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Although clinical severity scores have a diagnostic role in carpal tunnel syndrome, they do not correlate with recovery following carpal tunnel release. Favorable results and high patient satisfaction have been reported for patients with severe disease undergoing carpal tunnel release. We have recognized a subset of patients with severe disease who do not follow the typical, uneventful recovery pathway postoperatively. This group of patients develops transient worsening of their neuropathic pain in the median nerve distribution following release without other identifiable cause or symptoms meeting diagnostic criteria for complex regional pain syndrome. We have termed this “reawakening phenomenon.”

The purpose of this study was to compare the characteristics of patients with this phenomenon to those with a standard postoperative course. We hypothesize that preoperative variables can predict which patients are most at risk for this phenomenon, guiding patient expectations and improving perioperative care.

**PATIENTS AND METHODS**

A retrospective chart review was performed by three authors (J.M., P.H., and J.L.) on all patients who had undergone either open or endoscopic carpal tunnel release at a single institution between January of 2012 and December of 2017. Patients with any indication of isolated, worsened neuropathic pain in all, or a portion, of the median nerve distribution distal to the wrist that began shortly after their carpal tunnel release were then reviewed by a separate author (J.R.) and included in the case group as appropriate. The symptoms were described in the patient record as being more consistent with nerve pain (e.g., shocks, pins and needles, burning) rather than incisional pain in the palm or distal forearm. Patients in this study group must also have had improvement in postoperative electromyogram and nerve conduction studies or ultimately had resolution in their reawakening symptoms at long-term follow-up. Patients with signs and symptoms meeting criteria for complex regional pain syndrome were excluded. Additional exclusion criteria included patients under 18 years old, acute carpal tunnel syndrome, concern for incomplete release or need for early revision surgery, cervical radiculopathy, peripheral neuropathy, or concurrent procedures at the time of carpal tunnel release. A comparison group comprised all patients who were not a part of the case group and did not meet exclusion criteria. For patients who underwent bilateral carpal tunnel release, data were recorded for only one hand, which was selected at random (left or right). Comparison patients with an incomplete data set for individual variables were not included for that portion of the analysis. Demographic data, medical history, carpal tunnel history, and electromyogram and nerve conduction studies findings were collected. All details of reawakening patients’ symptoms and care were recorded.

A comparison of characteristics between patients who experienced reawakening syndrome and those who did not was made using t test for continuous characteristics and Fisher exact tests for binary and categorical characteristics. In addition, odds ratios for risk factors for reawakening syndrome were estimated using logistic regression; separate models were fit for each risk factor. Goodness of fit was assessed using the area under the receiver operating characteristic curve. Time to improvement among patients with reawakening phenomenon was estimated using the method of Kaplan and Meier. All analyses were performed using Stata software (version 15; StataCorp LLC, College Station, Texas). Statistical significance was defined as p less than 0.05. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. This article does not contain any studies with human or animal subjects. A retrospective review of existing, deidentified data was approved by the local institutional review board as exempt.

**RESULTS**

A total of 748 carpal tunnel releases were performed on 640 patients in the study period. Seventeen patients were found to have symptoms consistent with reawakening phenomenon of the median nerve. Two hundred patients were excluded [35 acute carpal tunnel syndrome; 36 carpal tunnel releases performed as exposure for another surgical indication (i.e., tendon retrieval for repair); 88 carpal tunnel releases performed in conjunction with another surgery; 41 revision carpal tunnel releases]. There were no exclusions of patients due to suspicion of postoperative complex regional pain syndrome or incomplete release. After exclusion criteria were met, 423 patients remained who comprised the comparison group. Postoperative follow-up was 13 months in the reawakening cohort and 7.1 months in the comparison group (p = 0.1039).

Demographic data and details associated with the patients’ carpal tunnel symptoms and release
are documented in Table 1. Older age at presentation \((p < 0.0001)\) and evidence of thenar atrophy on preoperative examination \((p < 0.0001)\) were strongly statistically significant indicators for developing reawakening phenomenon. Figure 1 presents odds ratios estimate from logistic regressions to quantify the risk of each potential risk factor. Goodness of fit varied by covariate, ranging from 0.501 for major depression to 0.769 for age. Increased length of symptoms before presentation to a hand surgeon was not statistically significant \((4.9 \text{ years in reawakening patients versus 2.9 years in the comparison group, } p = 0.069)\) (Fig. 2). Other clinical characteristics of interest that did not meet statistical significance include patient sex \((p = 0.027)\), open versus endoscopic release \((p = 0.644)\), smoking status \((p = 0.137)\), diabetes \((p = 0.165)\). Although the documented presence of osteoarthritis in the wrist and hand was statistically different between groups \((p = 0.001)\), it was not objectively measured and is unlikely clinically significant.

Electromyography testing data is shown in Table 2. In the reawakening cohort, 10 of 17 had a preoperative electromyogram. When present, abductor pollicis brevis fibrillations \((n = 7)\) were recorded a mean of 2.07 \((\text{range, 1 to 3})\). When abductor pollicis brevis sharp waves were present \((n = 7)\), there was a mean of 1.86 \((\text{range, 1 to 3})\). In the comparison cohort, 357 of 423 had a preoperative electromyogram. When present, abductor pollicis brevis fibrillations \((n = 47)\) were recorded a mean of 1.49 \((\text{range, 1 to 3})\). When abductor pollicis brevis sharp waves were present \((n = 40)\), there was a mean of 1.38 \((\text{range, 1 to 3})\). When factoring in the patient with negative findings, presence of abductor pollicis brevis fibrillations \((p = 0.0001)\) and sharp waves \((p = 0.027)\) were significantly more frequent in the reawakening cohort.

Fourteen of 17 patients who experienced reawakening after carpal tunnel release noted resolution of their neuropathic pain at an average period of 4.4 months \((\text{mean age, 75.2 years; length of symptoms, 5.4 months; nine of 14 had})\)

| Variable                      | Case \((n = 17)\) | Control \((n = 423)\) | \(p\) |
|-------------------------------|------------------|---------------------|------|
| Age, years                    | 71.1 (SD 15.54)  | 57.4 (SD 14.44)     | 0.0001 |
| Sex                           |                  |                     |      |
| Male                          | 11 (64.71%)      | 162 (38.30%)        | 0.04 |
| Female                        | 6 (35.29%)       | 261 (61.70%)        |      |
| Race                          |                  |                     |      |
| White                         | 15 (88.24%)      | 370 (88.10%)        | 0.99 |
| Non-white                     | 2 (11.76%)       | 50 (11.90%)         |      |
| Marital status                |                  |                     |      |
| Married                       | 8 (47.06%)       | 243 (57.45%)        | 0.591 |
| Single                        | 3 (17.65%)       | 70 (16.35%)         |      |
| Widowed                       | 3 (17.65%)       | 45 (10.64%)         |      |
| Divorced                      | 3 (17.65%)       | 11.35 (11.40%)      |      |
| Separated                     | 0 (0.00%)        | 17 (4.02%)          |      |
| Employment                    |                  |                     |      |
| Unemployed                    | 2 (12.50%)       | 57 (14.81%)         | 0.057 |
| Manual labor                  | 1 (6.25%)        | 49 (12.73%)         |      |
| Nonmanual labor               | 3 (18.75%)       | 137 (35.58%)        |      |
| Retired                       | 10 (62.50%)      | 99 (25.71%)         |      |
| Disabled                      | 0 (0.00%)        | 43 (11.17%)         |      |
| Surgery type                  |                  |                     | 0.99 |
| Open                          | 16 (94.12%)      | 387 (91.45%)        |      |
| Endoscopic                    | 1 (5.88%)        | 36 (8.55%)          |      |
| Smoking status                |                  |                     |      |
| Non-smoker                    | 11 (64.71%)      | 277 (65.48%)        | 0.113 |
| Former smoker                 | 3 (17.65%)       | 29 (6.88%)          |      |
| Smoker                        | 3 (17.65%)       | 117 (27.66%)        |      |
| Comorbidities                 |                  |                     |      |
| Diabetes                      | 8 (47.06%)       | 134 (31.67%)        | 0.18 |
| Osteoarthritis                | 6 (35.29%)       | 44 (10.40%)         | 0.006 |
| Hypertension                  | 10 (58.82%)      | 263 (62.17%)        | 0.806 |
| Anxiety                       | 6 (35.29%)       | 87 (20.57%)         | 0.224 |
| Depression                    | 6 (35.29%)       | 146 (34.31%)        | 0.99 |
| Opioids                       | 1 (5.88%)        | 5 (1.18%)           | 0.226 |
| Drug abuse                     | 1 (5.88%)        | 5 (1.19%)           | 0.192 |
| Thenar atrophy                | 10 (58.82%)      | 57 (13.48%)         | <0.0001 |
| Length of symptoms, years     | 4.92 (SD 7.88)   | 2.89 (SD 4.29)      | 0.069 |
Fig. 1. Odds ratios for risk of reawakening phenomenon. Note separate logistical regression models were fit for each risk factor.

Fig. 2. Histogram of the length of carpal tunnel symptoms for patients in each cohort.
thenar atrophy). The three patients who remained subjectively symptomatic had a normal (n = 2) or improved (n = 1) electromyogram and nerve conduction studies postoperatively (mean age, 51.6 years; length of symptoms, 2.5 years; one of three had thenar atrophy). A diagram of length of time to improvement is shown in Figure 3.

**DISCUSSION**

We have defined reawakening phenomenon as an increase in neuropathic pain in the median nerve distribution of the hand following an uneventful carpal tunnel release without any other identifiable cause. Our data suggest that this is most likely to occur in older individuals with evidence of thenar atrophy. Although it has not been described previously, it may be considered expected in this cohort of patients. We believe it is important to identify those patients at risk and provide appropriate perioperative counseling.

In our cohort of patients with reawakening phenomenon, we did find that there was some variation in the distribution of the pain they described postoperatively. Specifically, not all patients stated that the entirety of the median nerve distribution of their hand had worsened pain, but instead, it may have only affected their index or long finger. Nevertheless, it was problematic enough to draw attention to it at their first postoperative appointment often prompting additional diagnostic testing not routinely performed following carpal tunnel release at our institution. Documentation of the exact distribution of the pain was not precise enough to describe here. In addition, an objective measure of pain intensity, such as a visual analogue pain score, was not routinely documented.

Our reawakening cohort was followed for an average period of 13 months following their procedures. Over that time, 14 of the 17 patients had complete recovery (no persistent pain or paresthesia) at an average period of 4.4 months. During that time, providers occasionally treated patients with a gamma-aminobutyric acid analogue for nerve pain with modest improvement for some individuals. The remaining three patients in the cohort never experienced subjective improvement during their follow-up period but all had electromyogram and nerve conduction studies demonstrating objective improvement. The sample size for this group precluded statistical subgroup analysis.

The lack of improvement for some of our patients and the reported 2 to 5 percent rate of complex regional pain syndrome following carpal tunnel may raise suspicion that our findings are more indicative of a failure to diagnose complex regional

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**Table 2. Mean Value of Fibrillations and Sharp Waves on Electromyogram and Nerve Conduction Studies**

| Variable       | Case (n = 10) | Control (n = 357) | p   |
|----------------|--------------|-------------------|-----|
| Fibrillations  | 1.5 (SD 1.21)| 0.2 (SD 0.55)     | 0.0001|
| Sharp waves    | 1.3 (SD 1.16)| 0.1 (SD 0.48)     | 0.027 |

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**Fig. 3.** Time to improvement of symptoms among patients with reawakening phenomenon. Note that, as of the end of follow-up, three patients reported no subjective improvement.
pain syndrome than of the identification of new pathology. Complex regional pain syndrome is a distinct problem, however, with multiple, simultaneous symptoms that often present in a delayed fashion. Distinct clinical manifestations from autonomic dysfunction (e.g., sweating, swelling, changes in skin temperature, alterations to the hair and nail growth pattern) in combination with the neuropathic pain make this diagnosis discernible from the reawakening phenomenon described in this article. All charts were extensively reviewed for any signs concerning for complex regional pain syndrome, and patients having those symptoms were excluded.

Since we are unable to characterize the physiologic changes occurring at the nerve level during reawakening phenomenon, it is possible there is some overlap between the two processes. Development of complex regional pain syndrome has been extensively studied and is linked to inflammation and increased inflammatory cytokines like interleukin 1β and substance P. Conversely, there is a relative paucity of understanding or data behind the physiologic recovery of peripheral nerves following decompression. Certainly, one would expect some level of inflammation to return to the area as increased size of the carpal tunnel results in decreased pressure, improved perfusion, and an influx of inflammatory cells. As the hand that was once asleep reawakens, remyelination of the nerve takes place, and compound muscle action potential improves. However, data show that there is relatively limited improvement in the compound sensory action potential. Sensory nerves appear to be more susceptible to sustained compression, and the damage that results is more permanent. Limited recovery may also coincide with limited inflammation, and the physiologic reason for reawakening phenomenon may be entirely different from complex regional pain syndrome.

Ultimately, until further studies can identify the cause and interventions to prevent reawakening phenomenon, preoperative patient education for those at risk is important. Discussing this postoperative course with older patients who presented with prolonged carpal tunnel symptoms and the severe damage on examination or on electromyogram can improve patient satisfaction should it occur. If it does, short courses of gamma-aminobutyric acid analogues can be used for symptomatic relief, understanding that the process is self-limiting with resolution typically in less than 5 months.

There are limitations to this study. First, it was performed in a retrospective manner, potentially introducing bias. Inaccurate documentation of the phenomenon or overassessment of the process is always a possibility in any study performed in this fashion. Second, selection bias is a conceivable problem. Patients’ charts were reviewed by several authors with little interobserver variation, however. Third, the number of patients in the reawakening cohort is relatively small, and further studies or collaboration with other institutions may be beneficial to increase sample size and better elicit variables that put patients at risk. A prospective, multicenter study with defined objective measurement of multiple variables would be best suited to overcome these limitations.

**CONCLUSIONS**

Median nerve reawakening following carpal tunnel release has not been previously described but occurs in approximately 3.9 percent of all patients in our population. Positive predictors include advanced age, evidence of abductor pollicis brevis damage on electromyogram, and longer duration of symptoms before presentation. Preoperative counseling of patients at higher risk for the reawakening phenomenon is recommended.