

Review

# A Review of Carpal Tunnel Syndrome and Its Association with Age, Body Mass Index, Cardiovascular Risk Factors, Hand Dominance, and Sex

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Received: 10 April 2020; Accepted: 13 May 2020; Published: 18 May 2020



**Featured Application:** Researchers in the CTS area can use findings and summaries obtained in this research to quickly know their state of the art, the treatments used and the risk factors studied.

**Abstract:** Carpal tunnel syndrome (CTS) is one of the most common compressive, canalicular neuropathies of the upper extremities, causing hand pain and impaired function. CTS results from compression or injury of the median nerve at the wrist within the confines of the carpal tunnel. Parameters such as age, sex, and body mass index (BMI) could be risk factors for CTS. This research work aimed to review the existing literature regarding the relationship between CTS and possible risk factors, such as age, sex, BMI, dominant hand, abdominal circumference, respiratory rate, blood pressure, and cardiac rate to determine which ones are the most influential, and therefore, take them into account in subsequent applied research in the manufacturing industry. We performed a literature search in the PubMed, EBSCO, and ScienceDirect databases using the following keywords: carpal tunnel syndrome AND (age OR sex OR BMI OR handedness OR abdominal circumference OR respiratory rate OR blood pressure OR cardiac rate). We chose 72 articles by analyzing the literature found based on selection criteria. We concluded that CTS is associated with age, female sex, and high BMI. Trends and future challenges have been proposed to delve into the relationship between risk factors and CTS, such as correlation studies on pain reduction, analysis of weight changes to predict the severity of this pathology, and its influence on clinical treatments.

**Keywords:** carpal tunnel syndrome; influence; relationship; risk factors

## 1. Introduction

Entrapment neuropathies are the most frequent mono-neuropathies encountered in clinical practice. In these neuropathies, the nerve is damaged at sites where it passes through narrow, restricted spaces. Although entrapment neuropathies affect only a small portion of the nerve, they can have substantial physical, psychological, and economic consequences [1]. Carpal tunnel syndrome (CTS) is one of the most common compressive, canalicular neuropathies of the upper extremities, and a frequent cause of hand pain and impaired function. CTS results from compression or injury of the median nerve at the wrist within the confines of the carpal tunnel. Patients with CTS usually experience pain, numbness, tingling, and a sensation of swelling over the median nerve distribution area of the hand. A classic reported symptom is awakening at night due to numbness and pain in their hand, occasionally extending to the shoulders, but is relieved by shaking the wrist [2].

CTS represents a major occupational health problem with high social and economic implications [3]. Mexico has a yearly incidence of CTS of approximately 99 for every 100,000 persons, with a prevalence of about 3.4% in women and 0.6% in men [4].

The costs associated with this pathology are diverse, which are due to health care, surgical intervention, and rehabilitation, estimated that the United States spends one billion US dollars per year. Regarding to a loss of productivity from the employee, economic compensations from companies, and missing work, are calculated at 30 processing days [5].

The prevalence of CTS in the general population has been estimated to be between 7% and 19% given the caveats about the case definition, and its etiology is multifactorial and includes systemic disorders, such as diabetes mellitus, hypothyroidism, and obesity; post-menopausal females are also commonly affected [6].

Systemic, anatomical, idiopathic, and ergonomic factors could be significant in the etiology since some parameters such as age, sex, and body mass index (BMI) could be risk factors for CTS. A BMI value over 30 is classified as obesity; although some studies show a relationship between BMI and CTS, its relationship with anthropometric measurements, such as waist circumference and wrist circumference, is not clear [7].

This research work aimed to review the existing literature regarding the relationship between CTS and possible risk factors, such as age, sex, BMI, dominant hand, abdominal circumference, respiratory rate, blood pressure, and cardiac rate, to determine which ones are the most influential, and therefore, take them into account in subsequent applied research in the manufacturing industry.

Nevertheless, no studies that linked CTS to the abdominal circumference or respiratory rate were found; however, we identified articles that, in addition to the established factors, included anthropometric, occupational, and ergonomic factors, among others, which are described in this paper.

## 2. Methodology

### 2.1. Search Strategy

A bibliographic search carried out during November 2019 included the following keywords in PubMed, EBSCO, ScienceDirect databases: carpal tunnel syndrome AND (age OR sex OR BMI OR handedness OR abdominal circumference OR respiratory rate OR blood pressure OR cardiac rate). It is worth mentioning that these study factors were chosen because they have been considered for a practical study to be carried out in the manufacturing industry.

### 2.2. Screening and Eligibility Results

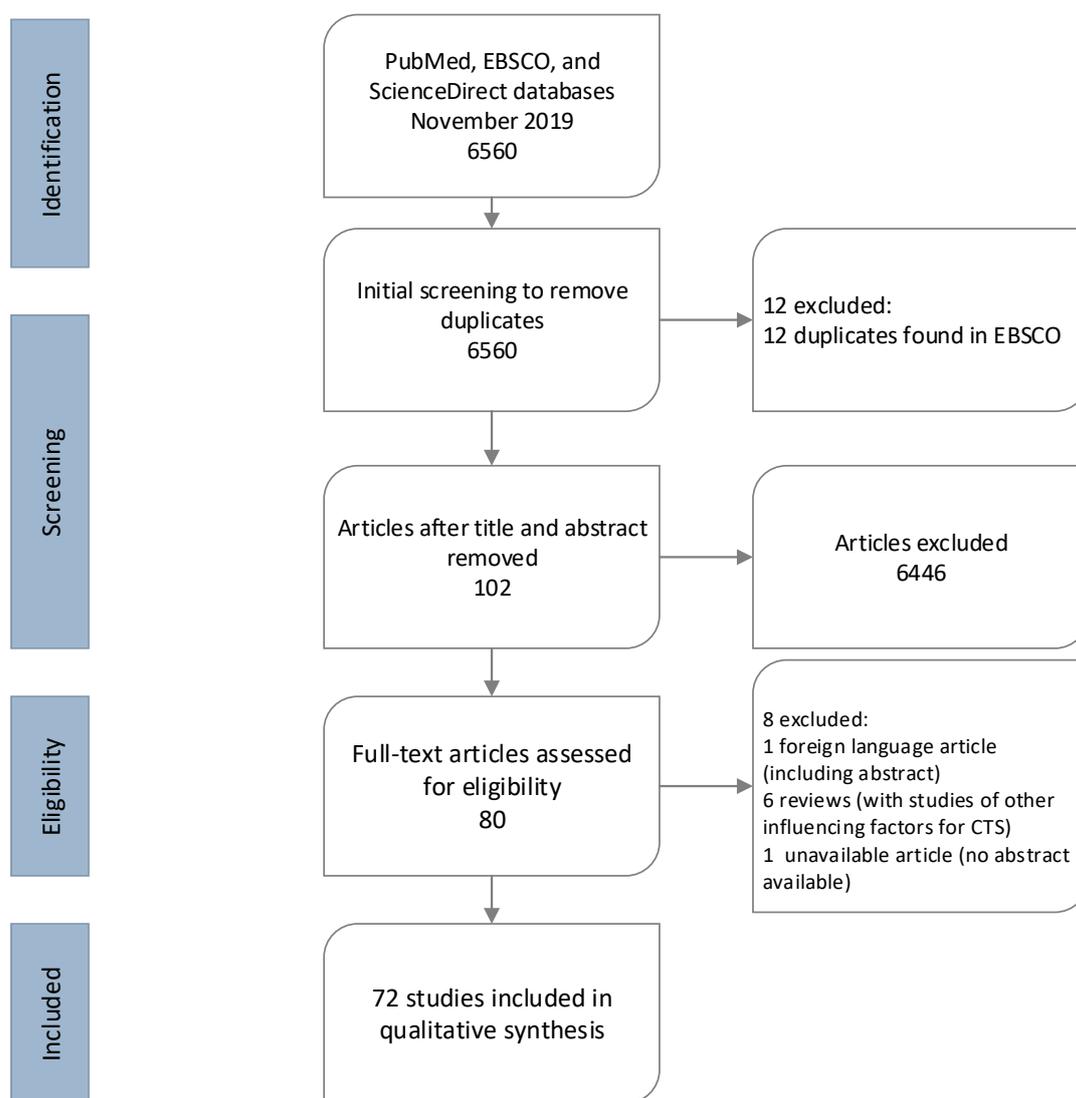
Initially, we reviewed the titles and abstracts of the articles displayed in each database used for this review, duplicated papers in databases were identified, and the selection criteria were established as described below:

First criterion: Throughout the review of the titles and abstracts, we kept the papers concerning CTS and the desired risk factors such as age, sex, BMI, dominant hand, abdominal circumference, respiratory rate, blood pressure, and heart rate.

Second criterion: No reviews were considered.

Third criterion: Articles written in a language other than English or Spanish were rejected.

Once we selected the works meeting the established criteria, we proceeded to carry out a complete review of each work, which meant recording the authors, year of publication, the title of the work, objectives, methodology, results obtained, conclusions, and future challenges. Next, we classified them according to the risk factors studied concerning CTS and then incorporated them into this work. It should be mentioned that the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statements were followed during the realization of the entire review. Figure 1 shows the respective PRISMA diagram, summarizing the results obtained in this methodology.



**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram, adopted from Sousa E., V. R., Teixeira S., Seixas A., Mendes J., & Costa-Ferreim A. [8]. CTS: carpal tunnel syndrome.

### 3. Results

According to the bibliographic search using PubMed, EBSCO, and ScienceDirect databases, 1679, 1146, and 3735 articles, respectively were found, totaling 6560 research papers. Subsequently,

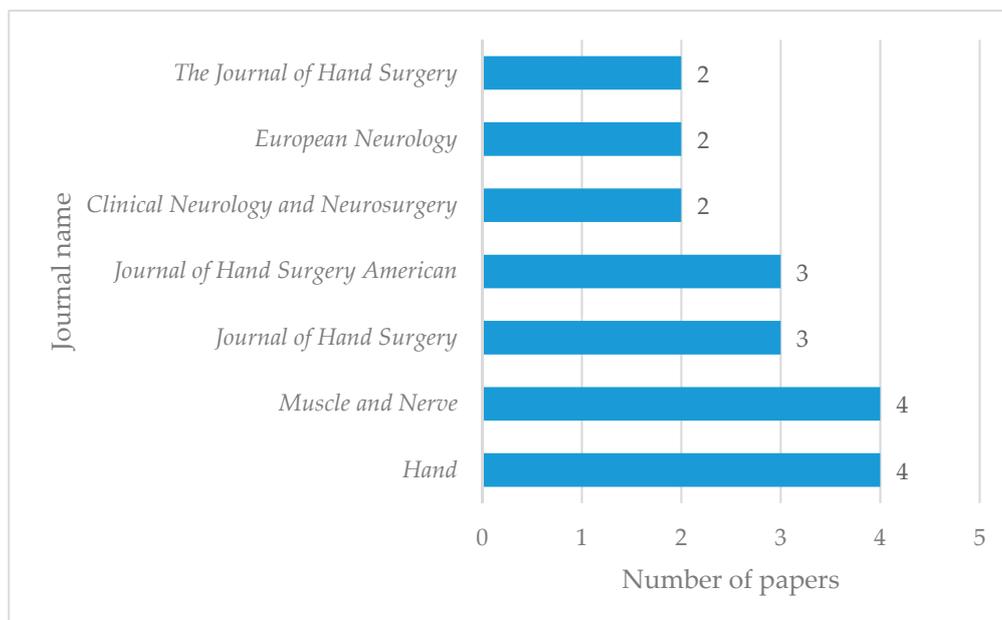
duplicates were identified among the information sources, and twelve cases were detected in EBSCO; therefore, 6548 papers remained for review. According to the first criterion (titles and abstracts), we eliminated a total of 6446 articles: 1593 from PubMed, 1124 from EBSCO, and 3729 from ScienceDirect.

We proceeded to thoroughly review the remaining 102 papers following the previously described criteria 2 and 3. According to the second criterion, we rejected six reviews because they related to CTS factors other than the ones examined in this work, such as psychosocial factors, clinical characteristics of patients, and hand-arm vibration syndrome, among others. Using the third criterion, we found that two articles were in a language other than English, so we reviewed them; however, one paper did not have an abstract in English and the other did not consider risk factors for CTS, therefore we discarded them.

Out of the 80 articles we selected for their complete review, eight did not investigate the relationship between CTS and the established factors; therefore, 72 articles were used in this work, which aimed to find out whether there is a relationship between the selected factors and CTS in terms of prevalence, diagnosis, severity, and surgical results, among others.

Finally, 72 articles were grouped according to the factors stipulated for this work, i.e., age, BMI, cardiovascular risks, dominant hand, sex, and multifactors except for the abdominal circumference and respiratory rate since no research was found regarding CTS for these factors. The classification of multifactors refers to the study of two or more of the factors involved; therefore, in several of the works reviewed, anthropometric, occupational, and ergonomic factors were also considered. The investigations were classified into six categories: (1) association of age with CTS, (2) association of BMI with CTS, (3) association of cardiovascular risk factors and CTS, (4) association of hand dominance with CTS, (5) association of sex with CTS, and (6) association of multifactors with CTS. These categories are described in the next paragraphs. At the end of this section, Table 1 shows a summary of the results obtained.

Figure 2 illustrates the leading journals that published topics associated with CTS for those that published more than one paper. The journals *Hand* and *Muscle & Nerve* have published at least four of these articles. Many journals specialize in topics associated with surgeries or problems in the hands. For a list of the journals with one published article included in this study, see Appendix A.



**Figure 2.** Journals published on CTS (only those with at least two articles included in the study are shown here).

**Table 1.** Summary of the results obtained from the research reviewed. BMI: Body mass index, PAF: Fraction attributable to the work-related population, SSS: Symptom severity scale.

Study	Influence Factors	Design Sample Size	p-Value	Effect Estimate	Related with CTS
Zyluk et al. [9]	Age	386 patients with CTS	Total grip strength: $p = 0.05$ Key pinch strength: $p = 0.18$	Total grip strength (%) ≤40 years: 138 (44) 41–65 years: 106 (53) >65 years: 87 (27) Key pinch strength: ≤40 years: 122 (43) 41–65 years: 102 (36) >65 years: 93 (22)	Yes
Porter et al. [10]	Age	Prospective study 87 patients with carpal tunnel decompression		Symptom severity score ≤50 years improvement: 1.60 >60 years improvement: 0.90 Functional status score ≤50 years improvement: 0.86 >60 years improvement: 0.49	Yes
Moschovos et al. [13]	Age	Case-control study 433 patients 92 healthy individuals	Age ≥65 years (moderate and severe CTS): $p < 0.01$	c-statistic (95%CI) Cross-sectional area <65 years: 0.94 (0.92–0.97) ≥65 years: 0.85 (0.78–0.92) Wrist to forearm ratio <65 years: 0.96 (0.93–0.99) ≥65 years: 0.86 (0.79–0.94)	Yes
Hansen and Larsen [11]	Age (patient >65 year at risk)	101 patients	$p = 0.001$	OR (95% CI): 17.85 (3.47–91.87)	Yes
Haghighat et al. [12]	Ages > 55	Cross-sectional descriptive study 240 dentists		Prevalence of CTS: 22.2%	Yes

Table 1. Cont.

Study	Influence Factors	Design Sample Size	p-Value	Effect Estimate	Related with CTS
Wilgis et al. [14]	Age	Prospective assessment 490 patients	Tinel's sign: $p = 0.001$ Phalen's test: $p < 0.001$ Semmes-Weinstein test: $p < 0.001$ Symptom status scores: $p < 0.001$	Tinel's sign Prior to surgery: 68% positive After surgery: 32% positive Phalen's test Prior to surgery: 89% positive After surgery: 11% positive Semmes-Weinstein test Prior to surgery: $2.4 \pm 0.05$ points After surgery: $1.97 \pm 0.04$ points Symptom status scores (average) Prior to surgery: $2.8 \pm 0.04$ After surgery: $1.1 \pm 0.04$	Yes
de Saboya et al. [15]	Age (continuous)	205 participants 285 hands with CTS diagnosed			
Ozcakir et al. [16]	BMI	27 patients with CTS symptoms 27 controls			
Sharifi et al. [17]	BMI	131 patients with CTS symptoms 131 controls	$p < 0.001$	OR (95% CI): 1.323, correlation coefficient: $r = 0.280$	
Ünaldı et al. [18]	BMI	100 patients with CTS 100 healthy volunteers	$p < 0.001$	Correlation coefficient CTS and BMI $r = 0.285$	Yes
Kurt et al. [19]	BMI	126 patients with BMI $\geq 30$			
Landau et al. [20]	BMI	50 patients with ulnar neuropathy at the elbow diagnosis 50 patients with CTS 50 control subjects	$p = 0.007$	Positive correlation between BMI and ulnar nerve conduction velocity: $r^2 = 0.22$	Yes

Table 1. Cont.

Study	Influence Factors	Design Sample Size	<i>p</i> -Value	Effect Estimate	Related with CTS
Hassan et al. [21]	BMI	120 patients with CTS symptoms	BMI and recurrence group: $p < 0.0001$	Recurrent group mean values BMI: 43.8, motor distal latency: 6.85 non-recurrent group mean values BMI: 37.99 motor distal latency: 5.4	Yes
Bodavula et al. [22]	BMI and sex	Prospective, longitudinal outcome study 598 cases (hands) with CTS diagnosed			
Mansoor et al. [23]	BMI	Cross-sectional survey 112 patients		Frequency of obesity: 34%	
Aygül et al. [24]	BMI	92 patients with CTS 30 healthy subjects	$p = 0.011$	Positive correlation between BMI and median motor distal latency: $r = 0.20$	Yes
Kim et al. [26]	BMI	15 players of wheelchair basketball	$p = 0.04$	Average BMI of subjects with CTS ( $26.0 \text{ kg/m}^2$ ) was greater than normal subjects ( $23.4 \text{ kg/m}^2$ )	Yes
Kouyoumdijan et al. [25]	BMI	141 patients with CTS	$p < 0.001$		Yes
Nageeb et al. [27]	BMI and vitamin D	50 CTS patients 50 controls	$p = 0.01$	Correlation coefficient between BMI and vitamin D: $r = -0.54$	Yes
Shiri et al. [28]	Obesity	Cross-sectional study 6254 participants		OR (95% CI): 2.4 (1.1–5.4)	Yes
Tang et al. [29]	Dominant hand	87 patients with bilateral CTS			

Table 1. Cont.

Study	Influence Factors	Design Sample Size	<i>p</i> -Value	Effect Estimate	Related with CTS
McDiarmid et al. [30]	Sex	29,937 CTS cases		CTS rate for data entry keyers Male: 1.17 Female: 1.10	Yes
Roquealure et al. [31]	Sex	1168 participants		OR (95% CI): Higher PAF in male blue-collar workers: 50% (41–57) Higher PAF in female white-collar workers: 24% (19–29)	
Giersiepen et al. [32]	BMI	Case–control study 808 participants with first surgery for CTS		OR (95% CI): 1.13 (1.06–1.20)	Yes
Çirakli et al. [33]	Age and sex	2516 patients with CTS symptoms			
Sassi and Giddins [34]	Sex	100 participants	Mean relative cross-sectional area (smaller in women than men): $p < 0.05$		Yes
El-Helaly et al. [35]	Sex	Cross-sectional study 279 laboratory technicians		CTS prevalence: 9.7%	Yes
Gruber et al. [36]	Sex	Retrospective study 170 cases			
Arslan et al. [37]	Age and BMI	165 subjects with pre-diagnosis of CTS	Age: $p = 0.60$ BMI: $p = 0.01$	OR (95% CI) Age: 0.96 (0.85–1.09) BMI: 0.59 (0.39–0.91)	Yes
Boz et al. [38]	BMI	Prospective study 198 CTS patients 194 control subjects			
Mondelli et al. [39]	BMI	Case–control study 340 patients with CTS 747 patients without CTS			

Table 1. Cont.

Study	Influence Factors	Design Sample Size	<i>p</i> -Value	Effect Estimate	Related with CTS
Kouyoumdijan et al. [40]	Age and BMI	210 symptomatic CTS patients 320 controls subjects	$p < 0.001$	OR (95% CI) BMI: 1.11 (1.05–1.16)	Yes
Hiebs et al. [41]	BMI	50 patients with CTS 50 controls			Yes
Thiese et al. [42]	Age, BMI, and sex	295 untreated CTS patients 50 healthy volunteers	Age: $p < 0.0001$ BMI: $p < 0.005$	Adjusted prevalence ratio Age: 1.04 (1.02–1.06) BMI: 2.67 (1.50–4.85) Female sex: 1.39 (0.84–2.29)	Yes
Moghtaderi et al. [43]	BMI and sex	Case–control study 128 CTS patients 109 controls	BMI: $p = 0.000$ Sex: $p = 0.001$	OR (95% CI) BMI: 1.75 (1.50–2.04) Sex: 9.95 (2.46–40.17)	Yes
Komurcu et al. [7]	Age and BMI	547 patients	Age: $p = 0.001$	OR (95% CI) Age $\geq 65$ : (1.86–9.35)	Yes
Iwuagwu et al. [44]	Age	31 patients with macromastia and CTS			Yes
Sousa et al. [45]	BMI and sex	Cross-sectional study 115 idiopathic CTS patients 115 controls			
Zambelis et al. [46]	Older age and higher BMI	130 subjects with CTS only, or mainly, in the left hand 130 subjects with CTS only, or mainly, in the right hand.	Age: $p = 0.006$ BMI: $p = 0.004$	OR (95% CI) Age: 1.03 (1.01–1.05) BMI: 1.09 (1.03–1.15)	Yes
Becker et al. [47]	Age, BMI, and sex	791 CTS cases 981 controls	$p < 0.001$	OR (95% CI) Age (41–60): 1.91 (1.58–2.31) BMI > 30: 2.90 (2.25–3.73) Female: 3.66 (2.84–4.71)	Yes
Kame et al. [48]	BMI	Cross-sectional study 36 patients	$p = 0.03$	CTS prevalence: 16.67%	Yes

Table 1. Cont.

Study	Influence Factors	Design Sample Size	p-Value	Effect Estimate	Related with CTS
Geoghegan et al. [49]	BMI	3391 cases		OR (95% CI): 2.06 (1.79–2.38)	Yes
Solmaz et al. [50]	Age and sex	Electrodiagnostic study 295 untreated CTS patients 50 patients with no risk factor (idiopathic) 50 healthy volunteers			
Zhang et al. [51]	Age, BMI, and sex	Retrospective cohort study 1114 patients with CTR 264 patients with cubital tunnel surgery 76 patients with both	$p < 0.05$	OR (95% CI) Age: 1.02 (1.00–1.04) BMI: 1.01 (0.97–1.05) Sex: 2.18 (1.34–3.55)	Yes
Law et al. [52]	Age, BMI, and sex	Interview survey 25,880 respondents (952 with CTS)		OR (95% CI) Age $\geq 65$ : 18% (15.0%–20.9%) Women: 66.5% (62.8%–70.3%) Obese: 42.9% (39.1%–46.7%)	Yes
Bland et al. [53]	BMI and sex	Observational study 145 patients with carpal tunnel decompressions	BMI: $p < 0.05$ Sex: $p = 0.05$	Correlation between SSS and BMI $r = -0.16$ Mean change in SSS Women = $-1.77$ Men = $-1.42$	
Bae et al. [54]	Age	Retrospective study 60 patients diagnosed with idiopathic CTS	$p = 0.001$	OR (95% CI): 0.922 (0.877–0.969)	Yes
Fakhauri et al. [55]	Sex	620 patients with CTS			

Table 1. Cont.

Study	Influence Factors	Design Sample Size	p-Value	Effect Estimate	Related with CTS
Hobby et al. [56]	Age and sex	97 patients with CTS		Age > 70 Symptom scale Preoperative: 3.05, Postoperative: 1.64 Function scale Preoperative: 2.88, Postoperative: 1.99 Male Symptom scale Preoperative: 2.65 Function scale Preoperative: 1.99 Female Symptom scale Preoperative: 3.08 Function scale Preoperative: 2.70	Yes
English et al. [57]	Age	Retrospective study 2313 patients with carpal tunnel decompression		Highest rates of carpal tunnel decompression 307 per 100,000 person-years (70–79 year age group)	Yes
Roh et al. [58]	Sex	Retrospective, nationwide cohort study Population of Korea during 2005–2007		Incidence rate ratio Male CTS diagnosed: 2.76 (2.74–2.78) Female CTS diagnosed: 7.12 (7.11–7.13)	
Ghasemi et al. [59]	BMI	Descriptive cross-sectional study 906 cases		CTS prevalence Men: 14% Women: 8.9%	

Table 1. Cont.

Study	Influence Factors	Design Sample Size	p-Value	Effect Estimate	Related with CTS
Bongers et al. [60]	Age and sex	355,201 listed patients in 1987 364,998 listed patients in 2001		Crude incidence rate 1.3 per 1000 (95% CI: 1.0 to 1.5) in 1987 1.8 per 1000 (95% CI: 1.7 to 2.0) in 2001. Males 0.6(95% CI: 0.5 to 0.7) in 1987 0.9 (95% CI: 0.8 to 1.0) in 2001 Females 1.9 (95% CI: 1.7 to 2.1) in 1987 2.8 (95% CI: 2.6 to 3.1) in 2001	Yes
Mattioli et al. [61]	Sex	8801 cases			
Ibrahim et al. [62]	Age and sex	479 patients			
Mondelli et al. [63]	Age, BMI, and sex	179 cleaners		OR (95% CI) older age: 3.82 (1.43–10.22) BMI: 1.79 (0.85–3.78)	Yes
Rosecrance et al. [64]	Age & BMI	Cross-sectional study 1142 participants	$p < 0.0001$	OR (95% CI) Age: 4.9 (2.40–10.02) BMI: 4.12 (2.10–8.08) CTS prevalence: 8.2%	Yes
Cosgrove et al. [65]	Age and BMI	900 subjects	Age and BMI: $p < 0.001$	Unstandardized coefficient Age: 0.01361 BMI: 0.04765	Yes

Table 1. Cont.

Study	Influence Factors	Design Sample Size	p-Value	Effect Estimate	Related with CTS
Nathan et al. [66]	Age, BMI, and sex	256 participants without CTS	Age: $p = 0.001$ Sex: $p = 0.02$ BMI: $p = 0.04$	OR (95% CI) Age $\geq 50$ : 6.58 (2.08–20.84) BMI $\geq 28.24$ : 4.02 (1.02–15.87) Sex: 1.53 (1.06–2.23)	Yes
Wolf et al. [67]	Age and sex	48,957 cases of CTS		OR (95% CI): 11.63 (10.90–12.41) Incidence rate ratio Women: 3.29(3.28–3.35) Age $\geq 40$ : 11.63 (10.90–12.41)	Yes
Harris-Adamson et al. [68]	Age, BMI, and sex	Pooled study cohort 3515 participants	Women: $p = 0.07$ Age and BMI: $p = 0.00$	HR (95% CI) Women: 1.30 (0.98–1.72) Age $\geq 50$ : 3.04 (1.96–4.71) BMI $\geq 30$ kg/m <sup>2</sup> : 1.67 (1.26–2.21)	Yes
Mohammad [69]	Age, BMI, and female sex	222 female touchscreen users		CTS prevalence: 34.20%	
Mondelli et al. [70]	Age, BMI, and sex	172 subjects (non-surgical) 219 patients (surgical)			
do Amaral et al. [71]	Age	200 hospital workers	$p < 0.0001$	OR (95% CI): 1.0 (0.97–1.03) CTS prevalence: 34%	Yes
Jerosch-Herold et al. [72]	Age, BMI, and sex	Prospective, multicenter cohort study 753 patients with CTS	$p < 0.0001$		Yes
Day et al. [73]	Age and sex	273 patients (with diagnosis of carpal or cubital tunnel syndrome)	Age (most important predictor of surgical release): $p < 0.001$ More surgeries performed on male patients: $p = 0.004$		Yes
Harada et al. [74]	Age and sex	875 idiopathic CTS cases			

Table 1. Cont.

Study	Influence Factors	Design Sample Size	<i>p</i> -Value	Effect Estimate	Related with CTS
McCabe et al. [75]	Age, BMI, and sex	Case-control study 68 CTS cases 138 controls	$p = 0.05$	OR (95% CI) Women aged < 60: 8.7 (1.9–39.4)	Yes
Kwon et al. [76]	Age, BMI, and sex	Prospective, case-control study 29 patients			
Rouq et al. [77]	Age and sex	Cross-sectional observational study 227 subjects with CTS			
Saeed and Irshad [78]	Age and sex	Observational study 213 patients with CTS			
Chan et al. [79]	Age, BMI, and sex	Cross-sectional design 215 patients with CTS			

Figure 3 illustrates the number of articles analyzed yearly, where the most common were ten in 2017; six in 2002, 2015, and 2018; and five in 2005, 2009, and 2016.

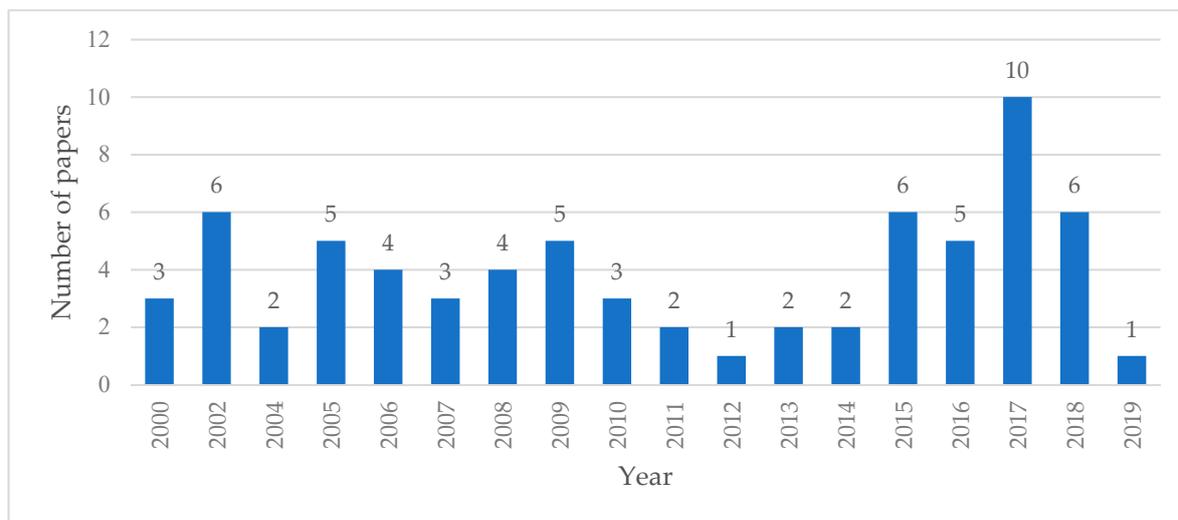


Figure 3. Yearly CTS publications.

Figure 4 illustrates the leading countries where the first author’s institution publishing the CTS articles is located (only those countries with at least two publications are shown; for a complete list, see the Supplementary Material). The United States presented 15 publications, followed by Turkey with 9, and the United Kingdom with 8; however, countries such as Brazil, Iran, and Italy have also deepened their study of CTS matters.

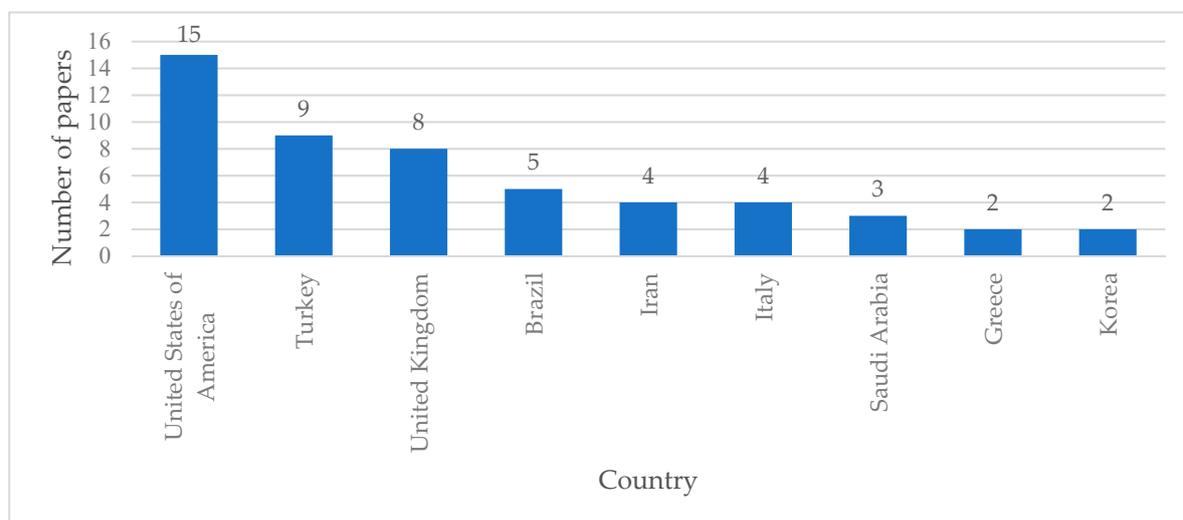


Figure 4. List of publications by country.

The departments with a high commitment regarding CTS are associated with neurology, orthopedic surgery, neurological sciences, physical medicine and rehabilitation, orthopedic and traumatology, among others. For a complete list of departments, please see the complementary material.

### 3.1. Association of Age with Carpal Tunnel Syndrome

Seven of 70 papers studied the relationship between age and CTS in various circumstances. Zyluk and Puchalski [9] and Porter et al. [10] found that improvements in patients after surgery decrease as age increases, especially in people over 60. Hansen, T. B. and K. Larsen [11] found unfavorable results

in patients over 65 years of age. Haghghat, A., S. Khosrawi, A. Kelishadi, S. Sajadieh and H. Badrian [12] found that CTS increases with age in people over 55 years old.

Zyluk and Puchalski [9] evaluated patients with CTS six months after surgery by utilizing the Levine questionnaire and measurements of grip and pinch strength, as well as the slight touch sensation via the filament test, finding that older patients (>60 years) showed less improvement in overall handgrip strength.

Porter P., V. B., Stephenson H., Wray C. C. [10] studied 87 patients with CTS who underwent decompression surgery to analyze the results of such surgery as a function of age. A validated self-administered questionnaire was applied and found that the improvement in symptoms and function decreased as the person gets older.

Moschovos, C., G. Tsivgoulis, A. Kyrozis, A. Ghika, P. Karachalia, K. Voumvourakis and E. Chroni [13] performed electrodiagnostic studies of median, ulnar, and radial nerve conduction. The effect of age on the accuracy of high-resolution ultrasound in the diagnosis and classification of CTS was evaluated. As a result, the authors found that in patients aged 65 and older with moderate and severe CTS, disease-related increases correlate negatively with increasing age.

Hansen, T. B. and K. Larsen [11] studied the influence of age as a possible short-term predictor of endoscopic carpal tunnel release (CTR). The authors recorded patients' satisfaction, symptoms, and function before and two months after endoscopic CTR and then analyzed all data using multivariate logistic regression. The results showed an accurate prediction in patients 65 years and older with unfavorable results; thus, he determined that this procedure is not suitable for elderly patients.

Haghghat, A., S. Khosrawi, A. Kelishadi, S. Sajadieh and H. Badrian [12] evaluated 240 dentists to assess the prevalence of CTS by applying a questionnaire where age, sex, experience, hours worked per week, type of activity, and clinical symptoms of CTS, such as pain and paresthesia in the hands, to make the diagnosis. The prevalence of CTS increases with age in such a way that it reaches 22.2% in ages over 55 years, as opposed to 6% among participants of ages between 25 and 34. Furthermore, Wilgis, E. F., F. D. Burke, N. H. Dubin, S. Sinha and M. J. Bradley [14] found that patients improved significantly in all age groups after carpal tunnel surgery. They evaluated the effect of increasing age on the outcome after CTS surgery of 635 cases with a CTS diagnosis, with a follow-up examination after 6 months. Pre-operatively, Tinel's signal, Phalen's test, Semmes-Weinstein sensory test, and grip and pinch resistance tests were applied. The test results showed that patients improved significantly in all age groups after carpal tunnel surgery.

Only one paper investigated the signs and symptoms in patients with CTS after using urban transportation [15]. A total of 205 patients were evaluated and CTS was diagnosed in 285 hands of these patients. After the diagnosis, the patients answered a questionnaire but no statistical significance with respect to age was found between groups.

### *3.2. Association of Body Mass Index with Carpal Tunnel Syndrome*

Eleven out of 70 studies were found to correspond to the group of research on the relationship between BMI and CTS. Ozcakir, S., D. Sigirli and H. Avsaroglu [16] recorded anthropometric hand and BMI measurements to determine whether they are independent risk factors for CTS. BMI and anthropometric measurements were highly significant in the CTS group and proved to be independent variables.

Similarly, Sharifi-Mollayousef, A., Yazdchi-Marand, M., Ayramlou, H., Heidar, P., Salavati, A., Zarrintan, S., & Sharifi-Mollayousefi, A. [17] sought to clarify the role of BMI and anthropometric hand measurements as independent factors in the development of CTS and its relation to the symptoms' severity to determine independent risk factors for CTS by performing a logistic regression analysis, and found that BMI, wrist radius, and a shape index are independent risk factors for CTS.

Furthermore, Ünalı, H. K., Kurt, S., Çevik, B., Mumcuoğlu, İ., & Sümbül, O. [18] evaluated the relationship between the wrist circumference, waist radius, and BMI in patients with CTS who

underwent neurological and nerve conduction studies (NCS), finding that there were statistically significant correlations between CTS and BMI, as well as patients' waist and wrist measurements.

Two investigations analyzed the influence of BMI on the median nerve conduction velocity in CTS patients. Kurt, S., B. Kisacik, Y. Kaplan, B. Yildirim, I. Etikan and H. Karaer [19] evaluated the presence or absence of recovery in the midline nerve conduction velocities in 126 obese patients after weight loss to find out whether excess weight or other factors influence the higher prevalence of CTS in obese patients. Two NCS in upper limbs were performed on patients who were included in dietary programs and the BMIs were statistically significant in the second test. Recovery of the mean nerve conduction velocity is expected in patients with CTS after weight loss.

Landau, M. E., K. C. Barner and W. W. Campbell [20] sought to determine whether BMI extremes are risk factors for ulnar neuropathy in the elbow or CTS and whether BMI affects the velocity of conduction of the median and ulnar nerves. Unidirectional analysis of variance of the control electrodiagnostic records and BMI was performed involving 50 patients with ulnar elbow neuropathy, 50 patients with CTS, and 50 control subjects. Patients with CTS have a higher average BMI; therefore, it was concluded that a higher BMI increases the risk for CTS.

Two out of 11 studies investigated the effect of BMI after the release of CTS. Hassan, M. M., & Al-Hawary, M. A. [21] clarified the role of BMI and distal motor latency at the first diagnostic visit as independent risk determinants in the recurrence of CTS after surgical release by measuring BMI and distal motor latency. The mean values of BMI and distal motor latency were significantly higher in the recurrent group compared to the non-recurrent group. Thus, a higher BMI and a higher value of distal motor latency were significantly correlated with recovery after operative release.

Bodavula, V. K., F. D. Burke, N. H. Dubin, M. J. Bradley and E. F. Wilgis [22] investigated the association between BMI and the effectiveness of CTR by employing physical testing and self-assessment of symptom severity and functionality before and after surgery. Patients with morbid obesity worsened on specific physical and self-assessment tests compared to normal preoperative BMI but all improved postoperatively regardless of BMI, in contrast with the findings of Hassan, M. M., & Al-Hawary, M. A. [21].

Mansoor, S., M. Siddiqui, F. Mateen, S. Saadat, Z. H. Khan, M. Zahid, H. H. Khan, S. A. Malik and S. Assad [23], Aygul, R., H. Ulvi, D. Kotan, M. Kuyucu and R. Demir [24], and Kouyoumdjian J. A., M. M. P. A., Roche P. R. F., Miranda R. C., Maciel G. [25] performed sensory and motor NCS to determine the relationship between BMI and CTS. All these studies address the association between obesity and the prevalence of CTS. Mansoor, S., M. Siddiqui, F. Mateen, S. Saadat, Z. H. Khan, M. Zahid, H. H. Khan, S. A. Malik and S. Assad [23] performed motor and sensory studies on both hands of each patient, finding an obesity frequency of 34%. They indicated that therapy given to CTS patients should also include weight reduction since obesity poses a cause-and-effect relationship for the severity and pathogenesis of CTS.

Aygul, R., H. Ulvi, D. Kotan, M. Kuyucu and R. Demir [24] assessed the sensitivities of electrophysiological techniques and investigated their relationship with BMI in a population of 92 CTS patients and 30 volunteers. It was found that the mean BMI was significantly higher in the CTS group than in the control group; thus, CTS is associated with increased BMI.

Among other studies, Kim, D. K., B. S. Kim, M. J. Kim, K. H. Kim, B. K. Park and D. H. Kim [26] investigated the factors contributing to CTS using electrodiagnostic and ultrasonographic findings of the median nerve and post-exercise median nerve change in wheelchair basketball players, determining that BMI and the period of wheelchair use contribute to the development of CTS in these patients..

Kouyoumdjian J. A., M. M. P. A., Roche P. R. F., Miranda R. C., Maciel G. [25] researched the relationship between BMI and CTS. NCS and sensory NCS were performed, as well as supramaximal intensity stimuli from the wrist to the index finger. It was found that CTS cases have a significant correlation with a higher BMI compared to control subjects.

Nageeb, R. S., N. Shehta, G. S. Nageeb and A. A. Omran [27] evaluated BMI and vitamin D levels in patients with CTS and discovered that CTS is significantly associated with hypovitaminosis D,

especially in patients with a high BMI; these patients had a lower level of vitamin D and a higher BMI compared to those in the control group.

### 3.3. Association of Cardiovascular Factor with Carpal Tunnel Syndrome

Shiri, R., M. Heliovaara, L. Moilanen, J. Viikari, H. Liira and E. Viikari-Juntura [28] studied the relationship of carotid artery intima-media thickness and clinical atherosclerotic diseases with CTS by studying surveys of medical examinations in five regions of university hospitals. The BMI was obtained and the thickness of the carotid artery intima-media was measured; then, logistic regression models were run to study the associations of atherosclerosis risk factors, carotid artery intima-media, and clinical vascular diseases with CTS. The findings indicate an association between CTS and obesity, high cholesterol, hypertension, cardiac arrhythmia, and high triglycerides in subjects 30 to 44 years old. Investigating the group of subjects that were 60 years or older showed that coronary artery disease, valvular heart disease, and carotid artery intima-media thickness are associated with CTS.

### 3.4. Association of Hand Dominance with Carpal Tunnel Syndrome

Tang, Q. Y., W. H. Lai and S. C. Tay [29] examined the effect of the dominant hand on the resolution of symptoms after surgical decompression in patients with moderate and severe CTS, and when performing a bilateral CTS release in 87 patients with moderate or severe CTS, the symptoms were recorded at follow-ups until complete resolution or until the last recorded consultation. The patients with severe CTS achieved a complete resolution in the non-dominant hand in a shorter time compared with the dominant one, and the symptoms diminished faster in the non-dominant hand after the release of CTS in patients with severe CTS.

### 3.5. Association of Sex with Carpal Tunnel Syndrome

Seven out of 70 papers were identified in this classification. McDiarmid, M., M. Oliver, J. Ruser and P. Gucer [30] argued that men and women doing the same job tasks will have similar rates of CTS. The Bureau of Labor Statistics about injuries at work and the data from the census of the current population survey were used to determine the injury rates of CTS for men and women in six high-risk occupations, such as assemblers, non-construction laborers, packaging and filling machine operators, janitors, cleaners, butchers and meat cutters, and data entry keyers. The male-to-female risk rate ratio ranged from 0.29 to 0.50; thus, an equal risk between sexes exists when the occupational tasks are genuinely similar.

Roquelaure, Y., Ha C., Fouquet, N., Descatha, A., Leclerc, A., Goldberg, M., & Imbernon, E. [31] conducted a study to assess the fraction attributable to the work-related population (PAF) of CTS in industrial sectors and occupational categories with a high CTS risk. The sectors were: agriculture, construction, manufacturing, and service industries. The PAF for women was higher in lower-grade white-collar workers. The PAF was high for men in blue-collar workers. The excess risk of CTS was statistically significant for two main occupational categories: blue-collar workers (for both sexes) and lower-quality services, white-collar salespeople, and clerks for women.

Giersiepen, K., A. Eberle and H. Pohlabein [32] conducted research to determine the role of the profession and the personal risk factors for CTS in men and women. Multivariate analyses adjusted according to BMI showed more pronounced risks for repetitive movements of the hand in men compared with women, especially those who had given birth more than twice or a history of hysterectomy. CTS is a work-related disease in both men and women, as seen in the fraction attributable to work in the Bremen population, which is estimated to be 33% in men and 15% in women under 65 years old.

One out of seven investigations concerning the association between sex and CTS assessed the correlation between patient history, physical examinations, and the electrophysiological method of evaluation in patients with suspected CTS [33]. The electrophysiological examinations performed on 2516 patients used the Kolmogorov–Smirnov test, Levine's test, and chi-square test for statistical

analyses detected CTS in 1383 patients (54.9%; female/male: 1019/364). No statistically significant association was found between CTS and sex.

Only one study contained information considering the size of the carpal tunnel between men and women [34]. A hypothesis was established stating that there would be no difference in the relative size of the carpal tunnel between men and women; to test this hypothesis, measurements were taken through magnetic resonance imaging of 50 men and 50 women with non-CTS-related symptoms. It was found that the mean relative carpal tunnel cross-sectional area was significantly smaller in women than in men.

One study considered the association between ergonomic and personal factors among laboratory technicians [35]. The study was conducted among 279 laboratory technicians, who were given a self-assessed questionnaire that included questions regarding their demographics, occupation history, work tasks, work tools, ergonomics, factors at work, and symptoms suggesting the existence of CTS. Univariate and multivariate analyses for both personal and physical factors were then performed in association with the confirmed CTS among them. The prevalence of CTS among laboratory technicians was 9.7% (27/279). The statistically significant risk factors for CTS among them were sex (all CTS cases were female), in addition to ergonomic factors, such as repetitive tasks and pipetting, among others. Gruber, L., H. Gruber, T. Djurdjevic, P. Schullian and A. Loizides [36] evaluated the sex differences for the diagnosis of CTS using high-resolution ultrasound in terms of the severity of neural alterations due to the wrist-to-forearm ratio (WFR), epineural thickening, loss of fascicular anatomy, and classical signs and symptoms. In this study, 170 cases were analyzed, where 149 were patients and 21 were healthy volunteers. A sex-specific analysis between patients and controls showed that symptomatic men had a significantly higher mean WFR ( $2.28 \pm 0.74$  vs.  $1.13 \pm 0.29$ ). In symptomatic cases, we found a significant difference in WFR between women ( $2.66 \pm 0.95$ ) and men ( $2.28 \pm 0.74$ ). Women differ significantly from men in terms of clinical presentation.

### 3.6. Association of Multifactors with Carpal Tunnel Syndrome

Forty-two research papers were identified that studied the association between multifactors and CTS pathology; however, these studies do not focus exclusively on the factors stipulated for this research but also involved others, which are described in this section.

Arslan, Y., I. Bulbul, L. Ocek, U. Sener and Y. Zorlu [37] conducted a study where they included 165 participants with 85 cases confirmed with idiopathic CTS. Age, sex, occupation, BMI, dominant hand, degree of idiopathic CTS, wrist circumference, proximal/distal width of the palm, hand/palm length, hand volume, and the palm length/proximal palm width were analyzed. The mean age identified was higher in the severe CTS group. Female sex, older age, and high BMI were found to be risk factors for idiopathic CTS. Boz, C., M. Ozmenoglu, V. Altunayoglu, S. Velioglu and Z. Alioglu [38] studied the anthropometry of wrists and hands as risk factors for CTS and found that for women, these are independent risk factors, while for men, they are not. BMI, wrist index, hand shape index, digit index, and hand length/height ratio were compared between the CTS patients and the control subjects for each sex separately through logistic regression analysis, where BMI was determined to be an independent risk factor in both males and females.

Mondelli, M., S. Curti, S. Mattioli, A. Aretini, F. Ginanneschi, G. Greco and A. Farioli [39] determined the relationship between the severity of CTS and selected anthropometric and obesity indexes. A total of 1087 patients, 340 with CTS and 747 without CTS, participated in the study. Anthropometric characteristics of the body and hand were measured. Relative risk ratios of CTS severity were analyzed using age and sex-adjusted multinomial logistic regression models. Although not properly established as an influential relationship between CTS and BMI in multivariate models, it was identified that BMI and the waist-to-height ratio seemed to convey different and relevant information, and suggested that both adiposity rates should be considered in the investigation of epidemiological studies. Kouyoumdjian, J. A., D. M. Zanetta and M. P. Morita [40] determined the association of CTS with wrist index and BMI. The study consisted of 210 patients with a diagnosis of

CTS and 320 control subjects who underwent NCS, and the BMI and wrist index values were obtained. The data were statistically analyzed through ANOVA and a logistic regression analysis. The presence of CTS was associated with increased BMI and wrist index values.

Fifty patients with CTS and 50 healthy volunteers participated in the study conducted by Hiebs, S., K. Majhenic and G. Vidmar [41], who were assessed for height, weight, BMI, wrist depth and width, hand shape index, digit index, palm length, palm width, third finger length, and the relationship between hand length and body height. A multiple logistic regression was used to determine the independent risk factors for CTS, identifying wrist index, BMI, and the relationship between hand length and body height as independent risk factors for CTS.

Thiese, M. S., A. Merryweather, A. Koric, U. Ott, E. M. Wood, J. Kapellusch, J. Foster, A. Garg, G. Deckow-Schaefer, S. Tomich, et al. [42] analyzed the database of a prospective multicenter prospective cohort study to determine the influence of CTS and wrist ratio in 1206 participants. Among their findings, they implied that BMI was a determinant modifier between WR and CTS. Meanwhile, Moghtaderi, A., S. Izadi and N. Sharafadinzadeh [43] determined that female sex, obesity, and a square wrist are independent risk factors for CTS in a study where 128 patients with CTS and 109 control subjects participated. A logistic regression analysis was conducted to evaluate the odds ratio of different risk factors. In their studies, they determined that female sex, obesity, and square wrists are independent risk factors for CTS.

One out of the multifactorial 42 studies focused on identifying a significant relationship between the degree of severity of CTS, age, BMI, wrist circumference, and waist circumference [7]. The 547 participating patients were classified into four CTS severity groups employing electrophysiological studies and anthropometric measurements were made. ANOVA, covariance analysis, and logistic regression analysis were performed. A significant relationship between CTS severity and age, BMI, and waist circumference were identified.

Iwuagwu et al. [44] included 31 patients with CTS and macromastia in their study, and their physical characteristics were recorded, such as age, BMI, and breast size. Clinical and electrophysiological assessments of the upper limb were performed, which found that age, chest circumference, and breast size have a positive correlation with the incidence of CTS.

Sousa et al. [45] conducted a study involving 115 idiopathic CTS patients and 115 controls. They analyzed their data using logistic regression analysis with pre-diabetes as the dependent variable and age, BMI, and CTS as independent variables. The results showed that CTS is closely related to age and being overweight.

Zambelis, T., G. Tsvigoulis and N. Karandreas [46] found that older age, higher BMI, and diabetes mellitus were more prevalent in patients with bilateral CTS, and that age and BMI were independently associated with bilateral CTS in a study that involved 130 subjects with CTS. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of CTS.

Becker, J., D. B. Nora, I. Gomes, F. F. Stringari, R. Seitensus, J. S. Panosso and J. A. C. Ehlers [47] confirmed through a case-control study with 791 CTS cases and 981 controls that female sex, obesity, and age are independent risk factors for CTS. The probability ratio between the two groups was calculated to analyze the ratio frequency, and the possible sources of bias were studied using stratified and multivariate analyses.

Karne, S. S. and N. S. Bhalerao [48] conducted a cross-sectional study involving 36 patients with a diagnosis of primary hypothyroidism and CTS by performing clinical examinations and electrophysiological NCS. An increase in BMI is a significant risk factor for CTS in hypothyroidism, and the clinical evidence of CTS proved to be a very sensitive parameter for it.

Geoghegan, J. M., D. I. Clark, L. C. Bainbridge, C. Smith and R. Hubbard [49] found that the musculoskeletal conditions of a previous wrist fracture, rheumatoid arthritis, and osteoarthritis of the wrist and carpus, an increase in BMI, diabetes, and hypothyroidism are important risk factors for CTS. The cases were patients with a diagnosis of CTS; four controls were individually matched by age, sex,

and general practice, and the data set included 3391 cases. The association between CTS and each exposure was analyzed using conditional logistic regression.

In a study involving 293 patients and 50 healthy individuals, Solmaz, V., S. Yavuz, A. Inanr, D. Aksoy, E. Pektas, A. Tekatas and S. G. Kurt [50] determined that there are electrodiagnostic differences between CTS patients with diabetes mellitus, CTS and hypothyroidism, CTS and fibromyalgia syndrome, CTS and rheumatoid arthritis, and idiopathic CTS cases via comparisons with NCS. There were no significant differences between the groups in terms of sex and age.

Zhang, D., J. E. Collins, B. E. Earp and P. Blazar [51] reported a retrospective cohort study via billing system queries using common procedural terminology codes for all patients who underwent open CTR and/or open cubital tunnel surgery. The study involved 1257 patients with CTS, 326 with an open cubital release, and 100 with open carpal and cubital tunnel release. In the multivariable analysis, older age, female sex, higher BMI, trigger finger, and de Quervain tenosynovitis were associated with CTR.

Data from the Adult Basic Module of the 2010 National Health Interview Survey was used as the basis for calculating the prevalence estimates of CTS and migraines. A total of 25,880 respondents were involved in the study. Through logistic regression, it was found that CTS was associated with older age, female sex, obesity, diabetes, and smoking [52].

Six of 42 multifactorial studies considered carpal tunnel surgery, including Bland, J. D. and S. M. Rudolfer [53], who conducted an observational study of the surgery, where women showed more considerable improvement than men (women success rate was 88% vs. 78% in men), also finding that there was a weak significant correlation among improvement in symptom severity scale and BMI. Regarding logistic regression models as predictors, it was identified that a higher BMI increased the probability of success. On the other hand, a higher age and male sex decreased the possibility of success.

Bae, J. Y., J. K. Kim, J. O. Yoon, J. H. Kim and B. C. Ho [54] performed multivariate analysis and determined that age and level of depression were preoperative predictors of patient satisfaction after CTR. The research involved 60 patients diagnosed with idiopathic CTS, in which they included age, sex, duration of symptoms, static two-point discrimination, the Semmes–Weinstein monofilament test, grip strength, electrophysiological category, scores for the Boston Carpal Tunnel Questionnaire (BCTQ), the Pain Anxiety Symptoms Scale, and the Center for the Epidemiological Study of Depression scale as preoperative predictors for patient satisfaction.

Fakhouri, F., R. A. Alsukhni, B. Altunbi, Z. Hawoot and R. Dabbagh [55] conducted a study to identify clinical and demographic baseline factors as possible predictors of a good surgical outcome, where 620 patients with CTS participated. Patients underwent open surgery for CTR and it was determined that elderly patients with a long-term disease, neurological deficits, and were Phalen negative did not respond to surgery as well as others.

In contrast, Hobby, J. L., R. Venkatesh and P. Motkur [56] justify surgery in the elderly based on the results of CTR in terms of improvements in symptoms and functional scores; however, surgical predictions are lower than in younger patients. A prospective study was conducted to evaluate the effect of age and sex on symptoms, self-reported disability, and surgical outcomes in 97 patients with CTS. The symptom severity, hand function, and patient satisfaction were assessed using the BCTQ and the patient assessment measure.

English, J. H. and D. P. Gwynne-Jones [57] determined that the highest incidence of CTS is found in older people who tend to have more severe neurophysiological changes by performing a retrospective review of 2313 patients who underwent carpal tunnel decompression, where age and sex were considered as parameters for comparison in the NCS. The highest rates of decompression were observed in the 70–79-year-old group in both women and men.

Roh, Y. H., M. S. Chung, G. H. Baek, Y. H. Lee, S. H. Rhee and H. S. Gong [58] found in their study of the Korean population that women with CTS are more likely than men to be treated surgically. Incidences of clinically diagnosed and surgically treated CTS were analyzed, as well as the influence of

age and sex. In comparison with Western studies, a similar incidence of CTS was found but a lower incidence of surgery.

Ghasemi, M., M. Rezaee, F. Chavoshi, M. Mojtahed and E. Shams Koushki [59] conducted their study on assembly workers in a detergent factory and computer users to determine the prevalence of CTS, as well as to assess the personal risk factors and level of exposure to occupational risk factors, where 906 cases (332 assembly workers and 574 computer workers) were analyzed. CTS cases were evaluated using the Katz's hand diagram and quick exposure check technique to assess environmental exposure to risk factors. The likely prevalence of CTS was 14% in men and 8.9% in women.

Bongers F. J. M., S. F. G., van den Bosch W. J. H. M., van der Zee J. [60] compared CTS incidence rates to the studied relationship between CTS and occupation, and data from the first and second Dutch National Survey of General Practice conducted in 1987 and 2001 were analyzed. A questionnaire was sent to patients, obtaining 118,208 responses in 1987 and 127,466 responses in 2001. The data were analyzed using an age-adjusted logistic regression to study the relationship between CTS and occupation. In 2001, the crude incidence rate of CTS was 1.5 times higher than in 1987 but the difference was not statistically significant after subdividing by age and sex. In both years, the female/male ratio was 3:1. Incidence rates were related to the job level of women, but not of men.

Mattioli, S., A. Baldasseroni, S. Curti, R. M. Cooke, A. Mandes, F. Zanardi, A. Farioli, E. Buiatti, G. Campo and F. S. Violante [61] studied surgical cases of idiopathic CTS in blue- and white-collar workers and housewives, where 8801 participants took part in the research and the data were obtained from public and private hospital records in the regional database of Tuscany, Italy. Blue-collar workers presented further surgical treatment of idiopathic CTS but no relationship between sex and age influence on idiopathic CTS was found in blue-collar workers.

Ibrahim, T., I. Majid, M. Clarke and C. J. Kershaw [62] investigated the effect of age, sex, and occupation on carpal tunnel decompression outcomes, where 479 patients participated. The results of the surgery were evaluated using the Brigham Hospital carpal tunnel questionnaire two weeks before surgery and six months after surgery. Cases were divided by age into four categories and two groups by occupation (repetitive and non-repetitive). Statistical analyses using the Kruskal–Wallis test to assess age and Mann–Whitney U test to assess sex and occupation were performed. No influence from age, sex, and occupation was found on the outcome of carpal tunnel decompression.

Using a hospital population of 179 cleaning workers, Mondelli, M., A. Grippo, M. Mariani, A. Baldasseroni, R. Ansuini, M. Ballerini, C. Bandinelli, M. Graziani, F. Luongo, R. Mancini, et al. [63] studied the appearance of CTS and elbow cube neuropathy (UNE) to check the differences between workers with and without CTS. The clinical and electrophysiological severity of CTS and UNE was evaluated using standardized severity scales and the symptoms were assessed with the self-administered Boston questionnaire. Univariate analysis showed that cleaners with CTS were older, had a higher BMI, and more prolonged exposure to cleaning with previous employers than those without CTS. Rosecrance, J. C., T. M. Cook, D. C. Anton and L. A. Merlino [64] reported in a study involving 1142 apprentices that the prevalence of CTS among apprentice construction workers was 8.2%, in comparison to metalworkers with 9.2%. It was determined that BMI, age, and self-reports of hard work were associated with the prevalence of CTS. The study was conducted by having participants complete a self-administered questionnaire and undergoing an electrophysiological study to assess the median nerve function.

In a study with 900 selected subjects, Cosgrove, J. L., P. M. Chase, N. U. Mast and R. Reeves [65] determined that CTS is related to job classification or other risk factors through an occupational evaluation considering written job analysis, videotaped job analysis, deposition transcripts, and direct interviews, where 50 subjects underwent extensive electrodiagnostic testing. In the population claiming to have CTS caused by railroad occupations, there was a significant association between CTS and BMI, age, and wrist index, but not job classification.

Nathan, P. A., K. D. Meadows and J. A. Istvan [66] conducted a study of the factors associated with CTS in industrial workers (steel pharmacy, meat/food packaging, electronics, and plastics). Their medical history, lifestyle factors, and symptoms were evaluated using interviews and electrodiagnostic studies

were done to measure the median nerve function. The sample consisted of 111 women and 145 men without CTS. The logistic regression analysis showed that older age, female sex, relative overweight, cigarette smoking, and the vibrations associated with job tasks significantly increased the risk for dominant-hand CTS.

Wolf, J. M., S. Mountcastle and B. D. Owens [67] studied CTS in the US military population with the hypothesis that young people would have a lower incidence of CTS than previously reported in populations in general. The unadjusted incidence of carpal tunnel diagnoses in the US military was 3.98 per 1000 person-years in a population of 12,298,088 person-years. Using Poisson regression, the rate ratios for sex were computed, using males as the referent, and controlling for differences in age, race, service, and rank between males and females. It was found that CTS incidence increased by age, with the age group  $\geq 40$  years having a significantly higher incidence. Increased age and advanced rank were risk factors for CTS.

Four studies considered the dominant hand in the analysis of CTS association and risk factors. Zambelis, T., G. Tsigoulis and N. Karandreas [46] found that right-hand CTS was more frequent in younger subjects and females. In contrast, Arslan, Y., I. Bulbul, L. Ocek, U. Sener and Y. Zorlu [37] found no dominant hand association in their study.

Harris-Adamson, C., E. A. Eisen, A. M. Dale, B. Evanoff, K. T. Hegmann, M. S. Thiese, J. M. Kapellusch, A. Garg, S. Burt, S. Bao, et al. [68] conducted cluster population analyses to examine the incidence of CTS in the dominant hand in terms of demographic characteristics and estimated associations with psychosocial occupational factors and years worked, adjusting for confounding personal risk factors, where 3515 participants without CTS were followed for 7 years. Personal factors associated with an increased risk of developing CTS were BMI, age, and being a woman. Mohammad, W. S. [69] conducted a study to explore the prevalence of CTS symptoms among touchscreen users at Majmaah University. A total of 222 female touchscreen users were enrolled in the study. Females with probable CTS and non-CTS were compared on each independent variable using the chi-square test or *t*-test, as appropriate. Regarding CTS risk factors, it was determined that age, BMI, work, predominant hand, years of use, and hours of touch screen use per day use are significantly associated with CTS symptoms.

Mondelli M., A. I., Ballerini M., Ginanneschi F., Reale F., Romano C., Rossi S. and Padua L. [70] aimed to determine whether differences in CTS between women and men are associated with age, education, or BMI in two populations; one with people with non-surgically treated idiopathic CTS and one with people with surgical-decompression-treated idiopathic CTS. The study consisted of 172 non-surgically treated and 219 surgically treated participants. Statistical differences between men and women were assessed using the non-parametric Mann-Whitney test for numerical variables, and with the chi-square test for ordinal scales (education, BMI groups, clinical and electrophysiological severity scales), finding that women have a more negative perception of CTS-related syndromes than men. Differences were not mediated by confounding factors (education, BMI, or age); therefore, sex emerged as the sole factor responsible for these differences.

According to do Amaral e Castro, A., T. L. Skare, P. A. Nassif, A. K. Sakuma and W. H. Barros [71], the prevalence of CTS in a population of hospital workers was of 34%, where age was found to influence CTS. Two hundred healthy individuals participated in the research, which established the respective epidemiological associations. They were questioned and examined for epidemiological data, BMI, signs and symptoms of CTS, and submitted to the BCTQ to assess severity. Then, data were collected and organized according to the frequency and contingency tables and the distribution of the sample was analyzed using the Kolmogorov-Smirnov test. The central tendency was expressed in mean values as a function of non-parametric sampling. Chi-square and Mann-Whitney tests were used for the association studies.

Jerosch-Herold, C., J. Houghton, J. Blake, A. Shaikh, E. C. Wilson and L. Shepstone [72] explored the association of the clinical and baseline severity of patients with anxiety, depression, health-related quality of life, and the costs of CTS in patients referred to secondary care, where 753 patients with CTS provided complete baseline data and self-reported symptom severity, and NCS for one hand

per patient were used. Multivariable linear regression, adjusting for age, sex, ethnicity, duration of CTS, smoking status, alcohol consumption, employment status, BMI, and comorbidities were performed. Patient-reported symptom severity in CTS is significantly and positively associated with anxiety, depression, health-related quality of life, and National Health Service and societal costs, even after adjusting for age, sex, BMI, comorbidities, smoking, drinking, and occupational status.

Day, C. S., E. C. Makhni, E. Mejia, D. E. Lage and T. D. Rozental [73] determined the effects of factors such as age, sex, and socioeconomic status on carpal and cubital tunnel management syndromes. The records of 273 patients diagnosed with CTS or cubital tunnel syndrome were analyzed. Information was collected regarding demographic, clinical, and socioeconomic (insurance) aspects (average income). A regression analysis was performed to determine which input variables contributed to surgical release of their neuropathy and to wait times for those who underwent surgery. The age of the patient was identified as the most critical predictor in terms of the surgical release, and among those with multiple neuropathies, men were more likely to have surgery than women.

One study considered trigger digit release with CTS. Harada, K., H. Nakashima, K. Teramoto, T. Nagai, S. Hoshino and H. Yonemitsu [74] studied 101 cases of patients with trigger digit release operations before and after the release of CTS in two comparison studies. The first study investigated cases that required endoscopic CTR using age, sex, and NCS data, while the second, conducted between the open CTR and endoscopic carpal tunnel release-trigger digit release groups regarding trigger digit release occurrence after CTR and NCS improvement after CTR. The statistical evaluations were done utilizing the Mann–Whitney U test. There was no evidence of any difference due to age or sex. McCabe, S. J., A. Gupta, D. E. Tate and J. Myers [75] considered the role of sleep position as a factor of CTS based on the prevalence of night symptoms, where 68 cases and 138 control subjects were analyzed. Comparisons between the preferred sleeping positions was made and the data were stratified by age and sex, controlled by BMI. The logistic regression models were developed in which sleep position was made a function of CTS, adjusting for BMI. A strong and significant association was found between a preference for sleeping on the side and the presence of CTS in men and women under 60 years of age, and BMI was associated with CTS in women but not in men.

One out of the 42 multifactorial studies determined whether ultrasound could be an alternative to NCS in the diagnosis of CTS [76]. Twenty-nine patients participated in the study and the cross-section of the median nerve was measured using ultrasound, finding that there was no significant difference in age, sex, BMI, and side involvement between the patients. Therefore, it was concluded that ultrasound is not accurate enough to replace the nerve conduction study to diagnose CTS.

Rouq et al. [77], when studying the disposition of clinical symptoms in patients with CTS through NCS, identified the primarily symptoms in the male sex in the three lateral fingers, hand, and forearm, while the female sex registered greater symptoms in the tips of the lateral fingers and the hand. Regarding the influence of age, patients 50 years and older had more significant symptoms in the three lateral fingers; in contrast, patients aged <50 years of age presented more symptoms in the wrist.

On the other hand, a study analyzed the effect of winter and summer seasons on CTS patients through NCS, and found the presence of CTS mostly occurred in winter. The female sex and the dominant hand had a more significant impact [78].

Finally, Chan, L., J. A. Turner, B. A. Comstock, L. M. Levenson, W. Hollingworth, P. J. Heagerty, M. Kliot and J. G. Jarvik [79] considered whether the results of the electrodiagnostic study are associated with symptom severity and functional limitations in patients with CTS after controlling for variables such as age, sex, BMI, depression, somatization, and pain-related catastrophe, where 215 patients with CTS participated in this research and the data were analyzed using descriptive statistics and linear regression analysis. The results obtained from the electrodiagnosis and the CTS symptoms and function were shown to be independent measurements, both with and without controlling variables.

#### 4. Trends and Future Challenges

Among the trends and future work to be done, we recommend verifying whether hypovitaminosis D correction could be of any benefit in treating and reducing pain severity in CTS patients [13]. It is necessary to explore anthropometric measurements that depend not only on unidimensional measures but also include the area or volume of the CTS [16]. The impact of approaches and treatments that address psychosocial stressors and biomedical factors on the relief of symptoms from CTS should first be understood [72]. Large prospective trials looking at an effective obesity countering regimen should be employed to explore the optimal weight reduction parameters for CTS in study populations [23].

The results of a shorter duration of time before complete resolution of symptoms in the non-dominant hand for severe CTS illustrates the need for further research in this area to better understand the recovery process following CTR. Furthermore, it may provide future research directions on post-operative rehabilitation following carpal tunnel surgery [29]. We proposed that additional studies should be carried out for further assessment of the relationship between a square-shaped wrist and CTS, especially as it relates to BMI since such research can more definitively identify the corresponding pathophysiological mechanisms [42].

Further studies are needed to confirm a broader hand volume tendency toward idiopathic CTS occurrence [37]; more specifically, future studies should investigate the natural history of CTS prospectively to assess whether changes in weight and waist circumference predict the severity of clinical and electrophysiological findings [39]. Further awareness is needed regarding a patient's sex, as women and men appear to present with a different set of symptoms and at different disease stages; therefore, prospective studies should be carried out to elucidate this [36]. Furthermore, an investigation of the possible correlation of the size of the canal relative cross-sectional areas (RCSAs) among CTS patients and healthy subjects is required [34].

The role of visceral and total body fat in CTS should also be considered in future studies [18]. Further analysis will identify the biomechanical risk factors associated with CTS and clarify possible interactions between occupational psychosocial factors, personal factors, and workplace physical exposures [68]. Further studies may be warranted to identify ethnic, sex, and socioeconomic factors that influence surgical treatment rates [58]. Other unidentified personal cofactors most likely become lost in the lateralization of CTS and must be investigated in the absence of known risk factors [46]. The next step is an analysis by occupation within this group to identify persons at high risk because of their jobs [67].

A more detailed, genetic-factor-targeted investigation may prove more beneficial to clarify this issue [19]. To further elucidate the role of hand anthropometries on the development of CTS, we proposed that future studies should have a larger sample size of male subjects, an even distribution of patients among severity subgroups, and use universal electrodiagnostic criteria [17]. Furthermore, the previously unreported finding of higher incidence in females requires further investigation [60].

Prospective cohort studies could be a better way of elucidating independent risk factors in CTS patients [43]. Future studies on diagnostic and treatment support for CTS should consider the possibility of diagnosing or treating two different conditions, even if both ultimately result in compromising the median nerve at the wrist, and examine whether their findings apply equally to patients above and below 63 years of age [53].

Becker, J., Nora, D.B., Gomes, I., Stringari, F.F., Seitensus, R., Panosso, J.S. and Ehlers, J.A.C. [47] state that a prospective study with diabetic patients could be a better way to elucidate the real association between diabetes and CTS. Longitudinal and genetic studies with physician verification of migraine headaches and CTS are needed to define this association further [52].

#### 5. Limitations

Despite the existence of several risk factors for CTS, this paper was limited to the study of age, sex, BMI, handedness, abdominal circumference, respiratory rate, and blood pressure because we intend to study these variables further research and apply them in the manufacturing industry.

## 6. Conclusions

CTS is associated with older age, female sex, and high BMI. Regarding age, it is considered the most important predictor of surgical release, and among those with multiple neuropathies, male patients were more likely to have surgery than female patients. CTS is a work-related disease in both men and women when the occupational tasks are similar. Women with CTS were more sensitive than men regarding reporting their symptoms. Older age, higher BMI, and diabetes mellitus were more prevalent in patients with bilateral CTS. Age and BMI were independently associated with bilateral CTS. Finally, there is an association between CTS and cardiovascular risk factors in young people and carotid intima-media thickness.

**Author Contributions:** M.A.C.-M.: conceptualization; M.A.C.-M., C.C.W., and R.V.: investigation; M.A.C.-M. and R.V.: data organization; M.A.C.-M. and C.C.W.: writing—original draft; J.L.G.-A. and M.A.C.-M.: writing—review and editing; J.A.L.-B., J.L.G.-A., and J.E.O.-T.: supervision; B.R.G.-R.: project administration. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received support from the Program for Professional Teacher Development (PRODEP). Authors appreciate the doctoral scholarship granted to Melissa Airem Cazares Manriquez from Mexican National Council for Science and Technology (CONACYT).

**Conflicts of Interest:** The authors state that they have no conflicts of interest to declare.

## Appendix A. Journals with One Publication

Journal	Year of Publication
<i>Pakistan Journal Medical Sciences</i>	2019
<i>Rev. Chir. Orthop. Traumatol</i>	2018
<i>Nigerian Journal of Clinical Practice</i>	2018
<i>Advanced Biomedical Research</i>	2018
<i>Clinical Neurophysiology</i>	2018
<i>Psychiatry Neurosurgery</i>	2018
<i>Clinical Anatomy</i>	2018
<i>Neurological Sciences Journal</i>	2017
<i>Journal of Occupational Health</i>	2017
<i>Asian Journal of Neurosurgery</i>	2017
<i>BMJ Open</i>	2017
<i>Annals of Rehabilitation Medicine</i>	2017
<i>Cureus</i>	2017
<i>Journal of Clinical Neurophysiology</i>	2017
<i>J. Med. Ultrason.</i>	2016
<i>J. Clin. Diagnostic Res.</i>	2016
<i>Ar. of Physical Medicine Rehab.</i>	2016
<i>Radiologia Brasileira</i>	2015
<i>Plastic. Reconstruction. Surgery</i>	2015
<i>J. of Turgut Ozal Medical Center</i>	2015
<i>Coll Antropol.</i>	2014
<i>Neurol. Med. Chir</i>	2014
<i>Occup. Environ. Med.</i>	2013
<i>Egyptian J. of Neurol., Psychiat. &amp; Neurosurg.</i>	2013
<i>Trauma Mon</i>	2012
<i>BioMed Central Musculoskeletal Disorders</i>	2011
<i>Clin. Orthop. Relat. Res.</i>	2010
<i>J. of Brachial Plexus and Peripheral Nerve Injury</i>	2009
<i>J. Hand Surgery—European</i>	2009

<i>Occupational and Environmental Medicine</i>	2009
<i>Scand. J. Work Environ. Health</i>	2009
<i>Int. Orthop.</i>	2008
<i>Folia Morphologica</i>	2008
<i>J. Gen. Pract.</i>	2007
<i>Arch. Phys. Med. Rehabil.</i>	2007
<i>British Society for Clinical Neurophysiology</i>	2006
<i>Neurophysiologie Clinique</i>	2006
<i>Ortopedia Traumatologia Rehabilitacja</i>	2006
<i>Hand Surg.</i>	2005
<i>Acta Neurologica Scandinavica</i>	2005
<i>European Journal of Neurology</i>	2005
<i>Clin. Neurol. Neurosurg.</i>	2004
<i>Clin. Neurophysiol.</i>	2002
<i>American J. of Physical Medicine &amp; Rehab.</i>	2002
<i>The Journal of Bone &amp; Joint Surgery</i>	2002
<i>Am. J. Ind. Med.</i>	2002
<i>Annals of Epidemiology</i>	2000
<i>Arq. Neuropsiquiatr.</i>	2000
<i>Environ. Res.</i>	2000

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