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Automated Nerve Monitoring in Shoulder Arthroplasty: A Prospective Randomized Controlled Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Evoked potential monitoring is used during surgery with the hope of averting neurologic injury
- Injury to the brachial plexus is possible during shoulder arthroplasty

What This Article Tells Us That Is New

- Using a prospective study design, automated nerve monitoring with feedback *versus* blinded monitoring during shoulder arthroplasty was not associated with a reduced duration of nerve alerts
- Secondary outcomes such as neurologic deficits and quality of life indices did not differ between the groups, although these outcomes improved in both groups over the course of the study

ABSTRACT

Background: Evoked potential monitoring is believed to prevent neurologic injury in various surgical settings; however, its clinical effect has not been scrutinized. It was hypothesized that an automated nerve monitor can minimize intraoperative nerve injury and thereby improve clinical outcomes in patients undergoing shoulder arthroplasty.

Methods: A prospective, blinded, parallel group, superiority design, single-center, randomized controlled study was conducted. Study participants were equally randomized into either the automated nerve-monitored or the blinded monitored groups. The primary outcome was intraoperative nerve injury burden as assessed by the cumulative duration of nerve alerts. Secondary outcomes were neurologic deficits and functional scores of the operative arm, and the quality of life index (Euro Quality of life-5 domain-5 level score) at postoperative weeks 2, 6, and 12.

Results: From September 2018 to July 2019, 213 patients were screened, of whom 200 were randomized. There was no statistically significant difference in the duration of nerve alerts between the automated nerve-monitored and control groups (median [25th, 75th interquartile range]: 1 [0, 18] and 5 [0, 26.5]; Hodges–Lehman difference [95% CI]: 0 [0 to 1] min; $P = 0.526$). There were no statistically significant differences in secondary outcomes between groups. However, in the ancillary analysis, there were reductions in neurologic deficits and improvements in quality of life index occurring in both groups over the course of the study period.

Conclusions: Protection from nerve injury is a shared responsibility between surgeons and anesthesiologists. Although a progressive improvement of clinical outcomes were observed over the course of the study in both groups as a consequence of the real-time feedback provided by the automated nerve monitor, this trial did not demonstrate that automated nerve monitoring by itself changes important clinical outcomes compared with no monitoring.

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Perioperative evoked potential monitoring is used to quantify the functional integrity of the peripheral nerves and spinal pathways and to detect and mitigate neurologic injury. However, this premise has yet to be proven, despite the routine use of evoked potential monitoring in various surgical procedures over the past four decades.[1] The lack of high-level evidence has given rise to long-standing controversies about the utility of evoked potential monitoring in the perioperative setting.[2,3] This uncertainty also results in difficulty formulating widely accepted clinical guidelines[1] for evoked potential monitoring in daily practice.[4–14] In addition, the current application of evoked potential monitoring is limited by the complicated logistics incurred in the perioperative settings.[15] This has triggered scrutiny from healthcare funders regarding the value of evoked potential monitoring.[1] To address some of these limitations, we wanted to assess the clinical effect of evoked potential monitoring in a surgical population that is at a higher risk of neurologic injury and in whom the mechanism of injury may be readily reversible with a timely alert/intervention.

Clinically apparent neuropathy after shoulder arthroplasty occurs in 4 to 8% of patients,[16–18] and intraoperative

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nerve conduction abnormalities vary from 24 to 80%.[16,19,20] Most nerve injuries during shoulder arthroplasty appear to result from indirect mechanisms, such as stretching of the brachial plexus beyond its mobility limits from extreme shoulder and arm positions, rather than direct surgical transection of nerves during surgery.[19,21,22] The nerve topography and anatomy of the brachial plexus vary substantially among individuals,[19,23,24] and a universal preventative strategy may be difficult to implement in the shoulder arthroplasty population. However, because the mechanism of injury in shoulder arthroplasty is often due to extreme arm positioning,[22] once identified, repositioning of the arm has been shown to reverse a majority of nerve dysfunction.[20,25,26]

The automated nerve monitor (EPAD, SafeOp Surgical, USA) is a simplified somatosensory evoked potentials (SSEP) monitoring device, that shares the same electrophysiologic principle as conventional SSEP monitoring. Importantly, unlike cortical SSEP, this device employs only subcortical SSEP monitoring and thus avoids any restriction on anesthetic medications.[25,27] This device also incorporates an algorithm to analyze SSEP waveforms and an artifact rejection system that allows the evoked potential monitoring to be conducted without the requirement of a designated technician or neurophysiologist.

In this clinical trial, we hypothesized that the use of automated nerve monitoring can minimize intraoperative nerve injury during shoulder arthroplasty surgery and thereby improve clinical outcomes. The primary objective of this prospective, blinded, randomized controlled trial was to assess the clinical effect of automated nerve monitoring to minimize intraoperative nerve injury during shoulder arthroplasty surgery. The secondary objectives of this study were to evaluate the effects of monitoring and event mitigation on the incidence of postoperative neurologic deficits, functional outcomes, and patient quality of life, as well as to explore the factors that determine these clinical and functional outcomes.

Materials and Methods

Trial Design

A prospective, blinded, parallel group, superiority design, single-center, randomized controlled study for assessing the effect of automated nerve monitoring on intraoperative nerve injury burden and postoperative outcomes in patients undergoing shoulder arthroplasty was conducted. For this study, 200 consecutive adult patients (older than 18 yr) scheduled to have a shoulder arthroplasty were randomly allocated into either nerve-monitored or blinded control groups using a one-to-one allocation ratio (*i.e.*, 100 patients in each group). The study was conducted at Roth|McFarlane Hand and Upper Limb Center (St. Joseph's Hospital, London, Ontario, Canada) from September 2018 to November 2019 (including the postoperative 3-month follow-up period). The trial protocol was approved by the Research Ethics Board at Western University (London, Ontario, Canada; Approval 108951). A pilot study[25] was performed to confirm the feasibility of this trial. This trial was registered at ClinicalTrials.gov on July 8, 2018 (NCT03624426, principal investigator Jason Chui). The trial registration was amended once to clarify the secondary outcomes. The trial was stopped when the target enrollment was obtained.

Participants

Participants were adult patients scheduled to have elective shoulder arthroplasty surgery under general anesthesia including anatomic total shoulder arthroplasty, reverse shoulder arthroplasty, hemiarthroplasty, and revision arthroplasty. We excluded patients who were unable to perform a complete neurologic examination or provide written informed consent, in whom we were unable to obtain baseline SSEP signals, or who had contraindications for SSEP monitoring, such as skin lesions at the sites of electrode placement. All study participants were recruited in a single, high-surgical-volume, university-affiliated hospital with a caseload of approximately 300 shoulder arthroplasty surgeries annually. Informed consent was obtained from all study participants.

Interventions

The study intervention used an automated nerve monitor to detect and mitigate nerve insult during shoulder arthroplasty surgery. This monitor incorporates an auto-acquisition and interpretation algorithm that allows automated subcortical SSEP monitoring. The setup of the automated nerve monitor is described in Supplemental Digital Content 1 (http://links.lww.com/ALN/C610), and the technical details of this device were reported previously.[25,27] In short, stimulating electrodes were attached to the median, ulnar, and radial nerves at the wrist level of the operative arm. A modified surgical draping technique was used to ensure sterility. The recording surface electrode was placed at the fifth cervical spine level at the posterior neck and referenced to the forehead electrode (Fz). The stimulating and recording electrodes were connected to a central control box that used a Bluetooth connection to a tablet for display and recordings. Subcortical SSEP monitoring was performed after anesthesia induction and continued until the end of the surgery.

Nerve-monitored Group. In the nerve-monitored group, when a nerve alert was signaled by the automated nerve monitor, the surgeon was informed and possible surgical interventions performed (*e.g.*, repositioning the operative arm into a more neutral position, avoidance of excessive traction, removal or adjustment of retractors, and/or using a smaller implant to avoid overcorrection/traction). For each nerve alert, the nerves involved, the stage of the procedure, the number and position of retractors, the position of the operative arm, and the time elapsed until return to normal were recorded.

Blinded Control Group. In the blinded control group, the automated nerve monitor was connected to the patient, but the screen of the monitor was covered by an opaque plastic bag, and the alarms were turned off. No monitor-based intervention was performed for this group.

General Procedures. Apart from the aforementioned intervention, all patients received standard anesthesia care, including a continuous brachial plexus block for postoperative pain management. A brachial plexus catheter was inserted under ultrasound guidance before induction of anesthesia, but local anesthetics were withheld until the end of surgery to enable intraoperative monitoring. A baseline clinical assessment of the sensory and motor functions of the upper limb was performed after the brachial plexus catheter insertion to ensure that any changes in neurologic symptoms were attributed to the surgery rather than to needle injury during the block procedure. The patient was then transferred to the operating room for the shoulder arthroplasty surgery. The anesthetic regimen was not restricted because only subcortical SSEP was monitored. After anesthesia induction and patient positioning, the stimulating and receiving electrodes were connected, and the monitoring was performed (Supplemental Digital Content 1, http://links.lww.com/ALN/C610). Once satisfactory baseline signals were obtained, the randomization allocation was disclosed, and surgery commenced. The monitoring was continued until the end of the surgery.

Outcomes

The primary outcome was the cumulative duration of nerve alerts of the operative arm, which has been previously used[28–31] as a measure of the extent of intraoperative nerve insult. Shortening the cumulative duration of nerve alerts reflects less intraoperative nerve insult.

The secondary outcomes were obtained by an independent assessor at 2, 6, and 12 weeks after surgery and included the following. (1) Neurologic deficit of the operative arm: The motor score was rated by a numeric rating score of 0 to 5 while sensory function was assessed by presence or absence of light touch. A reduction of power greater than or equal to 2/5 or complete loss of light touch sensation was defined as neurologic deficits. (2) The functional outcome of the operative arm using the American Shoulder and Elbow Surgeons score: The American Shoulder and Elbow Surgeons score[32] is a validated outcome measure.[33,34] (3) The quality of life measure using the Euro Quality of life-5 domain-5 level score: The Euro Quality of life-5 domain-5 level score consists of two components: a descriptive component to assess five dimensions of quality of life and a Euro Quality of life visual analogue scale. The Euro Quality of life-5 domain health state index is a single summary index, ranging from 0 to 1 (where 0 denotes death and 1 denotes full health/function), that is weighted to the country/region to describe the five dimensions of Euro Quality of life-5 domain.

Sample Size

The sample size calculation was based on the pilot data from our previous study on automated nerve monitoring in shoulder arthroplasty patients, in which the observed cumulative mean duration (± SD) of abnormal signals (nerve insults) was 40 ± 20 min.[7] To detect a difference of 10 min in the cumulative duration of nerve alerts in the intervention group using a two-tailed statistical test with a significance level of 5% with 90% power, 90 patients were required in each arm. Assuming a 10% dropout rate, the total sample size was adjusted to 200.

Randomization and Blinding

Stratified randomization was used to assign interventions into primary or revision operations because revision shoulder surgery has a significantly higher risk of nerve injury. In each stratum, a variable permuted block size of 4 to 6 was used. The allocation sequence was generated by the study statistician. To ensure allocation concealment, the assignment was stored in a password-protected electronic database (REDCap; Vanderbilt, USA). The research assistant evaluated eligibility, obtained informed consent, enrolled the participants, and accessed the database to assign the allocation in the operating room after satisfactory baseline SSEP signals were obtained.

Participants and outcome assessors were blinded to the treatment allocation. Intraoperative personnel were not blinded to the intervention group because the blinding of automated nerve monitoring was obvious. However, all clinicians and nurses for patients randomized to the control group were blinded to the data on the automated nerve monitor.

Statistical Methods

We summarized patient demographics along with the surgical and anesthetic characteristics in the two groups. Parametric data are presented as mean ± SD. Nonparametric data were presented as median (25th, 75th interquartile range). Numeric data are presented as numbers (frequencies). We assessed the adequacy of randomization by inspection. We constructed a CONsolidated Standards of Reporting Trials (CONSORT) flow diagram. The duration and the distribution of nerve alerts, as well as the intervention/maneuvers that mitigated nerve injury (reflected by reversing nerve alerts), in the five key stages of the surgery were summarized.

The primary outcome was evaluated using a two-tailed Mann–Whitney U test to assess the effect of automated nerve monitoring on the cumulative duration of nerve alerts. We further assessed the differences at each surgical stage between the two groups using the two-tailed Mann–Whitney U test. For the secondary outcomes, the American Shoulder and Elbow Surgeons score, the Euro Quality of life-5 domain health state index value, and the Euro Quality of life visual

analogue scale score were tested by the two-sample independent Student's *t* test (two-tailed). The effect of automated nerve monitoring on the neurologic deficit of the operative arm was assessed using the chi-square test.

An ancillary analysis examined changes in the duration of intraoperative nerve alerts and postoperative outcomes as time-dependent outcomes over the duration of the study period. Linear regression was used to assess the relationship between duration of nerve alerts (min) and the days since the study commenced (day). Linear regression was used to assess the relationship between and Euro Quality of life-5 domain health state index value (range, 0 to 1) and the days since the study commenced. Linear prediction plots were created to illustrate the results.

Logistic regression was also used to assess the relationship between neurologic deficits at postoperative 3 months (yes or no) and the duration since the study commenced (day). Predicted probabilities (95% CI) of neurologic deficits 3 months after surgery were determined for each 10-day interval since the study commenced. A margins plot was created to display the adjusted predicted probabilities (95% CI) of neurologic deficits 3 months after surgery over the days since the study commenced.

All analyses were done on an intention-to-treat basis using only complete-case analysis without imputation of missing data. A *P* value of less than 0.05 was considered significant. All analyses were performed using STATA (version 14.0, StataCorp, USA).

Results

Between September 2018 and July 2019, a total of 213 patients were assessed for eligibility. Of these patients, 13 patients were excluded because of failure to obtain baseline recordings. In total, 200 patients were recruited and randomly assigned into either the nerve-monitored group (100 patients) or the blinded control group (100 patients; fig. 1). There was no crossover between the two groups, and there were no protocol violations. Primary outcome data were obtained for all patients. The lost-to-follow-up rates at postoperative 2 weeks, 6 weeks, and 3 months were 4.5, 3.5, and 7.5%, respectively.

The baseline characteristics were similar between the nerve-monitored and control groups (table 1) except that there were more patients with diabetes mellitus in the control group (table 1). The baseline shoulder function as assessed with the American Shoulder and Elbow Surgeons score and the quality of life as assessed with the Euro Quality of life-5 domain-5 level score were similar between the two groups. The type, side, and median duration of surgery were also similar between the two groups.

Trial Treatment

Overall, 112 (56%) of 200 patients had at least one abnormal nerve alert during their surgery. The median (25th, 75th interquartile range) cumulative duration of abnormal nerve alerts was 3.5 (0, 20) min. The abnormal nerve alerts occurred most frequently during humeral component implantation (89 patients, 45%), followed by glenoid preparation and implantation (81 patients, 41%) and postreduction phase (66 patients, 33%). However, the duration of abnormal nerve alerts was longer in the glenoid preparation and implantation phase, followed by the humeral implantation phase and postreduction phases.

The distribution of nerve alerts at each stage of surgery is summarized in table 2. Nerve alerts occurred equally in all three monitored nerve distributions in the surgical stages of glenoid preparation and implantation, humeral implantation, and postreduction. In most instances, nerve alerts developed simultaneously in more than one nerve distribution, suggesting a global insult to the brachial plexus.

In the nerve-monitored group, the most common intervention in response to an abnormal nerve alert was repositioning of the operative arm, followed by adjustment of surgical retractors. In a few cases, the cause of nerve alerts was local tissue compression or surgical drape tension (table 2). These cases were treated with immediate tension release. Most of the nerve alerts resolved a few minutes after the intervention, resulting in shortening in cumulative duration of abnormal nerve alerts. There were 44 nerve alert events in which there were no identifiable causes of the abnormal alerts and no intervention was applied. There were 22 abnormal nerve alert events developed in the nonoperative arm, which resolved with repositioning.

Primary Outcome

The median (25th, 75th interquartile range) cumulative durations of abnormal nerve alerts were 1 (0, 18) and 5 (0, 26.5) min in the nerve-monitored group and control groups, respectively (table 3). There was no significant difference between the two groups ($P = 0.526$); the Hodges–Lehman difference (95% CI) was 0 (0, 1) min.

There were no differences in the duration of abnormal nerve alerts in each stage of shoulder surgery between the nerve-monitored and control groups. Table 3 shows the duration of nerve alerts numerically at each stage of shoulder surgery.

Secondary Outcomes

There were no differences in any of the secondary outcomes at postoperative week 2, week 6, and month 3 (table 3). Specifically, neurologic deficits identified during the 3-month postoperative clinical examination were found in 23 (13%) patients in the nerve-monitored group and in 16 (9%) patients in the control group ($P = 0.192$). The 3-month American Shoulder and Elbow Surgeons score was similar for the nerve-monitored and control groups (mean ± SD scores of 31.6 ± 13.8 and 31.4 ± 13.0, respectively; $P = 0.899$). The 3-month postoperative mean

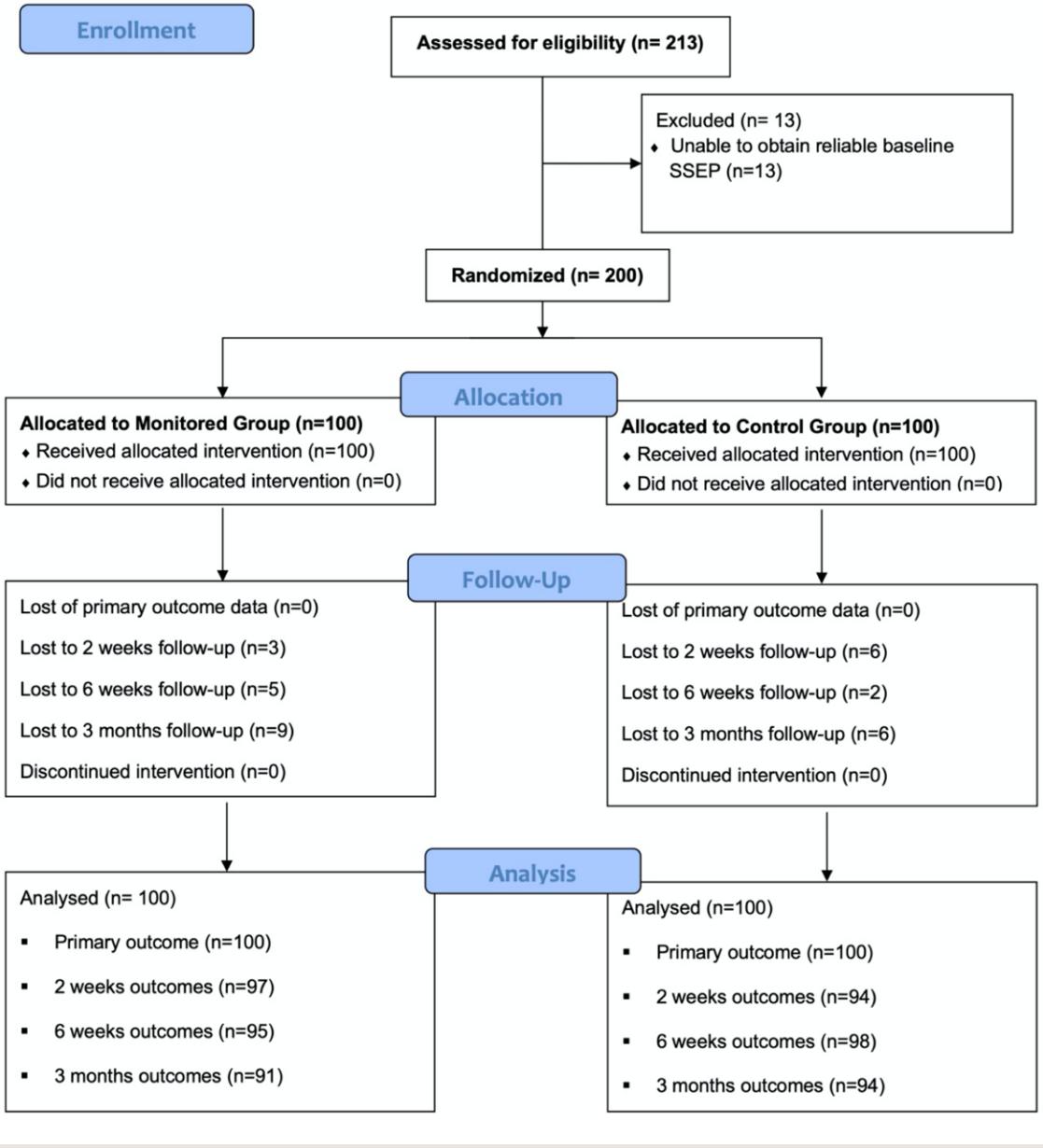

Fig. 1. Study flow chart. SSEP, somatosensory evoked potentials.

± SD Euro Quality of life-5 domain-5 level score health state index scores were 0.81 ± 0.12 in the nerve-monitored group and 0.82 ± 0.13 in the control group ($P = 0.679$).

Ancillary Analysis

In the ancillary analysis, there was a decrease of abnormal duration of nerve alerts (representing nerve insult burden) over the study period ($\beta = -1.01$ [95% CI, −2.16 to 0.18] every 36 days; $P = 0.094$), which is an approximately 1-min reduction of nerve alert every 36 days since the study commenced (fig. 2). This finding was consistent in both groups, suggesting a learning effect that was transferred from the intervention group to the control group. During the conduct of the study, we could also observe that the surgeons modified their surgical techniques in response to the experience they gained from nerve alerts patterns from the automated nerve monitor. One surgeon changed to removing the retractor in the surgical site every time the operative arm was repositioned, as well as the method of surgical drape application around the elbow to minimize ulnar nerve compression. The other two surgeons did not explicitly report any changes in their surgical techniques over the study period. However, the study team was aware of some

Table 1. Baseline Demographic and Perioperative Characteristics of the Patients

Characteristics	Nerve-monitored Group (n = 100)	Control Group (n = 100)
Age, yr, mean ± SD	67 ± 10	69 ± 8
Female sex, No.	41	48
Body weight, kg, mean ± SD	90 ± 21	86 ± 20
Height, cm, mean ± SD	170 ±10	166 ± 11
Body mass index, kg/m^2, mean ± SD	31 ± 6	31 ± 7
Coexisting medical condition, No.		
Hypertension	51	56
Diabetes mellitus	13	25
Neurologic disease	3	2
Peripheral neuropathy	9	6
Cervical spine disease	15	16
Peripheral vascular disease	3	2
Rheumatoid arthritis	9	9
Osteoarthritis	86	88
Surgical condition		
Right-handed, No.	86	89
Range of shoulder forward flexion, degrees, median (interquartile range)	70 (30, 90)	72.5 (40, 100)
Range of shoulder external rotation, degrees, median (interquartile range)	20 (10, 30)	20 (10, 40)
Previous fracture of the same arm, No.	16	16
Previous operation on the same shoulder, No.*	32	34
Avascular necrosis of the shoulder joint, No.	1	3
Methotrexate used, No.	11	7
Steroid used, No.	60	49
American Shoulder and Elbow Surgeons score, mean ± SD	42 ± 17	41 ± 14
Euro Quality of life-5 domain-5 level health state index score, mean ± SD	0.7 ± 0.2	0.7 ± 0.1
Euro Quality of life visual analogue scale score, mean ± SD	79 ± 12	79 ± 12
Perioperative care, No.		
Brachial plexus catheter inserted preoperatively	98	99
Maintenance anesthetic agents (sevoflurane/desflurane)	31/69	25/75
Surgery, No.		
Type of surgery		
Total shoulder arthroplasty	23	23
Reverse shoulder arthroplasty	76	77
Hemiarthroplasty	1	0
Redo shoulder replacement surgery	16	16
Left/right-sided surgery	36/64	46/54
Median duration of surgery, min, mean ± SD	99 ± 28	96 ± 26

Parametric data are presented as mean ± SD. Nonparametric data are presented as median (25th, 75th interquartile range). The numeric data are presented as frequencies. The American Shoulder and Elbow Surgeons score is a standardized functional outcome measures in shoulder and elbow surgery. The American Shoulder and Elbow Surgeons score ranged from 0 to 100 and is weighted equally for pain and function. The Euro Quality of life-5 domain-5 level score is an instrument to describe and value health state. "5D" denotes five dimensions, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five levels of health states.

*Previous surgery includes non–shoulder replacement operation such as shoulder arthroscopy, rotator cuff repair, and incision and drainage.

subtle changes in techniques over the study period. These findings suggest either a learning effect or Hawthorne effect, in which the surgeons have improved their surgical technique or behavior consciously or unconsciously in response to the feedback provided by the automated nerve monitor during the study period. We further examined the relationship of abnormal duration of nerve alerts over the study period across three participating surgeons. We found a differential learning effect among three surgeons; two surgeons (surgeons A and C) had marked reduction of duration of nerve alerts (representing reduction in nerve injury burden) over the study period, whereas one surgeon (surgeon B) had no substantial change (fig. 2).

We further examined the relationships of the incidence of neurologic deficits and quality of life during the study corresponding to the reduction in nerve injury over the study period. We found that there was a statistically significant reduction of the odds of neurologic deficits 3 months postoperatively over the study period (odds ratio, 0.85 [95% CI, 0.75 to 0.97] for every 30 days; $P = 0.012$; fig. 3). This represented a decrease of odds of 3-month postoperative neurologic deficits by a factor of 0.85 every 30 days since the study commenced. The predicted probabilities of 3-month postoperative neurologic deficits at days 100, 200, and 300 since the study commenced were 0.27, 0.18, and 0.11, respectively (fig. 3). There was also a statistically significant improvement of quality of life at postoperative 3 months across the study period ($\beta = 0.02$ [95% CI, 0.00003 to 0.0005] for every 100 days; $P = 0.022$; fig. 3). This corresponded to an improvement of Euro Quality of

Table 2. The Pattern of Nerve Alert and Intervention Used to Treat Abnormal Nerve Alerts

Variable	Exposure	Humerus Preparation	Glenoid Preparation and Implantation	Humeral Implantation	Wound Closure
Alerts in control group, No.					
Median	4	6	18	13	16
Ulnar	2	6	17	21	16
Radial		11	28	27	27
Nonoperative arm			2	4	1
Alerts in nerve-monitored group, No.					
Median	1	5	21	20	16
Ulnar	4	13	28	24	17
Radial		2	21	23	15
Nonoperative arm			4	6	5
Intervention in nerve-monitored group, No.					
No intervention	1	3	6	14	20
Reposition of the arm	4	11	19	20	7
Adjust surgical retractor		2	13	9	3
Other intervention			2*	1†	1‡

This table illustrates the nerve alert pattern at five stages of shoulder arthroplasty. "Median," "ulnar," and "radial" denote abnormal nerve alert showed on the median, ulnar, and radial nerve somatosensory evoked potentials, respectively. "Control" denotes abnormal nerve alert showed on the median nerve somatosensory evoked potentials on the contralateral arm. The number denotes the number of patients with nerve alert of each nerve at each stage of surgery.

*Other intervention: One case was due to soft tissue tension at the surgical site. The surgeon performed soft tissue release and was able to reverse the abnormal alert. The other case was due to tight forearm drape. The nerve alert was reversed with release of the surgical drape. †Other intervention: The surgeon reduced direct pressure and stopped dissection around the latissimus. ‡Other intervention: Radial nerve massage.

life-5 domain health state index value of 0.02 per 100 days since the study commenced.

Harms

No harm or unintended effects were noticed in this study.

Discussion

To address the current logistic limitations and lack of evidence of evoked potential monitoring in the perioperative setting, we carefully designed and conducted a prospective randomized controlled study to systematically assess whether a timely detection of nerve injury by the automated nerve monitor in company with simple reversing maneuvers can reduce intraoperative nerve injury and thereby improve clinical outcomes in shoulder arthroplasty. In this clinical trial, we did not demonstrate that automated nerve monitoring reduces intraoperative nerve injury and postoperative neurologic deficit or improves functional outcomes and quality of life up to postoperative 3 months compared with no monitoring.

The current utility of evoked potential monitoring is hampered by the lack of demonstrated clinical effect in the literature.[15] The guidelines on the use of electrophysiologic monitoring for surgery of the spinal column and spinal cord[1] only support the use of multimodality-evoked potential monitoring as a diagnostic adjunct in the perioperative setting (level I evidence) but not as a therapeutic adjunct or standard of care in spinal surgery because of the lack of high-quality evidence (*i.e.*, class I or II). After the publication of these guidelines, there were diverse opinions[4–14] among the societies of neurosurgeons, neurophysiologists, neurologists, and anesthesiologists about the interpretation of the evidence; for example, the lack of evidence should not be construed as a lack of therapeutic effect, which would call into question the validity of these recommendations. These diverse and conflicting opinions reflect the fact that there is a lack of high-level evidence in evoked potential monitoring to inform clinical decision-making.

Similar to the literature in spine surgery, the research of evoked potential monitoring in shoulder replacement surgery is limited to observational studies.[35–37] There are a few cohort studies that reported the use of evoked potential monitoring during shoulder replacement surgery; however, all these studies are limited to reporting the incidence of nerve injury and risk factor exploration.[35–37] Similar to the diverse views on the application of evoked potential monitoring in spinal surgery, some authors[20] conclude that all patients who are at high risk of nerve injury should be considered for routine monitoring, whereas others[16] refute the use of routine monitoring because of the lack of demonstrated clinical effects of evoked potential monitoring and the increased cost and length of surgery.

The current study adds important information to the literature of intraoperative evoked potential monitoring. First, to the best of our knowledge, no randomized control trial in the literature has been performed to systematically assess the evoked potential monitoring in shoulder arthroplasty. Second, this study employed an innovative technology that avoids the complicated logistics/expertise required for conventional neurophysiological monitoring. Most surgical centers do not perform evoked potential monitoring in shoulder replacement surgery because of

Table 3. Primary Outcome and Secondary Outcomes

Outcome	Nerve-monitored Group (n = 100)	Control Group (n = 100)	Group Difference	*P* Value
Primary outcome				
Duration of abnormal nerve alerts, min, median (25th, 75th)*	1 (0, 18)	5 (0, 26.5)	0 (0, 1)	0.526
Stage of surgery				
Exposure*	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.285
Humerus preparation*	0 (0, 0)	0 (0, 0)	0 (0, 0)	0.322
Glenoid preparation*	0 (0, 7)	0 (0, 7)	0 (0, 0)	0.828
Implantation*	0 (0, 6)	0 (0, 7)	0 (0, 0)	0.652
Wound closure*	0 (0, 1)	0 (0, 5)	0 (0, 0)	0.431
Secondary outcomes				
Postoperative 2 weeks				
Worsening of motor/sensory function†	84 (55)	65 (43)		0.426
American Shoulder and Elbow Surgeons score‡	16 ± 6	15 ± 7	0 (–3 to 1)	0.477
Euro Quality of life-5 domain-5 level health state index score‡	0.7 ± 0.1	0.7 ± 0.2	0.0 (–0.1 to 0.0)	0.301
Euro Quality of life VAS score‡	79 ± 14	78 ± 16	–1 (–5 to 4)	0.714
Postoperative 6 weeks				
Worsening of motor/sensory function†	23 (14)	17 (11)		0.294
American Shoulder and Elbow Surgeons score‡	22 ± 9	22 ± 8	0 (–2 to 3)	0.948
Euro Quality of life-5 domain-5 level health state index score‡	0.7 ± 0.1	0.7 ± 0.1	0.0 (0.0 to 0.0)	0.929
Euro Quality of life VAS score‡	79 ± 15	79 ± 16	0 (–5 to 4)	0.901
Postoperative 3 months				
Worsening of motor/sensory function†	23 (13)	16 (9)		0.192
American Shoulder and Elbow Surgeons score‡	31 ± 14	31 ± 13	–0 (–4 to 4)	0.899
Euro Quality of life-5 domain-5 level health state index score‡	0.8 ± 0.1	0.8 ± 0.1	0.0 (0.0 to 0.05)	0.679
Euro Quality of life VAS score‡	81 ± 13	82 ± 13	1 (–3 to 5)	0.614

The American Shoulder and Elbow Surgeons score is a standardized functional outcome measures in shoulder and elbow surgery. The American Shoulder and Elbow Surgeons score ranged from 0 to 100 and is weighted equally for pain and function. The Euro Quality of life-5 Domain-5 Level score is an instrument to describe and value health state. "5D" denotes five dimensions, including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has five levels of health states.

*Nonparametric data are presented as median (25th, 75th interquartile range). The outcome difference is tested by two-tailed Mann–Whitney U test, and the group difference is presented as the Hodges–Lehman median difference (95% CI for percentile differences). †Numeric data are presented as number (%). The outcome difference is tested by a chi-square test. ‡Parametric data are presented as mean ± SD. The outcome difference is tested by two-sample Student's *t* test (two-tailed), and the group difference is presented as mean difference (95% CI).

VAS, visual analogue scale.

the labor-intensive setup and monitoring requirements. The use of subcortical SSEP also negates the concerns of signal suppression from volatile agents.[25,27] Third, this study might be helpful in raising awareness of nerve injury prevention during surgery.

An interesting ancillary finding was observed in this study, in which the use of automated nerve monitoring was associated with improvement of clinical outcomes over the course of the study. We attributed these outcome benefits to surgical technique modifications over the study period in response to the real-time feedback learning experience provided by the automated nerve monitor. Importantly, these outcome benefits were observed in both monitored and blinded control groups. This learning or Hawthorne effect progressively reduced the baseline risk (*i.e.*, nerve insult) and thus markedly diluted the treatment effect of automated nerve monitoring and reduced the statistical power of this study. It is important to note that our center is among those performing the highest number of shoulder arthroplasty cases in Canada, implying that the learning effects of using an automated nerve monitor are observed in those with extensive surgical experience. This also reflects the fact that complete avoidance of intraoperative nerve injury is difficult to achieve without objective and tailored real-time feedback.

Limitations

The major limitation of this study was that the presence of learning or Hawthorne effect may confound the main results and conclusions of this study; future studies should consider this potential effect in their study design. Additionally, it was a single-center clinical trial. The nature of a single-center trial indicates that the benefits found may only be specific to our institution and may not generalizable. There was also a small proportion (less than 10%) of patients who were lost to follow-up.

Although we observed changes in the surgical technique over the study period, we cannot generalize these changes into a few recommendations for all surgeons. The changes must be tailored to the individual surgeons' techniques and may not be generalizable to other surgeons. In addition, some changes are very subtle and difficult to describe or reproduce clinically. It is also unknown whether the behavior changes to decrease nerve alerts that were learned by the surgeons during the course of the study will persist in the long term.

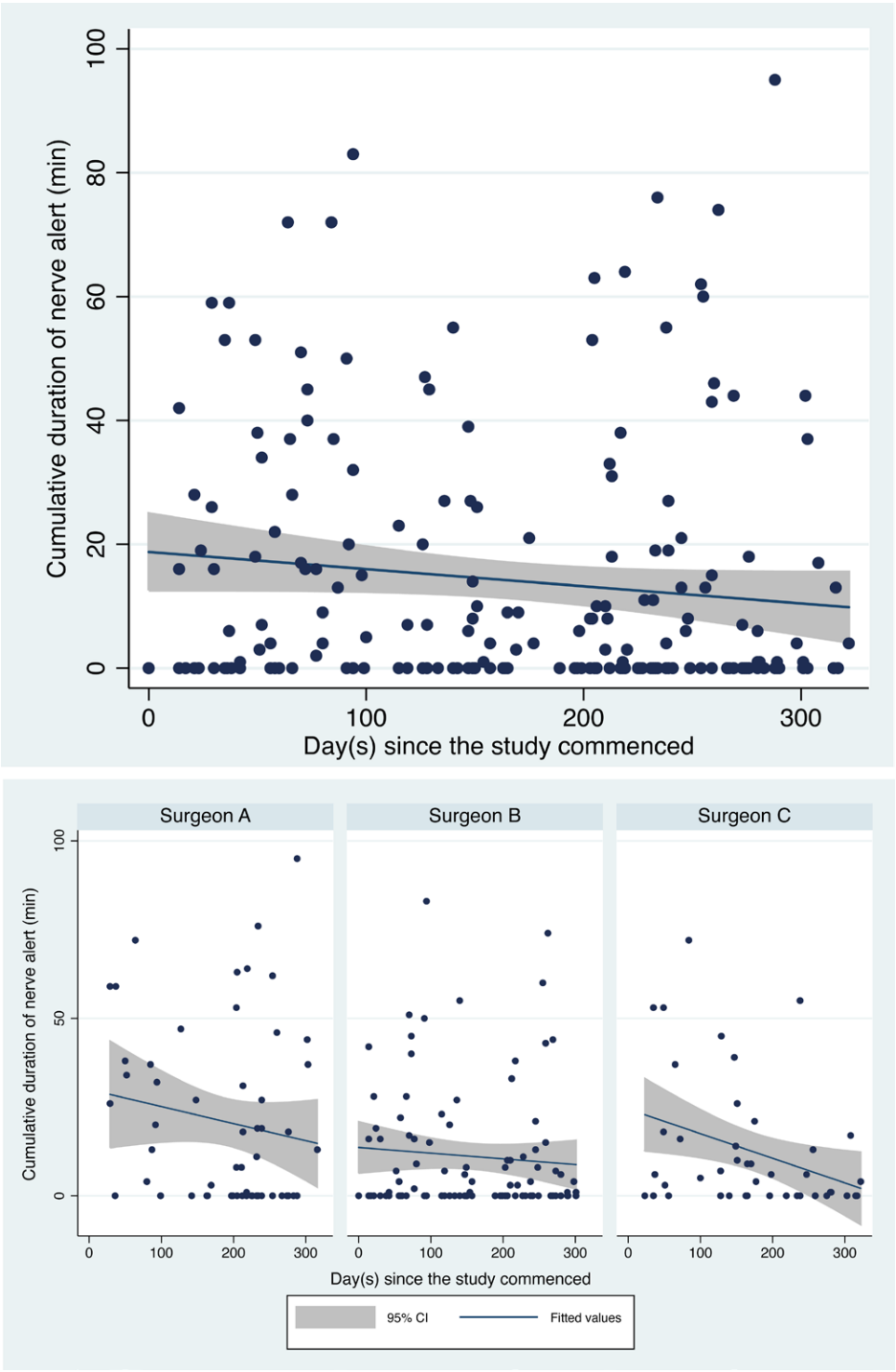

Fig. 2. The changes of cumulative duration of abnormal nerve alert across the study period. (*Top*) Linear prediction plot with 95% CI of the duration of nerve alerts across the study period. The duration of nerve alerts progressively reduces over the study period, suggesting a Hawthorne (or learning) effect, in which the surgeons has learned and improved their surgical skills to minimize the nerve alerts. (*Bottom*) Linear prediction plot with 95% CI of the duration of nerve alerts across the study period of three participating surgeons, reflecting different learning curves among three participating surgeons.

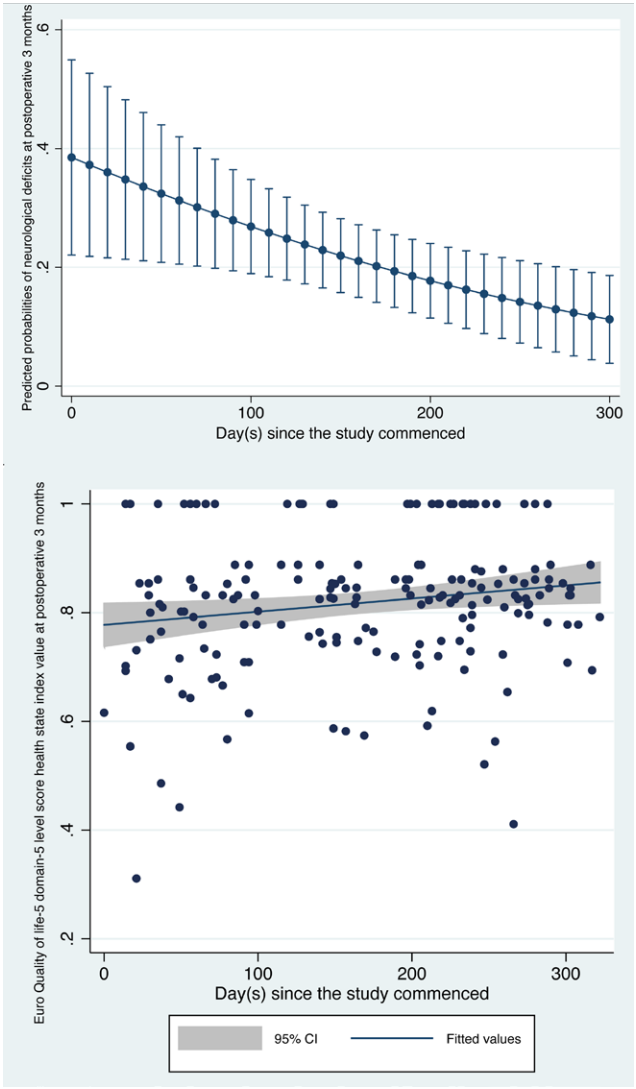

Fig. 3. The changes of predicted probabilities of neurologic deficits and Euro Quality of life-5 domain-5 level score and Euro Quality of life-5 domain-5 level score health state index value at postoperative 3 months over the study period. (*Top*) The 3-month postoperative margins plot of the predicted probabilities with 95% CI of neurologic deficits at across the study period. The 3-month postoperative predicted probabilities of neurologic deficits at days 100, 200, and 300 since the study commenced were 0.27, 0.18, and 0.11, respectively. (*Bottom*) The 3-month postoperative linear prediction plot with 95% CI of the Euro Quality of life-5 domain-5 level score health state index value across the study period. The 3-month postoperative Euro Quality of life-5 domain-5 level health state index value of patients improves over the study period ($\beta = 0.0002$ [95% CI, 0.00003 to 0.0005]; $P = 0.022$). This corresponds to an improvement of Euro Quality of life-5 domain health state index value of 0.02 per 100 days since the study commenced.

Conclusions

Protection from nerve injury is a shared responsibility between surgeons and anesthesiologists in the perioperative setting. This prospective, blinded, randomized controlled trial systematically assesses the outcome benefit of evoked potential monitoring with the application of a novel automated technology. Although a progressive improvement of clinical outcomes was observed over the course of the study in both groups as a consequence of the real-time feedback provided by the automated nerve monitor, this trial did not demonstrate that automated nerve monitoring by itself changes important clinical outcomes compared with no monitoring.

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Competing Interests

Dr. Murkin is a former scientific advisory board member of SafeOp Surgical (Hunt Valley, Maryland). He has provided technical support for the automated nerve monitoring technology in this study and reviewed the article but was not involved in the study conduct, data collection, or statistical analysis of this study. Dr. Faber is a scientific consultant for Exactech (Gainesville, Florida). The other authors declare no competing interests.

Reproducible Science

Full protocol available at: jason.chui@lhsc.on.ca. Raw data available at: jason.chui@lhsc.on.ca.

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