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“Combined Carpal Tunnel Release and Palmar Fasciectomy for Dupuytren’s Contracture Does Not Increase the Risk for Complex Regional Pain Syndrome”

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Abstract

Background

Hand surgery dogma suggests that simultaneous surgical treatment of carpal tunnel syndrome (CTS) and Dupuytren's contracture (DC) results in an increased incidence of Complex Regional Pain Syndrome (CRPS). As a result, many surgeons do not perform surgery for the two conditions concurrently. Our goal was to determine the extent of this association.

Methods

We identified all patients undergoing surgical treatment for CTS, DC, or both between April 1982 and March 2017 using the Indiana Network for Patient Care (INPC), a large, multi-institutional, statewide information exchange. Demographics, comorbidities, and 1-year post-operative incidence of CRPS were recorded.

Results

A total of 51,739 (95.6%) patients underwent carpal tunnel release (CTR) only, 2,103 (3.9%) underwent palmar fasciectomy (PF) only, and 305 (0.6%) underwent concurrent CTR and PF.

There was no difference in the likelihood of developing CRPS ($p=0.163$) between groups.

Independent risk factors for developing CRPS were younger age, anxiety, depression, epilepsy, gout, and history of fracture of the radius, ulna, or the carpus.

Conclusions

Concurrent CTR and PF is not associated with an increased risk for developing CRPS. Patient demographics, medical comorbidities, and a history of upper extremity trauma are associated with the development of CRPS after surgery and should be discussed preoperatively as potential risk factors.

Introduction

Complex regional pain syndrome (CRPS) is a chronic, debilitating syndrome characterized by pain, trophic changes, and autonomic dysfunction that can occur after minor upper extremity trauma or surgery[1, 2]. It has been reported to occur after common procedures in hand surgery, such as those used to treat carpal tunnel syndrome (CTS)[3] and Dupuytren's contracture (DC)[4]. CTS and DC can occur simultaneously and surgeons may have to consider concurrent surgical treatment.

Early observational studies of concurrent surgical treatment of CTS and DC suggest that there is an increased risk for developing CRPS[5, 6]. A recent meta-analysis, however, suggests that this increased risk may be smaller than previously thought[7]. Despite this, a survey of hand surgeons demonstrated that only half would be willing to perform surgical treatment of each condition simultaneously, given the concerns for development of CRPS[8].

The primary aim of this study is to assess whether simultaneous surgical treatment of DC and CTS results in an increased incidence of CRPS. Further, we sought to determine if other patient-related variables previously identified as risk factors for CRPS[9, 10] contribute to the development of CRPS after surgery.

Methods

Data Source

A database of unique, de-identified patients was built from the Indiana Network for Patient Care (INPC) using all patients who underwent treatment for DC or CTS from April 16, 1982 through March 27, 2017. The predecessor to the INPC was developed in 1972 as an electronic medical record; this evolved into a multi-institutional health information exchange containing longitudinal patient data throughout the continuum of inpatient and outpatient

healthcare in multiple settings, including outpatient surgery centers, predominantly in the state of Indiana[11-13]. Further, the majority of health care institutions in the state of Indiana participate in the INPC[14]. Each patient is assigned a unique global identifier and an algorithm is used to match patients with their health data based on associated unique identifiers, such as name, birth date, and demographic information[15]. Data are imported in real time directly from each institution's proprietary electronic medical record systems, and are subsequently validated by comparison to with insurance claims, billing submissions, operative reports, public health records, and pharmacy records. Data is reviewed by a clinical data analyst and provided by the Regenstreif Institute for research purposes[16]. The INPC currently includes data from over 38 health systems with greater than 13 million patients and 11 billion clinical data elements.

Patient Sample and Variables

Patients were divided into three cohorts—those who underwent CTR only (Current Procedural Terminology (CPT) codes 64721 or 29848), PF only (either CPT 26125, 26123, 26121, or 26045), or both CTR and PF during the same encounter. The diagnosis of CRPS, based on International Classification of Disease (ICD) codes (ICD-9 337.21, 354.4, 337.20; ICD-10 G56.4, G90.50, G90.51, G90.511, G90.512, G90.513, G90.519, G90.59), within one year of surgery was recorded. Comorbidities previously reported to be risk factors for CRPS were also recorded. Patient data were stored and analyzed using Indiana University Cloud computing and Microsoft Excel (Redmond, Washington, USA) in compliance with the Health Insurance Portability and Accountability Act of 1996 (HIPAA). All procedures followed were in accordance with the ethical standards of the Institutional Review Board of Indiana University.

Statistics

Univariate analyses were conducted to describe the population sample. Chi-square tests and Fisher's exact tests were computed to report the bivariate relationships between variables. To examine the extent of bivariate relationships, we calculated odds ratio with 95% confidence intervals and p-values using simple logistic regressions. To examine the relationship between different surgical treatments and CRPS we used multivariable logistic regression analysis controlling for the effect of sex, race, age, and comorbidities. Statistical analyses were conducted at 0.05 level of significance using Stata/SE 14.2 software (College Station, Texas, USA).

Results

A total of 54,147 patients met inclusion criteria; 51,739 (95.6%) underwent CTR only, 2,103 (3.9%) underwent PF only, and 305 (0.6%) underwent concurrent surgery. Table 1 illustrates demographic differences between groups. Those undergoing concurrent surgery were more likely to be male and white. Comorbidities were most prevalent in patients undergoing concurrent surgery and least prevalent in patients undergoing PF (Table 2). Diabetes, epilepsy, hypercholesterolemia, hyperlipidemia, osteoarthritis, and radius or ulna fractures were most common in patients undergoing concurrent surgery.

CRPS occurred in 298 patients (0.58%) after CTR only, 7 patients (0.33%) after PF only, and 3 patients (0.98%) who underwent concurrent surgery. There was no statistically significant difference in the risk for CRPS based on surgical group ($p=0.163$, and Table 3). Type of surgery within each group also did not significantly increase the risk of developing CRPS (See Table, Supplemental Digital Content 1, which shows the 1 year incidence of CRPS based on CPT code); specifically, endoscopic carpal tunnel release had the same risk for developing CRPS as open carpal tunnel release. Female sex, alcohol abuse, anxiety, depression, epilepsy, gout, radius or ulna fracture, wrist fracture, and wrist sprain were risk factors for CRPS in bivariate analysis.

On multivariable analysis, independent risk factors for CRPS were younger age, anxiety, depression, epilepsy, gout, radius or ulna fracture, and wrist fracture (Table 4). Having any comorbid condition increased the likelihood of CRPS 3.31 times ($p < 0.001$). The average age of patients developing post-operative CRPS was 47.9 (± 12.0) years, compared to 51.5 (± 14.7) years for patients who did not develop CRPS ($p < 0.001$). Multivariable analysis yielded similar results after applying a variable selection procedure (See Table, Supplemental Digital Content 2, which shows adjusted risk factors for developing CRPS after using a stepwise logistic regression to determine only variables whose p -values are ≤ 0.10).

Discussion

Many hand surgeons avoid simultaneous surgical treatment of CTS and DC because of concerns regarding development of CRPS[8]. In this study, we have shown that simultaneous CTR and PF does not increase the risk for developing CRPS. Thus, surgeons may consider performing the procedures concurrently without placing the patient at an increased risk for postoperative pain sequelae.

Rather than the type of surgery, we found that comorbidities were the best predictors for development of CRPS. Anxiety and depression were risk factors for CRPS in this study. This may be due to a shared neuropathophysiology, as similar brain regions are affected in CRPS[17, 18], depression[19, 20], and generalized anxiety disorder[21, 22]. Others have also shown that anxiety and anxious traits are risk factors for developing CRPS[17, 18, 23, 24], although this is controversial[25]. Abnormal neural functioning and pathways in the central nervous system being central to the pathogenesis of CRPS[26] may account for this and other studies[10, 27] finding epilepsy as a risk factor for CRPS. Understanding the neuropsychological profile of

patients most likely to develop CRPS allows the surgeon to identify at-risk patients during the initial consultation.

We found a statistically significant inverse correlation between age and incidence of post-operative CRPS. There is disagreement in the literature regarding age as a risk factor for CRPS. Some studies show increased age increases the risk for CRPS, other studies show decreasing age is a risk factor for CRPS, and yet other studies shows no correlation[9]. As one ages, the ability to develop new pathologic neuronal connections decreases and this may provide a modest level of protection against the development of CRPS. Further research is necessary to confirm the role of neuronal plasticity as it relates to CRPS.

Systemic disease has been inconsistently associated with an increased risk for developing CRPS. In this study, we found hyperlipidemia, hypercholesterolemia, and gout to be independent risk factors for CRPS. Hyperlipidemia was a risk factor for CRPS in some studies[28, 29], involved only in the initial stages of the disease in another[30], and unrelated in other studies[10, 30-32]. A mechanism by which hyperlipidemia may predispose the development of CRPS is by increasing the substrate used to synthesize pro-inflammatory 2-series prostanoids, 4-series leukotrienes, and other mediators of inflammation, vasomotor changes, and pain[28, 33, 34]. This hypothesis is supported by empiric data demonstrating that certain lipid derivatives are elevated in the serum of patients with CRPS compared with healthy controls[28, 35]. Hypercholesterolemia similarly has been inconsistently associated with the development of CRPS in other studies[10, 29, 36]. Lastly, our data is consistent with other research indicating an association between CRPS, elevated uric acid levels[29], and acute post-operative gout[37, 38].

In the majority of cases of CRPS, localized trauma is reported as the inciting event. We found that prior fracture of the radius, ulna, or wrist are independent risk factors for development

of CRPS; this is consistent with previously published data[10, 39]. Several theories regarding the pathophysiology of CRPS exist. Perhaps the most well accepted theory is that of a tissue or nerve injury causing aberrant release of chemical mediators in the susceptible individual. This, in turn, leads to maladaptive changes in the nervous and vascular systems[40]. These changes may cause immediate development of CRPS or predispose to future development with subsequent trauma[41]. This theory accounts for our findings of prior fracture of the radius, ulna, or wrist as independent risk factors for development of CRPS after surgery.

Whereas generalizability is a concern with all state-based patient registries, our patient demographics are consistent with those published in previous studies. Others have shown that DC is more prevalent in older, white male patients[42, 43] and CTS is more prevalent in younger, female patients[8, 44]. Further, consistent with other studies, we found that concurrent surgery is more frequently performed in males[5] and concurrent surgery patients are generally older than CTS patients[8].

Our study has several limitations related to the data source and the retrospective nature of the review. Patient attrition and missing data remain a concern with large databases and internal quality is difficult to confirm. For example, patient race was not reported by several institutions and this limited our demographic assessment. We attempted to minimize biases due to patient dropout and missing data by only including patients that had an INPC encounter before and after the study period. As a database built from input throughout the continuum of healthcare, there may be errors in diagnosis and procedural coding. The INPC mitigates this risk by comparing codes input directly by healthcare providers with those submitted for billing and insurance claims [13-15]. Finally, this study does not investigate complications other than CRPS after concurrent CTR and PF, yet these findings may be clinically significant.

Conclusion

This study demonstrates that concurrent CTR and PF does not increase the likelihood for developing CRPS. Factors associated with CRPS after surgery for CTS and DC include younger age, anxiety, depression, epilepsy, gout, and forearm and wrist fractures. Based on these data, we recommend simultaneous surgery for patients with CTS and DC after an informed discussion of the likelihood for CRPS in the at-risk population.

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Supplemental Digital Content Legends

Table, Supplemental Digital Content 1, which shows the influence of type of surgery for CTR and PF on developing CRPS. The 1-year postoperative incidence of CRPS based on CPT code is shown, [INSERT HYPER LINK](#).

Table, Supplemental Digital Content 2, which shows the adjusted Risk Factors for Developing CRPS after Surgery Using Variable Selection. A stepwise logistic regression was used to determine only the variables whose p-values are ≤ 0.10 , except forcing type of surgery into the model, [INSERT HYPER LINK](#).

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Table 1. Patient Demographics

	Carpal Tunnel Release		Palmar Fasciectomy		Concurrent Surgery	
	Patients (%)	<i>p</i>	Patients (%)	<i>p</i>	Patients (%)	<i>p</i>
Sex						
Female	35,266 (68.4)	<0.001	658 (31.4)	<0.001	146 (48.0)	<0.001
Male	16,305 (31.6)		1,440 (68.6)		158 (52.0)	
Race						
White	18,386 (85.6)	0.001	502 (89.5)	0.011	119 (93.7)	0.013
Non-white	3,092 (14.4)		59 (10.5)		8 (6.3)	
Age (years)						
Mean (±SD)	51.2 (±14.6)		58.3 (±14.0)		57.9 (±11.7)	

SD, Standard deviation.

Table 2. Patient Comorbidities

	CTR Only	PF Only	Concurrent Surgery
	Patients (%)	Patients (%)	Patients (%)
Alcohol abuse	3,448 (6.7)	162 (7.7)	27 (8.9)
Anxiety	10,235 (19.8)	229 (10.9)	62 (20.3)
Depression	22,638 (43.8)	558 (26.5)	128 (42.0)
Diabetes	19,357 (37.4)	714 (34.0)	146 (47.9)
Epilepsy	2,568 (5.0)	72 (3.4)	24 (7.9)
Fibromyalgia	1,235 (2.4)	15 (0.7)	4 (1.3)
Gout	3,695 (7.1)	157 (7.5)	25 (8.2)
Hypercholesterolemia	17,424 (33.7)	733 (34.9)	137 (44.9)
Hyperlipidemia	33,100 (64.0)	1429 (68.0)	235 (77.1)
Hyperparathyroidism	822 (1.6)	18 (0.9)	6 (2.0)
Multiple Sclerosis	731 (1.4)	6 (0.3)	3 (1.0)
Osteoarthritis	28,758 (55.6)	928 (44.1)	200 (65.6)
Finger fracture	1,571 (3.0)	62 (3.0)	12 (3.9)
Hand fracture	1,085 (2.1)	43 (2.0)	8 (2.6)
Radius or Ulnar fracture	3,249 (6.3)	81 (3.9)	29 (9.5)
Wrist fracture	1560 (3.0)	31 (1.5)	6 (2.0)
Wrist sprain	3,488 (6.7)	62 (3.0)	23 (7.5)
Any comorbidities	45,770 (88.5)	1786 (84.9)	284 (93.1)

CTR, carpal tunnel release; PF, palmar fasciectomy

Table 3. Risk Factors for Developing Complex Regional Pain Syndrome after Surgery

	Patients (%)	OR [95% CI]	<i>p</i>
Type of Surgery			
CTR only	298 (0.58)		
PF only	7 (0.33)	0.58 [0.27, 1.22]	0.15
Concurrent Surgery	3 (0.98)	1.71 [0.55, 5.38]	0.355
Sex			
Female	224 (0.62)	1.33 [1.03, 1.7]	0.028
Male	84 (0.47)		
Race			
White	127 (0.67)	0.81 [0.53, 1.24]	0.331
Non-white	26 (0.82)		
Comorbidity			
Alcohol Abuse	38 (1.04)	1.96 [1.40, 2.76]	<0.001
Anxiety	108 (1.03)	2.25 [1.78, 2.85]	<0.001
Depression	197 (0.84)	2.36 [1.87, 2.98]	<0.001
Diabetes	124 (0.61)	1.13 [0.90, 1.42]	0.288
Epilepsy	33 (1.24)	2.34 [1.62, 3.36]	<0.001
Fibromyalgia	10 (0.80)	1.42 [0.75, 2.67]	0.278
Gout	35 (0.90)	1.67 [1.17, 2.38]	0.005
Hypercholesterolemia	101 (0.55)	0.96 [0.75, 1.21]	0.712
Hyperparathyroidism	3 (0.35)	0.62 [0.20, 1.93]	0.408
Multiple Sclerosis	7 (0.95)	1.68 [0.79, 3.58]	0.174
Osteoarthritis	187 (0.63)	1.26 [1.00, 1.58]	0.051

Finger fracture	10 (0.61)	1.07 [0.57, 2.02]	0.831
Hand fracture	9 (0.79)	1.41 [0.72, 2.74]	0.314
Radius or Ulna fracture	38 (1.13)	2.14 [1.52, 3.01]	<0.001
Wrist fracture	24 (1.50)	2.81 [1.85, 4.27]	<0.001
Wrist sprain	41 (1.15)	2.19 [1.57, 3.04]	<0.001
Any comorbidities	295 (0.62)	3.00 [1.72, 5.24]	<0.001

OR, odds ratio; 95% CI, 95% confidence interval.

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Table 4. Adjusted Risk Factors for Developing Complex Regional Pain Syndrome after Surgery

	Adjusted OR [95% CI]	<i>p</i>
Type of Surgery		
CTR only		
PF only	0.807 [0.377-1.728]	0.581
Concurrent Surgery	1.854 [0.586-5.865]	0.293
Sex		
Male		
Female	1.076 [0.826-1.402]	0.587
Race		
Non-white		
White	0.741 [0.482-1.137]	0.170
Age	0.987 [0.978-0.997]	0.008
Comorbidities		
Alcohol abuse	1.237 [0.861-1.778]	0.249
Anxiety	1.498 [1.146-1.958]	0.003
Depression	1.777 [1.353-2.334]	<0.001
Diabetes	1.001 [0.773-1.297]	0.993
Epilepsy	1.520 [1.036-2.230]	0.032
Fibromyalgia	0.854 [0.448-1.628]	0.632
Gout	1.718 [1.188-2.483]	0.004
Hypercholesterolemia	0.965 [0.722-1.290]	0.810
Hyperlipidemia	0.796 [0.592-1.072]	0.133

Hyperparathyroidism	0.496 [0.157-1.563]	0.231
Multiple Sclerosis	1.179 [0.551-2.524]	0.672
Osteoarthritis	1.204 [0.925-1.567]	0.167
Finger fracture	0.688 [0.359-1.319]	0.260
Hand Fracture	0.854 [0.424-1.723]	0.660
Radius or Ulnar fracture	1.495 [1.000-2.235]	0.050
Wrist fracture	1.665 [1.013-2.737]	0.044
Wrist sprain	1.386 [0.974-1.972]	0.070

OR, odds ratio; 95% CI, 95% confidence interval

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SDC 1

The influence of type of surgery for CTR and PF on developing CRPS

CPTs Code	CRPS		p-value
	No CRPS Patients (percent)	CRPS Patients (percent)	
CTR			0.165
64721	47,846 (99.45)	265 (0.55)	
29848	3,376 (99.26)	25 (0.74)	
PF			0.052
26125	18 (100.00)	0 (0.00)	
26123	795 (100.00)	0 (0.00)	
26121	403 (99.26)	3 (0.74)	
26045	168 (98.82)	2 (1.18)	

CPT, Current Procedural Terminology; CTR, carpal tunnel release; PF, palmar fasciectomy.
CPTs in each category of CTR or PF is exclusive of the other CPTs in the same category.
The 1-year postoperative incidence of CRPS based on CPT code is shown.

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SDC 2

Adjusted Risk Factors for Developing CRPS after Surgery Using Variable Selection

	Adjusted OR [95% CI]	p
Type of Surgery		
CTR only		
PF only	0.777 [0.365-1.654]	0.513
Concurrent Surgery	1.843 [0.584-5.812]	0.297
Age	0.989 [0.981-0.998]	0.016
Comorbidities		
Anxiety	1.494 [1.151-1.940]	0.003
Depression	1.799 [1.386-2.335]	<0.001
Epilepsy	1.510 [1.036-2.199]	0.032
Gout	1.707 [1.188-2.452]	0.004
Hyperlipidemia	0.797 [0.620-1.023]	0.075
Radius or Ulnar fracture	1.475 [0.989-2.200]	0.057
Wrist fracture	1.669 [1.019-2.733]	0.042
Wrist sprain	1.383 [0.976-1.961]	0.068

CRPS, complex regional pain syndrome; OR, odds ratio; 95% CI, 95% confidence interval; CTR, carpal tunnel release; PF, palmar fasciectomy. A stepwise logistic regression was used to determine only the variables whose p-values are ≤ 0.10 , except forcing type of surgery into the model.

ACCEPTED