A Regression Model for Carpal Tunnel Syndrome[1] (42972)

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Abstract. **The purpose of this study was to determine whether a logistic regression model for the diagnosis of carpal tunnel syndrome (CTS) could be developed. Forty-eight variables were initially identified, for the 28 CTS and 34 non-CTS subjects, including 28 measures of nerve function, 6 anatomical measurements, 8 variables relating to disease symptoms, and 6 variables relating to physical attributes. An *a priori* clustering procedure was used to establish groups for the principal components analyses. The first principal component of each cluster was then used in a backward, stepwise logistic regression analysis. The best combination of candidate variables, as identified by the regression equation, was Raynaud's symptoms and median nerve motor function. The results of this study indicate that a model for CTS can be generated from a set of variables and that a linear combination of variables representing nerve function is closely associated with conduction decrements resulting from CTS.**

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A large body of literature exists on the symptoms, causes, treatment, and risk factors associated with carpal tunnel syndrome (CTS). The syndrome, an entrapment of the median nerve in the carpal canal, has been associated with personal (1), physical (2), and neurologic factors (3). Investigators have reported that women, especially those who are pregnant (4), using contraceptives (5), or near menopause (6) are susceptible to the syndrome. Both males and females appear to be more susceptible as they age (6), although others have found that age and CTS do not appear to be correlated (7, 8). Wrist trauma, both acute and cumulative, has been associated with CTS (9, 10). A small carpal canal area has been implicated as a risk factor for the syndrome (7, 11, 12). Furthermore, individuals with CTS report motor and sensory symptoms characteristic of an entrapment-induced neuropathy (6).

Despite this research, an attempt to provide a regression model for CTS has not been made. The development of a quantitative model for CTS would promote a better understanding of who develops CTS and could eventually be used in directing intervention strategies. Ultimately, refinements on a model could allow for predicting the occurrence of the syndrome, thus reducing the financial and personal costs associated with CTS. The purpose of this study, therefore, was to develop a regression model, based on variables that have been previously associated as risk factors for CTS. This exploratory model may be helpful in better understanding factors associated with the syndrome and may ultimately lead to the research to develop a prediction model for CTS.

Method

Subjects. All subjects were volunteers between the ages of 20 and 65. CTS cases and controls were matched for sex and generation (e.g., 20–30, 30–40, etc.). CTS cases were workers employed in the Baltimore Metropolitan Area who were being seen in the Neurology Clinic at the Francis Scott Key Medical Center, Baltimore, MD. A worker was considered a possible "case" if he reported one or more of the median nerve sensory symptoms or two or more of the median nerve motor symptoms listed in Table I. Controls responded to advertisements on public bulletin boards and were screened by telephone for the absence of symptoms noted in Table I. Each subject was examined by the same neurologist. The results of the neurologic examinations were not used to define or select cases for

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Table I. Criteria for Assignment as a Carpal Tunnel Case

A positive response to one or more of the following median nerve sensory symptoms:

1. Numbness in hands or fingers.
2. Pain in shoulder, arm, hand, or finger.
3. Wake in morning with symptoms listed in 1 or 2 above.

or

A Positive Response to two or more of the following motor symptoms:

1. Decrease in grip strength.
2. Difficulty in opening jars or lifting.
3. Tendency to drop small objects.

inclusion in the study. The examination was used to exclude those individuals with disorders other than CTS or those who exhibited dermatologic abnormalities which might have interfered with testing. Sixty-two subjects were classified and subsequently examined by the neurologist, resulting in a sample where 15 males and 13 females were diagnosed as CTS cases and 16 males and 18 females were diagnosed as controls. Incomplete data reduced this number to 58 (12 males and 13 females in the CTS group, 15 males and 18 females in the control group). Because of the way in which the subjects were recruited and the manner in which they were matched (i.e., by sex and generation) this sample may not be representative of the population of carpal tunnel subjects.

Procedure. Subjects were required to complete a medical questionnaire and undergo an examination by a neurologist. Functional capacity of the subject's hands and wrists was evaluated from measures derived from computerized axial tomography (CT), nerve conduction velocity (NCV), and vibratory threshold studies. The procedure used for obtaining the CT (GE8800 CT/T scanner), as well as the methods for ensuring proper wrist alignment, has been described by Bleecker *et al.* (7). Three CT slices taken at the wrist crease and approximately 12 and 25 mm distal to the crease were used for analyses. NCV studies provided measures of amplitude, latency, and velocity for sensory and motor fibers of the median and ulnar nerves for both the right and left hands. Vibratory thresholds were measured from the second (median nerve) and fifth (ulnar nerve) digits of the left and right hands using the Optacon instrument and following a procedure outlined by Arezzo *et al.* (13). These procedures yielded 48 variables for the analyses, including 14 from the questionnaire, 24 from the NCV studies, 6 from the CT measurements, and 4 from the vibration threshold data. Table II provides a list of these variables.

Multiple regression analysis is a potent statistical technique for predicting a single, dependent variable from multiple independent variables (14). In the current study, the number of independent variables is large relative to the sample size. Such a large number of variables can lead to a model in which the inclusion of additional candidate variables does not produce a corresponding gain in the yield of the model (15). To reduce the number of independent variables, data reduction techniques were used prior to performing the regression analysis (16). The first reduction technique was an *a priori* clustering procedure to divide the 48 variables into groups before performing the principal components analyses (15, 17). Principal components analyses were then performed to further reduce the number of variables without adversely affecting the results of the regression (18). The final reduction technique entailed removing variables not significantly correlated with the criterion variable. A backward, stepwise logistic regression procedure was subsequently used to develop the model in which the criterion variable was dichotomized (i.e., CTS = 0; non-CTS = 1) (19, 20).

Results

Thirty-nine variables (numbers 10 through 48, Table II) fell into eight clusters (identified by topical headings in Table II). Of the nine unclustered variables, six (numbers 3, 4, 5, 6, 7, and 9) were excluded because of low response rates which remained low even after the responses to these questions had been dichotomized; the remaining three variables (numbers 1, 2, and 8) were excluded because they were not significantly correlated with the criterion variable.

Principal components analyses were performed on each of the eight clusters of variables. The resulting factors were then rotated using a varimax solution. Since rotating the factors did not change the factor patterns, the decision was made to use the nonrotated values in the subsequent analyses. The first principal component from each cluster was used in the regression analysis. Each of the variables in the size, carpal canal area, and Optacon clusters correlated positively ($0.82 \le r \le 0.93$) with the corresponding first principal component. Thus, for the principal component representing carpal canal area, the larger the magnitude of the component score, the larger the carpal canal area of the patient. For vibration threshold (Optacon), the larger the magnitude of the component score, the higher the vibration threshold of the patient, whereas for size, the larger the component score, the greater was the height and weight of the subject.

Table III contains the loadings and eigenvalues of the first principal components extracted from the four nerve conduction velocity clusters. Distal latency was negatively correlated with the median motor, median sensory, and ulnar sensory nerve functions. Distal amplitude and velocity were positively correlated with the median motor, median sensory, and ulnar sensory nerve functions (i.e., the larger the component score, the more efficient the particular nerve fiber functions).

Table II. Variables Evaluated in Regression Analysis

1. Sex (0 = male; 1 = female)
2. Age (years)
3. Dominant hand (1 = right; 2 = left)
4. History of wrist fracture (0 = no; 1 = yes, right; 2 = yes, left; 3 = yes, both)
5. Diagnosed arthritis (0 = no; 1 = yes, degenerative; 2 = yes, rheumatoid; 3 = yes, type unknown; 4 = don't know)
6. Diagnosed thyroid disorder (0 = no; 1 = yes; 2 = don't know)
7. Diagnosed diabetes (0 = no; 1 = yes; 2 = don't know)
8. Do you drink? (0 = no; 1 = yes)
9. Do you experience burning pain in your little finger? (0 = no; 1 = yes, right; 2 = yes, left; 3 = yes, both hands)

SIZE

10. Height (inches)
11. Weight (lbs)

RAYNAUD'S SYMPTOMS

12. Do your fingers turn white in cold weather? (0 = no; 1 = yes, right; 2 = yes, left; 3 = yes, both hands)
13. Do your fingers appear bluish and cold? (0 = no; 1 = yes, right; 2 = yes, left; 3 = yes, both hands)
14. Do your fingers become numb in cold weather? (0 = no; 1 = yes, right; 2 = yes, left; 3 = yes, both hands)

MEDIAN NERVE MOTOR FUNCTION

15. Median nerve motor distal latency, left hand (msec)
16. Median nerve motor distal latency, right hand (msec)
17. Median nerve motor distal amplitude, left hand (mV)
18. Median nerve motor distal amplitude, right hand (mV)
19. Median nerve motor velocity, left hand (meters/sec)
20. Median nerve motor velocity, right hand (meters/sec)

ULNAR NERVE MOTOR FUNCTION

21. Ulnar nerve motor distal latency, left hand (msec)
22. Ulnar nerve motor distal latency, right hand (msec)
23. Ulnar nerve motor distal amplitude, left hand (mV)
24. Ulnar nerve motor distal amplitude, right hand (mV)
25. Ulnar nerve motor velocity, left hand (meters/sec)
26. Ulnar nerve motor velocity, right hand (meters/sec)

MEDIAN NERVE SENSORY FUNCTION

27. Median nerve sensory distal latency, left hand (msec)
28. Median nerve sensory distal latency, right hand (msec)
29. Median nerve sensory distal amplitude, left hand (mV)
30. Median nerve sensory distal amplitude, right hand (mV)
31. Median nerve sensory velocity, left hand (meters/sec)
32. Median nerve sensory velocity, right hand (meters/sec)

ULNAR NERVE SENSORY FUNCTION

33. Ulnar nerve sensory distal latency, left hand (msec)
34. Ulnar nerve sensory distal latency, right hand (msec)
35. Ulnar nerve sensory distal amplitude, left hand (mV)
36. Ulnar nerve sensory distal amplitude, right hand (mV)
37. Ulnar nerve sensory velocity, left hand (meters/sec)
38. Ulnar nerve sensory velocity, right hand (meters/sec)

CARPAL CANAL AREA

39. Proximal measure of carpal canal area, right hand (cm^2)
40. Middle measure of carpal canal area, right hand (cm^2)
41. Distal measure of carpal canal area, right hand (cm^2)
42. Proximal measure of carpal canal area, left hand (cm^2)
43. Middle measure of carpal canal area, left hand (cm^2)
44. Distal measure of carpal canal area, left hand (cm^2)

OPTACON (VIBRATION THRESHOLD)

45. 2nd digit threshold of right hand (Hz)
46. 5th digit threshold of right hand (Hz)
47. 2nd digit threshold of left hand (Hz)
48. 5th digit threshold of left hand (Hz)

DIAGNOSIS

49. Carpal tunnel syndrome (0 = CTS; 1 = control)

Table III. Eigenvalues and Factor Loadings of the Principal Components for Nerve Functions

	Factor Loadings[a]			
	Ulnar motor	Ulnar sensory	Median motor	Median sensory
Measurements				
Distal Lat[b] LH	0.77	−0.84	−0.71	−0.87
Distal Lat RH	0.78	−0.81	−0.68	−0.88
Distal Amp LH	0.18	0.49	0.59	0.60
Distal Amp RH	0.27	0.45	0.70	0.63
Velocity LH	−0.72	0.77	0.69	0.76
Velocity RH	−0.60	0.83	0.67	0.89
λ[c]	2.19	3.07	2.72	3.65

[a] A factor loading represents the correlation between a variable and the principal component from which it is derived.

[b] Lat, latency; Amp, amplitude; LH, left hand; RH, right hand.

[c] Eigenvalue for the factor.

Latency was positively correlated, amplitude was slightly correlated, and velocity was negatively correlated with the principal component for the ulnar motor nerve. These results indicate that for the ulnar motor fiber, the larger the component score, the less efficient the nerve functioned.

The eighth cluster consists of three variables, each representing a Raynaud's symptom. Each variable was coded 0 or 1 depending on whether or not the patient reported experiencing or not experiencing that symptom in either hand. The three variables were summed to obtain a total score.

A correlation matrix of variables used in the logistic regression analysis is presented in Table IV. The variables entered into the regression equation were diagnosis (carpal tunnel or noncarpal tunnel), Raynaud's symptoms, and the principle components representing Optacon (vibration threshold), carpal tunnel area, median nerve motor function, and median nerve sensory function.

The Raynaud's symptoms cluster was positively correlated with the diagnosis, indicating that those diagnosed as having CTS reported more Raynaud's symptoms. Median motor and sensory functions were negatively correlated with CTS (i.e., CTS patients had less efficient median nerve function). The vibration thresh-

Table IV. Correlation Matrix of Variables Used in Logistic Regression Study

	Age	Sex	Size	Raynaud's Symptoms	Optacon	CT area	Median nerve motor	Ulnar nerve motor	Median nerve sensory	Ulnar nerve sensory	Diagnosis
Age	1.00	0.00	0.03	−0.10	0.42	0.23	−0.47	0.11	−0.29	−0.30	0.14[a]
	0.00	1.00	0.83	0.46	0.00	0.08	0.00	0.38	0.02	0.02	0.30[b]
Sex		1.00	−0.66	0.00	−0.07	−0.62	0.02	−0.18	0.20	0.20	−0.05
		0.00	0.00	1.00	0.60	0.00	0.88	0.15	0.12	0.13	0.72
Size			1.00	−0.04	−0.07	0.65	−0.06	0.06	−0.12	−0.14	−0.06
			0.00	0.76	0.58	0.00	0.72	0.72	0.34	0.27	0.63
Raynaud's symptoms				1.00	0.24	0.09	−0.12	0.23	−0.13	−0.14	0.63
				0.00	0.06	0.50	0.36	0.07	0.30	0.27	0.00
Optacon (vibration threshold)					1.00	0.04	−0.45	−0.03	−0.39	−0.09	0.35
					0.00	0.79	0.00	0.82	0.00	0.49	0.01
Carpal tunnel area						1.00	−0.31	0.26	−0.35	−0.31	0.30
						0.00	0.02	0.05	0.01	0.02	0.02
Median nerve motor							1.00	−0.24	0.72	0.41	−0.38
							0.00	0.06	0.00	0.00	0.00
Ulnar nerve motor								1.00	−0.42	−0.47	0.14
								0.00	0.00	0.00	0.28
Median nerve sensory									1.00	0.60	−0.37
									0.00	0.00	0.00
Ulnar nerve sensory										1.00	−0.16
										0.00	0.21
Diagnosis											1.00
											0.00

[a] Pearson correlation coefficient.
[b] Probability for Ho:$P = 0$.

old (Optacon) and the carpal tunnel area clusters were positively correlated with CTS. This correlation indicates that CTS patients had higher vibration thresholds and larger carpal canal areas than non-CTS subjects. Generation (age), sex, size, alcohol use, and ulnar nerve functions had very small negative or positive correlations with CTS diagnosis and were not entered into the regression equation. Generation and sex were not correlated because CTS and non-CTS cases were matched on these variables.

A backward, stepwise procedure was used to obtain the regression equation. The significance level for variables to be retained in the model and to reenter the model was $\alpha' = 0.05/5 = 0.01$. The parameter estimates from the regression analysis are presented in Table V. The two variables included in the solution to the regression equation were Raynaud's symptoms and median nerve motor function.

Discussion

The results indicate that a logistic regression model can be developed for the diagnosis of CTS. The best combination of cluster variables consisted of Raynaud's symptoms and median nerve motor function. Both variables have previously been associated with CTS; however, median nerve motor conduction is not considered as sensitive a criterion for establishing a diagnosis of CTS as median nerve sensory conduction. Kemble (21), Dawson *et al.* (22), and Downie (23) have reported that the median nerve sensory components are superior to the median nerve motor components for differentiating CTS. The difference between this study and previous findings is probably the way in which NCV values were calculated. Traditionally, NCV studies of CTS have focused on single components (i.e., amplitude, latency, or velocity) of nerve conduction. This study considered all three components simultaneously. The correlation between the median nerve motor and median nerve sensory components was 0.72, indicating that the two variables share a good deal of common variance and are probably comparable measures of median nerve integrity. By using the three components simultaneously, a second measure, at least as effective as median nerve sensory velocity, may be available for differentiating CTS. Further research is needed to replicate this finding.

Table V. Parameter Estimates of the Logistic Regression Equation

Variable	β	SE	χ^2	P
Intercept	−1.653	0.493	11.23	<0.001
Raynaud's symptoms	3.005	0.813	13.65	<0.001
Median nerve motor function	−1.159	0.433	7.15	<0.010

Females appear to be especially susceptible to CTS. Several studies have tried to account for these sex differences with varying degrees of success (4, 5). They have reported that wrist size (7) and body weight (9) do not appear to be related to CTS. In this study both carpal tunnel area and size were correlated to sex and each other. The correlations between carpal tunnel area and size to the criterion variable (i.e., diagnosis) were weak. In addition, neither size or carpal tunnel area were included in the regression model. This suggests that carpal canal area and size (i.e., the relationship of height to weight) are not related to carpal tunnel syndrome and that reported sex differences in CTS are probably not a result of physical dimensions.

These results should be interpreted with caution. The purpose of this study was to determine whether a model could be developed using multiple regression techniques, not to develop an equation that could be used clinically for prediction. This is, to our knowledge, the first reported attempt to derive a regression model for CTS and should be viewed as such. The present model should be replicated and validated before practical uses are considered. The end point for this line of research is to develop a valid and reliable model for predicting the development of CTS. The equation developed in this effort is too crude and cumbersome for clinical use. Research should evaluate other variables besides the ones used in this study for inclusion in a model. One set of variables that merits future attention is the work conditions under which CTS is most likely to occur, as discussed by Silverstein *et al.* (24).

Even though this study dealt with generating a model for carpal tunnel syndrome through the use of regression techniques, several points need to be raised regarding the key variables in the regression equation. The two variables included in the regression equation are the best combination of the 48 variables examined. The results do not suggest that either one of these two variables is more important than the other three variables in the equation. The decision was made to not evaluate the importance of the individual variables within this equation. Additions or deletions to the original set of 48 variables could change not only the importance of the variables but what variables appear in the equation. Given the preliminary nature of this line of research, the importance of the variables in this equation are best determined through replication. Dismissing the importance of variables not selected could therefore be premature. In addition, variables not selected for the equation have been shown to function adequately in discriminating between those individuals who have developed CTS and controls. These variables may prove useful and practical in diagnosing CTS if data are not available for either of the key variables identified in the regression equation.

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