

Competing Interests

The authors declare no competing interests.

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In Reply:

We thank Drs. Petrar and Montemurro for their letter regarding our case scenario[1] and for outlining the impact of local anesthetic dosing on this case. These considerations are all important and relevant; the subject of this case scenario may indeed have received a relative overdose of local anesthetic. Although local anesthetic dosing is certainly germane to a discussion of systemic toxicity itself, we do not feel the dosing is central to the purpose of this article. Accepting that the case was performed in the manner it was with the dosing and technique used, there is still much to learn from this case. Because diagnostic error is now recognized as a critical problem of huge clinical and financial consequence by safety experts and both the Joint Commission and the American Medical Association, occurring with unacceptable frequency across all medical specialties,[2] we chose to focus on the cognitive factors that impacted the clinical decision making. These lessons are broadly applicable to all decision-making situations, well beyond the reach of this particular clinical situation.

We also thank Drs. Barrington and Weinberg for their comments on the possibility that fixation error occurred, and the importance of crisis resource management. The