ORIGINAL ARTICLE

Biomechanical risk factors for carpal tunnel syndrome: a pooled study of 2474 workers

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ABSTRACT

Background Between 2001 and 2010, five research groups conducted coordinated prospective studies of carpal tunnel syndrome (CTS) incidence among US workers from various industries and collected detailed subject-level exposure information with follow-up of symptoms, electrophysiological measures and job changes.

Objective This analysis examined the associations between workplace biomechanical factors and incidence of dominant-hand CTS, adjusting for personal risk factors.

Methods 2474 participants, without CTS or possible polyneuropathy at enrolment, were followed up to 6.5 years (5102 person-years). Individual workplace exposure measures of the dominant hand were collected for each task and included force, repetition, duty cycle and posture. Task exposures were combined across the workweek using time-weighted averaging to estimate job-level exposures. CTS case-criteria were based on symptoms and results of electrophysiological testing. HRs were estimated using Cox proportional hazard models.

Results After adjustment for covariates, analyst (HR=2.17; 95% CI 1.38 to 3.43) and worker (HR=2.08; 95% CI 1.31 to 3.39) estimated peak hand force, forceful repetition rate (HR=1.84; 95% CI 1.19 to 2.86) and per cent time spent (eg, duty cycle) in forceful hand exertions (HR=2.05; 95% CI 1.34 to 3.15) were associated with increased risk of incident CTS. Associations were not observed between total hand repetition rate, per cent duration of all hand exertions, or wrist posture and incident CTS.

Conclusions In this prospective multicentre study of production and service workers, measures of exposure to forceful hand exertion were associated with incident CTS after controlling for important covariates. These findings may influence the design of workplace safety programmes for preventing work-related CTS.

What this paper adds

► Few large prospective studies using rigorous case-criteria, individual-level exposure data and appropriate control for confounding have examined associations between occupational biomechanical risk factors and carpal tunnel syndrome (CTS) incidence.

► Biomechanical risk factors associated with increased risk of developing CTS include time-weighted average peak hand force, forceful hand exertion repetition rate and the per cent time of **forceful** hand exertion.

► In this cohort, total repetition rate, per cent time of **any** hand exertion and wrist posture measures were not significantly associated with an increased risk for developing CTS.

INTRODUCTION

Carpal tunnel syndrome (CTS) is a common peripheral entrapment neuropathy resulting from compression of the median nerve at the wrist that often results in high medical treatment costs, lost work time and associated disability.[1] Although prior studies have related CTS to personal as well as workplace biomechanical factors such as hand force, repetition, awkward posture and vibration,[2-6] exposure-response relationships are not well described. Additionally, these studies were methodologically limited by cross-sectional design, non-specific CTS case-criteria (eg, symptoms only), self-reported or group-level exposure assessment, or limited sample size. Thus, for some prior studies, the observed risk factors may have been associated with true CTS, symptoms 'consistent with' CTS (but not necessarily including mononeuropathy), or other distal upper extremity musculoskeletal disorders (MSDs).

Prior studies also used different methods to assess workplace biomechanical exposures. For each exposure domain (force, repetition, posture), multiple assessment tools are available to quantify exposure at the task level.[7] For example, hand-activity level (HAL) ratings, repetition rate, or the duration of exertion (eg, duty cycle) have all been used as metrics of hand activity. Furthermore, for jobs involving multiple tasks, there are several ways to summarise exposure at the job level. For example, job-level hand force can be estimated from multiple tasks by using peak force, average force, time-weighted average (TWA) force, or typical (most common) force.[7] Currently there is little guidance regarding which of these techniques best predicts risk, nor consensus on which technique to use.

The importance of interaction between force and repetition on MSDs has been documented at the tissue level[8,9] and in epidemiological studies of working populations.[4,10] However, when tasks

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include multiple exposure domains, there is little consensus on methods for estimating the combined risk. Most studies measure each domain separately.[11] Although some exposure assessment methods, such as the threshold limit value (TLV) for HAL,[12] which estimate a single index for biomechanical hazard from multiple physical exposure domains may implicitly consider interaction, few studies have examined associations between CTS and exposures estimated with such multidomain methods.[3 13–15] Therefore, methods of estimating the combined effects of concurrent exposures across domains (eg, repetition rate of forceful exertions) have been limited and are recognised as a barrier to furthering our understanding of risk factors for occupational MSDs.[11 16]

To address these gaps, six research groups designed coordinated, multiyear, prospective epidemiological studies of US production and service workers from a variety of industries and used rigorous case-criteria and individual-level exposure assessments. After completion of data collection, subject-level demographic and longitudinal data including symptom assessments, physical examination findings, electrophysiological measures and workplace biomechanical factors were pooled.[11 17] Previously, we described the relationships between personal factors, occupational psychosocial factors and duration of employment with CTS incidence.[18] This analysis pooled data from five of the six study sites to examine associations between biomechanical exposures and incident CTS while adjusting for personal factors.

METHODS
Study participants and procedures
Participants
The pooled study cohort consisted of data from five research groups. Participants in all studies were at least 18 years of age, employed at a company where some workers performed hand-intensive activities. Details on the study designs and methods of pooling exposure[11] and health outcome[17] data are provided elsewhere (site F, a sixth site, was not eligible for pooling because subject-level exposure data were not collected). A total of 3214 workers were eligible for participation. Participants were excluded from analysis if they met the case criteria for CTS or possible polyneuropathy at enrolment (ie, baseline). Most of the participants worked in the manufacturing (83%), service (9%) or agriculture (6%) sectors.

Data collection
In all five studies, questionnaires were administered to participants at enrolment to collect information on work history, demographics, medical history and musculoskeletal symptoms. Electrodiagnostic studies (EDS) of median and ulnar nerve function across the wrist were administered to all participants and are described elsewhere.[17] Depending on the study group, EDS was either administered to all participants at regular intervals regardless of symptom status or only to those reporting upper limb symptoms.[17] Follow-up assessments of symptoms and EDS were performed at different intervals across the five studies.[11 17] Investigators responsible for collecting health outcome data were blinded to participant exposure status.

Biomechanical exposure
Ten measures of workplace biomechanical exposures were collected at the task level for all participants: two measures of hand force, three measures of hand repetition, two measures of hand exertion duty cycle, two measures of wrist posture and one measure of hand vibration.[11] Exposure estimates were

based on a trained analyst's observation of each participant performing his/her usual work tasks, measurement of hand forces applied to complete each task, videotape analysis of the task, and interviews of participants or their supervisors. These analysts were blinded to health outcome.

Specifically, the pooled data set included estimates of the highest hand force requirements for a task as estimated by the worker (*worker-rated peak hand force*) and the analyst (*analyst-rated peak hand force*) using the Borg CR-10 rating scale.[19] The repetitiveness of tasks was estimated by the analyst using the HAL scale. The HAL scale is one variable used in the HAL for TLV; the HAL for TLV is an index that combines repetition and peak hand force. The association of HAL for TLV with CTS will be evaluated in a separate publication. Other temporal exertion patterns for repetition, duty cycle and posture were determined by detailed time studies of task-level videos.[11] These included the number of **all** exertions per minute (*total hand repetition rate*) and the number of **forceful** exertions per minute (*forceful hand repetition rate*). Forceful exertions were those requiring ≥9N pinch force or ≥45N of power grip force or a Borg CR-10 ≥2. Estimates of force were based on measurement of the force required for the task, the weights of parts or tools, or force matching. Duty cycle was quantified for **all** hand exertions (*% time all exertions*) and **forceful** hand exertions (*% time forceful exertions*). Posture was quantified as the % time in ≥30° wrist extension (*% time ≥30° wrist extension*) and the % time in ≥30° wrist flexion (*% time ≥30° wrist flexion*). Finally, exposure to hand vibration (yes/no) observed by the analyst during a task was recorded.

Exposures were measured at the individual task level at all study sites at the time of participant enrolment and measured again if the job changed, thus creating a time series of exposure information. Three standard approaches were applied to summarise the task-level exposures at the job level: *peak* (the highest exposure across all tasks), *typical* (the exposure of the most commonly performed task) and *TWA* (a proportional weighting of each task's exposure value by the proportion of time the task was performed across the week). Peak, typical and TWA exposures were highly correlated across participants (r=0.84–0.99); therefore, only TWA measures (which included information from all tasks performed) were used for this analysis.

Outcome
The study outcome was incident CTS of the dominant hand and required (1) symptoms of tingling, numbness, burning or pain in the thumb, index finger or long finger **and** (2) EDS results demonstrating median mononeuropathy at the wrist.[20] Median mononeuropathy was defined as (1) peak median sensory latency >3.7 ms or onset median sensory latency >3.2 ms at 14 cm, (2) motor latency >4.5 ms, (3) transcarpal sensory difference of >0.85 ms (difference between median and ulnar nerve sensory latency across the wrist), or (4) an absent latency value consistent with an abnormal EDS *and* EDS evidence of normal ulnar nerve physiology (ulnar sensory peak latency <3.68 ms). Participants with symptoms consistent with CTS and concurrent abnormal median and ulnar nerve EDS were classified as *possible polyneuropathy* and were censored at the time that the possible polyneuropathy case definition criterion was met.[18] All EDS latency values were temperature adjusted to 32°C. Individuals who were symptomatic without a subsequent EDS were censored at the last date of known case status. Person-time was calculated as the number of days from enrolment to an abnormal EDS with symptoms or censoring due to possible polyneuropathy, dropout or study termination.

Personal factors

All studies collected participant age, gender, body mass index (BMI), race/ethnicity, education, smoking status, hand dominance, and comorbid medical conditions such as rheumatoid arthritis, diabetes mellitus and thyroid disease. Prior carpal tunnel release and disorders of the distal upper extremity were also assessed. General health was assessed on a five-point scale. Total years worked at the current employer was self-reported at study enrolment.

Statistical analysis

HRs were estimated using Cox proportional hazards regression with robust CIs adjusted for potential confounding. For each exposure measure, the cohort was split into three equal size groups based on the exposure distribution. Potential confounding by personal factors was evaluated empirically. Specifically, covariates that were associated with each outcome (p≤0.20 and had less than 10% missing data) were initially included in each model and then removed sequentially, in descending order of probability (with the covariate having the highest p value removed first). Covariates that, when removed from the model, resulted in a change of the effect estimate of the primary exposure variable by more than 10% were considered confounders and subsequently retained in the final multivariable model. To further minimise bias, models were also adjusted by study site and the exposure variable from each of the other domains (force, repetition, duty cycle and posture) with the least amount of missing data. As previous distal upper extremity disorders are (1) expected to be associated with the same exposures as CTS and (2) are not believed to be an independent risk factor for CTS, this variable was not considered a confounder for these analyses.[21] The interactions of force and repetition were assessed by stratifying models using a median split of the exposure distribution at baseline. The healthy worker survivor effect was assessed by stratifying models on more or less than 3 years of work at enrolment, a threshold chosen to achieve an adequate sized referent group. To examine the impact of our definition of possible polyneuropathy, an additional post-hoc analysis was performed using concurrent abnormal median and ulnar nerve latencies regardless of median nerve symptoms as the definition for possible polyneuropathy. The functional form of the relationships between CTS and biomechanical exposures were assessed using penalised splines[22] in a Cox model (R Core Team, Vienna, Austria). All other analyses were implemented with the Stata statistical package (Stata, College Station, Texas, USA).

RESULTS

Of the initial 3214 workers, 364 were excluded due to CTS (N=309) or possible polyneuropathy (N=55) at enrolment. Of the remaining 2850 eligible workers, 376 were dropped due to lack of exposure data or loss to follow-up for a participation rate of 86.8% (figure 1). There were 179 (7.2%) incident CTS cases occurring over 5103 years of follow-up, for an incident rate of 3.51 per 100 person-years (table 1). The mean age at baseline was 40.8 years (SD=11.1) and 88% had no reported medical condition. The median years worked at the same company at baseline was 6.1 years (IQR 2.3–12) and most participants (84%) worked the day shift. The median follow-up time was 2 years (IQR=1–2.9) with 10% of participants having less than 6 months of follow-up time and 10% having more than 4.7 years.

Correlations between most demographic and exposure variables were low (r=−0.01 to 0.19). However, as expected,

working years and age were correlated (r=0.48). Among the biomechanical variables, correlations greater than r=0.5 were observed for *forceful hand repetition rate* and *total hand repetition rate* (r=0.54) and *forceful hand repetition rate* and % time in *forceful hand exertion* (r=0.76).

Baseline exposure results are presented in table 2. Differences between all (total) exertions and forceful exertions are best observed by inspection of the metrics used to depict repetition rate and duty cycle. Specifically, the median *total hand repetition rate* (18.0 exertions/min; IQR 10.1–31.6) was more than three times the *forceful hand repetition rate* (5.3 exertions/min; IQR 1.4–13.3). Similarly, the median % *time all hand exertions* (67.2% time; IQR 53.6–80.4) was more than three times the % *time forceful hand exertions* (20.0% time; IQR 6.3–37.9). Approximately 63% of participants were exposed to vibration during all of their tasks, 8% were exposed to vibration during some tasks and 29% were not exposed to vibration at all.

Crude and adjusted estimates of the associations between each biomechanical exposure and incident CTS are presented in table 3. When models were adjusted for age, gender, BMI, study site and exposure to other biomechanical domains, several statistically significant exposure-response relationships were observed.

Statistically significant monotonic increases in risk were observed for participants in the middle and upper tertiles of *worker* as well as *analyst-rated peak hand force*. Specifically, for the *analyst-rated peak hand force*, those in the middle tertile had a 60% increase in CTS risk (HR=1.59; 95% CI 1.09 to 2.34) and those in the highest tertile had a 117% increase in CTS risk (HR=2.17; 95% CI 1.38 to 3.43) when compared with the reference group. Similar magnitude increases were observed for *worker-rated peak hand force*. The penalised cubic spline fit of the adjusted association also demonstrated a near linear association between *analyst-rated peak force* and incident CTS over peak hand force ratings of zero to seven (see online supplementary figure S1a). For values greater than seven the CI was wider and the precision of the estimate was lower due to relatively few workers having such high exposure.

The adjusted model for the *analyst HAL scale* demonstrated a statistically significant increased risk for the middle tertile (HR=1.54; 95% CI 1.02 to 2.32) but not the upper tertile (HR=1.32; 95% CI 0.87 to 2.02). For the two video analysis measures of hand repetition, an increased rate of CTS in the adjusted models was observed for *forceful hand repetition rate*
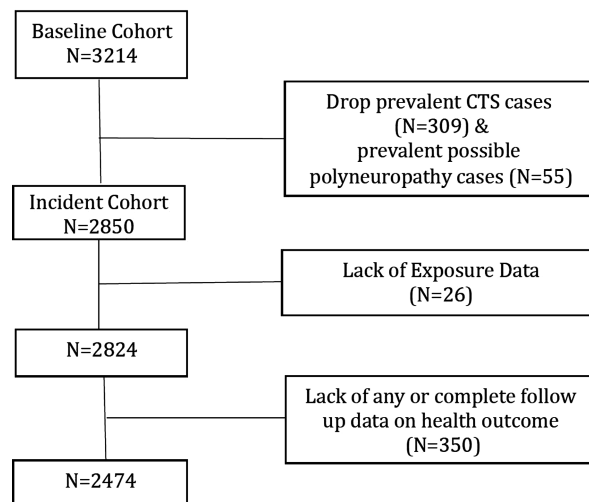

Figure 1 Cohort description (CTS, carpal tunnel syndrome).

but not for *total hand repetition rate*. When compared with the lowest tertile of *forceful hand repetition rate*, the HRs for the middle tertile and upper tertile were 1.53 (95% CI 1.05 to 2.25) and 1.84 (95% CI 1.19 to 2.86), respectively.

Additionally, a penalised cubic spline fit demonstrated a near linear association up to 30 exertions/min, at which point the precision declined due to the low number of participants with exposures above this level (see online supplementary figure S1b).

A similar pattern was observed for the duty cycle measures of hand exertion. In the adjusted models, the per cent time that the fingers were exerting **any** level of force (*% time all hand exertions*) was not associated with incident CTS (table 3). A post-hoc analysis of *% time all hand exertions*, using cut-points of 30% duration (HR=0.85; 95% CI 0.41 to 1.76) and 60% duration (HR=1.00; 95% CI 0.50 to 1.99) also demonstrated no significant associations (data not shown). In contrast, CTS incidence was significantly and monotonically associated with per cent time performing a **forceful** grip or pinch (*% time forceful hand exertions*). Specifically, those in the upper tertile of this measure had twice the rate of incident CTS compared with those in the lowest tertile (HR=2.05, 95% CI 1.34 to 3.15). A model using a penalised cubic spline demonstrated a near linear increase in rate of CTS up to 50% time in forceful *hand exertions* beyond which the precision declined due to small sample size at the higher exposure level (see online supplementary figure S1c).

No associations were observed in the crude or adjusted models between measures of wrist posture or vibration and CTS incidence (table 3).

In a post-hoc analysis, the interaction of hand force and repetition rate on CTS risk was investigated by stratifying the *analyst-rated peak hand force* HRs by *total hand repetition rate* (table 4A) and *total hand repetition rate* by *analyst-rated hand force* (table 4B). For the first stratification, the cohort was split on median *total hand repetition rate* (18.1 repetitions /min; table 4A). A stronger association between *analyst-rated peak force* and CTS was observed in the high repetition group compared with the lower repetition group. However, when *total hand repetition rate* was stratified by *analyst-rated peak hand force* (Borg CR-10 of 3), there was no association with incident CTS in either the low-force or high-force subgroups.

To explore the effect of years worked on the exposure-response relationships, analyses of associations between incident CTS and *analyst-rated peak hand force*, *forceful hand repetition rate* and *% time forceful hand exertions* were

Table 1 Demographics and related characteristics

	Total N=2474	N	CTS cases (n)
Gender*		2474	179
Male	1200 (48%)		65
Female	1274 (52%)		114
Age (years)		2474	179
<30 years	490 (20%)		25
≥30 & <40 years	614 (25%)		39
≥40 & <50 years	793 (32%)		64
≥50 years	577 (23%)		51
Ethnicity†		2151	158
Caucasian	1267 (51%)		112
Hispanic	509 (21%)		16
African American	164 (7%)		14
Asian	139 (6%)		9
Other	72 (3%)		7
Education		2449	175
Some high school or less	495 (20%)		32
High school graduate or above	1954 (79%)		143
Handedness		2474	179
Left handed	192 (8%)		16
Right handed	2282 (92%)		163
Body mass index*		2462	178
Body mass index (<25)	804 (33%)		35
Body mass index (≥25 & <30: overweight)	826 (33%)		59
Body mass index (≥30: obese)	832 (34%)		84
General health†		2041	161
Very good or excellent	884 (36%)		55
Good	881 (36%)		83
Fair or poor	276 (11%)		23
Medical condition		2469	179
No medical condition	2182 (88%)		153
Current medical condition	287 (12%)		26‡
Diabetes	99 (4%)		7
Rheumatoid arthritis	54 (2%)		5
Thyroid disease (hyper/hypo)	131 (5%)		15
Pregnancy	19 (1%)		0
Previous DUE disorder		1830	134
No previous DUE	1578 (64%)		105
Previous DUE	252 (10%)		29
Smoking status		2459	176
Never smoked	1344 (54%)		93
Currently smoke	649 (26%)		50
Previously smoked	466 (19%)		33
Years worked at enrolment		2455	176
≤1 year	262 (11%)		17
>1 & ≤3 years	503 (20%)		26
>3 & ≤7 years	564 (23%)		46
>7 & ≤12 years	567 (23%)		50
>12 years	559 (23%)		37

Missing per cent for each characteristic represents missing data.
*p≤0.20 and retained in models.
†p≤0.20 but excluded from models due to missing >10% data.
‡One participant had two medical conditions.
CTS, carpal tunnel syndrome; DUE, distal upper extremity.

Table 2 Summary of baseline job-level time-weighted average exposures

	(N)	Median (IQR)	Range
Force measures			
Peak hand force: worker rated	2168	3 (2.0–4.5)	0– 10
Peak hand force: analyst rated	2408	3 (1.8–4)	0–10
Repetition measures			
HAL scale: analyst	2423	4.9 (4–6)	0–10
Total hand repetition rate	2165	18.0 (10.1–31.6)	0.7–100
Forceful hand repetition rate	2442	5.3 (1.4–13.3)	0–95.7
Duty cycle			
% time all hand exertions	2165	67.2 (53.6–80.4)	0.7–100
% time forceful hand exertions	2442	20.0 (6.3–37.9)	0–100
Posture measures			
% time ≥30°wrist extension	2433	5.6 (0–18.2)	0–100
% time ≥30°wrist flexion	2432	0.6 (0–3.5)	0–62.5

HAL, hand-activity level.

Table 3 Crude and adjusted hazard rate ratios for carpal tunnel syndrome and individual time-weighted average biomechanical exposures

		Crude				Adjusted			
	Cutoffs	Cohort (N)	Cases (n)	HR	95% CI	Cohort (N)	Cases (n)	HR	95%CI
Force measures									
Peak hand force: worker rated*		2233	157			1955	142		
Lower tertile	≤2.1		38	1.00			33	1.00	
Middle tertile	>2.1 & ≤4		62	1.22	0.81 to 1.84		57	1.70	1.08 to 2.68
Upper tertile	>4		57	1.62	1.07 to 2.44		52	2.08	1.31 to 3.29
Peak hand force: analyst rated*		2410	176			2038	153		
Lower tertile	≤2.5		58	1.00			49	1.00	
Middle tertile	>2.5 & ≤4		75	1.16	0.82 to 1.64		65	1.59	1.09 to 2.34
Upper tertile	>4		43	1.65	1.11 to 2.46		39	2.17	1.38 to 3.43
Repetition measures									
HAL scale: analyst rated†		2425	177			2299	164		
Lower tertile	≤4		66	1.00			59	1.00	
Middle tertile	>4 & ≤5.3		50	1.36	0.94 to 1.95		48	1.54	1.02 to 2.32
Upper tertile	>5.3		61	1.21	0.85 to 1.73		57	1.32	0.87 to 2.02
Total hand repetition rate: video analyst†		2107	159			2038	153		
Lower tertile	≤13		61	1.00			57	1.00	
Middle tertile	>13 & ≤26		57	0.94	0.66 to 1.35		56	1.12	0.76 to 1.65
Upper tertile	>26		41	0.77	0.52 to 1.15		40	0.94	0.59 to 1.5
Forceful hand repetition rate: video analysis‡		2384	170			2354	166		
Lower tertile	≤2.6		60	1.00			59	1.00	
Middle tertile	>2.6 & ≤9.6		60	1.16	0.81 to 1.66		57	1.53	1.05 to 2.25
Upper tertile	>9.6		50	1.26	0.87 to 1.84		50	1.84	1.19 to 2.86
Duty cycle									
% duration all hand exertions: video analysis†		2107	159			2038	153		
Lower tertile	≤59%		45	1.00			42	1.00	
Middle tertile	>59% & ≤76%		57	1.20	0.81 to 1.77		56	1.12	0.75 to 1.67
Upper tertile	>76%		57	1.29	0.87 to 1.91		55	1.13	0.75 to 1.68
% duration forceful hand exertions: video analysis‡		2384	170			2354	166		
Lower tertile	≤11%		57	1.00			56	1.00	
Middle tertile	>11% & ≤32%		55	1.12	0.78 to 1.62		53	1.46	0.98 to 2.17
Upper tertile	>32%		58	1.48	1.03 to 2.13		57	2.05	1.34 to 3.15
Posture measures									
% time ≥30°wrist extension: video analysis§		2373	168			2038	153		
Lower half	≤5%		96	1.00			88	1.00	
Upper half	>5%		72	0.90	0.66 to 1.23		65	0.87	0.59 to 1.29
% time ≥30°wrist flexion: video analysis§		2374	168			2038	153		
Lower half	≤1%		86	1.00			83	1.00	
Upper half	>1%		82	0.94	0.69 to 1.27		70	0.83	0.60 to 1.15
Other									
Vibration: analyst rated¶		2092	162			1719	139		
Lower half	0		96	1.00			82	1.00	
Upper half	>0		66	1.07	0.78 to 1.47		57	1.04	0.69 to 1.55

All models include age, gender, body mass index, study site.
*Adjusted for total repetition rate, % duration all exertions, % time ≥30° wrist flexion.
†Adjusted for peak force, % time ≥30° wrist flexion.
‡Adjusted for % time ≥30° wrist flexion.
§Adjusted for peak force, total repetition rate, % duration all exertions.
¶Adjusted for peak force, total repetition rate, % duration all exertions, % time ≥30° wrist flexion.
HAL, hand-activity level.

conducted for the subgroup with less than 3 years of work at baseline and the subgroup with three or more years of work (table 4C–E). Somewhat higher HRs were observed for those who worked less than 3 years compared with those who had worked three or more years.

In a post-hoc analysis, when we changed the definition of possible polyneuropathy to be patients with concurrent abnormal median and ulnar nerve latencies regardless of symptoms (N=121), the adjusted HRs increased for the middle analyst-rated peak hand force tertile (HR=1.82; 95% CI 1.22 to 2.71), the upper analyst-rated peak hand force tertile (HR=2.61; 95% CI 1.62 to 4.2), forceful hand repetition rate (HR$_{middle\ tertile}$=1.74; 95% CI 1.17 to 2.59; HR$_{upper\ tertile}$=2.1; 95% CI 1.32 to 3.32) and % time forceful hand exertions (HR$_{middle\ tertile}$=1.6; 95% CI 1.05 to 2.42; HR$_{upper\ tertile}$=2.39; 95% CI 1.54 to 3.71). There was minimal change in the effect estimates of the other exposure variables.

Table 4 Associations between selected workplace biomechanical exposures and incident carpal tunnel syndrome stratified by (A) repetition, (B) peak hand force, or (C–E) years worked at time of enrolment

	Cohort (N)	Cases (n)	HR	95% CI
(A) Analyst-rated peak hand force stratified by total hand repetition rate				
Analyst peak force: subgroup with ≤18.1 repetitions/min	1100	82		
Lower tertile		35	1.00	
Middle tertile		27	1.03	0.60 to 1.77
Upper tertile		20	1.82	0.99 to 3.37
Analyst peak force: subgroup with >18.1 repetitions/min	1033	71		
Lower tertile		14	1.00	
Middle tertile		38	2.78	1.51 to 5.14
Upper tertile		19	2.97	1.41 to 6.27
(B) Total hand repetition rate stratified by analyst-rated peak hand force				
Total repetition rate: subgroup with lower peak hand force (≤3)	1308	91		
Lower tertile		36	1.00	
Middle tertile		29	1.01	0.59 to 1.73
Upper tertile		26	1.11	0.60 to 2.07
Total repetition rate: subgroup with higher peak hand force (>3)	878	62		
Lower tertile		21	1.00	
Middle tertile		27	1.36	0.76 to 2.44
Upper tertile		14	0.64	0.30 to 1.37
(C) Analyst-rated peak hand force stratified by years worked at enrolment				
Analyst peak hand force: subgroup with <3 years of work	674	37		
Lower tertile		10	1.00	
Middle tertile		16	1.83	0.80 to 4.17
Upper tertile		11	3.37	1.16 to 9.81
Analyst peak hand force: subgroup with ≥3 years of work	1345	113		
Lower tertile		39	1.00	
Middle tertile		46	1.46	0.94 to 2.28
Upper tertile		28	1.88	1.12 to 3.18
(D) Forceful hand repetition rate stratified by years worked at enrolment				
Forceful repetition rate: subgroup with <3 years of work	727	40		
Lower tertile		12	1.00	
Middle tertile		17	2.18	0.97 to 4.89
Upper tertile		11	2.78	0.93 to 8.27
Forceful repetition rate: subgroup with ≥3 years of work	1608	123		
Lower tertile		45	1.00	
Middle tertile		39	1.45	0.93 to 2.28
Upper tertile		39	1.75	1.07 to 2.86
(E) % duration forceful hand exertion stratified by years worked at enrolment				
% duration forceful exertions: subgroup with <3 years of work	727	40		
Lower tertile		11	1.00	
Middle tertile		17	1.94	0.86 to 4.40
Upper tertile		12	2.53	0.90 to 7.09
% duration forceful exertions: subgroup with ≥3 years of work	1608	123		
Lower tertile		44	1.00	
Middle tertile		34	1.32	0.83 to 2.12
Upper tertile		45	2.16	1.36 to 3.43

All models are adjusted for age, gender, body mass index, study site and the other biomechanical variables listed in table 3.

DISCUSSION

In this prospective study of a working population, exposure-response relationships were observed between several measures of forceful hand exertion and incident CTS. The observed associations provide strong evidence for modifiable physical risk factors in the workplace. The strengths of the study were the large sample size, specific case-criteria and detailed exposure measures at the individual level. The wide range of industries, jobs and locations represented increases the heterogeneity of exposures and the generalisability of the findings. The incidence of CTS was 3.51 per 100-person-years, which was higher than the 0.17 rate reported from workers compensation data[23] and lower than some studies of specific working populations (1.2–11.0 per 100-person-years).[13][14][23]

Since there are several approaches to summarising exposure at the job level when workers perform more than one task, job-level exposure based on (1) peak, (2) typical and (3) TWA methods were calculated for each worker across all of his/her tasks. For this data set, regardless of the exposure domain (force, repetition, duty cycle, posture or vibration), the correlations between the three summary methods were high (range: r=0.84–0.99) because most jobs consisted of just one (57%)

task. Future studies using various summary methods among only participants who worked jobs with two or more tasks are needed in order to (1) compare the risk prediction performance among the exposure summary techniques, and (2) explore the implications of each technique on workplace injury prevention strategies.

The risk of CTS incidence increased monotonically across peak hand force categories, regardless of whether it was rated by the analyst or worker (r=0.52). Approximately two-thirds of analyst and worker-rated peak hand force scores differed with 38% of scores rated higher by the worker (mean=1.9; SD=1.5) versus 28% rated higher by the analyst (mean=1.5; SD=1.1). Despite the differences between the two measures, both were associated with increased risk of CTS, thus validating the use of either scale for surveillance.

When hand repetition rate was considered independent of force (eg, *total hand repetition rate*), we observed no significant increase in rate of CTS. On the other hand, *forceful hand repetition rate*, a measure of simultaneous exposure to forceful and repetitive hand exertions, was significantly associated with an increased risk of CTS. The CTS incidence rate appeared to increase linearly with *forceful hand repetition rate* up to 30 repetitions/min (see online supplementary figure S1b), at which point the HR plateaued with widening CIs. Very few workers performed work that required more than 30 hand exertions/minute at greater than a 45N grip or 9N pinch force, possibly due to the difficulty performing work at such exposure levels. Contrary to our results, several cross-sectional studies have reported associations between total hand repetition or wrist angular velocity and CTS.[4 6 10 24] One explanation may be that their repetition rates were, to some extent, a measure of forceful repetition rates (ie, the analyst may have only counted a hand motion as a repetition if it exceeded some minimum level of applied force). Alternatively, it could be that repetition is a risk factor for CTS only during low force tasks. However, this was not observed in the low force subgroup post-hoc stratified analysis of *total hand repetition rate* by *analyst-rated peak hand force* (table 4B).

The analyst-rated HAL scale captures hand repetition as well as recovery time[12] and has been associated with distal upper extremity disorders and CTS in some prior studies[13 25] but not others.[15] In our cohort, a 54% increase in rate of CTS occurred among participants with exposure in the middle tertile (eg, HAL scale=4–5.3) but the rate declined modestly in the upper tertile. These findings differ from a prospective study[13] that reported a monotonic 37% increase in risk of CTS for every unit increase in HAL scale. Although the Bonfiglioli[13] study and our study had similar sample sizes (2921 vs 2474), there were different CTS incidence rates (2.20 vs 3.51 per 100-person-years), different jobs and different exposure levels. For example, the median value for HAL in the Bonfiglioli study[13] was lower than in our study. In addition, the correlation between HAL and peak force was larger in the Bonfiglioli study (Spearman r=0.42 vs 0.18), suggesting that the minimum force threshold required for a 'hand exertion' was higher than in our study.

Similar to the findings for repetition, the per cent time performing **any** finger pinch or power grip (including light-force and high-force exertions) was not associated with CTS incidence regardless of whether exposure cut-points were based on the study population distribution or *a priori* selected values. However, the per cent time spent in forceful pinch or power grip increased the rate of CTS in a dose-response pattern. Participants with a per cent of time in forceful hand exertion between 11% and 32% (second tertile) had a 46% increase in

the rate of CTS and those with per cent time in forceful hand exertion of more than 32% (third tertile) had twice the rate of CTS compared with the lowest tertile (<11%). The decline in risk for CTS observed for those who spent more than 50% of their time in forceful exertion (see online supplementary figure S1c) could be a reflection of the scarcity of data above that exposure level. It could also indicate an attenuation commonly observed in other studies of associations between occupational exposures and adverse health effects and represent a healthy worker survivor bias resulting from the self-selection of the most affected workers out of jobs with the highest levels of exposure.[26]

Although several cross-sectional and case-control studies have identified wrist posture as a risk factor for CTS,[5 6 27–30] National Institute for Occupational Safety and Health (NIOSH) found insufficient evidence that posture increased risk for CTS in a comprehensive review.[31] In our study, posture, measured as the per cent time with >30° of wrist flexion or extension, was not associated with incident CTS. It is possible that the lack of association was due to the particular category cut-points used. Many studies have reported an increase in carpal pressure with increasing wrist extension or flexion[32] and one study suggested that wrist extension greater than 33° or wrist flexion greater than 49° would increase CTS risk.[33] Other literature suggests that 15° of extension is the functional neutral wrist posture[34]; therefore, using a threshold of 45° (15°+30°) of extension may be a better cut-point for risk assessment. However, the tasks performed by the workers in our cohort did not require much wrist extension or flexion. The cohort median per cent time in wrist flexion and wrist extension greater than 30° were 5.6% and 0.6%, respectively. Therefore, the postures observed among these study participants may have been of insufficient duration to increase risk. Another approach would have been to measure the per cent time in non-neutral wrist postures during forceful hand exertions. Fung *et al*[5] found increased risk of CTS among those with wrist flexion or extension that was forceful. Unfortunately, this type of analysis was not possible with our data set.

The interaction between force and repetition makes the relative distributions of their exposure levels important when estimating their individual associations with incident CTS. For example, in the stratified analysis (table 4A) workers exposed to a lower repetition rates (<18 repetitions/min) were not at elevated risk of CTS until exposed to high levels of peak hand forces (>4). However, for those performing jobs with higher hand repetition rates (>18 repetitions/min), CTS risk increased nearly threefold with only moderate peak hand force (>2.5 and ≤4). This suggests that, at lower repetition rates workers may tolerate greater levels of force than they tolerate at higher repetition rates.

Although the presence of vibration exposure was not associated with CTS incidence in this cohort, the vibration metrics used were prone to substantial non-differential misclassification and may have biased findings towards the null. Studies with more precise measures of vibration have found associations between vibration and CTS.[6 35 36] The relationship between hand vibration exposure and risk of CTS should be explored with more complete and accurate exposure assessments.

Healthy worker survivor bias can attenuate exposure-response results due to the inclusion of participants hired well before study enrolment and the exclusion of prevalent cases diagnosed at baseline.[37] To some extent, this bias may explain the increased rate of CTS that was observed among recent hires; for example, those hired within 3 years of enrolment. In this recent

hire group, the rate of CTS among those exposed to high peak hand forces was approximately 50% greater than those with the same physical exposure, but hired more than three years prior to enrolment. A similar, albeit weaker, pattern was observed for those exposed to high forceful hand repetition rates. Yet the pattern for exposure to high per cent time in forceful hand exertions was no different between the two hire-date subgroups. It may be that the recently hired workers who are most susceptible to CTS leave high exertion jobs in less than 3 years. When estimating the same associations using cut-points of 5 or 7 years, there were no differences between subgroups, regardless of exposure metric or magnitude (data not shown in table 4). These findings suggest that the dropout associated with the healthy worker effect likely occurs in only the first few years of employment. The findings also suggest that effect estimates are likely underestimated in this analysis. Further research focused on new hires may clarify when and why workers choose to leave the workforce due to injury or difficulty tolerating certain physical exposures.

Our case definition for possible polyneuropathy, concurrent abnormal ulnar and median latency and CTS symptoms, was used to exclude incident CTS cases who might have polyneuropathy. The analysis was repeated after excluding all participants with concurrent abnormal median and ulnar nerve latencies regardless of symptoms; effect estimates were slightly increased for the exposure variables that included some measure of forceful hand exertion. There were no other important differences due to this change in definition of possible polyneuropathy.

Limitations

Several limitations should be considered based on differences in study designs between the five studies pooled for these analyses.[11 17] Exposure data were not collected with identical methods across studies, likely increasing the possibility of non-differential exposure misclassification and underestimation of effect estimates.[11] The findings for vibration should be interpreted with caution because the assessments were simply dichotomised and the sample set was smaller than for the other analyses. The differences between study groups in the frequency of outcome assessments likely affected the temporal precision of diagnosis leading to some non-differential misclassification. In addition, it would have been useful to adjust for psychosocial factors in the analyses; the independent role of psychosocial factors in this cohort was investigated in a prior publication.[18] However, the psychosocial variables were not available from one study group and an analysis was only possible with a substantially smaller sample size. Finally, the work history used in the assessment of healthy worker survivor bias only included the total years worked at the current employer and not prior employment.

CONCLUSION

In this prospective multicentre study of production and service workers, several measures of forceful occupational hand exertion were significantly associated with incident CTS after controlling for important covariates. Peak hand force, forceful hand repetition rate, and the per cent time in forceful hand exertion were each associated with the incident CTS in a dose-dependent pattern. Repetition rate for all hand exertions and the per cent time in any hand exertion (regardless of hand force) were not associated with an increased rate of CTS in this cohort. These findings support the conclusion that hand force is an important risk factor for CTS and do not support the conclusion that hand repetition, as distributed among the members of this study sample, is a risk factor for CTS. Workplace safety programmes may incorporate these findings into their strategies to prevent work-related CTS in production and service work.

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