Epidemiologic Associations of Carpal Tunnel Syndrome and Sleep Position: Is There a Case for Causation?

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Abstract

Introduction Carpal tunnel syndrome (CTS) is thought to be due to compression of the median nerve in the carpal tunnel. It is known that carpal tunnel pressures are elevated in wrist postures of flexion and extension and in those patients with CTS. Classic symptoms of CTS include night waking with pain, tingling, and numbness. These classic symptoms stimulated our interest in the relationship of sleep to the development of CTS.

Method We reviewed the literature surrounding the epidemiology of CTS and the literature regarding sleep disturbances. Through careful distillation of these studies and a process of reasoning, we have developed a hypothesis for a causal mechanism of CTS.

Results Epidemiologically, it has been shown that CTS is associated with age, gender, increased body mass index (BMI), diabetes, pregnancy, and is more common in some populations. The same associations noted above for CTS are strongly associated with sleep disturbances. Sleep disturbances due to age, gender, BMI, pregnancy, and population variations are all associated with sleeping in the lateral position supporting the hypothesis that a common causative mechanism of CTS is sleeping in a lateral position. **Discussion** We believe that the epidemiologic associations with CTS act through a common causative mechanism, increased sleeping in the lateral position which puts the wrist at increased risk of flexion or extension, compressing the median nerve in the carpal tunnel. This hypothesis is simple and explains the connection between a previously unconnected group of epidemiologic associations. This realization has real clinical significance in that it focuses our attention on the early disorder when it is completely reversible. It clarifies previously confused clinical circumstances, creates research questions that can be tested, and it invites us to change our clinical perspective in this most common form of nerve compression.

Keywords Carpal tunnel syndrome · Causation · Sleep disturbance · Sleep position

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Introduction

Carpal tunnel syndrome (CTS) is the most common form of peripheral nerve compression. An estimated 400,000 surgical cases are performed in the United States each year [24]. Despite the familiarity with clinical care of patients with CTS, an understanding of the causation of CTS remains elusive. There has been no unifying theory that

links together the multiple known associations of CTS into a common causative mechanism.

There is no standard approach that can be applied as proof of causation. The criteria of Hill are often used to support or refute causation; however, epidemiologic checklists are useful but not definitive (see Rothman for a discussion [51]). Rothman suggests that we use the concept of a sufficient cause for a disease, which is “a set of minimal conditions and events that inevitably produce disease” [51]. Following from this idea of a sufficient cause, a causal mechanism is the sequence of events that leads to the disease. One important aspect of this concept is that only one component of the causal mechanism need be blocked or eliminated to result in disease prevention or reduction.

Using Rothman’s term, compression of the median nerve in the carpal tunnel is widely perceived as the sufficient cause of CTS. Nighttime symptoms, usually attributed to wrist position, are common in CTS, motivating us to consider the possible role of sleep position in the genesis of this disorder. To evaluate this, we reviewed the epidemiologic associations of CTS and the literature regarding sleep disturbances and sleep position. Through distillation of these studies and a process of reasoning, we developed a hypothesis that links the known associations of CTS through an underlying causative mechanism for CTS.

This new hypothesis helps us to understand the multiple associations of CTS that were not previously linked in a

simple theory. In addition, this hypothesis makes predictions that can be tested. Finally, this new hypothesis invites us to think of CTS in a different fashion that has real management implications for patients.

CTS and Pressure

Increased pressure in the carpal tunnel in patients with CTS and increased pressure in the carpal tunnel with wrist flexion and extension has been consistently and repeatedly shown. Table 1, summarizing a review of the literature, is copied from the report by Weis et al. [60]. Gupta has shown that pressure causes early ultrastructural changes in nerve before changes occur in electrodiagnostic testing [19]. It is widely accepted that pressure on the median nerve is a “sufficient cause” of CTS as defined by Rothman.

CTS and Sleep

In a review of CTS published in 1962, it was noted that symptoms “often increase at night” [61]. In a study comparing clinical features of patients with the results of electrodiagnostic studies, Katz et al. [23] found 77% of those with a positive electrical test to have nocturnal symptoms. These numbers are almost identical to results published by others in 2005 [59].

Table 1 Summary of the review of literature.

Study	Patients Who Had Carpal Tunnel Syndrome				Control Subjects			
	Number of Wrists	Neutral ^a	Flexion ^a	Extension ^a	Number of Wrists	Neutral ^a	Flexion ^a	Extension ^a
Gelberman et al. ⁹ (1981)	15	32 (4.27)	94 (12.53)	110 (14.66)	—	—	—	—
Werner et al. ³⁶ (1983)	16	31 (4.13)	75 (10.00)	105 (14.00)	—	—	—	—
Szabo and Chidgey ³⁴ (1989)	22	10 (1.33)	32 (4.27)	51 (6.80)	6	5 (0.67)	16 (213)	27 (3.60)
Okutsu et al. ²³ (1989)	62	43 (5.73)	192 (25.60)	222 (29.60)	32	14 (1.87)	144 (19.20)	27 (3.60)
Luchetti et al. ³⁰ (1989)	30	26 (3.47)	—	—	4	13 (1.73)	—	—
Rojviroj et al. ²⁸ (1990)	61	12 (1.60)	27 (3.60)	33 (4.40)	32	4 (0.53)	9 (1.20)	13 (1.73)
Graham et al. ¹⁴ (1991)	22	20 (2.67)	—	—	13	12 (1.60)	—	—
Average	—	26 (3.47)	—	—	—	9 (1.20)	—	—

^a Values are given as millimeters of mercury with kilopascals in parentheses.

Copied from Weiss ND, Gordon L, Bloom T, So Y, Rempel DM. Position of the wrist associated with the lowest carpal-tunnel pressure: implications for splint design. *J Bone Joint Surg Am* 1995;77:1695–1699.

Figure 1 Prevalence of insomnia: age and sex distribution (copied from Cirignotta F, Mondini S, Zucconi M, Lenzi PL, Lugaresi E. Insomnia: an epidemiological survey. *Clin Neuropharmacol* 1985;8 Suppl 1:S49–S54).

Epidemiology of Carpal Tunnel Syndrome and Sleep Disturbances

Age The development of CTS is related to age. Phalen reported the number of cases increased for each decade of age to 59 years, after which, the number of cases in each decade decreased [45]. Atroshi et al. [3] observed a similar age distribution with the highest prevalence of CTS in men of 45–54 years and of women of the age of 55–64. Bland and Rudolfer [7] found that cases of CTS had a bimodal distribution for age with a peak at age 50–54 and a second peak at age 75 to 84 years. Similarly, Mondelli et al. reported: “The age-specific incidence for women increased gradually with age, reaching a peak between 50 and 59 years, after which, it declined. In men, there was a bimodal distribution with peaks between 50 and 59 years and between 70 and 79 years” [31].

Gender Phalen noted in 1966 that the gender distribution of CTS was two-thirds to one-third female to male [45]. The increased presentation of women with CTS was also noted by Mondelli et al. [31] with 79.7% of cases in women. Atroshi et al. found the male to female ratio to be 1:1.4 [3]. Within women, using a nested case-control design, Ferry et al. [14] found associations with previous history of another musculoskeletal complaint, OR 1.98, past use of oral contraception, OR 1.38, obesity, OR 1.68, and diabetes and myxoedema.

Age, Gender, and Insomnia There is extensive literature that links age and gender with sleep disturbances [5, 26]. Insomnia is more common in women and increases with age, increasing more in women than in men [11]. Figure 1 shows the age and sex distribution of prevalence of insomnia in a large survey in Italy, whereas Fig. 2 shows the age and gender distribution of cases of CTS confirmed electrically at two locations in the UK [7]. There is

similarity in gender and age distribution of insomnia and the development of CTS. Both increase with increasing age, both show a bimodal distribution primarily in women, and both are more prevalent in women. Recently, Shepertycky [54] has shown that women with obstructive sleep apnea often presented with complaints of insomnia. This suggests some of these women with insomnia may have also had obstructive sleep apnea.

BMI The association of CTS with obesity or increased BMI has been noted and found repeatedly [9]. Nordstrom et al. [37] found the risk of CTS increased 8% for each unit of increase in BMI (about 6 lbs.). Nathan and Keniston summarized that being overweight, older, and physically inactive are major risk factors for slowing (of the median

Figure 2 Age and gender distribution of cases of CTS confirmed electrically at two locations in the UK (copied from Bland JP, Rudolfer SM. Clinical surveillance of carpal tunnel syndrome in two areas of the United Kingdom, 1991–2001. *J Neurol Neurosurg Psychiatry* 2003;74:1674–1679).

nerve) and clinical CTS [33]. Bland found some complexity in the relationship between age and obesity, and CTS. Bland noted that “increased BMI is a significant independent risk factor for CTS in patients under the age of 63 years but is less important in older patients” [6] and further suggested that “...CTS in the elderly population may have different underlying pathogenetic mechanisms” [6].

BMI can be influenced by exercise, and Nathan reported that people with CTS who embarked on an exercise program decreased body fat, BMI, sensory latency at the carpal tunnel and carpal tunnel symptoms [32]. Mondelli et al. notes an increase in age-adjusted incidence from 1960–1980 [31]. The authors suspected this could be partially the result of more sensitive diagnostic testing and the opening of an Orthopedic Department.

Age, Gender, BMI, and sleep disorders Snoring and sleep apnea are known to be associated with age and BMI. Gislason et al. [17] reported that 15.5% of Swedish men and 11.2% of Icelandic women reported habitual snoring. They reported an increase with age for men and women until the age of 60 years after which there was some decline in men. These authors found sleep apnea to be more common in older postmenopausal women than in men, but this specific finding is not typical.

Most studies of snoring and sleep apnea find these problems to be related to age and in contrast to insomnia, more common in men [52]. Snoring and obstructive sleep apnea increase with age in adulthood and decrease in the elderly. Men are affected more than women. Redline looked at age strata found that BMI > 28 kg/m² (OR 11.7) and male gender (OR 12.2) are significant risk factors for sleep apnea in subjects aged 22 to 55 years but not younger or older [48]. Through its influence on sleep position, sleep apnea may offer insight to the potential causal relationship of sleep disturbances and sleep positions related to CTS.

Pregnancy There is a general belief that CTS is associated with pregnancy. Padua reported that 59% of women in their eighth or ninth month of pregnancy complained of paresthesia in at least one hand (56% R, 45% L, and 41% bilateral) [43]. Electrodiagnostic studies were consistent with CTS in 43%. The duration of symptoms was a mean of 3.4 months. Stolp-Smith [58] noted 50% of CTS cases in pregnant women occurred in the third trimester. It is widely recognized that CTS will usually resolve after pregnancy.

Pregnancy and Sleep Position The relationship of pregnancy and sleep position offers further evidence of the association of sleep position to CTS. As noted above, CTS is common in the third trimester of pregnancy. Because of the enlarging uterus, clinicians recommend that pregnant women adopt a sleeping position on the left side.

Populations Nathan found the prevalence of probable and definite CTS much lower in Japanese compared to American populations but the prevalence of slowing of the median nerve to be similar [34].

Sleep Position Related to a Specific Population In our review, we were intrigued by a sleep disorder called “Sleep Paralysis (SP) and Associated Hallucinations” because “it is widely believed that lying in the supine position is a proximate cause of SP” [10]. We do not believe CTS is related to SP; however, research into SP has created some interesting information about sleep position. In one study of sleep positions in Japan and Canada, Fukuda found that 58.8% of Canadian university students and 32.4% of Japanese university students sleep on their side, whereas 40.5% of Japanese and 3.5% of Canadian students sleep on their back [15].

Diabetes Singh et al. wrote CTS occurs in 6–30% of individuals with diabetes and in 2–3% of the general population. The prevalence increases with the duration of diabetes [55]. Those who had developed CTS had had diabetes longer than those who had not yet developed CTS. The calculated lifetime risk of CTS was 50% after 44 years and 85% after 54 years of having type 1 diabetes [55]. Becker et al. [4] showed that while diabetes may be a significant risk factor for CTS in women, diabetes only appears to be a risk factor for CTS when combined with BMI.

Diabetes, Obesity, and Sleep Disturbance According to the National Sleep Foundation’s survey, 11% of those who claim that sleep problems also have been diagnosed with diabetes [35]. Khuram et al. [25] concluded that diabetes mellitus (65%) and sleep disorders (35%) were obesity-related complications in subjects of age range 50–59 years. Sleep disturbances and insomnia are more common in diabetics than in control groups [22, 57]. Skomro et al. [56] concluded that adult type 2 diabetics had higher incidences of insomnia than control groups. Compounding the problem of reduced sleep in DM patients, Gottlieb et al. [18] showed that a study on sleep restriction suggested a causal association between shortened sleep and impaired glucose tolerance.

Sixty-four percent of the respondents to the 2005 Sleep in America Poll conducted by the National Sleep Foundation had a BMI > 25.0. These individuals were more likely to get less than 6 h of sleep a night, experience insomnia, and are at a higher risk for sleep apnea [35].

BMI and obesity has been found to be predictors of heavy snoring [13]. As elevated BMI/obesity is an elevated risk for sleep problems, in kind, it puts an individual at a higher risk for acquiring diabetes. Obstructive sleep apnea is more common among diabetic populations [22], as heavy snoring can lead to “oxygen desaturation which increases

catecholamine and cortisol levels, thereby increasing insulin resistance” [2]. Snoring caused by obstructive sleep apnea, or sleep-disordered breathing has been found to elevate the risk for acquiring type II diabetes [2, 47, 49]. There is a high prevalence of insomnia in diabetic hemodialysis patients [20].

Shift Work Shift work and night work are probably the most severe precipitating factors of insomnia [12, 30]. Shift-work is one of the leading circadian rhythm disorders causing insomnia [1, 12, 50]. Roth and Roehrs suggest that shift work is one of the leading risk factors for developing chronic insomnia [50].

Arthritis A number of studies have noted that sleep disturbances are a common problem in children with juvenile rheumatoid arthritis [8, 28, 44]. In a study by Power et al., [46] pain was determined to be a key mediator in the correlation between arthritis and sleep disturbances. Similarly, Ohayon found that arthritis as a chronic painful condition was a cause of major sleep disturbances [40]. Nicassio and Wallston observed that RA appeared to be a strong cause of sleep disturbances and that RA patients attributed their sleep problems to their arthritic pain more often than other stresses in their life [36].

BMI/Obesity Trends in USA

In a 6-year study examining obesity trends in the United States from 1999–2004, Odgen et al. [39] observed that overall obesity appears to be increasing among children, adolescents, and male adults. This latest study confirming a continuing trend noted by Odgen: “Between 1980 and 2002, obesity prevalence doubled in adults aged 20 years or older, and overweight prevalence tripled in children and adolescents aged 6 to 9 years” [39]. Sixty-four percent of the respondents to the 2005 Sleep in America Poll conducted by the National Sleep Foundation had a BMI > 25.0.

Sleep-Related Problems in the United States

The National Sleep Foundation’s 2005 Survey notes that sleep problems in America have been on a steady increase since 1999, with 75% of Americans reporting regular sleep problems. Sleep problems included disturbances such as insomnia, frequent waking, snoring, restless leg syndrome, and pauses in breathing [35].

Approximately one-third of the population surveyed reported experiencing insomnia every night of the week,

while half reported insomnia or other sleep problems at least a few nights a week. Some of the most common complaints of individuals suffering from sleep problems were snoring, sleep apnea, and restless leg syndrome. According to respondents from the national sleep survey, women were more likely than men to report that they get less sleep than they need [35].

Hypothesis Development

We were interested in sleep from the perspective of CTS because of the frequency of night time complaints in CTS patients and the prevalence of sleep disorders in the US population. Using the knowledge that wrist position causes increased pressure in the carpal tunnel, we were vigilant for information that could lead to inference about wrist position. Looking closely at the shared relationship of CTS and insomnia with age and gender, as evidenced by Figs. 1 and 2, it became apparent that the relationship was unlikely to be a random event. We could not think of an obvious link to sleep or wrist position or a direct biologic mechanism for insomnia to cause CTS, although at first glance, the opposite could be true. The prevalence of CTS is much less than insomnia, so we felt the direction of this relationship could not be that CTS caused insomnia.

We then focused our interest on snoring and sleep apnea. Both snoring and sleep apnea increase in prevalence until some age threshold, when they, like CTS, decrease. In contrast to CTS, they are both more common in men. Snoring and sleep apnea, like CTS, are also associated with increased BMI. Once again, there is an age threshold for the effect of BMI. Increased BMI is reported to have an influence on both sleep apnea and CTS in adults but not in the elderly. We are not sure of the explanation of this observation.

Looking further into the biology of sleep apnea provides a potential mechanism for the development of CTS. In sleep apnea, cessation of breathing is believed to be caused by collapse and obstruction of the upper airway. This is more likely when sleeping in the supine position and is exacerbated by age and increased body weight. The cessation of breathing results in “arousals” that prevent satisfying sleep. It is known that sleeping in the lateral position can improve sleep apnea. In normal weight individuals, 90.0% had a good response to sleep position change, 74% in the mildly obese group, and 57.4% in the obese group [21].

Obstructive sleep apnea is divided into positional and non-positional, depending on the influence of sleeping on the side on the degree of respiratory disturbance. Positional patients have been found to have less severe and fewer breathing abnormalities than non-positional patients. This is

thought to be due to improved sleep quality from sleeping in the lateral position [42]. Oksenberg suggests that many patients of both sleep apnea groups avoid the supine posture spontaneously during sleep [41]. One treatment for obstructive sleep apnea is to encourage sleeping on the side. Research does support that people will seek out sleep positions that provide the most comfort. Kubota has shown that men have a favorite sleeping position, and the stated position correlates with the most frequent sleeping position observed [27].

People with higher BMI and of older age may be more likely to sleep on their side to improve their upper airway mechanics. If sleeping on the side is related to positioning the wrist in flexion or extension, this could be a causal pathway for nerve compression. This is also supported by sleep position in pregnancy. Although we have been unable to find literature to link sleeping on the side with the presence of insomnia, Sheperdycky [54] has recently shown that women with obstructive sleep apnea often presented with complaints of insomnia.

The observations of sleep position in Japan and Canada and the observation of the prevalence of CTS in the US and Japanese populations also support our hypothesis.

The relationship between diabetes and CTS could be mediated by increased BMI and sleep position. Other associations with CTS such as certain occupations and arthritis may also be associated with sleep position, sleep disturbances, and insomnia but once again, the relationship to sleep position is less clear.

Although not specifically related to CTS in the detail we describe, sleep position has been suggested in the literature as a causative mechanism in nerve compression, and the importance of posture has been extensively discussed by Novak and Mackinnon [29, 38].

Removal of a Step in a Causative Pathway

Rothman [51] has noted that if any step in a causative mechanism is interrupted, the presence of the disease can be prevented. Sevim et al. showed that in patients with mild and moderate CTS, night splinting gave a significant improvement at 1 year. Gerritsen [16] showed 37% success for patients treated with splinting alone after 18 months. Nathan has shown a reversal in CTS with a reduction in BMI, and it is known that CTS in pregnancy will usually resolve after delivery.

When sleeping on ones side, we have observed and experienced flexed and extended wrist positions due to the angle of attack of the uppermost arm as it contacts the bed or lower arm. The lower arm can assume a vertical position and with gravity causing flexion or extension of the wrist.

Direct pressure from sleeping with the hand and wrist under the pillow could occur in any sleep position.

This is the only hypothesis that links the commonly known epidemiologic features of CTS. The common pathway pointing to sleep position through unrelated sleep-related conditions that closely correspond to epidemiologic features associated with CTS give credibility to this hypothesis.

Sleep Position-Attributed Nerve Compression

We do not know the attributable risk of sleeping on the side, which is the difference in risk of developing CTS between those sleeping on the side compared to those who do not. Neither do we know the etiologic fraction, which is the percentage of cases that could be prevented by removing the exposure.

Our hypothesis does not negate other causes of CTS. It is known that there is a redistribution of body fluid to the upper body during sleep. This added volume could sensitize the carpal tunnel to the effects of wrist position. It is also possible that other features of sleep and sleep disturbance could be causing CTS. Activities other than sleep that cause the wrist to be in a flexed or extended posture or that directly compress the carpal tunnel can also be implicated as causative. Similarly, any disorder or activity that causes a mass effect in the carpal tunnel could cause nerve compression.

Hypothesis

We believe, after review of the literature, that the associations of CTS have a common causative pathway through sleep position and can be best explained as resulting from a sleep position on the side causing the wrist position to be deviated into flexion or extension, compressing the median nerve in the carpal tunnel, and initiating the sequence of events resulting in CTS. This hypothesis can be tested by clinical research. We predict an association between women, people with higher BMI, and people who are older, and sleeping on the side. We predict that in the elderly, BMI is supplanted by a search for comfort in the cervical spine or back causing older people to sleep on their side. These predictions can be evaluated with a cross-sectional survey. We predict that patients with CTS will sleep on their side more than other persons and that when sleeping on the side is controlled by study design, the association of age, BMI, and gender with CTS will be reduced or will disappear. This prediction can be tested using a case-control study design.

We predict that patients with sleep apnea and early CTS will improve with treatment for sleep apnea that encourages a supine sleeping position even without wrist splinting. This could be tested using a cohort study. Finally, we predict that a randomized trial of preventative splint wear in pregnant women will prevent CTS.

This type of further research can add evidence to determine if these known associations with CTS and sleep disorders act through a common causative pathway by increasing the probability a person will sleep on their side.

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