Original Article

Incidence of and Risk Factors for Peripheral Nerve Block-Related Complications after Orthopedic Surgery

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Objective: To determine the incidence of and risk factors for peripheral nerve block-related complications after orthopedic surgery at a single-tertiary hospital.

Materials and Methods: The prospective observational study included 500 patients scheduled to undergo orthopedic surgery with peripheral nerve block [PNB] guided by ultrasound, nerve stimulation, paresthesia elicitation, or landmark during the period October 2015 to September 2017 study period. Intra-operative complications related to PNB (e.g., pneumothorax, local anesthetic systemic toxicity) were recorded. All patients were assessed for nerve block resolution within 48 h and followed to evaluate for postoperative neurological symptoms [PONS] at postoperative day [POD] 3, 4, 5, 10 and 6 weeks after surgery. If already discharged, they were followed-up by phone. Those with remaining PONS were continually evaluated at 6 months postoperatively. The incidence of and risk factors for PONS were analyzed.

Results: The incidence of PONS at POD 3 was 2.2% (95% confidence interval [CI] 1.2 to 3.9), at POD 4 was 1.6% (95% CI 0.8 to 3.1), at POD 5 was 1.4% (95% CI 0.7 to 2.9), at POD 10 was 1.2% (95% CI 0.6 to 2.6), and at 6 weeks postoperatively was 0.8% (95% CI 0.3 to 2.0). Only two patients with open reduction internal fixation [ORIF] of distal humerus fracture had persistent PONS lasting longer than 6 months ($p<0.001$). Male gender (adjusted odds ratio [AOR] 4.92, 95% CI 1.26 to 19.29; $p = 0.022$), body mass index [BMI] $\geq$30 kg/m^2 (AOR 4.35, 95% CI 1.18 to 16.03; $p = 0.027$), and 0.5% bupivacaine (AOR 3.95, 95% CI 1.11 to 14.03; $p = 0.034$) were significantly risk factors for PONS. Neither pneumothorax nor local anesthetic systemic toxicity was occurred.

Conclusion: The incidence of PNB-related complications is low. Risk factors for PONS after PNB are male gender, BMI $\geq$30 kg/m^2, and 0.5% bupivacaine.

Keywords: Incidence, Risk factors, Peripheral nerve block, Postoperative neurological symptoms, Orthopedic surgery

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Peripheral nerve block [PNB] provides superior pain control after painful orthopedic surgery. Similar to many pain management modalities, the benefits of PNB are not without some associated risks and complications. According to the American Society of Anesthesiologists [ASA] Closed Claims Project[1], the most common PNB complications were nerve injury (51%), death (11%), pneumothorax (6%), and brain damage (5%). The incidence of PONS after PNB varied from 0.02% to 8.2%[2-5]. The incidence of persistent PONS lasting longer than 6 months was reported to range from 0.014% to 0.6%[2-9]. With specific regard to local anesthetic systemic toxicity [LAST], incidence rates ranging from 0.08 to 0.98 per 1,000 patients were reported[3,9-11].

The variation of the incidence rates among complications is likely due to multifactorial etiology. Few studies have explored the incidence of complications associated with PNB following orthopedic surgery. Accordingly, the aim of the prospective observational study was to determine the incidence of and risk factors for peripheral nerve block-related complications after orthopedic surgery at a single-tertiary hospital.

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Materials and Methods

After approval by the Siriraj Institutional Review Board (Si. 543/2015), a prospective observational study included patients scheduled to undergo orthopedic surgery with peripheral nerve block guided by ultrasound, peripheral nerve stimulation, elicitation of paresthesia or anatomical landmark at a single-tertiary hospital during the October 2015 to September 2017 study period. Patients having one or more of the following were excluded: aged <18 years, scheduled for truncal blockade, and/or difficulty communicating. Written informed consent was obtained from all study participants.

Patient demographics, underlying diseases, and pre-existing neurological deficits were recorded. Collected intra-operative data included type of orthopedic surgery, tourniquet times, PNB and nerve localization technique, local anesthetic type and dosage, and sequence of nerve blocks (before/after spinal block, epidural block, or general anesthesia). During nerve blocks, the occurrence of adverse events, such as LAST and pneumothorax, was documented. Postoperatively, all patients were evaluated daily regarding the nerve block resolution by two physician members of the research team. The daily postoperative evaluation also included sensory and motor examinations of the operative limb. Sensory examination was conducted with pinprick and cold application compared with the contralateral side. Motor function was assessed as ability or inability to move the affected limb compared to the contralateral side. If the block had not resolved within 48 hours after surgery, surgeons and staff anesthesiologists involved in the case were contacted for formal evaluation. Patients with PONS were followed daily until resolution of symptoms or discharge. PONS was defined as clinical features of numbness or abnormal sensation in the blocked limb, and muscle weakness or pain unrelated to surgery lasting longer than 48 hours. After discharge, all patients were evaluated by phone at POD 3, 4, 5, 10, and 6 weeks postoperatively. Those with remaining PONS were continually evaluated at 6 months postoperatively. The follow-up telephone call was made by a nurse member of the research team. Incidence of PONS at POD 3, POD 4, POD 5, POD 10, and 6 weeks postoperatively was reported. Risk factors associated with PONS were identified.

Statistical analysis

Previous study reported an incidence of PONS of 8.2% in orthopedic surgery patients who received PNB[4]. The sample size was calculated using a two-sided 95% CI for a single proportion that extends 0.025 to both sides of the estimated proportion of 0.082. That calculation yielded a minimum sample size of 463 patients. To compensate for a 5% loss to follow-up, 23 patients were added for a total study population of 486 patients.

Demographic data were summarized using descriptive statistics. Categorical data are presented as number and percentage, and continuous data are presented as mean $\pm$ standard deviation or median and range (minimum and maximum). Univariate analysis was used to test factors for significant association with PONS (Chi-square test, Fisher's exact test, and independent t-test). All factors found to be statistically significant in univariate analysis were included in multiple logistic regression analysis. A p-value less than 0.05 was considered to be statistically significant for all tests. Statistical analysis was performed using PASW Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA).

Results

Five hundred orthopedic surgery patients were included in the study. All enrolled patients completed 6 weeks of follow-up. Patient characteristics and perioperative data are shown in Table 1. Among patients with PONS versus those without PONS, male gender (72.7% versus 36.0%, respectively, $p = 0.022$), ORIF of distal humerus fractures (18.2% versus 0.0%, respectively, $p<0.001$), and using 0.5% bupivacaine (63.6% versus 30.3%, respectively, $p = 0.041$) were significantly associated with the presence of PONS. Patient age, BMI, diabetes mellitus, hypertension, dyslipidemia, pre-existing neuropathy, tourniquet time, nerve localization using paresthesia technique, sequence of nerve block performed, volume of local anesthetic, and addition of dexamethasone to local anesthetic were not significantly associated with the development of PONS (all $p>0.05$).

Of the 500 patients, 140 (28.0%) received upper limb blocks, and 360 (72.0%) patients received lower limb blocks. The most frequently performed blocks for lower limbs were femoral (36.6%), adductor canal (25.6%), and popliteal (7.4%) blocks-comprising 69.6% of all blocks performed (Table 2). The most frequently performed upper limb blocks were interscalene (14.2%), axillary (6.8%), and supraclavicular (5.2%) blocks. Ultrasound guidance was the most commonly performed nerve localization technique. Paresthesia technique was only used for interscalene and supraclavicular brachial blocks; whereas, landmark

Table 1. Patient characteristics and perioperative data of the study population

Variables	Total (n = 500)	Patients with PONS (n = 11)	Patients without PONS (n = 489)	*p*-value
Male	184 (36.8)	8 (72.7)	176 (36.0)	0.022*
Age (year)	55.5±18.3	46.3±17.3	55.7±18.3	0.092
Body mass index (kg/m^2)	25.5±4.5	28.0±6.8	25.5±4.4	0.250
Diabetes mellitus	75 (15.0)	2 (18.2)	73 (14.9)	0.674
Hypertension	196 (39.2)	4 (36.4)	192 (39.3)	1.000
Dyslipidemia	122 (24.4)	4 (36.4)	118 (24.1)	0.475
Preexisting neuropathy	3 (0.6)	0 (0.0)	3 (0.6)	1.000
Surgery type: ORIF distal humerus	2 (0.4)	2 (18.2)	0 (0.0)	<0.001*
Tourniquet time (min)	91.1±31.1	104.4±41.2	91.1±30.7	0.229
Block technique: paresthesia	25 (5.0)	1 (9.1)	24 (4.9)	0.435
Block sequence: after GA, SB, or EB	72 (14.4)	2 (18.2)	70 (14.3)	0.641
Local anesthetic: 0.5% bupivacaine	155 (31.0)	7 (63.6)	148 (30.3)	0.041*
Local anesthetic: volume (mL)	17.5±3.6	17.7±3.4	17.5±3.6	0.855
Local anesthetic + dexamethasone	18 (3.6)	1 (9.1)	17 (3.5)	0.335

The data are presented as standard deviation or n (%). * $p<0.05$ indicates statistical significance
PONS = postoperative neurological symptoms; ORIF = open reduction internal fixation; GA = general anesthesia; SB = spinal block; EB = epidural block

Table 2. Peripheral nerve block techniques relative to different nerve localization techniques

Nerve block technique	Total	Nerve localization technique				
		Landmark	Paresthesia	NS	US	US + NS
Interscalene	71 (14.2)	0 (0.0)	17 (23.9)	1 (1.4)	50 (70.4)	3 (4.3)
Supraclavicular	26 (5.2)	0 (0.0)	6 (23.1)	0 (0.0)	20 (76.9)	0 (0.0)
Infraclavicular	7 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	6 (85.7)	1 (14.3)
Axillary	34 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	33 (97.1)	1 (2.9)
Median	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)
Femoral	183 (36.6)	5 (2.7)	0 (0.0)	65 (35.6)	112 (61.2)	1 (0.5)
Adductor	128 (25.6)	0 (0.0)	0 (0.0)	0 (0.0)	128 (100.0)	0 (0.0)
Sciatic	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (75.0)	1 (25.0)
Popliteal	37 (7.4)	0 (0.0)	0 (0.0)	0 (0.0)	37 (100.0)	0 (0.0)
Ankle	2 (0.4)	2 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Saphenous	4 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)
Tibial	2 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (100.0)	0 (0.0)
Total	500 (100.0)	7 (1.4)	23 (4.6)	66 (13.2)	397 (79.4)	7 (1.4)

The data are presented as n (%)
NS = nerve stimulator; US = ultrasound; US+NS = combined ultrasound and nerve stimulator

technique was used only for femoral and ankle blocks. Mostly of cases used single-injection technique (98%). Only 2% of cases used continuous perineural catheter. Fifty-six percent and 44% of blocks were performed by staff anesthesiologists and supervised trainees (40% residents, 4% fellows), respectively. Regarding the use of local anesthetic, 0.25% bupivacaine was mostly used (38.2%). The other drugs were 0.5% bupivacaine (31.0%), 0.33% bupivacaine (22.4%), 2% lidocaine (5.2%), 0.5% levobupivacaine (1.8%), 0.5% ropivacaine (0.6%), 0.25% levobupivacaine (0.4%), 0.33% levobupivacaine (0.2%), and 1% lidocaine (0.2%).

The incidence of PONS at POD 3 was 2.2% (11/500 blocks) (95% CI 1.2 to 3.9) (Table 3). The

Table 3. Characteristics of patients with postoperative neurological symptoms [PONS]

No.	Patient-related factors				Surgery-related factors		Anesthesia-related factors		Presentation of PONS
	Age	Sex	BMI	Comorbidity	Surgery	Tourniquet	Block	Guidance	
1	64	F	33.9	DM, HT, DLP, obesity	ORIF distal humerus	None	ISB	P	Persistent weakness, numbness at 6 mo
2	35	M	26.8	None	ORIF distal humerus	None	SCB	US	Persistent weakness, numbness at 6 mo
3	29	M	24.0	None	Ankle fusion	28 min	PSB	US	Persistent numbness at 6 wk, pain on POD 5
4	37	M	23.2	None	ORIF radius	62 min	Med	US	Persistent numbness at 6 wk
5	78	F	31.7	DM, HT, DLP, obesity	Revision TKA	115 min	ACB	US	Persistent numbness at POD 10
6	65	M	25.7	HT, DLP	RCR	None	ISB	US	Persistent numbness at POD 10
7	30	M	24.7	None	ACLR	125 min	FNB	US	Persistent numbness at POD 5
8	62	M	21.8	HT, DLP	Bilateral TKA	90, 65 min	ACB	US	Persistent numbness at POD 4
9	36	M	44.1	Obesity	Meniscus repair	145 min	FNB	US	Persistent numbness at POD 3
10	37	M	31.6	Obesity	DRUJ repair	135 min	AXB	US	Persistent numbness at POD 3
11	36	F	20.7	None	ORIF tibia	135 min	PSB	US	Persistent numbness at POD 3

BMI = body mass index; F = female; M = male; DM = diabetes mellitus; HT = hypertension; DLP = dyslipidemia; ORIF = open reduction and internal fixation; RCR = rotator cuff repair; ACLR = anterior cruciate ligament reconstruction; TKA = total knee arthroplasty; DRUJ = distal radioulnar joint; ISB = interscalene block; SCB = supraclavicular block; PSB = popliteal sciatic block; Med = median nerve block; FNB = femoral nerve block; ACB = adductor canal block; ICB = infraclavicular block; AXB = axillary block; P = paresthesia technique; US = ultrasound; min = minute; mo = months; wk = weeks; POD = postoperative day incidence of PONS at POD 4 was 1.6% (8/500 blocks) (95% CI 0.8 to 3.1). On POD 5, 7 patients (7/500 blocks) reported persistent numbness for incidence of 1.4% (95% CI 0.7 to 2.9). Of those 7 patients, one patient developed shooting pain in his foot after a popliteal sciatic block for an ankle fusion. This symptom developed between the POD 5 to 6 weeks postoperatively. No electromyography [EMG] was performed in this case. On POD 10, 6 patients (6/500 blocks) reported persistent numbness for an incidence of 1.2% (95% CI 0.6 to 2.6). At 6 weeks postoperatively, 4 patients (4/500 blocks) still had numbness for an incidence of 0.8% (95% CI 0.3 to 2.0). At 6 months postoperatively, 2 patients still had unresolved numbness, and both also had clinical muscular weakness. One patient had weakness and numbness in the 4th and little fingers after an open reduction internal fixation [ORIF] of a distal humerus fracture with an interscalene block using paresthesia technique. EMG was performed, which indicated radial nerve injury distal to the triceps muscle, ulnar nerve injury proximal to the flexor carpi ulnaris, and median nerve injury proximal to the pronator teres. The other patient had wrist drop and persistent numbness in the dorsum of the hand after ORIF for distal humerus fracture with a supraclavicular block under ultrasound guidance. EMG indicated radial nerve injury above the branch to the triceps muscle, and ulnar nerve injury across the elbow region. EMG investigation confirmed that the neurologic deficits in these two cases were not related to PNB. No incidence of pneumothorax, LAST, or cardiac arrest related to PNB was observed in the study.

Table 4 summarizes the risk factors associated with PONS. From univariate analysis, the factors associated with PONS were male gender (crude OR 4.74, 95% CI 1.24 to 18.11; p = 0.022) and 0.5% bupivacaine (crude OR 4.03, 95% CI 1.16 to 13.98; p = 0.041). Even though BMI ≥30 kg/m^2 was not found to be significant in univariate analysis, it was still included in multivariate analysis, because it remained a factor of interest and suspicion. Multivariate logistic analysis revealed male gender (adjusted OR [AOR] 4.92, 95% CI 1.26 to 19.29; p = 0.022), BMI ≥30 kg/m^2 (AOR 4.35, 95% CI 1.18 to 16.03; p = 0.027), and 0.5% bupivacaine (AOR

Table 4. The univariable and multivariable regression analysis for risk factors associated with postoperative neurological symptoms [PONS]

Variables	Crude OR	95% CI	*p*-value	Adjusted OR	95% CI	*p*-value
Male gender	4.74	1.24 to 18.11	0.022*	4.92	1.26 to 19.29	0.022*
Age ≥60 year	0.52	0.15 to 1.81	0.300	-	-	-
BMI ≥30 kg/m^2	3.26	0.93 to 11.40	0.073	4.35	1.18 to 16.03	0.027*
Diabetes mellitus	1.27	0.27 to 6.00	0.674	-	-	-
Hypertension	0.88	0.26 to 3.06	1.000	-	-	-
Tourniquet time			0.809			
No tourniquet	1.00	-	-	-	-	-
>45 min	0.64	0.16 to 2.52	-	-	-	-
≤45 min	0.85	0.09 to 8.44	-	-	-	-
Nerve localization		-	0.435	-	-	-
Others[a]	1.00	-	-	-	-	-
Paresthesia	1.94	0.24 to 15.76	-	-	-	-
Block sequence		-	0.641	-	-	-
Before GA/SB/EB	1.00	-	-	-	-	-
After GA/SB/EB	1.22	0.26 to 5.78	-	-	-	-
Local anesthetics			0.041*			0.034*
Others[b]	1.00	-	-	1.00	-	-
0.5% bupivacaine	4.03	1.16 to 13.98	-	3.95	1.11 to 14.03	-

* p<0.05 indicates statistical significance

OR = odds ratio; CI = confidence interval; BMI = body mass index; GA = general anesthesia; SB = spinal block; EB = epidural block

[a] Other nerve localization techniques included ultrasound, nerve stimulation, and anatomical landmark

[b] Other local anesthetics included 0.33% bupivacaine, 0.25% bupivacaine, 0.5% levobupivacaine, 0.33% levobupivacaine, 0.25% levobupivacaine, 0.5% ropivacaine, 2% lidocaine, and 1% lidocaine

3.95, 95% CI 1.11 to 14.03; $p = 0.034$) to be factors independently associated with PONS. Regarding type of orthopedic surgery, ORIF distal humerus was found to be significantly associated with PONS ($p<0.001$). It was not possible to include this procedure in univariate and multivariate analysis due to the small number of events. Of the 500 patients, only 2 patients received ORIF of distal humerus fractures. They developed PONS that persisted at 6 months postoperatively.

Discussion

The prospective observational study found an incidence of PONS of 2.2% for PONS at POD 3, 1.6% at POD 4, 1.4% at POD 5, 1.2% at POD 10, and 0.8% at 6 weeks postoperatively. Compared with previous study, the 1.4% incidence of PONS at POD 5 in the present study was higher than the 0.18% incidence at POD 5 reported by Sites et al[9]. In contrast, the 1.2% incidence of PONS at POD 10 in the present study was less than the 8.2% incidence at POD 10 reported by Fredrickson and Kilfoyle[4]. Obviously, the incidence of PONS associated with PNB is quite variable. Differences in reported incidence may depend on the definition of nerve injury, follow-up duration, risk factors, data collection, and probable cause of nerve injury[3,8].

In the present study, symptoms that persisted for more than 24 hours but resolved within 48 hours after surgery or after removal of the perineural catheter were considered to be prolonged residual anesthetic effects[12]. Unresolved symptoms that persisted for more than 48 hours were considered neurologic sequelae, and symptoms that persisted for more than 6 months were considered long-term PONS[9]. Forty-eight hours is used as a cutoff point to define as prolonged sensory loss or muscle weakness, since symptoms lasting longer than 48 hours can interfere with rehabilitation, can cause distress to patients and their families, and is a matter of concern to the attending surgeon and anesthesiologist.

Of the 11 patients that developed PONS in the present study, three patients had symptom resolution between POD 3 and POD 4, one patient between POD 4 and POD 5, one patient between POD 5 and POD 10, two patients between POD 10 and 6 weeks postoperatively, and two patients between 6 weeks and 6 months postoperatively. Two patients had persistent neurological deficits for more than 6 months with clear etiology unrelated to PNB that was confirmed by EMG. Nerve injury in those 2 cases was likely caused by either the humerus fracture itself or the surgery to correct the fracture. Radial nerve injury is the most common peripheral nerve injury following a humerus fracture[12,13], with an incidence of 2% to 17%[13]. Primary radial nerve palsy occurs after trauma in humerus fracture, whereas secondary radial nerve palsy occurs after fracture manipulation or surgery[14]. Accordingly, the risks and benefits should be considered before performing PNB in patients at risk for nerve injuries specific to certain types of surgery[8]. In addition, PNB should be avoided if exploration of nerve or assessment of postoperative nerve function is required[8].

The cause of nerve injury may be classified as patient-related, surgery-related, anesthetic-related, or a combination of factors. Patient-related risk factors included male gender, elderly, body mass index extremes, smoking, diabetes, hypertension, vasculitis, peripheral vascular disease, and preexisting neurologic disease[15,16]. Similarly, the present study found male gender and BMI ≥ 30 kg/m^2 to be significantly associated with increased risk of developing PONS. Regarding anesthetic-related factors, the present study identified 0.5% bupivacaine as a risk factor for PONS, which is similar to the findings of other studies[17,18]. Yang et al[17] conducted animal and in vitro studies that showed that nerve injury can occur from continuous infusions of 0.5 or 0.75% bupivacaine for 72 hours. Yu et al[18] studied neurotoxicity in human neuroblastoma cell culture and showed that both bupivacaine and procaine could induce nerve damage. However, further studies are needed to clarify the risk of local anesthetic-induced neurotoxicity. Concerning nerve localization techniques, the present study was not able to identify association between PONS and paresthesia elicitation, which is similar to results reported by Liguori et al[19]. In contrast, Fredrickson and Kilfoyle[4] reported elicitation of paresthesia as a risk factor for PONS. An American Society of Regional Anesthesia and Pain Medicine [ASRA] Practice Advisory[8] recommends that practitioners should not force needle-to-nerve contact. No nerve localization technique has been shown to be more or less safe relative to reducing nerve injury[20]. Regarding local anesthetic systemic toxicity and pneumothorax, LAST can cause central nervous system toxicity and cardiovascular toxicity[10,11], whereas pneumothorax causes respiratory compromise. No events associated with these complications were observed in the present study.

Limitations

The present study has some mentionable limitations. Firstly, this was a single-center study.

A multicenter clinical trial is needed to increase the generalizability of the results. Secondly, the data in the present study was observational in nature. Therefore, the incidence of complications may differ between experts and novices. Thirdly, a variety of nerve localization techniques were used, including ultrasound, nerve stimulation, ultrasound plus nerve stimulation, elicitation of paresthesia, and landmark-based techniques. These factors were not stratified into an equal distribution, which introduced a confounding bias. Fourthly, the present study was unable to identify the absolute cause of nerve injury. More specifically, the study was not able to conclusively determine whether a nerve injury was related to PNB or to some other cause. To confirm a diagnosis, EMG and/or nerve conduction studies are required, but these investigations are difficult to perform in all cases. Finally, the incidence rate of long-term PONS is not reported. Only four patients with unresolved neurological symptoms were contacted at 6 months after surgery, and two patients had persistent neurological symptoms at the 6-month postoperative follow-up.

Conclusion

The incidence of PNB-related complications is low. Male gender, BMI $\geq$30 kg/m^2, and 0.5% bupivacaine are significantly associated with increased PONS risk.

What is already known on this topic?

Postoperative complications associated with peripheral nerve block are multifactorial, including patient, surgical, and anesthetic factors. The complications of most concern are LAST and neurologic deficit. The incidence of PONS is variable, and the cause of nerve injury may be difficult to identify.

What this study adds?

Orthopedic surgery with ORIF of distal humerus fracture was significantly associated with nerve injury. Male gender, BMI $\geq$30 kg/m^2, and 0.5% bupivacaine are associated with increased PONS risk.

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Potential conflicts of interest

The authors declare no conflict of interest.

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