

# Incidence of Local Anesthetic Systemic Toxicity in Orthopedic Patients Receiving Peripheral Nerve Blocks

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**Background and Objectives:** Peripheral nerve blocks are increasingly used. However, despite low complication rates, concerns regarding local anesthetic systemic toxicity remain. Although recent studies suggest that this severe complication has decreased considerably, there is a paucity of data about it on a national level. We sought to elucidate the incidence of local anesthetic systemic toxicity on a national level and therefore provide guidance toward the need for preparedness in daily anesthetic practice.

**Methods:** We searched a large administrative database for patients who received peripheral nerve blocks for total joint arthroplasties from 2006 to 2014. Their discharge and billing data were analyzed for *International Classification of Diseases, Ninth Revision, Clinical Modification* codes coding for local anesthetic systemic toxicity or surrogate outcomes including cardiac arrest, seizures, and use of lipid emulsion on the day of surgery. Rates for these outcomes were determined cumulatively and over time.

**Results:** We identified 238,473 patients who received a peripheral nerve block within the study period. The cumulative rate of outcomes among these patients in the study period was 0.18%. There was a significant decrease of overall outcome rates between 2006 and 2014. Use of lipid emulsion on the day of surgery increased significantly in total knee replacement from 0.02% 2006 to 0.26% in 2014.

**Conclusions:** The incidence of local anesthetic systemic toxicity is low but should be considered clinically significant. Since it may cause substantial harm to the patient, appropriate resources and awareness to identify and treat local anesthetic systemic toxicity should be available wherever regional anesthesia is performed.

(*Reg Anesth Pain Med* 2017;42: 442–445)

Peripheral nerve blocks (PNBs) are increasingly used as effective and safe anesthetic and analgesic techniques.<sup>1</sup> However, despite low complication rates that may be facilitated by advances in application methodology and pharmacology, concerns regarding local anesthetic systemic toxicity (LAST) remain. In this context, recent studies suggest that the incidence of this potentially fatal complication has decreased considerably,<sup>2,3</sup> thus leading some to question the need for the widespread allocation of resources to avoid and treat LAST. In a single-institutional case series of 80,661 patients receiving a PNB in a specialty surgical

setting between 2009 and 2014, Liu et al<sup>2</sup> determined the overall incidence of LAST to be 0.04 per 1000 PNBs. However, with external validity limited, data evaluating the incidence of this complication on a national level are needed. Thus, we sought to elucidate the incidence of LAST in a database reflecting the practice of more than 400 hospitals in the United States and therefore provide guidance toward the need for preparedness in daily anesthetic practice. We hypothesized that among patient populations commonly receiving PNBs, such as joint arthroplasty recipients, the rate of LAST would be low but within the range of clinical relevance.

## METHODS

In this retrospective cohort study, we obtained data from a large administrative database (Premier Perspective Database, Premier Inc, Charlotte, North Carolina)<sup>4</sup> for patients who received PNBs for elective, primary total hip replacement (THR), total knee replacement (TKR), or total shoulder replacement (TSR) from 2006 to 2014. The cohorts THR, TKR, and TSR were defined using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9 CM)* codes 81.51, 81.54, and 81.80, respectively. To determine the incidence of potential LAST cases, we queried hospital discharge claims for either direct evidence of this complication by *ICD-9 CM* codes (968.6, Poisoning by peripheral nerve- and plexus-blocking anesthetics; 968.9, Poisoning by other and unspecified local anesthetics), or surrogate outcomes such as *ICD-9 CM* codes for seizures (780.39, Other convulsions), cardiac arrest (427.5, Cardiac arrest) and the billing file was used to obtain administration of 10% and 20% lipid emulsions on the day of surgery. Rates for these outcomes were determined cumulatively and over time. When admission entries had more than one of the mentioned outcomes, it was counted as one case to avoid overlap. Rates are displayed as percentage of patients who received a block. We further differentiated if patients who had codes for at least one of the previously mentioned outcomes were treated at rural or urban hospitals, teaching or nonteaching hospitals, and whether they died before hospital discharge. Cochran-Armitage trend test was performed to test for significance in complication rates over time.<sup>5</sup> Statistical analyses were performed using SAS version 9.4 statistical software (SAS Institute, Cary, North Carolina) and Microsoft Excel 2010 (Microsoft Corp, Redmond, Washington). The data for this study met the de-identification requirements set forth by the Health Insurance Portability and Accountability Act and was exempt from consent requirements by the Institutional Review Board of Mount Sinai Medical Center (New York, NY; #14-00674) and the Hospital for Special Surgery (New York, NY; #2012-050-CR2).

## RESULTS

A total of 1,407,668 patients were identified who underwent elective primary total joint arthroplasties. Of those, 238,473 patients received a PNB within the study period. Of those patients, 434 had at least one of the studied outcomes listed. The cumulative

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The authors declare no conflicts of interest. Stavros G. Memtsoudis is a nonpaid consultant for B. Braun. He is funded by the Anna Maria and Stephen Kellen Career Development Award, New York.

This work received no funding.

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ISSN: 1098-7339

DOI: 10.1097/AAP.0000000000000544

rate of all studied outcomes (cardiac arrest, seizures, and use of fat emulsion on the day of surgery) in all procedures (THR, TKR, and TSR) in the study period was 0.18 % (Table 1). Figure 1 shows the overall and procedure specific rates over time. There was a significant decrease in the combined outcome rate for all procedures between 2006 and 2014 with the most pronounced decrease happening between 2006 and 2008. Interestingly, no patient claims documented an ICD-9 CM code specifically coding for poisoning by a local anesthetic. There were only 7 patients with more than one outcome listed, thus limiting bias by overlap diagnoses.

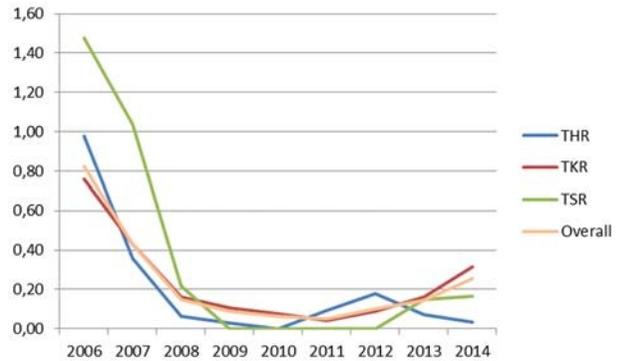
Among the 434 patients who had at least one of the studied outcomes listed 91.94% (n = 399) were treated in an urban and 8.06% (n = 35) in a rural hospital. Furthermore, 43.09% (n = 187) were treated in a teaching and 56.91% (n = 247) in a nonteaching hospital. Sixty-three (14.52%) of the patients died before discharge from the hospital.

Figure 2, A–C show the rates of the studied outcomes over time. The incidence of a seizure diagnosis showed a decreasing trend from 0.91% in THR, 0.68 % in TKR, and 1.48% in TSR in 2006 to 0.02%, 0.01, and 0% in 2014, respectively, without this finding reaching statistical significance. There was no significant change in coding for cardiac arrest in all procedures (0.00 %–0.07%). Use of lipid emulsion on the day of surgery increased significantly from 0.02% in TKR in 2006 to 0.26% in 2014. There was an increasing trend for patients receiving lipid emulsion in TSR from 0.00% in 2006 to 0.16% in 2014 without reaching statistical difference. We found no documentation on the use of lipid emulsion on the day of surgery in THR during the study period. The cumulative rate of use of lipid emulsion on the day of surgery was 0.04%.

**DISCUSSION**

In this analysis of population-based data, we identified a low but relevant incidence of surrogate outcomes potentially indicating the occurrence of LAST in patients receiving PNBs in the context of total joint arthroplasty. Outcomes suggestive of LAST decreased significantly in incidence during the study period, with the use of lipid emulsion significantly increasing in recent years.

Our finding suggesting that LAST-related symptoms have decreased over time is concordant with previous reports. In his review of the literature published before 2002, Mulroy<sup>3</sup> already described a significant decrease of LAST after PNBs. In recent studies, LAST has become even rarer.<sup>1,2,6</sup> Nevertheless, with 0.18%, the cumulative rate of all outcomes we found is higher than the rates reported in the past few years by other groups. Barrington and Kluger<sup>6</sup> found LAST to occur in 0.08% of PNBs from 2007 to 2012. Neal<sup>7</sup> found an incidence of 0.026% in an



**FIGURE 1.** Cumulative rate of outcomes among patients receiving PNBs. Cumulative rate (%) of the studied outcomes (cardiac arrest, seizures, and use of fat emulsion on the day of surgery combined) for each surgical procedure separately and for all surgical procedures combined. Overall = THR, TKR, and TSR combined.

evidence-based review of recent literature. Heinonen et al<sup>8</sup> found an incidence of 0.007% in a nationwide survey in Finland from 2011 to 2013. Rohrbaugh et al<sup>9</sup> report an incidence of LAST in 0.053% of interscalene nerve blocks performed for ambulatory shoulder surgery from 2001 to 2011. Sites et al<sup>1</sup> reported an incidence of LAST in 0.008% of PNBs from 2003 to 2011, and Liu et al<sup>2</sup> found LAST to occur in only 0.004% of PNBs from 2009 to 2014.

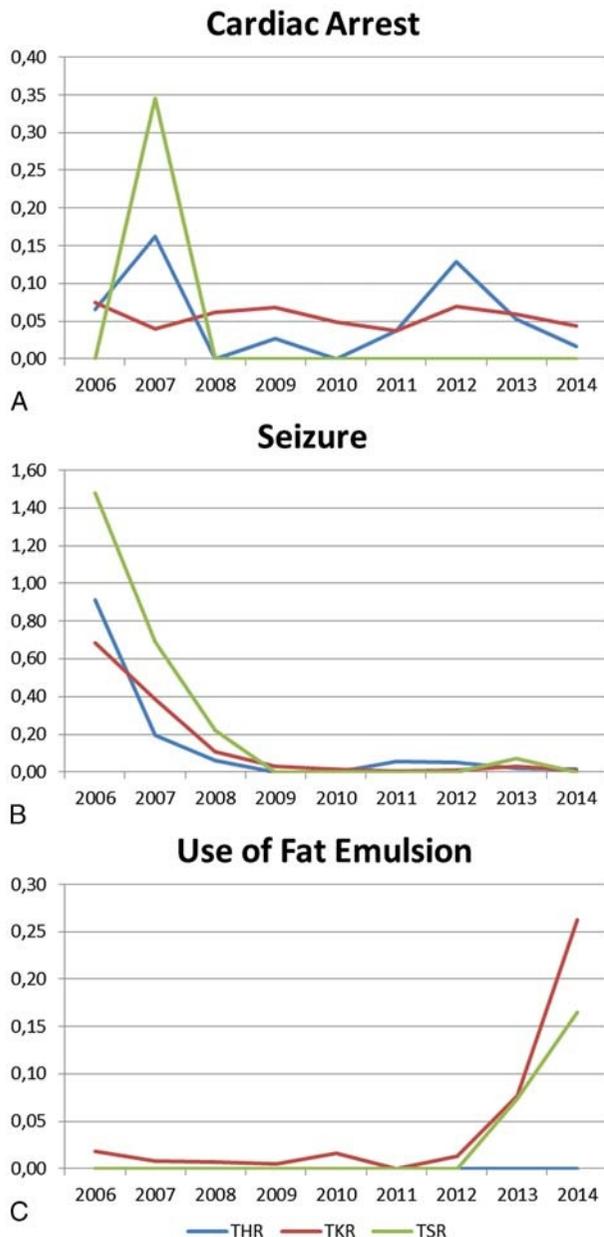
One of the reasons for the declining incidence of LAST may be that advances in localization techniques and implementation of safety steps may have reduced intravascular injection.<sup>9–11</sup> These newer technologies may not be as widespread in smaller rural or nonacademic hospitals as in the academic centers that are usually reporting on these outcomes. Therefore, the rates reported by single-center studies might be lower than the actual rates in the general medical community. However, it must be considered, that the rates from our analysis might overestimate the incidence of LAST, since we used surrogate parameters not specific for LAST, including cardiac arrest and seizures. The most specific of our surrogate parameters was the use of lipid emulsions on the day of surgery. The cumulative rate of this parameter might reflect the actual incidence of LAST better than the cumulative rate of all outcomes combined. However, it must be taken into account that administrations may include those cases in which LAST was suspected but may not have been the actual cause for treatment.

Whereas the decreasing incidence of complications associated with LAST, such as cardiac arrests and seizures, specifically in the years 2006 to 2008, might possibly be attributed to technical

**TABLE 1.** Cumulative Outcomes Among Patients Receiving PNBs

	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
<b>THR</b>	0.98 (30)	0.36 (11)	0.06 (2)	0.03 (1)	0.00 (0)	0.09 (5)	0.18 (11)	0.07 (4)	0.03 (2)	0.16 (66)
<b>TKR</b>	0.76 (82)	0.43 (55)	0.16 (24)	0.10 (20)	0.08 (19)	0.04 (11)	0.09 (27)	0.16 (46)	0.31 (73)	0.19 (357)
<b>TSR</b>	1.48 (3)	1.04 (3)	0.22 (1)	0.00 (0)	0.00 (0)	0.00 (0)	0.00 (0)	0.15 (2)	0.16 (2)	0.15 (11)
<b>Overall</b>	0.82 (115)	0.43 (69)	0.15 (27)	0.09 (21)	0.06 (19)	0.05 (16)	0.10 (38)	0.15 (52)	0.25 (77)	0.18 (434)

Ratio (%) and crude number (n) of charts coding for one or more of the studied outcomes among patients receiving a PNB during the study period. Overall = THR, TKR, and TSR combined. All numbers are shown as % (n).



**FIGURE 2.** A–C, Incidence of outcomes among patients receiving PNBs. The graphs show the incidence of complications (%) itemized for the outcomes: cardiac arrest (A), seizure (B), and use of lipid emulsion on the day of surgery (C).

advances, the increased use of lipid emulsions from 2012 to 2014 might indicate a higher level of awareness of this potentially life-saving intervention. Given its good safety profile practitioners may err on the side of caution when deciding to administer lipid emulsions. Furthermore, an increase in the availability of lipid emulsions in places where regional anesthesia is performed, as suggested in several guidelines, may contribute to this finding.<sup>12,13</sup> Ultimately, the true incidence of LAST in the medical community remains unknown but is likely to lie in the range reported by the studies previously mentioned with our study, marking a possible high value.

There are several limiting factors to our analysis. The analyzed data are derived from an administrative database, where

only billable procedures, diagnoses, and medications are documented. Thus, no clinical details can be taken into account for interpretation. Although Premier Inc. conducts thorough quality controls to ensure that the reliability of their data is as high as possible, there is no possibility to completely rule out incorrect billing. Furthermore, documentation may be nonspecific and vary widely. Whereas some institutions code for a complication related to LAST or bill for an intervention, it seems that none use actual codes descriptive of local anesthetics being the cause of the complication. This may point to the unfamiliarity with this rare code among administrative staff or at least in some case be indicative of a missed diagnosis of LAST. Since there was no direct documentation of LAST, we used surrogate markers so we may have missed atypical cases of LAST while including events not related to LAST.<sup>14</sup> The occurrence of seizures and cardiac arrests on the day of surgery may be due to other reasons than LAST, thus overestimating the incidence of LAST. The use of lipid emulsions on the day of surgery should be a more specific indicator for cases with at least suspected LAST. However, there might have been cases of LAST that were not treated with this intervention.<sup>15</sup> Furthermore, Premier database does not give information on why a medication is used. Therefore, patients might have received lipid emulsion because of LAST-unrelated neurologic symptoms, seizures, cardiac arrests or early, minor symptoms of LAST we did not take into account.

Irrespective of these limitations, the study analyzed a large sample of 238,473 PNBs performed at more than 400 hospitals nationwide describing situations in which LAST can feasibly be suspected. Therefore, the data help to outline the magnitude of the problem in need of attention and resources. The fact that the rates we found are higher than those previously reported does not invalidate these data but adds information about rates in the general medical community. Furthermore, our findings highlight the need for proper reporting and documentation of LAST to facilitate quality assurance.

In conclusion, improvements in the application of PNBs may have led to decreased rates of LAST and/or related complications. The incidence of LAST is low but considerably higher than the incidence of other important complications in anesthesia such as malignant hypothermia, which has been reported to occur at a rate of 0.001%<sup>16</sup> or epidural hematoma after neuraxial anesthesia at 0.05%<sup>17</sup> and should by this measure be considered clinically significant. Since LAST may cause substantial harm<sup>18</sup> to the patient and is potentially treatable, our data support that adequate resources and awareness measures be expended and enacted to counter this complication wherever regional anesthesia is performed.

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