Importance of Tissue Morphology Relative to Patient Reports of Symptoms and Functional Limitations Resulting From Median Nerve Pathology

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MeSH TERMS
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- tissues
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Significant data exist for the personal, environmental, and occupational risk factors for carpal tunnel syndrome. Few data, however, explain the interrelationship of tissue morphology to these factors among patients with clinical presentation of median nerve pathology. Therefore, our primary objective was to examine the relationship of various risk factors that may be predictive of subjective reports of symptoms or functional deficits accounting for median nerve morphology. Using diagnostic ultrasonography, we observed real-time median nerve morphology among 88 participants with varying reports of symptoms or functional limitations resulting from median nerve pathology. Body mass index, educational level, and nerve morphology were the primary predictive factors. Monitoring median nerve morphology with ultrasonography may provide valuable information for clinicians treating patients with symptoms of median nerve pathology. Sonographic measurements may be a useful clinical tool for improving treatment planning and provision, documenting patient status, or measuring clinical outcomes of prevention and rehabilitation interventions.

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Carpal tunnel syndrome (CTS), the most frequently occurring of all compression neuropathies, primarily occurs as a result of compression of the median nerve in the carpal tunnel, which eventually leads to sensorimotor and occupational performance deficits. Significant research has investigated physical, occupational exposure, and personal factors related to CTS, and limited research has investigated the impact of psychosocial risk factors. However, little research has evaluated how these factors relate to the physiological status of the median nerve among people with varying levels of symptomatology.

Hazardous occupational exposures, such as vibration, direct compression, and prolonged highly repetitive and forceful hand–wrist tasks, are the most common risk factors researched for CTS (Barr, Barbe, & Clark, 2004; Bongers, Ijmker, van den Heuvel, & Blatter, 2006). Additionally, evidence has indicated that increased compression of the median nerve occurs as a result of various wrist positions (Viikari-Juntura & Silverstein, 1999). Forearm pronation and supination increase pressure in the carpal tunnel (Rempel, Bach, Gordon, & So, 1998), wrist flexion and extension can reduce the area within the carpal tunnel (Skie, Zeiss, Ebraheim, & Jackson, 1990), and prolonged or repetitive ulnar deviation of the wrist causes lateral compression of the median nerve (Hägg, Oster, & Byström, 1997). Of all positions, the anterior movement of the large flexor tendons during wrist flexion, combined with decreased space in the canal, creates the greatest compression of the median nerve (Keir, 2001).

Gender and anthropometry are two personal factors with the highest association with CTS (Feuerstein, Shaw, Nicholas, & Huang, 2004; Huang,

Feuerstein, & Sauter, 2002). The prevalence of musculoskeletal disorders is 2–4 times higher among women (Lundberg, 2002; Park, Krebs, & Mirer, 1996), and women are significantly more likely to develop symptoms in the hand and wrist (Hagberg, Vilhemsson, Tornqvist, & Toomingas, 2007). Secondary to gender, wrist ratio (anterioposterior depth divided by mediolateral width) is one of the primary factors with a strong relationship to CTS (Gordon, Johnson, Gatens, & Ashton, 1988; Kamolz et al., 2004; Radecki, 1994). Among people with CTS, >75% have a square-shaped wrist (ratio >0.70; Radecki, 1994), and as the ratio increases (>0.75), so does the association with CTS (Lim, Tan, & Ahmad, 2008).

Despite the extent of hazardous occupational exposures and contributory personal factors, an increase in exposure to psychological stressors in the environment can be related to musculoskeletal symptoms (Devereux, Vlachonikolis, & Buckle, 2002). Negative psychological stress is correlated with a significant increase in motor unit activation in muscles of the upper extremity (Rissén, Melin, Sandsjö, Dohns, & Lundberg, 2000), and psychological demands of a job and the ability to control work tasks have been linked to changes in health (Bongers, Kremer, & ter Laak, 2002). Additionally, increased psychological strain can have a fundamental impact on quality of life and health across various occupations (Brisson et al., 1999; Edimansyah, Rusli, Naing, Mohamed Rusli, & Winn, 2007; Kawakami, Kobayashi, Araki, Haratani, & Furui, 1995).

Physiological changes in the median nerve leading to increased incidence of CTS are likely the result of a combination of occupational, personal, and environmental factors. Although a plethora of researchers have evaluated the predictive relationship of various personal and physical exposures to subjective symptoms (Farmer & Davis, 2008; Mattioli et al., 2009; Moghtaderi, Izadi, & Sharafadinzadeh, 2005; Sharifi-Mollayousefi et al., 2008), no studies have commented on the relationship of risk factors to median nerve morphology as predictors of these subjective reports.

Diagnostic ultrasonography is an accepted tool for observing median nerve morphology for diagnosis of CTS (Roll, Case-Smith, & Evans, 2011), and ultrasonography may be a valuable screening tool to identify median nerve pathology in an acute stage (Roll, Evans, Li, Freimer, & Sommerich, 2011). Ultrasonography is a pain-free, relatively inexpensive, and portable technology that can provide real-time images of tissues under the skin. Using ultrasonography, the size, shape, and overall appearance of the median nerve can be visualized, documented, and measured. Sonographic measurements are correlated to subjective symptoms of median nerve pathology (Kaymak et al., 2008), and these measures provide a method for documenting outcomes after carpal tunnel release (Mondelli, Filippou, Aretini, Frediani, & Reale, 2008). No studies have investigated the relationship of acute median nerve morphology to various risk factors, nor has it been investigated as an outcome measure for conservative treatments.

Successful prevention and rehabilitation techniques for median nerve pathology require an understanding of the acute physiology of the median nerve. The objectives of this research were to identify risk factors that may be predictive of subjective reports of symptoms or functional deficits and to determine the utility of including a measurement of morphology when planning or providing interventions for median nerve pathology. Our primary research question was, What is the relationship between current evidence-based risk factors for CTS and innovative measures of median nerve morphology, using gray-scale diagnostic ultrasonography, among people with varying symptomatology?

Method

The biomedical institutional review board of The Ohio State University approved the protocol, and all participants provided signed consent to participate.

Participants

The study sample was heterogeneous, maximizing the distribution and variability of data for an exploratory regression analysis. The sample included patients referred to a neurology clinic for evaluation of median nerve pathology and participants from a convenience population of nonpatient working adults. To be included, participants had to be of working age (18–65 yr old). Before consent, history of fracture or surgery in the dominant wrist, pregnancy or ≤3 mo postpartum, or any known rheumatic disorder, polyneuropathy, or uncontrolled thyroid disorder led to participant exclusion. The discovery of anatomic anomalies during data collection (i.e., bifurcated median nerve or Martin Gruber anastomosis) was a cause for exclusion after consent.

Independent Variables

A chart review provided each participant's gender and date of birth for calculation of age (in years). Participants provided hand dominance, level of education, and occupational information on a questionnaire. Level of education was categorized as high school, college (i.e., associate's or bachelor's degree), or graduate education

(i.e., master's or doctoral degree). Participants indicated their level of employment (i.e., unemployed, part time, full time, retired) and provided their occupational title. Body mass index (BMI) was calculated for each participant on the basis of height (cm) and mass (kg). Researchers used an electronic caliper to measure the dominant wrist. We calculated wrist ratio as the depth (mm) divided by the width (mm) of the wrist.

We used a modified version of the Job Content Questionnaire (JCQ; Karasek et al., 1998) to obtain ratings of psychosocial strain in the workplace on the basis of decision latitude (control) and psychological demands. The JCQ has high validity (αs = .73–.74), and responses to psychological demands have a moderate correlation to job control (rs = .220–.293), making it a good tool for categorizing job strain in various occupations (Karasek et al., 1998). Job control and psychological demand scores on the modified version of the questionnaire can range from 12 to 48. Participants categorized as having *active* jobs had both control and demands scale scores >30 points, and those in *passive* occupations had scores <30 on both scales. Participants who indicated having high control and low demands were categorized as having *low-strain* occupations, and participants who indicated having high demands and low control were categorized as having *high-strain* occupations.

A Logiq i hand-carried ultrasound console with a 12-MHz linear array transducer (GE Healthcare Ultrasound, Milwaukee, WI) was used to collect images of the median nerve for every participant. Ultrasonography was completed using a previously published protocol (Roll & Evans, 2009). Locations for collection of cross-sectional images in the dominant upper extremity of each participant included (1) forearm 6 cm from the distal wrist crease, (2) middle carpal tunnel at the level of the pisiform, and (3) distal carpal tunnel at the hook of the hamate.

After collection of the three cross-sectional images, researchers blinded to participant complaints completed measurements of the median nerve images. Median nerve morphology was observed using three different measures:

1. A direct trace along the inner hypoechoic (i.e., bright) border of the median nerve provided a measurement of the cross-sectional area (CSA) of the median nerve in forearm and mid–carpal tunnel.
2. Subtracting the CSA at the pisiform from the CSA in the forearm provided a measurement of the change in CSA, an indication of median nerve swelling.
3. Measurement of the perpendicular distance from the outer edge of the flexor retinaculum to a line drawn from the insertion points of the ligament on the trapezium and hook of the hamate indicated the amount of anterior bulging of the retinaculum.

To minimize error resulting from overestimating or underestimating the measures, the researchers completed each measurement 5 times, dropped the highest and lowest measures, and averaged the remaining three measures.

Dependent Variable

Subjective report of symptoms or functional deficit resulting from median nerve pathology (e.g., numbness and pain, decreased ability to complete fine motor tasks) provided a grouping mechanism that served as the dependent measure in the regression model. Participants completed the Boston Carpal Tunnel Questionnaire (BCTQ; Levine et al., 1993) to provide a measure of subjective symptom and functional status in the dominant hand. Cronbach's α values for the BCTQ range from .80 to .90 for the Symptom Severity scale and from .88 to .93 for the Functional Status scale, and both scales have high test–retest reliability (rs = .91 and .93, respectively; Leite, Jerosch-Herold, & Song, 2006). Respondents to this questionnaire provide a rating that indicates severity of symptoms or functional deficits resulting from median nerve pathology on a scale ranging from 1 to 5, where 1 = *no symptoms or limitations* and 5 = *maximum symptoms or limitations.* Participant responses to questions on each scale were coded, and average scores for both symptom severity and functional status were obtained. Categorization as having complaints of median nerve pathology included those participants with average symptom severity or functional status scores >1.0, and participants with average scores of 1.0 on both scales had no complaints related to median nerve pathology.

Statistical Analysis

We calculated descriptive statistics for each independent variable, and participants were categorized on the basis of BCTQ results. Occupations were categorized on the basis of JCQ results to obtain a descriptive grouping for qualitative discussion and comparison. We evaluated differences between participants with and without complaints for each independent variable, using t tests or χ^2 analysis as indicated by the level of measurement. Unadjusted odds ratios were calculated for the contribution of each individual variable to the BCTQ grouping outcome. Variables with small units of measure were adjusted to provide appropriate odds ratios relative to the other variables. Multicollinearity analysis was completed to ensure that no variables were highly correlated.

An exploratory stepwise binary logistic regression analysis was completed to evaluate the relationship of the independent variables to complaints of median nerve pathology. We entered variables into the stepwise model on the basis of unadjusted odds ratios. Because of published literature relating gender, age, and wrist ratio to symptoms, these variables were included in the final stepwise regression regardless of individual significance to ensure the model controlled for the contribution of these factors to the other variables. Final odds ratios were calculated for variables that met the selection criteria ($p = .10$) and that remained in the model after forward and backward stepwise iterations.

Results

Ninety-five participants consented to participate in the study; anatomic anomalies led to the exclusion of 7 participants after consent. On the basis of BCTQ scores, 56 of the remaining 88 participants (63.6%) reported symptoms or functional limitations in their dominant hand. The *t* tests and χ^2 analyses indicated no differences in age, gender, hand dominance, height, or wrist ratio between the two groups (Table 1). Participants with complaints had less education and higher BMI ($p < .05$). Additionally, participants with complaints of symptoms and functional deficits had larger median nerve measurements than participants without complaints.

Categorization of the reported occupations by JCQ scores resulted in most participants being categorized as having active (42.0%; $n = 37$) or low-strain jobs (36.4%; $n = 32$). Ten participants (11.4%) reported being unemployed and were not included in the descriptive report. Nearly all participants with high-strain or passive jobs (10.2%; $n = 9$) were in the complaint group. Approximately two-thirds of participants with active jobs (e.g., nurse assistant, registered nurse, attorney) fell into the complaint group, whereas only half of participants with low-strain jobs (e.g., occupational therapists, physical therapists, professor) had complaints. Table 2 provides a descriptive listing of all the occupational titles reported by participants, categorized by responses on the JCQ and BCTQ.

Of the unadjusted odds ratios, those for BMI, education, and all sonography measures were significant predictors of symptoms or functional deficits ($p < .05$). CSA change was highly correlated with CSA at the pisiform and CSA in the forearm, but the latter two measures were not highly correlated. Therefore, the evaluation of the final model did not include CSA change because of the assumption that this measure shared too much information with the other uncorrelated variables. Although age, gender, and wrist ratio were not individually significant, previous literature dictated consideration of these variables in the final regression model. Independent variables were entered into the iterative stepwise model on the basis of the unadjusted odds ratios (Table 3) for predicting complaints of median nerve pathology on the basis of BCTQ responses.

A significant stepwise binary logistic regression model ($r^2 = .281$, $p = .002$) combined BMI, education, and CSA at the pisiform to predict the presence of complaints of symptoms or decreased function among the participants (Table 4). For every 1 mm^2 increase in CSA at the pisiform, participants were 1.3 times more likely to complain of symptoms, and odds were 1.1 times higher for each unit increase in BMI. Although not significant,

Table 1. Participant Demographic Characteristics, by Subjective Complaints of Symptoms or Functional Deficits ($N = 88$)

Characteristic	Participants With Complaints ($n = 56$)	Participants Without Complaints ($n = 32$)	*p*
	Frequencies		
Gender, female:male	44:12	22:10	.306
Hand dominance, right:left	51:5	27:5	.341
Education, high school:college:graduate	27:18:11	5:17:10	.001
	Mean (Standard Deviation)		
Age, yr	44.4 (11.5)	40.8 (12.3)	.163
Height, cm	166.3 (8.4)	169.0 (8.6)	.155
Mass, kg	88.5 (21.6)	74.2 (17.5)	.002
Body mass index	32.1 (7.7)	26.0 (6.1)	<.001
Wrist ratio	0.726 (0.044)	0.717 (0.044)	.351
Cross-sectional area			
Forearm, mm^2	6.06 (1.30)	5.55 (0.94)	.038
Pisiform, mm^2	11.11 (4.01)	8.32 (1.68)	<.001
Change, mm^2	5.06 (3.82)	2.77 (1.62)	<.001
Retinacular bulge, mm	3.26 (0.49)	2.86 (0.49)	.001

Table 2. Occupations Reported by Participants With and Without Complaints of Symptoms or Functional Deficits, by Job Content Questionnaire Results

Active (n = 37)	Passive (n = 2)	Low Strain (n = 32)	High Strain (n = 7)
		Participants With Complaints	
Administrative assistant (2)	Personal banker	Administrative assistant (2)	Bus driver (2)
Attorney	Surgical technician	Babysitter	Registered nurse (3)
Audiologist		Customer service representative	Telemarketing representative
Cook, food service (2)		Dock worker	
Educator, faculty (5)		Fellowship coordinator	
Hospital administrator		Home health aide	
Lifeguard		Homemaker	
Lift operator		Insurance broker	
Medical technologist		Janitor	
Nurse anesthetist		Physical therapist	
Nurse assistant		Physical therapist assistant	
Painter, drywall (union)		Respiratory therapist	
Paramedic		School librarian	
Pharmacist		Therapy attendant	
Registered nurse (2)			
Scheduler			
Service manager			
Sprinkler fitter			
		Participants Without Complaints	
Accountant		Administrative assistant (3)	Undergraduate student
Administrative assistant		Electromyography technician	
Educator, faculty (3)		Graduate student (5)	
Finance director		Manager	
Medical transcriptionist		Occupational or physical therapist (2)	
Nurse case manager		Physical therapist assistant (2)	
Registered nurse		Professor	
Sonographer (2)		Speech–language pathologist	
Tax reporting manager		Substitute teacher, emergency medical technician	

Note. N = 88; 10 participants were unemployed and not included in the analyses.

this exploratory model indicated a trend resulting from education whereby individuals with a high school education were 3.5 times more likely to complain of symptoms or functional limitations than those with graduate-level education.

Discussion

This preliminary study indicates that measures of median nerve morphology (i.e., CSA) may be more valuable for understanding symptoms of median nerve pathology than other previously studied factors. Previously, gender and wrist ratio were the primary personal factors studied for their relationship to CTS, whereas this analysis indicates that physiological measures of the median nerve using diagnostic ultrasonography have a stronger contribution to this disorder when considered with a patient's BMI and level of education.

The outcomes of this exploratory analysis contrast with the results of previous studies exploring the predictability of sonographic measures. Kaymak et al. (2008) indicated that CSA measurements of the median nerve in the carpal tunnel had no correlation to the BCTQ symptom severity and functional status scales (−0.04–0.18).

Table 3. Unadjusted Odds Ratios of Predicting Symptoms and Functional Deficits on the Basis of Individual Characteristic Variables (N = 88)

Variable	Odds Ratio	95% Confidence Interval	p
Age	1.027	0.989, 1.067	.163
Gender (female vs. male)	1.667	0.624, 4.454	.308
Body mass index	1.146	1.057, 1.242	<.001
Education			
High school vs. graduate	4.909	1.362, 17.692	.015
Undergraduate vs. graduate	0.963	0.326, 2.843	.945
Wrist ratio (×100)	1.050	0.949, 1.163	.345
CSA at pisiform	1.390	1.137, 1.699	.001
Retinacular bulge (×10)	1.193	1.069, 1.331	.002
CSA change forearm–pisiform	1.326	1.091, 1.611	.005

Note. CSA = cross-sectional area.

Table 4. Final Stepwise Binary Logistic Regression Odds Ratios for Factors Predictive of Symptoms and Functional Deficits ($N = 88$)

Factor	Odds Ratio	95% Confidence Interval	*p*
Body mass index	1.097	1.003, 1.200	.043
Cross-sectional area at pisiform	1.3338	1.071, 1.672	.010
Education			
High school vs. graduate	3.489	0.823, 14.796	.090
Undergraduate vs. graduate	0.822	0.236, 2.861	.758

Note. Model statistics: $r^2 = .281$, $p = .002$.

Similarly, Mondelli et al. (2008) found no direct correlation between sonographic measures and the BCTQ in a surgical population with median nerve pathology. However, after including additional personal and occupational factors in a regression analysis of the same data, a relationship of sonographic measures to subjective reports was found (Mondelli et al., 2008). For every reduction in 1 mm^2 of CSA after surgery, the odds of subjective symptoms being normalized on the BCTQ increased by 20%–24%. Although this regression may support the success of surgical intervention rather than the relationship of physiology to symptoms, when combined with the results of our study, the data support continued investigation of the utility of sonographic measures in clinical practice.

The results in our study support previous research identifying BMI as a significant predictor of median nerve pathology. Our regression analysis indicated a slightly increased chance of symptoms with each unit increase in BMI, but the increased risk of CTS per unit increase in BMI has been noted to be as much as nearly double (Moghtaderi et al., 2005). Although the current study sample was not large enough to allow for a stratified comparison of various BMI levels, those with BMI >30 may be 4–9 times more likely to require surgical intervention for CTS than those with BMI <25 (Mattioli et al., 2009). Further evaluation is needed to better understand the relationship of BMI to tissue morphology and the presence of symptoms or functional deficits.

The significant influence of education on subjective reports was an unexpected outcome. Although we did not control for occupation, in theory more physically demanding jobs frequently require less education, whereas college and graduate education often lead to less physical occupations. Workers in blue-collar occupations may be up to 9 times more likely to have been surgically treated for CTS than workers in white-collar jobs (Mattioli et al., 2009). In a study of medical transcriptionists, those without a college education self-reported more upper-extremity symptoms than those with college education (Gelfman, Beebe, Amadio, Larson, & Basford, 2010). In our study, although the limited distribution of data from the JCQ disqualified those data from inclusion in the regression analysis, blue-collar occupations tended to be more typically associated with complaints. However, on the basis of the descriptive data set, many participants with skilled occupations also had complaints.

Although interesting, because none of these studies measured physical exposure, the relative importance of educational level and other occupational exposure data in development of pathology remains unclear. Moreover, the relative relationship of all personal, environmental, and occupational factors to tissue morphology requires further investigation. Use of sonography to measure CSA of the median nerve within the carpal tunnel appears to have value for predicting symptoms and functional deficits. Future studies using linear regression of the various independent factors on sonographic measures would provide stronger evidence and understanding of these relationships.

Limitations

A small, heterogeneous sample limits the ability to make broad generalizations on the basis of the results. Because of the disproportionate ratio of female to male participants in our sample, statistical power may not have been adequate to identify the contribution of gender. Matching participants on age and gender between clinical and nonclinical populations would provide better control of variables previously considered important. Categorization of participants relied on subjective reports, and diagnosis by electrodiagnostic studies was not considered; therefore, the study's results are more applicable to an acute, clinical population with symptoms of median nerve pathology instead of a population with a chronic disorder. Finally, inclusion of precise psychosocial and physical exposure variables may enhance the interpretation of this study's results.

Implications for Occupational Therapy Practice

The goal of rehabilitation research is to inform interventions that will prevent, reduce, or remediate disorders. CTS is often managed with splinting (Rempel, Dahlin, & Lundborg, 1999), but protective equipment alone will usually not completely remediate the problem. Similarly, effectiveness of workplace redesign to reduce physical loads remains inconclusive (van den Heuvel, de Looze, Hildebrandt, & Thé, 2003). A better understanding of physiology and tissue morphology may provide valuable

information to improve or validate positive effects of therapeutic treatments.

The results of this cross-sectional data collection indicate that the physiological state of the median nerve is related to a person's subjective experiences and occupational performance. Diagnostic ultrasonography has been successfully used in the workplace to quickly collect images of median nerve physiology without being obtrusive (Evans, Roll, Li, & Sammet, 2010), demonstrating significant implications for clinical practice. With the ability to visualize and appreciate swelling of the median nerve at the start of treatment, a therapist can confirm the pathophysiology that requires treatment.

The portability and advancing quality of sonographic equipment situates this technology perfectly for documentation of physiological changes within rehabilitation clinical practice (Roll & Evans, 2009). Continuous innovation in equipment designs and development of preset sonography parameters is making sonography equipment easier for nontraditional users to adopt. Sonography could be a highly useful tool for monitoring changes in the median nerve resulting from various physical exposures (Missere et al., 1998), and it follows that it could be useful in monitoring changes resulting from treatment exposure.

To summarize, the results of this study have the following implications for occupational therapy practice:

- Clinicians providing interventions for carpal tunnel syndrome and other work-related musculoskeletal disorders should consider how to best target these interventions to the underlying physiological mechanisms, an approach that may ultimately affect symptoms and functional status.
- Real-time visualization of pathophysiology and tissue morphology may improve the evaluation and interpretation of personal, environmental, or occupational risk factors for musculoskeletal disorders, leading to improved individualized treatment planning.
- Sonographic imaging is highly portable and can provide real-time visualization of tissue morphology. It may be a valuable clinical and research tool to enhance decision making and monitor changes in tissue morphology subsequent to therapeutic interventions.

Conclusion

In summary, this study demonstrates that morphology of the median nerve measured with diagnostic ultrasonography has an important relationship to subjective complaints of symptoms and functional limitations resulting from median nerve pathology. Additional research with larger samples is required to understand the interrelationship of various personal, environmental, and occupational factors with physiological changes. This study provides preliminary evidence for the use of sonography as a clinical tool for evaluating and monitoring median nerve pathology and measuring intervention outcomes. ▲

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