

# Association Between Cardiovascular Risk Factors and Carpal Tunnel Syndrome in Pooled Occupational Cohorts

Kurt T. Hegmann, MD, MPH, Matthew Steven Thiese, PhD, MSPH, Jay Kapellusch, PhD, Andrew S. Merryweather, PhD, Stephen Bao, PhD, Barbara Silverstein, PhD, Eric M. Wood, MD, MPH, Richard Kendall, DO, Jacqueline Wertsch, MD, James Foster, MD, Arun Garg, PhD, and David L. Drury, MD, MPH

**Objective:** The aim of the study was to ascertain if cardiovascular (CVD) risk factors are carpal tunnel syndrome (CTS) risk factors. **Methods:** Analysis of pooled baseline data from two large prospective cohort studies ( $n = 1824$ ) assessed the relationships between a modified Framingham Heart Study CVD risk score both CTS and abnormal nerve conduction study prevalence. Quantified job exposures, personal and psychosocial confounders were statistically controlled. Odds ratio and 95% confidence intervals were calculated for individual risk scores. **Results:** There was a strong relationship between CVD risk score and both CTS and abnormal nerve conduction study after adjustment for confounders, with odds ratios as high as 4.16 and 7.35, respectively. Dose responses were also observed. **Conclusions:** In this workplace population, there is a strong association between CVD risk scores and both CTS and abnormal nerve conduction study that persisted after controlling for confounders. These data suggest a potentially modifiable disease mechanism.

The strongest and most consistent risk factors for carpal tunnel syndrome (CTS) appear to include age, obesity, and combinations of force and repetition.<sup>1–8</sup> These factors have now been confirmed in several prospective cohort studies.<sup>9–16</sup> Whereas some have suggested work-related factors are the greatest risks, a population-based estimate of risk of CTS in the state of Wisconsin with an approximate population of 5 million demonstrated both high and increased risk among those over 65 years of age<sup>17</sup> apparently at least partially contradicting the assumption of a large overall magnitude of impact of occupational factors.

There is no consensus on a unifying theory for the mechanism of CTS.<sup>18–20</sup> The lack of a unifying theory impairs the testing of the purported root cause(s), as well as hinders effective prevention programs.

Recently, some data have suggested cardiovascular (CVD) risk factors may raise risk of CTS.<sup>3,21–29</sup> This is particularly suggested by both the data on metabolic syndrome<sup>26–28</sup> and insulin resistance<sup>30</sup> as well as a few retrospective studies suggesting an association with carotid intima-media thickness.<sup>31–33</sup> CVD disease association has

been further suggested by a protective effect of vigorous exercise with and without wrist strain reported in a case-control study.<sup>34</sup>

As both obesity and diabetes appear to be risk factors, this also suggests a potential relationship with CVD disease. Support is found in the literature investigating body shape that appears to be a risk factor with waist circumference having been shown to have a stronger correlation with CTS than hip circumference in men, and both waist-to-hip ratio and body mass index (BMI) have overall comparable associations with CTS.<sup>35</sup> A case-control study found waist circumference and waist-to-hip ratio as independent risks that amplify risk above that from BMI alone.<sup>27</sup> Waist circumference was also identified as an independent risk in another study that also found a relationship with electrodiagnostic severity of CTS.<sup>36</sup>

There are numerous other reported risk factors such as diabetes mellitus (DM).<sup>3,21–25</sup> Fewer studies have assessed risk from metabolic syndrome, although it also is reportedly a risk.<sup>26–28</sup> Low-density lipoprotein is another purported risk, although data are sparse.<sup>29</sup> A recent meta-analysis reported tobacco use doubled risk of CTS in cross-sectional studies, but was not found to increase risk in either case-control or cohort studies.<sup>37</sup> Yet, many of the occupational epidemiological studies reported<sup>9–15,38</sup> are severely underpowered for diseases such as DM, as the prevalence of various diseases are naturally low in younger, employed workforces. The occupational cohorts were also largely not designed to test associations with CVD disease.

The purpose of this study was to analyze pooled data from two large prospective cohort studies to evaluate for an association between modified Framingham Heart Study-based CVD risk data and risk of CTS.

## METHODS

This study was approved by the institutional review boards of the University of Wisconsin-Milwaukee, the University of Utah, and the State of Washington. Detailed methods and data collection instruments are available elsewhere,<sup>12,39,40</sup> thus abbreviated methods follow.

Workers were recruited from 35 facilities involving 25 diverse industries located in the states of Illinois, Utah, Washington, and Wisconsin. These employees worked manufacturing, food processing, and office jobs. Workers were consented.

The Health Outcomes Assessment Teams collected data from computerized questionnaires, structured interviews, standardized physical examinations, and nerve conduction studies (NCS). Questionnaire data included demographics, hobbies, physical activities outside of work, psychosocial (eg, job satisfaction), and medical history data (eg, DM, hypertension). Structured interviews included data on the presence and distribution of tingling/numbness and pain. Body mass indices were calculated from measured heights and weights. Blood pressure was measured after being seated for at least 5 minutes, and most often after at least 20 minutes, using automated cuffs (Omron HEM-780, Kyoto, Japan).

All workers underwent a NCS of each hand regardless of symptoms at baseline. The examiners were blinded to the worker's

From the Rocky Mountain Center for Occupational and Environmental Health (Dr Hegmann, Dr Wood, Dr Thiese), University of Utah, Salt Lake City, Utah; Center for Ergonomics (Dr Kapellusch, Dr Foster, Dr Garg), University of Wisconsin-Milwaukee, Milwaukee, Wisconsin; Department of Mechanical Engineering (Dr Merryweather), University of Utah, Salt Lake City, Utah; Safety and Health Assessment and Research for Prevention (SHARP) Program (Dr Bao, Dr Silverstein), Washington State Department of Labor and Industries, Olympia, Washington; Physical Medicine and Rehabilitation (Dr Kendall), University of Utah, Salt Lake City, Utah; Physical Medicine and Rehabilitation (Dr Wertsch), Medical College of Wisconsin, Milwaukee, Wisconsin; Allina Health Clinics, Minneapolis, Minnesota.

Address correspondence to: Kurt T. Hegmann, MD, MPH, Rocky Mountain Center for Occupational and Environmental Health, Department of Family and Preventive Medicine, School of Medicine, University of Utah, 391 Chipeta Way, Suite C, Salt Lake City, UT 84108 (kurt.hegmann@hsc.utah.edu).

Copyright © 2015 American College of Occupational and Environmental Medicine

DOI: 10.1097/JOM.0000000000000573

symptoms and job physical exposures. The NCS protocol followed the recommendations of the American Association of Neuromuscular & Electrodiagnostic Medicine.<sup>41</sup> A minimal hand temperature of 30°C was assured before conducting NCS. Standard antidromic sensory, motor, and transcarpal (mixed nerve) studies were done for both the median and ulnar nerves bilaterally.<sup>42</sup> Distances of 14 cm for sensory, 8 cm for motor, and 8 cm for transcarpal studies were used with reference values of 0.55 ms or less for transcarpal delta (difference between the transcarpal sensory latencies for the median and ulnar nerves), 3.7 ms or less for sensory latency and 4.5 ms or less for motor latency. Workers with diffuse nerve conduction abnormalities (both the median and ulnar nerves) were excluded. Workers with a peak ulnar latency at least 3.68 ms at 14 cm were classified as having polyneuropathy and were also excluded. Those workers with transcarpal delta >0.55 ms were classified as having an “abnormal” NCS consistent with median mononeuropathy at the wrist. Workers classified as having “abnormal NCS” may or may not have had abnormal median nerve sensory and/or motor latencies.

A symptomatic episode was tingling, numbness, burning, and/or pain in at least one of the first three digits (thumb, index finger, and/or middle finger). The CTS case definition required the following: (1) either four or more symptomatic episodes or one or more symptomatic episode lasting at least 7 days in the past 12 months, and (2) an abnormal NCS consistent with CTS.

Jobs were measured and videotaped by the Job Exposure Assessment Teams. Strain Index scores, a combination of six job physical variables (force, repetition rate, duration of exertion, posture, speed of work, and task duration per day), were computed from these analyses.<sup>12,43,44</sup>

CVD variables of age, treated and untreated, measured or self-reported past diagnosis of hypertension, tobacco use, and DM assigned a point value, stratified by gender, in accordance with the Framingham Heart Study (Table 1).<sup>45</sup> The Framingham score does not use BMI and cholesterol was excluded from the score metric because it was not measured. In addition, blood pressure scores in the Framingham score were modified from the original Framingham score. Participants in Washington (n = 746) and Wisconsin (n = 3) did not have a blood pressure measurement. If participants did not have a blood pressure measurement but had the past diagnosis of hypertension, they were assigned a blood pressure value of 1 point. If participants did have a blood pressure measurement, they were assigned points for the measure and past diagnosis as described in Table 1. If male and female participants were diagnosed with DM they were given a point value of 3 and 4, respectively, in accordance with the published Framingham Heart Study scoring rubric.<sup>45</sup> Similarly, in accordance with the Framingham Heart Study scoring rubric,<sup>45</sup> if male and female participants reported currently smoking, they were given a point value of 4 and 3, respectively. An individualized CVD risk score was calculated by summing up

**TABLE 1.** Modified Framingham Risk Profiles by Gender

CVD Risk Scores for Women						
Score	Age (yrs)	Reported High BP, Not Measured	Measured Systolic BP + No High BP Diagnosis	Measured Systolic BP + Yes High BP Diagnosis	Tobacco Use	DM
0	≤34.9	No	<130	<120	No	No
1		Yes	130–139			
2	35–39.9		140–149	120–129		
3				130–139	Yes	
4	40–40.9		150–159			Yes
5	45–49.9		≥160	140–149		
6				150–159		
7	50–54.9			≥160		
8	55–59.9					
9	60–64.9					
10	65–69.9					
11	70–74.9					
12	≥75					
CVD Risk Scores for Men						
Score	Age (yrs)	Reported High BP, Not Measured	Measured Systolic BP + No High BP Diagnosis	Measured Systolic BP + Yes High BP Diagnosis	Tobacco Use	DM
0	≤34.9	No	<130	<120	No	No
1		Yes	130–139			
2	35–39.9		140–159	120–129		
3			≥160	130–139		Yes
4				140–159	Yes	
5	40–40.9			≥160		
6	45–49.9					
7						
8	50–54.9					
9						
10	55–59.9					
11	60–64.9					
12	65–69.9					
13						
14	70–74.9					
15	≥75					

BP, blood pressure; CVD, cardiovascular disease; DM, diabetes mellitus; mm Hg, points allotted based on the Framingham Heart Study CVD risk tables.<sup>40</sup>

individual CVD variable point values for each participant. Individualized CVD risk scores range from 0 to 29; however, an a priori decision was made without knowledge of the relationships to CTS or NCS to collapse scores at least 16 into one category as scores above 16 were too infrequent to provide accurate statistical power.

**Statistical Analyses**

Logistic regression was performed to assess the risk between individualized CVD risk score and prevalence of CTS or abnormal NCS. Univariate analyses were done with each variable individually to conclude separate association with CTS then combined in a multivariate logistic regression to assess the influence of confounders. All analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC). Statistical significance is  $P < 0.05$ . Potential confounding variables with meaningful evidence of association to CTS ( $P < 0.20$ ) were considered for inclusion in multivariate models. Potential confounders assessed include job physical exposures (Strain Index for the typical job task on the right hand), measured BMI, and job satisfaction. Collinearity between potential confounders was assessed. The final main effects model included all confounders that were statistically significant or had an epidemiological basis for a causal relationship and were trending toward statistical significance ( $P < 0.20$ ). Spearman correlations were calculated for individual CVD risk factors. Logistic regression was used to assess adjusted relationships between individual CVD risk factors and CVD risk score for both CTS and NCS. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated.

**RESULTS**

The population consisted of 1824 workers, of which 1088 (59.6%) were female (Table 2). A total of 308 (16.9%) had CTS. The mean age was greater among those with CTS at  $45.1 \pm 9.8$  years compared with those without CTS at  $40.3 \pm 11.5$  years. DM was

**TABLE 2.** Population Demographics Stratified by CTS Case Status

CVD Risk Characteristics*	CTS (n = 308, 16.9%)	No CTS (n = 1,516, 83.1%)
Variable (N = 1,824)		
Age (yrs)	45.1 (9.8)	40.3 (11.5)
Gender		
Female	227 (73.7%)	861 (56.8%)
Male	81 (26.3%)	655 (43.2%)
DM†		
Yes	28 (9.1%)	58 (3.8%)
No	280 (90.9%)	1,458 (96.2%)
Hypertension‡		
Yes	70 (22.7%)	218 (14.4%)
No	238 (77.3%)	11,298 (85.6%)
Average systolic BP‡ (mm Hg)	129.8 (18.0)	127.1 (16.9)
Tobacco use		
Never	179 (58.1%)	916 (60.4%)
Ever	129 (41.9%)	600 (39.6%)
BMI (kg/m <sup>2</sup> )	31.0 (7.3)	28.2 (6.2)
CVD risk score	7.7 (4.4)	5.8 (4.3)

Percentages reported as a total of those with or without CTS. BMI was calculated using measured heights and weights. Diabetes, hypercholesterolemia, and hypertension were yes/no based on self-reported previous physician diagnosis. BP was measured; CVD risk index score based on the modified Framingham Heart Study. BP, blood pressure; BMI, body mass index; CTS, carpal tunnel syndrome; CVD, cardiovascular disease; DM, diabetes mellitus.

\*Data reported as mean ± standard deviation or n (%).

†“Yes” responses to physician diagnoses.

‡For the subset (n = 1,075) with measured systolic BP.

present in 86 (4.7%) and hypertension in 288 (15.8%). Among the 1075 participants who had measured blood pressure, the systolic blood pressure was somewhat higher in the CTS case group  $129.8 \pm 18.0$  mm Hg compared with the non-CTS case group at  $127.1 \pm 16.9$  mm Hg. Past or current tobacco use was common and reported by 729 (40.0%). The BMI was higher in the CTS group  $31.0 \pm 7.3$  compared with the non-CTS case group’s BMI of  $28.2 \pm 6.2$  kg/m<sup>2</sup>. The overall mean individualized CVD risk score was higher in the CTS case group  $7.7 \pm 4.4$  compared with the non-CTS case group at  $5.8 \pm 4.3$ . Correlations between individual CVD risk factors were also calculated (Table 3). The correlations between CVD risk factors were relatively low, ranging from  $-0.047$  (between DM and tobacco use) to  $0.272$  (between age and high blood pressure).

Data were analyzed to assess associations between the person’s individual CVD risk factors and CVD risk factor score and risk of CTS (Tables 4 and 5). Separate analyses analyzed associations between CVD risk factor scores and abnormal NCS. For unadjusted associations, there was a trend of increasing risk of CTS across the CVD risk factor scores with a peak OR of 4.94 (95% CI 2.51, 9.71). For analyses of risk for an abnormal NCS, the results showed mostly stronger associations than for CTS and peaked at an OR of 8.06 (95% CI 3.43, 18.90). Body mass indices and the Strain Index scores that assessed job physical demands were also significant in the univariate analyses. Job dissatisfaction had significant association with CTS, but not with abnormal median NCS. Relationships between individual CVD risk factors and both CTS and NCS were assessed, adjusting for gender, BMI, and Strain Index (Table 5). These data demonstrate statistically significant relationships between hypertension and both CTS and NCS. Tobacco use was statistically significantly related to NCS and was trending toward statistical significance ( $P = 0.101$ ) in relationship to CTS.

Multivariate analyses were performed that included BMIs, Strain Index scores, and job satisfaction (Table 6 and Fig. 1). Both the CVD disease risk factors and these potential confounders demonstrated comparable results with adjusted analyses as with the univariate analyses. The adjusted OR across the CVD risk categories mostly rose across the categories although modestly less strongly than in the unadjusted analyses. The peak adjusted OR for CTS was 4.16 (95% CI 2.28, 7.61). The peak adjusted OR for NCS was 7.35 (95% CI 3.09, 17.53).

**DISCUSSION**

CVD disease risk factors were strongly associated with risk of both CTS prevalence and objectively measured NCS abnormalities in this large cross-sectional study. These findings persisted after adjustments for job physical factors, body mass indices, and job satisfaction. The relationships were higher in magnitude for the purely objective measure of median NCS abnormalities as compared with the case definition of CTS that included symptoms.

These data suggest CTS is a multifactorial disorder that may have CVD disease risk as an underlying mechanism. Numerous studies have suggested job physical factors are risk factors<sup>9-16</sup>;

**TABLE 3.** Correlations Between CVD Risk Factors in This Workplace Population (n = 1,824)

	Age	BP	Tobacco	DM
Age	1.00000			
BP	0.27210	1.00000		
Tobacco	0.01573	0.03775	1.00000	
DM	0.16362	0.19671	-0.04709	1.00000

BP, blood pressure; CVD, cardiovascular disease; DM = diabetes mellitus.

**TABLE 4.** Crude OR and 95% CI for Associations Between CVD Risk Factor Scores and CTS and Abnormal NCS

CVD Risk Factor	Cases/Total	CTS	Cases/Total	Abnormal NCS
Modified Framingham score		OR (95% CI)		OR (95% CI)
0	24/279	1.00 (Reference)	71/279	1.00 (Reference)
1	3/34	1.03 (0.29, 3.61)	10/34	1.22 (0.56, 2.68)
2	10/122	0.95 (0.44, 2.05)	38/122	1.33 (0.83, 2.12)
3	12/91	1.61 (0.77, 3.37)	<b>36/91</b>	<b>1.92 (1.16, 3.16)</b>
4	<b>33/211</b>	<b>1.97 (1.13, 3.45)</b>	<b>80/211</b>	<b>1.79 (1.22, 2.64)</b>
5	<b>28/185</b>	<b>1.90 (1.06, 3.39)</b>	<b>89/185</b>	<b>2.72 (1.83, 4.03)</b>
6	<b>19/95</b>	<b>2.66 (1.38, 5.11)</b>	<b>55/95</b>	<b>4.03 (2.47, 6.56)</b>
7	<b>27/142</b>	<b>2.49 (1.38, 4.51)</b>	<b>82/142</b>	<b>4.00 (2.61, 6.14)</b>
8	<b>25/154</b>	<b>2.06 (1.13, 3.75)</b>	<b>77/154</b>	<b>2.93 (1.93, 4.44)</b>
9	<b>19/96</b>	<b>2.62 (1.36, 5.04)</b>	<b>59/96</b>	<b>4.67 (2.86, 7.64)</b>
10	<b>30/110</b>	<b>3.98 (2.20, 7.21)</b>	<b>66/110</b>	<b>4.39 (2.76, 7.01)</b>
11	<b>15/57</b>	<b>3.79 (1.84, 7.82)</b>	<b>34/57</b>	<b>4.33 (2.39, 7.84)</b>
12	<b>16/77</b>	<b>2.79 (1.40, 5.56)</b>	<b>56/77</b>	<b>7.81 (4.42, 13.80)</b>
13	<b>11/37</b>	<b>4.50 (1.98, 10.20)</b>	<b>27/37</b>	<b>7.91 (3.65, 17.15)</b>
14	7/41	2.19 (0.88, 5.46)	<b>23/41</b>	<b>3.74 (1.91, 7.34)</b>
15	<b>9/30</b>	<b>4.55 (1.88, 11.04)</b>	<b>22/30</b>	<b>8.06 (3.43, 18.90)</b>
≥16	<b>20/63</b>	<b>4.94 (2.51, 9.71)</b>	<b>39/63</b>	<b>4.76 (2.68, 8.46)</b>
CVD test for Trend <i>P</i> value		<0.0001		<0.0001
BMI (per kg/m <sup>2</sup> )	<b>308/1,824</b>	<b>1.06 (1.04, 1.08)</b>	<b>864/1,824</b>	<b>1.07 (1.05, 1.08)</b>
Strain Index (per unit)	<b>308/1,824</b>	<b>1.01 (1.00, 1.02)</b>	<b>864/1,824</b>	<b>1.02 (1.01, 1.03)</b>
Job satisfaction				
Satisfied	64/519	1.00 (Reference)	237/519	1.00 (Reference)
Neither satisfied or dissatisfied	<b>166/937</b>	<b>1.53 (1.12, 2.09)</b>	441/937	1.06 (0.85, 1.31)
Dissatisfied	<b>78/368</b>	<b>1.91 (1.33, 2.75)</b>	186/368	1.22 (0.93, 1.59)

BMI, body mass index; CI, confidence interval; CTS, carpal tunnel syndrome; CVD, cardiovascular; NCS, nerve conduction study; OR, odds ratio. All bold values are *P* < 0.05.

however, mechanisms of the disease are unclear and many theoretical disease mechanisms have been postulated.<sup>20</sup> Mostly cross-sectional studies have suggested individual factors such as DM<sup>3,21–25</sup> and metabolic syndrome<sup>26–28</sup> are associated with CTS. This study's findings also support some prior findings of

associations with hypertension,<sup>17,33,46</sup> although some studies of hypertension have also been negative.<sup>47,48</sup> This study supports findings from cross-sectional studies of risks from smoking, although those findings also are counter to findings of a lack of risk in case-control and cohort studies<sup>37</sup>; however, combinations of

**TABLE 5.** Adjusted OR and 95% CIs for Relationships Between Individual CVD Risk Factors and Both CTS and Abnormal NCS Adjusted for Gender, BMI, and Strain Index

CVD Risk Factor	Cases/Total	CTS	Cases/Total	Abnormal NCS
		OR (95% CI)		OR (95% CI)
Blood Pressure				
No diagnosis of hypertension or elevated blood pressure at enrollment	181/1,259	1.00 (Reference)	525/1,259	1.00 (Reference)
Diagnosis of hypertension and/or elevated blood pressure at enrollment	<b>127/565</b>	<b>1.34 (1.03, 1.76)</b>	<b>339/565</b>	<b>1.66 (1.34, 2.06)</b>
Smoking				
Never smoker	179/1,095	1.00 (Reference)	502/1,095	1.00 (Reference)
Ever smoker	129/729	1.24 (0.96, 1.60)	<b>362/729</b>	<b>1.29 (1.07, 1.57)</b>
Age category				
<25	9/161	1.00 (Reference)	38/161	1.00 (Reference)
25–29	17/191	1.36 (0.58, 3.17)	56/191	1.19 (0.73, 1.94)
30–34	24/205	1.90 (0.84, 4.28)	<b>77/205</b>	<b>1.86 (1.16, 3.00)</b>
35–39	29/224	2.02 (0.91, 4.46)	<b>82/224</b>	<b>1.70 (1.06, 2.72)</b>
40–44	<b>54/284</b>	<b>3.12 (1.47, 6.62)</b>	<b>146/284</b>	<b>3.19 (2.03, 5.01)</b>
45–49	<b>61/276</b>	<b>3.77 (1.78, 7.96)</b>	<b>160/276</b>	<b>4.14 (2.63, 6.51)</b>
50–54	<b>68/243</b>	<b>5.07 (2.40, 10.72)</b>	<b>155/243</b>	<b>5.29 (3.31, 8.45)</b>
55–59	<b>33/169</b>	<b>2.88 (1.30, 6.35)</b>	<b>103/169</b>	<b>4.26 (2.59, 7.00)</b>
60–64	11/63	2.49 (0.95, 6.49)	<b>42/63</b>	<b>5.71 (2.95, 11.04)</b>
65+	2/8	5.34 (0.89, 31.95)	<b>5/8</b>	<b>5.83 (1.30, 26.27)</b>
DM				
No	280/1,738	1.00 (Reference)	804/1,738	1.00 (Reference)
Yes	<b>28/86</b>	<b>1.91 (1.18, 3.11)</b>	<b>60/86</b>	<b>2.04 (1.26, 3.31)</b>

CI, confidence interval; CTS, carpal tunnel syndrome; CVD, cardiovascular; DM, diabetes mellitus; NCS, nerve conduction study; OR, odds ratio.

**TABLE 6.** Adjusted\* OR and 95% CI for Associations Between Factors and CTS and Abnormal NCS

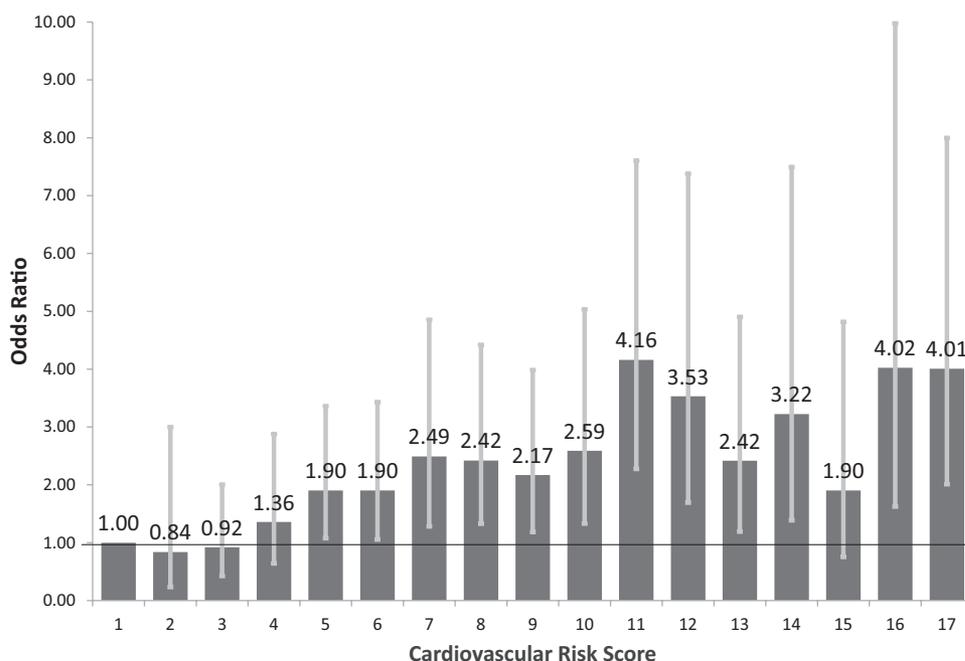
Adjusted analyses	Cases/Total	CTS OR (95% CI)	Cases/Total	Abnormal NCS OR (95% CI)
Modified Framingham score		OR (95% CI)		OR (95% CI)
0	24/279	1.00 (Reference)	71/279	1.00 (Reference)
1	3/34	0.84 (0.23, 3.00)	10/34	1.02 (0.46, 2.29)
2	10/122	0.92 (0.42, 2.01)	38/122	1.27 (0.78, 2.05)
3	12/91	1.36 (0.64, 2.88)	<b>36/91</b>	<b>1.70 (1.02, 2.85)</b>
4	<b>33/211</b>	<b>1.90 (1.08, 3.36)</b>	<b>80/211</b>	<b>1.75 (1.17, 2.60)</b>
5	<b>28/185</b>	<b>1.90 (1.05, 3.43)</b>	<b>89/185</b>	<b>2.74 (1.83, 4.12)</b>
6	<b>19/95</b>	<b>2.49 (1.28, 4.85)</b>	<b>55/95</b>	<b>3.96 (2.40, 6.52)</b>
7	<b>27/142</b>	<b>2.42 (1.33, 4.42)</b>	<b>82/142</b>	<b>3.98 (2.57, 6.18)</b>
8	<b>25/154</b>	<b>2.17 (1.18, 3.99)</b>	<b>77/154</b>	<b>3.07 (2.01, 4.70)</b>
9	<b>19/96</b>	<b>2.59 (1.33, 5.04)</b>	<b>59/96</b>	<b>4.57 (2.76, 7.56)</b>
10	<b>30/110</b>	<b>4.16 (2.28, 7.61)</b>	<b>66/110</b>	<b>4.57 (2.83, 7.38)</b>
11	<b>15/57</b>	<b>3.53 (1.69, 7.38)</b>	<b>34/57</b>	<b>4.28 (2.33, 7.86)</b>
12	<b>16/77</b>	<b>2.42 (1.19, 4.91)</b>	<b>56/77</b>	<b>7.02 (3.92, 12.58)</b>
13	<b>11/37</b>	<b>3.22 (1.39, 7.49)</b>	<b>27/37</b>	<b>6.30 (2.85, 13.97)</b>
14	7/41	1.90 (0.75, 4.82)	23/41	3.40 (1.71, 6.77)
15	<b>9/30</b>	<b>4.03 (1.62, 9.98)</b>	<b>22/30</b>	<b>7.35 (3.09, 17.53)</b>
≥16	<b>20/63</b>	<b>4.01 (2.01, 8.00)</b>	<b>39/63</b>	<b>3.90 (2.16, 7.04)</b>
CVD test for trend P value		<0.0001		<0.0001
BMI (per kg/m <sup>2</sup> )	<b>308/1,824</b>	<b>1.06 (1.04, 1.08)</b>	<b>864/1,824</b>	<b>1.06 (1.04, 1.08)</b>
Strain Index (per unit)	<b>308/1,824</b>	<b>1.01 (1.00, 1.02)</b>	<b>864/1,824</b>	<b>1.02 (1.01, 1.03)</b>
Job satisfaction				
Satisfied	64/519	1.00 (Reference)	237/519	1.00 (Reference)
Neither Satisfied or dissatisfied	<b>166/937</b>	<b>1.52 (1.10, 2.09)</b>	441/937	1.03 (0.82, 1.30)
Dissatisfied	<b>78/368</b>	<b>1.98 (1.36, 2.88)</b>	186/368	1.26 (0.94, 1.68)

CI, confidence interval; BMI, body mass index; CTS, carpal tunnel syndrome; CVD, cardiovascular; NCS, nerve conduction study; OR, odds ratio.  
\*Adjusted for all other factors in the model.

CVD risk factors are, to our knowledge, previously unassessed. These data suggest that there is a meaningful association between CVD risk score and both CTS and abnormal NCS, demonstrating strength of association, consistency with other studies evaluating individual CVD factors, a biological gradient response, and biological plausibility. Stronger relationships of age, BMI, and DM with NCS have been previously reported.

Strengths of this study include the large sample size, multi-state population, universal measurement of NCS regardless of

symptoms, and objective measures for obesity and blood pressure. The systematic measurement of these factors in a large population-based study is an important strength. The systematic approach to use a modified Framingham CVD risk score to quantify CVD risks is another strength. The adjustment for measured job physical risk factors is another particularly unique strength and helps to remove that potential confounder for these analyses. The Framingham score does not incorporate obesity, which is another potential study strength as obesity may have a direct physical impact on the carpal canal.



**FIGURE 1.** Adjusted odds ratios for carpal tunnel syndrome by cardiovascular risk score.

Weaknesses include the cross-sectional design, although the extraordinary cost to measure job physical factors makes a prospective cohort study to replicate these results with sufficient powering impractical. Another potential limitation is the large proportion of workers from the manufacturing sector, although this study included workers from the services and healthcare sectors. In addition, the primary exposure is a modified Framingham CVD risk score. Although this is a weakness, it is likely biased toward the null. If all data were available (eg, blood pressure measured in all participants, hypertension medication use, cholesterol measures), it appears likely that associations would have been stronger.

CTS prevalence is related to CVD disease risk factors, although this modeling did not include hyperlipidemia and some other risk factors. This relationship remains after statistical adjustment for known and suspected confounders. The relationship with median NCS abnormalities, a purely objective finding, was modestly stronger than those for CTS. This suggests a potent and potentially modifiable disease mechanism; however, whether CVD disease risk factor modification reduces risk of CTS and/or median NCS abnormalities requires further investigation.

## CONCLUSIONS

These data demonstrate that individual CV factors of hypertension, tobacco use, age, and diabetes are independently related to carpal tunnel outcomes of CTS diagnosis and/or abnormal NCS. Obesity is not included in this model and lipids were not assessed. Yet, a modified Framingham CVD risk score is strongly related to both CTS diagnosis and abnormal NCS. This strong relationship persists after adjustment for known and suspected risk factors including BMI, Strain Index, and job satisfaction.

## REFERENCES

- Bernard BP, ed. Musculoskeletal disorders and workplace factors. A critical review of epidemiologic evidence for work-related musculoskeletal disorders of the neck, upper extremity, and low back. Washington, DC: National Institute for Occupational Safety and Health; 1997; DHHS (NIOSH) Publication No. 97-141, pp. 5a-1 to 5a-67.
- Gelfman R, Melton 3rd LJ, Yawn BP, Wollan PC, Amadio PC, Stevens JC. Long-term trends in carpal tunnel syndrome. *Neurology*. 2009;72:33–41.
- Geoghegan JM, Clark DI, Bainbridge LC, Smith C, Hubbard R. Risk factors in carpal tunnel syndrome. *J Hand Surg Br*. 2004;29:315–320.
- Maghsoudipour M, Moghimi S, Dehghan F, Rahimpanah A. Association of occupational and non-occupational risk factors with the prevalence of work related carpal tunnel syndrome. *J Occup Rehab*. 2008;18:152–156.
- Melhorn JM, Ackerman WE, Glass LS, Deitz DC. *Guides to the Evaluation of Disease and Injury Causation*. Chicago: AMA Press; 2008.
- Roquelaure Y, Ha C, Nicolas G, et al. Attributable risk of carpal tunnel syndrome according to industry and occupation in a general population. *Arthritis Rheum*. 2008;59:1341–1348.
- Wolf JM, Mountcastle S, Owens BD. Incidence of carpal tunnel syndrome in the US military population. *Hand (N Y)*. 2009;4:289–293.
- Kuorinka I, Hannu H, Ilkka E. Prevention of musculoskeletal disorders at work: validation and reliability in a multicenter intervention study. *Int J Ind Ergon*. 1995;15:437–446.
- Armstrong T, Dale AM, Franzblau A, Evanoff BA. Risk factors for carpal tunnel syndrome and median neuropathy in a working population. *J Occup Environ Med*. 2008;50:1355–1364.
- Bonfiglioli R, Mattioli S, Armstrong TJ, Ryan D, Franzblau A. Validation of the ACGIH TLV for hand activity level in the OCTOPUS cohort: a two-year longitudinal study of carpal tunnel syndrome. *Scand J Work Environ Health*. 2013;39:155–163.
- Evanoff B, Dale AM, Deych E, et al. Risk factors for incident carpal tunnel syndrome: results of a prospective cohort study of newly-hired workers. *Work*. 2012;41(suppl 1):4450–4452.
- Garg A, Hegmann KT, Wertsch JJ, et al. The WISTAH hand study: a prospective cohort study of distal upper extremity musculoskeletal disorders. *BMC Musculoskelet Disord*. 2012;13:1–17.
- Gell N, Werner RA, Franzblau A, Ulin SS, Armstrong TJ. A longitudinal study of industrial and clerical workers: incidence of carpal tunnel syndrome and assessment of risk factors. *J Occup Rehabil*. 2005;15:47–55.
- Harris-Adamson C, Eisen EA, Dale AM, et al. Personal and workplace psychosocial risk factors for carpal tunnel syndrome: a pooled study cohort. *Occup Environ Med*. 2013;70:529–537.
- Kapellusch JM, Gerr FE, Malloy EJ, et al. Exposure-response relationships for the ACGIH threshold limit value for hand-activity level: results from a pooled data study of carpal tunnel syndrome. *Scand J Work Environ Health*. 2014;40:610–620.
- Werner RA, Franzblau A, Gell N, Hartigan AG, Ebersole M, Armstrong TJ. Risk factors for visiting a medical department because of upper-extremity musculoskeletal disorders. *Scand J Work Environ Health*. 2005;31:132–137.
- Hanrahan LP, Higgins D, Anderson H, Smith M. Wisconsin occupational carpal tunnel syndrome surveillance: the incidence of surgically treated cases. *Wis Med J*. 1993;92:685–689.
- Hand, wrist, and forearm disorders not including carpal tunnel syndrome. Hegmann KT, Hughes MA, Biggs JJ, eds. *Occupational medicine practice guidelines*. 3rd ed., Elk Grove Village, IL: American College of Occupational and Environmental Medicine (ACOEM); 2011. p. 621–622.
- Moore JS. Carpal tunnel syndrome. *Occup Med*. 1992;7:741–763.
- Moore JS. Biomechanical models for the pathogenesis of specific distal upper extremity disorders. *Am J Ind Med*. 2002;41:353–369.
- Gulliford MC, Latinovic R, Charlton J, Hughes RA. Increased incidence of carpal tunnel syndrome up to 10 years before diagnosis of diabetes. *Diabetes Care*. 2006;29:1929–1930.
- Karpitskaya Y, Novak CB, Mackinnon SE. Prevalence of smoking, obesity, diabetes mellitus, and thyroid disease in patients with carpal tunnel syndrome. *Ann Plast Surg*. 2002;48:269–273.
- Seror P, Seror R. Prevalence of obesity and obesity as a risk factor in patients with severe median nerve lesion at the wrist. *Joint Bone Spine*. 2013;80:632–637.
- Singh R, Gamble G, Cundy T. Lifetime risk of symptomatic carpal tunnel syndrome in type 1 diabetes. *Diabet Med*. 2005;22:625–630.
- Solomon DH, Katz JN, Bohn R, Mogun H, Avorn J. Nonoccupational risk factors for carpal tunnel syndrome. *J Gen Intern Med*. 1999;14:310–314.
- Balci K, Utku U. Carpal tunnel syndrome and metabolic syndrome. *Acta Neurol Scand*. 2007;116:113–117.
- Mondelli M, Aretini A, Ginanneschi F, Greco G, Mattioli S. Waist circumference and waist-to-hip ratio in carpal tunnel syndrome: a case-control study. *J Neurol Sci*. 2014;338:207–213.
- Onder B, Yalcin E, Selcuk B, Kurtaran A, Akyuz M. Carpal tunnel syndrome and metabolic syndrome co-occurrence. *Rheumatol Int*. 2013;33:583–586.
- Nakamichi K, Tachibana S. Hypercholesterolemia as a risk factor for idiopathic carpal tunnel syndrome. *Muscle Nerve*. 2005;32:364–367.
- Plastino M, Fava A, Carmela C, et al. Insulin resistance increases risk of carpal tunnel syndrome: a case-control study. *J Peripher Nerv Syst*. 2011;16:186–190.
- Durakoglugil ME, Cicek Y, Kocaman SA, et al. Increased pulse wave velocity and carotid intima-media thickness in patients with carpal tunnel syndrome. *Muscle Nerve*. 2013;47:872–877.
- Park JH, Kim SN, Han SM, et al. Carotid intima-media thickness in patients with carpal tunnel syndrome. *J Ultrasound Med*. 2013;32:1753–1757.
- Shiri R, Heliövaara M, Moilanen L, Viikari J, Liira H, Viikari-Juntura E. Associations of cardiovascular risk factors, carotid intima-media thickness and manifest atherosclerotic vascular disease with carpal tunnel syndrome. *BMC Musculoskelet Disord*. 2011;80:1–12.
- Goodson JT, DeBerard MS, Wheeler AJ, Colledge AL. Occupational and biopsychosocial risk factors for carpal tunnel syndrome. *J Occup Environ Med*. 2014;56:965–972.
- Mondelli M, Curti S, Farioli A, et al. Anthropometric measurements as a screening test for carpal tunnel syndrome: receiver operating characteristic curves and accuracy. *Arthritis Care Res*. 2015;67:691–700.
- Komurcu HF, Kilic S, Anlar O. Relationship of age, body mass index, wrist and waist circumferences to carpal tunnel syndrome severity. *Neurol Med Chir (Tokyo)*. 2014;54:395–400.
- Pourmemari MH, Viikari-Juntura E, Shiri R. Smoking and carpal tunnel syndrome: a meta-analysis. *Muscle Nerve*. 2014;49:345–350.
- Werner RA, Franzblau A, Gell N, Hartigan AG, Ebersole M, Armstrong TJ. Incidence of carpal tunnel syndrome among automobile assembly workers and assessment of risk factors. *J Occup Environ Med*. 2005;47:1044–1050.
- Silverstein BA, Fan ZJ, Bonauto DK, et al. The natural course of carpal tunnel syndrome in a working population. *Scand J Work Environ Health*. 2010;36:384–393.

40. Bao S, Silverstein B, Howard N, Spielholz P. The Washington State SHARP approach to exposure assessment. *Fundamentals and Assessment Tools for Occupational Ergonomics USA*. Boca Raton, FL: Taylor & Francis Group; 2006:44-1 to 44-22.
41. Jablecki C, Andary M, Floeter M, et al. Practice parameter: electrodiagnostic studies in carpal tunnel syndrome. Report of the American Association of Electrodiagnostic Medicine, American Academy of Neurology, and the American Academy of Physical Medicine and Rehabilitation. *Neurology*. 2002;58:1589–1592.
42. Buschbacher R, Koch J, Emsley C, Katz B. Electrodiagnostic reference values for the lateral antebrachial cutaneous nerve: standardization of a 10-cm distance. *Arch Phys Med Rehab*. 2000;81:1563–1566.
43. Moore JS, Garg A. The Strain Index: a proposed method to analyze jobs for risk of distal upper extremity disorders. *Am Ind Hyg Assoc J*. 1995;56:443–458.
44. Garg A, Kapellusch J, Hegmann K, et al. The Strain Index (SI) and threshold limit value (TLV) for hand activity level (HAL): risk of carpal tunnel syndrome (CTS) in a prospective cohort. *Ergonomics*. 2012;55:396–414.
45. D'Agostino RB, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care the Framingham Heart Study. *Circulation*. 2008;117:743–753.
46. Tseng CH, Liao CC, Kuo CM, Sung FC, Hsieh DP, Tsai CH. Medical and non-medical correlates of carpal tunnel syndrome in a Taiwan cohort of one million. *Eur J Neurol*. 2012;19:91–97.
47. Ferry S, Hannaford P, Warskyj M, Lewis M, Croft P. Carpal tunnel syndrome: a nested case-control study of risk factors in women. *Am J Epidemiol*. 2000;151:566–574.
48. Cannon LJ, Bernacki EJ, Walter SD. Personal and occupational factors associated with carpal tunnel syndrome. *J Occup Med*. 1981;23:255–258.