Optimal timing for repair of peripheral nerve injuries

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BACKGROUND: Data regarding outcomes after peripheral nerve injuries is limited, and the optimal management strategy for an acute injury is unclear. The aim of this study was to examine timing of repair and specific factors that impact motor-sensory outcomes after peripheral nerve injury.

METHODS: This was a single-center, retrospective study. Patients with traumatic peripheral nerve injury from January 2010 to June 2015 were included. Patients who died, required amputation, suffered brachial plexus injury, or had missing motor-sensory examinations were excluded. Motor-sensory examinations were graded 0 to 5 by the Modified British Medical Research Council system. Operative repair of peripheral nerves was analyzed for patient characteristics, anatomic nerve injured, level of injury, associated injuries, days until repair, and repair method.

RESULTS: Three hundred eleven patients met inclusion criteria. Two hundred fifty-eight (83%) patients underwent operative management, and 53 (17%) underwent nonoperative management. Those who required operative intervention had significantly more penetrating injuries 85.7% versus 64.2% ($p < 0.001$), worse initial motor scores 1.19 versus 2.23 ($p = 0.004$), and worse initial sensory examination scores 1.75 versus 2.28 ($p = 0.029$). Predictors of improved operative motor outcomes on univariate analysis were Injury Severity Score less than 15 ($p = 0.013$) and male sex ($p = 0.006$). Upper arm level of injury was a predictor of poor outcome ($p = 0.041$). Multivariate analysis confirmed male sex as a predictor of good motor outcome ($p = 0.014$; Adjusted Odds Ratio, 3.88 [1.28–11.80]). Univariate analysis identified distal forearm level of injury ($p = 0.026$) and autograft repair ($p = 0.048$) as predictors of poor sensory outcome. Damage control surgery for unstable patients undergoing laparotomy ($p = 0.257$) and days to nerve repair ($p = 0.834$) did not influence motor-sensory outcome. Outcomes did not differ significantly in patients who underwent repair 24 hours or longer versus those who were repaired later.

CONCLUSION: Outcomes were primarily influenced by patient characteristics and injury level rather than operative characteristics. Peripheral nerve injuries can be repaired after damage control surgery without detriment to outcomes. (*J Trauma Acute Care Surg.* 2017;83: 875–881. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Prognostic study, level III.

KEY WORDS: Peripheral nerve injury; epidemiology; timing of repair; damage control; outcomes.

Traumatic peripheral nerve injuries (PNI) have an incidence of approximately 2% to 3% in civilian trauma patients.[1,2] Not only are these injuries relatively common, but their impact is also magnified by the potential for lifelong disabilities and the young patient population at risk, with an average age ranging from 28 years to 35 years.[1,3–6] This represents a significant number of work-years lost for society. The average cost of a single median nerve injury, accounting for hospital costs and loss of production, has been conservatively estimated to be US $61,500.[5]

The surgeon's role in minimizing the morbidity of PNIs is important, yet there is still no consensus on the optimal timing of repair after injury. Even for completely transected nerves, the recommended time to surgical repair ranges from 3 days to 3 weeks.[4,7–10] Belzberg et al.[11] surveyed 126 experienced peripheral nerve surgeons and not only was there disagreement on the timing of repairs, but also the decision to operate at all for certain cases. Due to the lack of evidence supporting a universally acceptable management algorithm for these injuries, this study was performed to examine the optimal timing of repair and prognostic factors of motor-sensory outcomes for patients with PNIs. For variables under the influence of the trauma surgeon specifically, we hypothesized that earlier repair would yield improved motor-sensory outcomes for patients.

PATIENTS AND METHODS

Study Population

This is a single center retrospective study from a Level I trauma center. Traumatic PNIs (January 2010 to June 2015) were identified by ICD-9 coding (see Appendix, Supplemental Digital Content 1, http://links.lww.com/TA/A975). We excluded patients who had any of the following criteria: mortality, amputation of the affected limb, brachial plexus injuries, operative repairs performed at outside hospitals, or patients who were missing initial or follow-up motor-sensory examinations (Fig. 1).

Study Design

For all patients meeting inclusion criteria, we analyzed each individual chart, identifying the specific anatomic nerve injured, associated local injury (vascular, bone, muscle or tendon), initial and follow-up motor-sensory scores, and time between injury and last recorded follow-up. For upper extremity PNIs, we also categorized the level of injury (upper arm, proximal forearm, distal forearm, palmar or digital). Indications for peripheral nerve repair were preoperative documentation of motor deficit or PNIs discovered intra-operatively while being explored for concurrent associated injuries. For all patients who underwent operative repair, we identified the need for damage control surgery (DCS), defined as patients who underwent laparotomy and were too unstable for peripheral nerve repair, days from injury to repair (early repair if performed ≤1 day), tourniquet time, and repair method (primary repair, autograft, allograft, nerve tube).

Motor-sensory examinations were graded 0 to 5, using the Modified British Medical Research Council system. Only

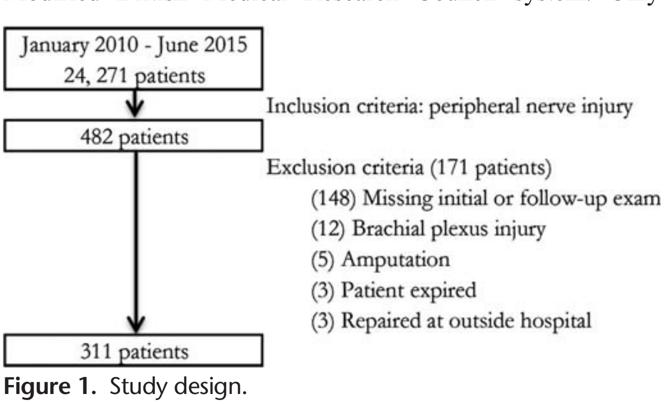

Figure 1. Study design.

patients with initial motor scores of 0 and initial sensory scores of 0 to 3 were included for analysis of motor-sensory improvement. Follow-up motor-sensory scores of 4 to 5 were considered as significant improvement. The motor-sensory scores were determined retrospectively from chart reviews.

Statistical Analysis

Descriptive statistics were calculated for all variables. Kolmogorov-Smirnov test was performed to confirm normal distribution in the continuous data. Independent t-test was used for continuous data, which were reported as means with standard deviations. Pearson's χ^2 test and Fisher's exact test were used for categorical data which were reported as percentages. Univariate analysis was used to identify variables predictive of significant motor-sensory improvement. Variables with p values less than 0.2 were further analyzed with multivariate analysis. Linear regression with manual method for variable selection was used. p Values less than 0.05 were considered statistically significant. Statistical analysis was performed using SPSS statistics, version 23 (IBM Corporation, 1 New Orchard Road, Armonk, New York 10504-1722, USA).

RESULTS

Epidemiology of PNIs

During the 5.5-year study period, 482 (2.0%) patients were identified to have peripheral PNIs. Exclusion criteria removed 171 patients; 148 were due to missing initial or follow-up examinations, 12 had brachial plexus injuries, five required amputations, three died, and three had nerve repairs performed at outside hospitals. Our final study population consisted of 311 patients (Table 1). The average age of our patients was 35.2 years, and they presented with an average Injury Severity Score (ISS) of 5.5. The majority of patients were male, 83.9%. Although the incidence of penetrating mechanisms for all institutional trauma activations during this period was 16.9%, the PNIs attributed to penetrating mechanisms was 82%. Average length of follow-up was 15.4 weeks.

Digital nerves were most commonly injured, followed by ulnar nerves, multiple upper extremity nerves, median nerves, radial nerves, lower extremity nerves, and other upper extremity nerves. For upper extremity nerve injuries, the level of injury was most common at the digital level, followed by distal forearm, upper arm, palmar, and finally proximal forearm (Fig. 2). Although few in number, the lower extremity PNIs included three peroneal nerves, one sciatic nerve, one posterior tibial nerve and one unspecified nerve of the pelvic girdle. Regarding associated regional vascular, bony, and tendon or muscle injuries, 17 (5.5%) patients had all three structures injured, 103 (33.1%) had two, 145 (46.6%) had one, and 46 (14.8%) had no associated injuries.

Of all PNIs, 258 (83%) patients underwent operative management, and 53 (17%) underwent nonoperative management. The nonoperative group was significantly more likely to have suffered blunt trauma, have higher ISS, have more associated fractures, and have the lower extremity affected. The operative

TABLE 1. Demographics

Variables	Total PNIs n = 311	Operative Management n = 258	Nonoperative Management n = 53	p
Patient characteristics				
Age, y	35.2 ± 14.9	34.7 ± 15.0	37.6 ± 14.5	0.183
Age > 65	10 (3.9%)	9 (3.5%)	1 (1.9%)	1.000
Sex, male	261 (83.9%)	219 (84.9%)	42 (79.2%)	0.309
Weight, kg	76.3 ± 18.8	75.9 ± 19.0	78.3 ± 17.9	0.399
Glasgow Coma Scale	14.9 ± 0.6	15.0 ± 0.3	14.7 ± 1.2	0.139
SBP	129.6 ± 21.8	128.8 ± 21.8	133.7 ± 21.5	0.150
SBP < 90	8 (2.6%)	7 (2.8%)	1 (1.9%)	1.000
ISS	5.5 ± 5.6	4.9 ± 5.0	8.66 ± 7.0	<0.001
ISS > 15	21 (5.8%)	14 (5.4%)	7 (13.2%)	0.064
Mechanism, penetrating	255 (82%)	221 (85.7%)	34 (64.2%)	<0.001
Follow-up time, wk	15.4 ± 19.4	15.9 ± 19.6	12.9 ± 18.5	0.293
Injured peripheral nerves				
Digital	88 (28.3%)	76 (29.5%)	12 (22.6%)	0.316
Ulnar	63 (20.3%)	47 (18.2%)	16 (30.2%)	0.048
Multiple upper extremity	55 (17.7%)	53 (20.5%)	2 (3.8%)	0.004
Median	48 (15.4%)	40 (15.5%)	8 (15.1%)	0.940
Radial	46 (14.8%)	35 (13.6%)	11 (20.8%)	0.179
Lower extremity	6 (1.9%)	2 (0.8%)	4 (7.5%)	0.009
Other upper extremity	5 (1.6%)	5 (1.9%)	0 (0%)	0.593
Associated injuries				
Tendon/muscle	212 (68.2%)	191 (74%)	9 (39.6%)	<0.001
Vascular	103 (33.1%)	94 (36.4%)	9 (17%)	0.006
Bone	87 (28%)	56 (21.7%)	31 (58.5%)	<0.001

SBP, systolic blood pressure.

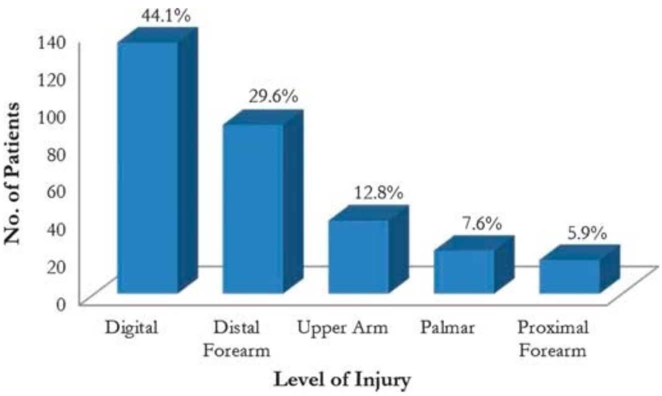

Figure 2. Upper extremity level of injuries.

group had significantly worse initial motor scores, and worse initial sensory examination scores (Table 2). However, the operative and nonoperative groups had insignificant differences in score improvement and follow-up motor-sensory exam. There were only two patients during this time to have either a thoracotomy or a traumatic brain injury, who also had a diagnosed PNI, neither of whom underwent nerve repairs.

Operative Management of PNIs

For patients that underwent operative repair of their PNIs, average length of time between injury and repair was 3.5 days. Of the 258 peripheral nerve repairs, 252 were performed by orthopedic surgeons, and six were performed by trauma surgeons. DCS was required in 23 (8.9%) patients. Tourniquet time was on average 99.2 minutes. The repair method was predominately by primary repair (72.9%), followed by autograft repair (12.8%), nerve tube (8.5%), allograft repair (3.5%), and finally nerve transposition (1.9%).

Predictors of Improved Motor-Sensory Outcome With Operative Repair

We analyzed patients with initial motor scores of zero and those with initial sensory scores of 0 to 3. There were 170 patients with such initial motor scores, and 220 patients with such initial sensory scores. With our definition of significant motor-sensory improvement being follow-up scores of 4 to 5, we used univariate analysis to identify variables that would predict significant improvement (Table 3). There were 91 of 170 patients with motor deficits that had clinically significant improvements, and there were 117 of 220 patients with sensory deficits that had clinically significant improvements. Predictors of improved operative motor outcomes were ISS less than 15 ($p = 0.013$) and male sex ($p = 0.006$). Upper arm level of injury was a predictor of poor outcome ($p = 0.041$). Multivariate analysis (Table 4) confirmed male sex as a predictor of significantly improved motor outcome ($p = 0.014$; AOR, 3.88 [1.28–11.80]).

When factors affecting operative sensory outcomes were examined, distal forearm level of injury ($p = 0.026$) and autograft repair ($p = 0.048$) were found to be predictors of poor sensory outcome. Patients who had both motor and sensory deficits (n = 152) were compared with those who had only motor (n = 22) or sensory (n = 71) deficits, and the outcomes after repair were not significantly different ($p = 0.305$, $p = 0.215$). Comparing primary repair with autograft repair head-to-head also showed that primary repair has superior results for sensory outcomes ($p = 0.043$). Tourniquet time ($p = 0.660$, 0.100), DCS ($p = 0.257$, 0.648), and days to nerve repair ($p = 0.834$, 0.294) did not influence motor or sensory outcomes, respectively. For patients with early repair, 54.7% had clinically significant improvement in motor outcome, compared with 53% of patients with later repairs. In regards to patients with early repair, 38.1% had clinically significant improvement in sensory outcome, compared with 45.9% of patients with later repairs.

DISCUSSION

There is a lack of evidence based consensus in the management of PNIs. In particular, there is tremendous variability in expert recommendations for the timing of repair. This study intended to examine the relationship of patient, injury, and operative characteristics with motor-sensory outcomes.

Our patient population is similar to other institutional experiences, with PNI incidences of 2% to 3%,[1,2] young male prevalence of 81% to 84%,[1,4,6,12,13] and proportions of penetrating injury mechanism between 62% and 86%.[1,4] Our study is the first to report that patient characteristics of ISS less than 15 and male sex are predictors of improved motor outcome after surgical repair. Although we did not show any differences in sensory outcomes based on patient characteristics, it is notable that Hundepool et al.[12] demonstrated poor sensory recovery associated with male sex. Of all patient characteristics, age as a prognostic factor has the most discrepancy in the literature, with many contradicting studies.[7,14–17] Our study suggests that age is not a prognostic factor in functional outcome.

We found that our distribution of anatomic nerves injured was consistent with other civilian studies, in which upper extremity peripheral nerves are more commonly injured than lower extremity ones.[9,18] However, most of these studies only focused on specific peripheral nerves and excluded digital nerves.[4,12] Our study showed that the most commonly injured peripheral nerves were digital, followed by ulnar nerves in the distal forearm. Excluding digital nerves, our study confirmed Saadat et al.'s[1] findings that ulnar nerves in the forearm are the most commonly injured. For associated injuries, Puzović et al.[4] reported similar percentages of vascular and bony injuries, but a

TABLE 2. Outcomes: Operative Versus Nonoperative Management

Variables	Total PNIs n = 311	Operative Management n = 258	Nonoperative Management n = 53	*p*
Motor				
Initial Score	1.37 ± 2.2	1.19 ± 2.1	2.23 ± 2.4	0.004
Latest score	3.42 ± 2.0	3.35 ± 2.3	3.76 ± 1.9	0.160
Score improvement	1.96 ± 2.3	2.06 ± 2.3	3.28 ± 2.5	0.352
Sensory				
Initial score	1.84 ± 1.7	1.75 ± 1.7	2.28 ± 1.6	0.029
Latest score	3.30 ± 1.3	3.25 ± 1.3	3.57 ± 1.1	0.064
Score improvement	1.50 ± 1.8	1.49 ± 1.9	1.28 ± 1.8	0.713

TABLE 3. Predictors of Improved Motor-Sensory Outcomes: Univariate Analysis

	Motor, n = 170		Sensory n = 220	
Variables	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**
Patient characteristics				
Glasgow Coma Scale > 9	—	—	—	—
SBP > 90	0.188	4.69 (0.51–43.48)	1.000	0.78 (0.13–3.95)
ISS < 15	0.013	10.14 (1.24–82.98)	0.519	1.86 (0.47–7.37)
Age < 65	0.735	0.68 (0.18–2.63)	1.000	1.30 (0.30–5.59)
Sex, male	0.006	4.03 (1.39–11.67)	0.819	0.92 (0.44–1.93)
Mechanism, penetrating	0.308	0.62 (0.25–1.57)	0.196	1.67 (0.77–3.63)
Injured peripheral nerve				
Digital	0.190	1.50 (0.82–2.76)	0.209	1.41 (0.83–2.41)
Ulnar	0.849	0.92 (0.41–2.10)	0.793	0.91 (0.47–1.79)
Multiple upper extremity	0.096	1.86 (0.89–3.87)	0.830	0.93 (0.48–1.80)
Median	0.448	1.41 (0.71–2.08)	0.636	0.84 (0.40–1.75)
Radial	0.089	0.47 (0.19–1.14)	0.783	1.12 (0.49–2.55)
Lower extremity	0.214	0.46 (0.39–0.54)	1.000	0.56 (0.50–0.63)
Other upper extremity	0.249	1.90 (1.64–2.19)	0.582	2.62 (0.23–29.30)
Level of injury				
Upper arm	0.041	0.38 (0.14–0.98)	0.430	1.46 (0.57–3.65)
Proximal forearm	0.220	0.46 (0.13–1.63)	0.752	1.29 (0.36–4.58)
Distal forearm	0.595	1.20 (0.61–2.37)	0.026	0.51 (0.28–0.93)
Palmar	0.514	1.52 (0.43–5.40)	0.595	1.30 (0.50–3.41)
Digital	0.244	1.44 (0.78–2.65)	0.251	1.37 (0.80–2.34)
Associated injuries				
Tendon/muscle	0.109	1.81 (0.87–3.76)	0.509	0.82 (0.45–1.50)
Vascular	0.818	0.93 (0.50–1.73)	0.590	0.86 (0.49–1.50)
Bone	0.484	0.78 (0.39–1.57)	0.981	0.99 (0.52–1.91)
Multiple associated injuries	0.364	1.33 (0.72–2.45)	0.841	1.06 (0.62–1.82)
Operative characteristics				
Initial damage control	0.257	0.52 (0.16–1.65)	0.648	1.31 (0.41–4.20)
Days from injury to repair ≤1	0.834	1.07 (0.56–2.06)	0.294	1.38 (0.76–2.50)
Short tourniquet time	0.660	1.19 (0.55–2.59)	0.100	0.56 (0.29–1.12)
Repair method				
Primary repair	0.467	1.29 (0.65–2.55)	0.091	1.76 (0.91–3.38)
Autograft	0.146	0.54 (0.24–1.25)	0.048	0.41 (0.17–1.01)
Allograft	0.452	2.24 (0.42–11.87)	1.000	1.30 (0.26–6.59)
Nerve tube	0.944	1.05 (0.31–2.56)	0.672	0.81 (0.30–2.17)

OR, odds ratio.

much lower incidence of soft tissue injuries (33.3%) compared with ours (68.2%).

Regarding the level of upper extremity nerve injuries, Secer et al.[19,20] have demonstrated that lower levels of repair were critical for good outcomes in the military population. However, their study population only consisted of gunshot and blast injuries, whereas our study encompassed all injury mechanisms for injured peripheral nerves in the civilian setting. With our greater diversity of PNIs and their mechanisms, we confirmed that a high level of injury has a worse prognosis for motor recovery after surgical repair ($p = 0.041$).

Previous studies have been conflicted with respect to which anatomic nerve has the best prognostic recovery.[20,21] For the upper extremity, Barrios and de Pablos[21] found the median nerve to have the best recovery, whereas Secer et al.[20] found the radial nerve to be the best. Our study did not find any statistically significant difference among the anatomic peripheral nerves for motor-sensory recovery.

Multiple studies have shown that primary repair of transected peripheral nerves is the preferred surgical method.[9,20,22,23] Specifically, Secer et al.[20] found that sural nerve autografts had the worst outcomes. Our study also showed a trend of worse motor outcomes with autograft repairs; however, this did not achieve significance.

There is a general consensus that for nerve injuries belonging to the classes of neurapraxia and axonotmesis, early surgical exploration is not indicated due to the possibility of spontaneous recovery.[18,20,24] These types of injuries can be closely followed up for 6 months, possibly a year, before surgical exploration is warranted.[7,10,21,25] For cases of neurotmesis, the time to repair is more urgent, but still varies from a three day to a 3-week window. Campbell recommends repair within 72 hours for sharp transections,[9] whereas Seddon argues that

TABLE 4. Predictors of Improved Motor-Sensory Outcomes: Multivariate Analysis

	Motor, n = 170		Sensory, n = 220	
Variables	***p***	**OR (95% CI)**	***p***	**OR (95% CI)**
Patient characteristics				
SBP > 90	0.222	4.78 (0.39–58.82)	—	—
ISS < 15	0.218	4.67 (0.403–54.07)	—	—
Sex, male	0.017	3.88 (1.28–11.80)	—	—
Mechanism, penetrating	—	—	0.061	3.13 (0.95–10.36)
Injured peripheral nerve				
Digital	0.946	1.03 (0.49–2.16)	—	—
Multiple upper extremity	0.116	2.00 (0.84–4.76)	—	—
Radial	0.274	0.57 (0.21–1.56)	—	—
Level of injury				
Upper arm	0.491	0.65 (0.19–2.21)	—	—
Distal forearm	—	—	0.064	0.49 (0.23–1.04)
Associated injuries				
Tendon/muscle	0.847	1.09 (0.45–2.67)	—	—
Operative characteristics				
Tourniquet time <100	—	—	0.184	0.62 (0.30–1.26)
Repair method				
Primary repair	—	—	0.973	1.02 (0.36–2.92)
Autograft	0.330	0.61 (0.22–1.66)	0.663	0.74 (0.19–2.91)

by waiting 3 weeks, fibrosis offers a mechanical advantage for nerve suturing,[26] which is also around the time Wallerian degeneration is completed.[4] In this study, transected nerves were repaired within an average of 3.5 days, and earlier repair (within the first 24 hours) did not demonstrate improved outcomes.

In addition, we showed that for patients who required DCS and thus had delayed surgical repair of their injured peripheral nerves, there was no difference in motor or sensory recovery. To the best of our knowledge, this study is the first to specifically address this issue, one that is not uncommon for the trauma surgeon. Discovering a transected peripheral nerve in a patient that is coagulopathic, hypothermic, and acidotic, who cannot tolerate a lengthy nerve repair, occurred in 8.9% of our study population. These results demonstrate that life-threatening injuries can be addressed first without compromising motor-sensory recovery for patients who need surgical repair of their PNIs.

The main limitations to this study are the retrospective nature, and the relatively short follow-up time, 15.9 weeks on average. Ideally, we would have brought all 311 patients back to our clinic for a formal motor-sensory evaluation, but compliance with follow-up is limited in our patient population. Despite these limitations, this study has supported previous work on PNIs, showing that patient characteristics and injury level are the most reliable predictors of motor-sensory outcomes and suggests that later repair does not affect functional outcomes for patients who need other life-threatening issues addressed first.

AUTHORSHIP

K.I. participated in the conception, design, overall responsibility. E.W. participated in literature search. E.W., S.B., D.E. participated in data collection. E.W., J.C. participated in statistical analysis. E.W., S.B., J.C., K.I. participated in analysis and interpretation. E.W. participated in writing the article. K.I., S.B., J.C., M.S., A.G., D.D. participated in the critical revision of the article. K.I. participated in the final approval of the article.

DISCLOSURE

The authors declare no conflicts of interest.

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