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In Reply:—We thank Dr. Chappell *et al.* for their interest in our article and insightful review. They first question the abstract's conclusion that "The use of vasopressor and diuretics is also associated with acute renal failure," and specifically highlight concern regarding the applicability of the conclusion to "healthy individuals."[1] Dr. Chappell *et al.* seem to be using the concepts of "healthy patients" and "patients with previously normal renal function" interchangeably. We agree that the patient population we examined does not represent "healthy patients," as demonstrated by the variety of comorbidities affecting the patients and delineated in table 1 of the original article.[1] However, the data are explicitly based on patients with normal preoperative renal function, given that we excluded patients with preexisting renal dysfunction or the failure to demonstrate a preoperative estimated creatinine clearance of 80 ml/min or greater. As we stated in the limitations section, although these criteria do exclude patients with renal dysfunction, they probably also exclude healthy patients who did not warrant preoperative serum creatinine testing. Our article does not attempt to make commentary regarding "healthy patients," simply those with normal renal function.

Next, Dr. Chappell *et al.* suggest that it is inappropriate to claim an association between vasopressor or diuretic administration and acute renal failure (ARF) because of their analysis of the details in table 5 of the original article. They compared the 0.8% and 1.5% ARF incidences experienced by patients receiving vasopressor and diuretics, respectively, to existing literature documenting an ARF rate of 1–5% for hospitalized patients.[2–4] They conclude that an association cannot exist because 0.8% and 1.5% are less than the 1–5% incidence described in epidemiologic studies.[2–4] We disagree with this interpretation. The quoted 1–5% incidence is for an entirely different patient population: all hospitalized patients, without regard for their reason for admission. The 1–5% incidence presumably also includes patients at very high risk for ARF: urologic surgery patients, cardiac surgery patients, and patients receiving intravenous contrast postoperatively. Most importantly, that population and literature include patients with preexisting renal dysfunction, a group well known to be at high risk for postoperative ARF. A careful review of the original article's table 5 demonstrates that among low-, medium-, and medium–high-risk patients, 1.5% of those who received a diuretic experienced ARF, whereas only 0.3% of those who did not receive a diuretic experienced ARF. Similarly, among low-, medium-, and medium–high-risk patients, 0.8% of those who received a vasopressor infusion experienced ARF, whereas only 0.4% of those who did not receive a vasopressor infusion experienced ARF. We believe these are the most relevant comparisons. Most importantly, given that diuretic and vasopressor infusion administration were identified as independent predictors in a logistic regression analysis, they are independently associated with the ARF outcome. Our abstract conclusion only states this observation, without interpreting causation or speculating on pathophysiology.

Dr. Chappell *et al.* also highlight an important element of our data that may have warranted additional attention in the discussion section: the observation that intraoperative urine output is not associated with postoperative ARF. We completely agree with Dr. Chappell *et al.* that this is an important observation that contrasts existing clinical assumption and demands increased focus. We were reticent to expound more aggressively on this observation given that our data could not discern a causal relation or extract out the effect of fluid administration, preoperative fasting, or the timing of diuretics. We are uncomfortable concluding that these data suggest "limiting the crystalloid amount to reduce perioperative complication" as Dr. Chappell *et al.* suggest. In addition, Dr. Chappell *et al.* have brought to our attention a typographical error in table 5: The label of the second row from the bottom should include a greater-than symbol rather than a less-than symbol to read: "Urine >0.5 ml $\cdot$ kg^{-1} $\cdot$ h^{-1}." This typographical error does not change the interpretation of the data: Urine output was not associated with ARF. In fact, most patients who experienced ARF did not demonstrate oliguria. We are delighted that Dr. Chappell *et al.* support our hypothesis-generating work. We hope these data will spur "further prospective investigations" as they suggest.

Dr. D'souza *et al.* raise an interesting point regarding the choice of the Cockcroft–Gault formula *versus* the Modification of Diet in Renal Disease formula when estimating creatinine clearance. As mentioned in the discussion section, the use of a single serum marker as a measure of renal function during a nonsteady postoperative state suffers from questionable accuracy, regardless of which formula is chosen. The Modification of Diet in Renal Disease formula was derived from data in patients with existing chronic kidney disease.[5] Later, it was modified to incorporate race-specific variations, providing additional accuracy in African-Americans. Conversely, the Cockcroft–Gault formula was derived using patients with and without chronic kidney disease.[6] The Cockcroft–Gault formula suffers from the absence of any race-specific measures. The Modification of Diet in Renal Disease formula suffers from the absence of any weight-based measures. We used the Cockcroft–Gault formula for several reasons: (1) It is more accurate across a broad range of renal function,[7] (2) it incorporates weight and the effect of weight on anticipated normal serum creatinine, (3) it is used more widely in pharmacologic dosing practice, and (4) the Modification of Diet in Renal Disease formula is known to underestimate glomerular filtration rate in patients with normal renal function.[7] Identifying patients with normal preoperative renal function was the foundation of our methodology and guided us to the use of the Cockcroft–Gault formula.

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Minimizing the Risk of Intravascular Injection during Ultrasound-guided Peripheral Nerve Blockade

To the Editor:—We read with interest the recently published case reports by Loubert *et al.*[1] and Zetlaoui *et al.*[2] regarding suspected inadvertent intravascular injection of local anesthetic (LA) and LA toxicity during ultrasound-guided axillary brachial plexus blockade. While ultrasound likely reduces the risk of accidental vascular puncture compared with "blind" peripheral nerve stimulation,[3] these two case reports demonstrate that the risk of intravascular injection persists despite ultrasound guidance.[1,2] In 2006 and 2007 at the Toronto Western Hospital, we performed 1,797 ultrasound-guided brachial plexus blocks without any sign or symptom of LA toxicity. Good fortune notwithstanding, there are several important principles that merit thoughtful consideration to improve detection of accidental intravascular injection and possibly prevent LA toxicity during ultrasound-guided peripheral nerve blockade. We believe that the most reliable feature during real-time ultrasound imaging indicative of intravascular injection is the failure to visualize a hypoechoic fluid bolus on the ultrasound monitor during and/or after injection of as little as 1 ml of injectate. Indeed, we customarily initiate LA injection with a 1-ml bolus to exclude intravascular or intraneural[4,5] needle tip placement before proceeding with 5-ml increments of injectate. Visualization of the needle tip does not preclude intravascular injection *per se*; it is the real-time observation of hypoechoic fluid causing tissue dispersion that most consistently excludes intravascular injection. The absence of a discernible extraneural hypoechoic fluid bolus on the ultrasound monitor means that either the needle tip is intravascular or the plane of imaging is inaccurate.

We are also hesitant to recommend the use of ultrasound for perivascular block techniques as described by Loubert *et al.*[1] Rather, we contend that perineural LA deposition is the safest application of ultrasound technology. There can be multiple veins traveling alongside landmark pulsatile arteries, especially in the axilla. Veins are exquisitely collapsible with even the slightest amount of pressure applied by the transducer to the skin, and can therefore vanish from sonographic view, fooling even the most experienced providers, as demonstrated by these two recent case reports.[1,2] We therefore use systematic scanning of the intended block site before needle insertion. Our systematic sonographic survey includes sliding the transducer distally and proximally to trace the target nerve along its expected course and examine the surrounding vasculature and tissues. Scanning is performed with varying degrees of pressure, with and without the use of color Doppler, to identify any hazards that may cross the planned trajectory of the needle. In addition, applying pulse wave Doppler over a nearby vessel during perineural injection may help to detect inadvertent intravascular injection by the characteristic high-pitch sound of turbulent flow associated with a sudden rush of fluid. Finally, however contentious,[6] we strongly believe that patients undergoing ultrasound-guided peripheral nerve blockade should remain awake with judicious sedation so that signs and symptoms of LA toxicity can be recognized, communicated, and treated immediately upon onset.

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Ultrasound-guided Peripheral Nerve Blocks and Intravascular Injection

To the Editor:—In the April issue of ANESTHESIOLOGY, Loubert *et al.*[1] and Zetlaoui *et al.*[2] reported about possible intravascular injection after an ultrasound-guided axillary block. Their reports highlight the need for vigilance in the performance of ultrasound-guided blocks. This and similar reports of complications[3–5] after ultrasound-guided regional blocks reinforce the need for proper training, and the understanding that ultrasound, after all, is only a tool. Any tool should be used with full cognizance of its limitations. The major limitations of ultrasound-guided blocks are technical,[6] including the angle of incidence, needle visualization, and possibly artifacts.[7,8] Training in the proper holding of the probe while analyzing and while injecting help overcome some of the complications. Sometimes even with proper training, complications do occur.[4]

The reports[1,2] have similarities and differences besides the ultrasound-guided axillary block and intravascular complication leading to seizure. One of them described the changes in vital signs,[1] and the