Arbejdsmarkedsudvalget
AMU alm. del - Bilag 84
Offentligt

Den Videnskabelige Komite

Dansk Selskab for Arbejds- og Miljømedicin

Carpal tunnel syndrome
and the use of computer mouse and keyboard
A Review

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Oktober 2005

Forord

Dansk Selskab for Arbejds- og Miljømedicin (DASAM) har i december 2004 etableret en videnskabelig komité, som har til opgave løbende at formidle udbud med henblik på udarbejdelse af opdateret videnskabelig dokumentation vedrørende arbejdsbetingede sygdomstilstande samt forestå redigeringsprocessen af det videnskabelige dokument.

Komiteens oprettelse var foranlediget af, at Arbejdsskadestyrelsen har ønsket en række referencedokumenter om det videnskabelige grundlag for at antage, at særlige arbejdsmæssige påvirkninger kan være årsag til bestemte sygdomme. Komiteen står til rådighed for andre rekvirenter af lignende referencedokumenter. Komité-medlemmer blev udpeget af DASAM efter indkaldelse af forslag ved offentligt opslag.

Komiteen består af

overlæge dr. med. Sigurd Mikkelsen, Arbejdsmedicinsk Klinik, Glostrup (formand).
overlæge ph.d. Johan Hviid Andersen, Arbejdsmedicinsk Klinik, Herning
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De første opgaver har været udbudt per e-mail og over internettet til relevante forskningsinstitutioner i Norden, og komiteen har blandt kvalificerede ansøgere udvalgt den bedst kvalificerede til at løse opgaven.

Det første dokument foreligger hermed. Det vedrører spørgsmålet om det videnskabelige grundlag for at antage, at computerarbejde kan forårsage karpaltunnelsyndrom. Opgavens indhold har været beskrevet af Arbejdsskadestyrelsen, der har finansieret udarbejdelsen af dokumentet.

Graden af evidens for en årsagsmæssig sammenhæng er rubriceret efter en standard, som DASAM's videnskabelig komite har udarbejdet på baggrund af internationale standarder. Den anvendte standard er vist i Appendix 1.

Opgaven er løst af overlæge, ph.d. Jane Frølund Thomsen, Arbejdsmedicinsk Klinik i Glostrup. Opgaven har været uafhængigt bedømt af to særligt sagkyndige reviewere, professor Fred Gerr, University of Iowa, USA, og docent overlæge Isam Atroshi, Ortopediska kliniken Hässleholm-Kristianstad og der er herudover indhentet skriftlige bemærkninger fra komiteens medlemmer Dokumentet er efterfølgende gennemgået og drøftet på et heldags-møde med reviewerne, komiteen og Jane Frølund Thomsen. Sluttelig har Jane Frølund Thomsen revideret referencedokumentet i forhold til de fremkomne bemærkninger.

Komiteen og reviewerne kan tiltræde dokumentets konklusioner og de præmisser, der ligger til grund herfor.

København oktober 2005

Sigurd Mikkelsen
Formand for DASAM's Videnskabelige Komite.

Resumé på dansk

Litteraturen omhandlende udførelse af computerarbejde, både anvendelse af tastatur og mus, og forekomst og udvikling af karpaltunnelsyndrom (KTS) blev gennemgået. Gennemgangen var baseret på en litteratursøgning i relevante databaser (juni 2005). Der anvendtes flg. søgetermer til identifikation af den epidemiologiske litteratur: Carpal tunnel syndrome or cts or median nerve and computer or visual display unit or keyboard or mouse. Flg. kriterier skulle være opfyldt for at indgå: Tværsnitsundersøgelser eller longitudinelle undersøgelser med en eksponeret gruppe, der udførte computerarbejde (mus eller tastatur) og en kontrolgruppe uden denne eksponering eller case-referent undersøgelser, hvor computerarbejde (mus eller tastatur) var belyst særskilt. Desuden skulle diagnosen KTS indeholde både symptomer forenelige med KTS samt enten et klinisk interview udført af en læge der bekræftede disse symptomer eller en neurofysiologisk undersøgelse (NFU). Studier der undersøgte nervefunktionen i armen og hånden ved computerarbejde indgik ligeledes. Herudover blev der foretaget litteratursøgning af longitudinelle undersøgelser der omhandlede repetitivt og ikke kraftfuldt arbejde og udvikling af KTS, idet denne type arbejde har visse lighedspunkter med computerarbejde. Endelig foretoges litteratursøgning af studier, der beskriver ledstillinger og kraftudøvelse ved computerarbejde samt studier, hvor undersøgelser af karpaltunneltryk undersøgtes ved forskellige ledstillinger, kraftudøvelse og egentlige arbejdsfunktioner. Sidstnævnte med henblik på at vurdere, om computerarbejde indebærer belastninger, der kan medføre skadelige virkninger på medianusnerven. Litteraturlister fra relevante artikler blev gennemgået. I alt blev der ved litteratursøgningen gennemlæst ca. 800 titler samt relevante abstracts forud for udvælgelsen af artikler til litteraturgennemgangen.

Der fandtes i alt 5 studier der opfyldte kriterierne for at kunne belyse epidemiologisk evidens, 3 longitudinelle, 1 case-referent studie og 1 tværsnitsstudie med et case-referent element indeholdt. Det ene longitudinelle studie (Nathan et al. 2002) var ikke veludført, idet eksponeringen var dårligt bestemt, KTS diagnosen var ved den indledende undersøgelse kun baseret på NFU og først ved opfølgningen suppleredes med symptomer. Jobændringer i de 11 år undersøgelsen forløb var ikke beskrevet. Hertil kom, at gruppen af personer der udførte computerarbejde var lille, kun 22 personer af de i alt 471 deltagere. De to andre longitudinelle studier var veludførte men indebar forskellige fortolkningsmæssige problemstillinger (Andersen et al. 2003, Thomsen et al. 2002). Begge studier viste en signifikant forøget risiko for den eksponerede gruppe. I studiet af Andersen et al (NUDATA studiet) var diagnosen imidlertid ikke sikker, idet der ikke blev foretaget NFU. I studiet af Thomsen et al. var det ikke muligt at foretage analyser af follow-up data, fordi forekomsten af KTS var for lille. Dertil kom, at eksponeringen var blandet op med manuel brevsortering. Begge studier antydede en eksponerings-respons sammenhæng men kunne ikke pege på en egentlig tærskelværdi for antal timer om ugen eller antal uger, måneder eller år med computerarbejde.
Case-referent studiet viste ingen positiv sammenhæng mellem computerarbejde og KTS. Studiet (de Krom et al. 1990) havde meget få eksponerede blandt deltagere med KTS, hvilket betød at det var svært at opnå signifikante resultater.
Det sidste studie (Stevens et al. 2001) viste, at computerbrugere ansat på en stor medicinsk afdeling, som fik diagnosticeret KTS, i højere grad end computerbrugere uden KTS brugte mus hyppigt. Artiklens forfattere konkluderede, at der ikke var nogen forskel, men foretog ingen statistiske analyser. En simpel analyse af de oplyste tal viste imidlertid, at forskellen var statistisk signifikant.

Flere af studierne viste at kønnet (kvinde) i sig selv var en risikofaktor. Ingen af studierne undersøgte om computerarbejde havde en forskellig effekt for kvinder sammenlignet med mænd. De longitudinelle studier indeholdt ikke oplysninger om computerarbejdes betydning for prognosen for KTS eller om symptomerne aftog eller forsvandt ved eksponeringsophør. Det er således ikke muligt at drage konklusioner på disse punkter ud fra et videnskabeligt grundlag.
Der fandtes 2 longitudinelle studier af repetitivt ikke kraftfuldt arbejde, hvor det ene fandt en positiv sammenhæng og det andet ingen sammenhæng. De epidemiologiske fund er således ikke entydige. Der fandtes i alt 7 studier, der undersøgte en mulig påvirket nervefunktion hos computerbrugere. Der anvendtes enten NFU eller vibrometri. En enkelt undersøgelse viste nedsat nerveledningshastighed henover karpaltunnelen hos personer med intensivt computerarbejde sammenlignet med personer, der ikke havde computerarbejde (Murata et al. 1996), men som i de øvrige 5 studier var det ikke muligt at adskille en mulig effekt af computerarbejdet fra en effekt pga. symptomer i øvre bevægeapparat. Et nyere og velgennemført studie kunne ikke vise nogen forskel i hverken vibrationssans eller nerveledning hos computerbrugere sammenlignet med sygeplejersker stort set uden computerbrug (Sandén et al. 2005). Dette fund var det samme før og efter der kontrolleredes for smertestatus. Samlet set kunne disse studier således ikke bidrage til en vurdering af den samlede evidens.
Undersøgelser af ledstillinger af fingre, håndled og underarm samt af kraftudøvelsen ved computerarbejde viste, at leddene holdes indenfor det naturlige funktionsområde og bringes ikke i yderstillinger. Håndleddet holdes typisk bagoverbøjet i en 20-30 graders vinkel og let drejet til lillefingersiden, mest udtalt ved anvendelse af tastatur. Det er den almindelige antagelse, at KTS opstår pga. forøget tryk i karpaltunnelen. Der er derfor foretaget en række undersøgelser af trykket i karpaltunnelen under forskellige forhold, herunder forskellige håndledsvinkler og ved anvendelse af forskellige grader af kraft. Ved de ledstillinger og den kraftanvendelse der anvendes ved computerarbejde øges trykket i karpaltunnelen noget, men til under det niveau hvor der eksperimentelt er vist begyndende nerveskade. Trykket i karpaltunnelen er i et enkelt studie målt under udførelsen af musearbejde (Keir et al. 1999). Ret overraskende fandt man her, at klik og træk med musen medførte en øgning af karpaltunneltrykket til over det niveau, hvor der menes at kunne opstå nerveskade. Der er således en mulig patofysiologisk mekanisme for udvikling af KTS ved computerarbejde. Dette studie er imidlertid ikke forsøgt gentaget og man har i dag ingen viden om, hvad et således let forhøjet tryk tilstede i kortere eller længere perioder kan betyde for nervefunktionen på længere sigt.

Samlet vurdering

Der er utilstrækkelig (insufficient) evidens for, at computerarbejde (mus og tastatur) forårsager KTS.

Review

Introduction

Carpal tunnel syndrome (CTS) is a compression neuropathy of the median nerve as it passes through the carpal tunnel. It is regarded as the most frequent compression neuropathy. Reported prevalences and incidences vary according to the choice of case definition and the method of nerve conduction test (NCT) used. The prevalence and incidence are higher in women than in men. This differs somewhat between studies but is approx. in the ratio of 3 to 1. Overall prevalences from 3.0-5.8% for women and 0.6-2.1% for men has been found in the general population based on both clinical symptoms and NCT (1,2). Annual CTS incidences also vary between studies. For women the peak incidence is in the age group from 50-64 years. For men the annual incidence rate gradually increases with age but levels out in the higher age groups (3,4,5). In studies where the CTS case definition was based on symptoms and NCT or performed surgery the annual incidence in women varied from 1.2 (4) to 1.5 (3) and up to 5.1 (5) cases per 1000 persons and from 0.4 (4) to 0.5 (3) up to 1.4 (5) in men. The incidence of CTS based on workers' compensation claims (calculated per 1000 full time workers, USA) was in the same level, though the peak incidences were in the lower age groups and the differences between men and women were not as pronounced (6).

This review focuses on epidemiological studies testing a causal relationship between computer work and CTS. This subject has been reviewed recently but these former reviews focused on the possible pathophysiological mechanisms with the implicit assumption that a causal relationship exists between computer work and CTS (7,8). However, this remains controversial.

The core of this review is a detailed evaluation of the existing epidemiological literature concerning computer work and CTS. However, there are similarities between computer work and repetitive, low force work. Therefore, studies on the causal relationship between repetitive work and CTS are considered too (longitudinal studies only). Though not epidemiological in design, studies of median nerve function in computer users with and without symptoms compared to others will also be reviewed. Information concerning the possible pathophysiological mechanisms leading to CTS in computer users may support the epidemiological evidence. Thus, the literature on exposure characteristics in computer work and especially the influence of force and hand/arm position on the carpal tunnel pressure (CTP) and the median nerve is reviewed in detail.

Methods

The review on the epidemiological aspects was based on a literature search in the following databases: Pubmed, Embase, Web of Science, Ergonomic Abstracts, and Arbline. The language had to be English and the article should be published in a journal with a peer-review process. Only papers with original data were considered. The search was performed in June 2005.

The text search terms were: 'carpal tunnel syndrome or CTS or median nerve and computer (approx. 100 articles) or visual display unit (approx. 5 articles) or keyboard (approx. 25 articles) or mouse' (approx. 10 articles) with number of retrieved references varying a little between databases. The search term 'computer use and ergonomic risk factors' was also used (31 articles in Pubmed). All titles and relevant abstracts were read. Reference lists in relevant articles were also searched.

The criteria for inclusion in the review of epidemiological evidence were: Cross-sectional or longitudinal studies including groups exposed to computer work (mouse or keyboard) and unexposed groups. Or case-referent studies where computer work (mouse or keyboard) was specified as an exposure. The case definition had to be CTS (for further definition, see below).

Studies using workers' compensation data were not included.
With the use of the above search terms studies of nerve conduction and vibration sense in the peripheral nerves in the arms and hands of computer users were retrieved and included. Also studies describing the arm and hand position and force level in computer work were retrieved and included in the review. Furthermore longitudinal studies of CTS and repetition with low force were identified with the search terms 'carpal tunnel syndrome and repet*' (221 articles, Pubmed only). All titles and relevant abstracts were read. Only the few studies with a prospective design and a focus on the causal relationship between repetitive work and CTS were included.
The search term 'carpal tunnel pressure' identified 253 articles (Pubmed only). All titles and relevant abstracts were read and human studies with a focus on carpal tunnel pressure (CTP) and the effect of force and position of arm, wrist and fingers were included. No cadaver studies were considered.

The CTS case definition

Clinically, the CTS diagnosis is based on a detailed interview revealing typical symptoms. An NCT is recommended but in obvious cases this may be omitted (9). The conditions for making a correct diagnosis in the epidemiological setting are different. In a working population only few will present with a fully developed syndrome. Therefore the case finding procedure must be able to detect early and less pronounced CTS cases without confusing the condition with other disorders. Information about symptoms may be obtained from questionnaires or interviews. Though highly sensitive questionnaire symptoms are not very specific and often cover several other conditions (10). Therefore questionnaire symptoms need to be confirmed by qualitative interviews. Only a smaller proportion of persons with interview confirmed CTS symptoms show NCT changes consistent with CTS (11). Thus, the optimal case definition requires a combination of interview based symptoms and a NCT consistent with CTS. NCT alone cannot be regarded as a gold standard. Dependent on the method used it produces varying numbers of false positive and negative tests. Some of the tests used in epidemiological studies produce 20% or more positive tests among asymptomatic persons (2,12). If a high false positive rate is combined with imprecise symptom information then differential misclassification may occur and the estimate of association between exposure and CTS may be biased. This is not unlikely since symptom reporting may very well be influenced by the level of exposure. On the other hand, a high false negative rate will influence the exposed *and* the controls equally and make an association weaker, if there is one, but the estimate will not be biased. Tinel's and Phalens tests on their own have too low sensitivity and specificity to discriminate CTS cases from persons with other disorders (13,14,15,16).
The positive predictive value (PPV), i.e. the probability that the person has CTS if the "test" is positive, has been established for different combinations of symptoms and clinical tests with NCT used as the gold standard (17). In the calculations a rather high CTS prevalence of 10% was assumed. The PPV of having CTS was 0.44 when CTS symptoms were present in at least 2 of the fingers innervated by the median nerve, the physical examination was positive (Tinel's, Phalen's, two point discrimination or carpal compression test) and night symptoms were present. The PPV was reduced to 0.31 if night symptoms were left out and to 0.25 without the physical examination.
In this review epidemiological studies using a case definition including symptoms (both questionnaire and interview) in combination with NCT or symptoms alone but confirmed by interview are discussed in detail. However, studies with a case definition based on questionnaire symptoms only, NCT only or Tinel's or Phalen's test only are also mentioned.

Exposure assessment in computer work

As in other epidemiological studies on ergonomic exposure there are different methods of obtaining exposure information. Especially in cross sectional studies information based on questionnaire self-report introduces a significant risk of information bias because symptom level may influence evaluation of exposure and vice versa. This may be solved in a longitudinal design but only partly because the participant may still be influenced, e.g. by responses given at baseline. In order to establish a causal relationship between computer work and CTS you need information on the duration and the intensity of both keyboard and mouse work. Many kinds of computer work involve pauses to some extent because of other tasks or reflections of what is happening on the screen. Intensive computer work has not been clearly defined but involves work where either keyboard or mouse is used with few interruptions, e.g. in graphical work or data entering of figures from lists. In all the epidemiological studies on computer work cited in this review the analyses were based on self report of exposure duration. In one of the studies, the intensity of exposure was objectively characterised but this information was not used in the statistical analyses (18). In the NUDATA study (Neck and Upper extremity Disorders Among Technical Assistants) (19) very detailed exposure information was obtained objectively by a computer programme installed in the participant's computer but this has not been included in any published analyses of causality yet (personal communication, Sigurd Mikkelsen, Dr. Med. Sci.).

Results

Pathophysiological mechanisms

In order to understand and explain the possible pathophysiological mechanisms in the development of CTS associated with computer work information about actual position of arm and hand and exertion of force during computer work is important. It is generally assumed that the dominating pathophysiological mechanism in the development of CTS because of biomechanical factors is increased pressure in the carpal tunnel leading to nerve damage because of impaired circulation (20). This is also the rationale behind the surgical treatment. Therefore, in addition to epidemiological evidence an important question to be answered would be: is it possible that the biomechanical load in computer work affects the median nerve in a harmful way?

Wrist position and exertion of force in computer work

Both wrist position and exerted force in computer work has been measured. In the study of Keir (21), wrist extension ranged from 23° to 30° and ulnar deviation from -3.2° to 5.2° during mouse work. Keyboard work seemed to involve more ulnar deviation. In a study of data entry work goniometer measurements showed wrist extension of 14° and 20° at the 50^{th} and 90^{th} percentile, respectively (11). In another study of keyboard work, mean ulnar deviation using a conventional keyboard was 18.9° (SD 6.8) (22).

The finger tip force exerted in keying varied between less than 1 N up to 7 N but in most studies between 1-4 N (23,24,25). One study measured both the finger tip force and the tendon force simultaneously when pressing a keyboard key during open surgery (26). The mean force applied to the tendon was 7.2 N (SD 1.4 N). Johnson et al measured the force exerted on the computer mouse bottom. All values were below 1 N corresponding to 0.4-1.5 % of MVC (27).

Carpal tunnel pressure

Several studies have measured the carpal tunnel pressure (CTP) under different conditions (21,28,29,30,31,32,33,34,35). The normal resting CTP with the wrist in neutral position varies between 3-13 mmHg (results

from 7 studies summarized in (30) and (32)). CTP in CTS patients varies between 10-43 mmHg (32) though higher values have been found (31). In an often cited study by Lundborg et al (28), CTP was increased experimentally in 16 human volunteers. At 60 and 90 mmHg the sensory and subsequently the motor response was blocked within an hour whereas a CTP of 30 mmHg had minor and varying effects but produced "pins and needles" in 2 of 4 subjects. This was further studied by Gelberman et al. who found some functional loss at 40 mmHg and complete motor and sensory block at 50 mmHg in healthy subjects (29).
Several studies have measured the CTP profile associated with different wrist angles, finger flexion and forearm position (21,32,33,35). The studies show that CTP is dependent on the position of the forearm, wrist and metacarpophalangeal joint (MCP). Thus, supination showed higher values than pronation and MCP flexion increased the pressure (21,32,35). With wrist movements between 40° flexion and 40° extension and varying angles of MCP the CTP did not exceed 20 mmHg. Ulnar and radial deviation did not alter the CTP much (33).
CTP has been studied while performing actual work tasks. Rempel et al. measured CTP in 19 healthy subjects (30). CTP increased from 8 (SD 6) mmHg in rest to 18 (SD 13) mmHg after lifting half kilo cans for 5 minutes, 20 cans per minute. Mean recovery time for CTP was 14 (SD 15) sec. The effect on CTP of different levels of exerted force was studied in 20 healthy subjects by Keir et al. (34). With the finger tip exerting 0, 5, 10, and 15 N the CTP increased to 7.8, 14.1, 20.0, and 33.8 mmHg, respectively. The same research group conducted a study on the effect of computer tasks. In 14 healthy subjects the mean CTP rose from 5.3 mmHg in rest to 16.8-18.7 mmHg (varying between different kinds of computer mice) with the hand static on the computer mouse and to 28.8-33.1 mmHg when dragging or pointing and clicking with the mouse (21). This was the only study found on computer work and CTP.

Epidemiological studies

Computer work and carpal tunnel syndrome

Five epidemiological studies were found with a focus on the causal relationship between computer work and CTS fulfilling the outcome criteria (11,18,19,36,37,38,39). Three of these studies were prospective in design (11,18,19,38), one was a case-referent study (37,39) and one was cross-sectional but with a case-referent approach (36). The studies are listed in Table 1 with information on design, population, gender, response rate, type of computer work, control group, CTS case definition and prevalence, confounders controlled for, results and comments. In the extensive prospective study of computer users by Gerr et al. the prevalence of CTS was too low to allow any analyses of causality (40). The CTS prevalence was 0.5% (3 cases) and the annual incidence 0.9% (3 cases). Thus, this study is not further considered.
In the study of Andersen et al., 6943 technical assistants and machine technicians were studied at baseline and after 1 year of follow up, the NUDATA study (19). The CTS case definition was based on information obtained by questionnaire interviews. No NCT was performed. Three case definitions were used: 1. tingling/numbness at least once a week the last 3 months (questionnaire) or 2. the same but confined to the distribution area of the median nerve and confirmed by clinical interview (performed by physicians) or 3. as the second definition but including tingling, numbness or pain *at night*. At follow-up only the second definition was used. Mouse and keyboard use were self-reported in a questionnaire as hours per week (h/w). The study showed an increasing risk for case definition 2 with odds ratios from 2.3 (95% CI 1.2-4.5) when using the mouse 5-9 hours per week (h/w) increasing to 3.6 (95% CI 1.8-7.1) with mouse use 20-24 h/w. There was no

further increase of risk with increasing hours above 24 h/w. Almost the same pattern was seen for case definition 1 but clearly different from definition 3 which showed only borderline significance at 30+ hours and a very irregular pattern with no significant findings for hours below 30. 77 fulfilled the third case definition. As results were presented for 5-hour groups, the number of cases in each group was quite small. This may explain the insignificant results but cannot explain the non-existing exposure-response pattern. In the follow-up analyses the exposure-response pattern was clearer (case definition 2) and a significantly increased risk was found when working more than 20 h/w with the mouse. In contrast to the findings for mouse use the results for hours working with the keyboard showed no significantly elevated risks whatsoever and no signs of an exposure-response relationship.

As a substudy of the Danish PRIM study (Project on Intervention and Research in Monotonous work), a study on CTS was carried out by Thomsen et al. (11). 731 participants from 3 companies, a bank and 2 postal centres, were included. The study population was divided into 4 exposure groups, 389 with repetitive work (data entry, manual letter sorting), 73 with forceful work (lifting boxes), 28 with forceful and repetitive work (sorting bundles and parcels) and 219 with varied work (office work). In 22 participants the exposure could not be characterised. Data entry was the main repetitive task comprising 25% of the total work hours and 59% of the work hours in the repetitive group. Keying speed was 214 strokes pr. minute. Goniometer measurements of wrist movements showed that this work task was highly repetitive with mean power frequency (MPF) = 0.68 Hz (SD 0.13), 2.2% time with pauses (SD 1.0) and wrist extension 39° and 17° at the 10^{th} and 90^{th} percentile, respectively. The same figures for the non-repetitive tasks were MPF=0.23-0.32 Hz, pauses 3.7-21.5%, wrist extension 34°-38° (10^{th}) and 6°-19° (90^{th}). CTS cases were identified by clinical interviews performed by a physician of participants reporting tingling in the median area at least once a week in the last 3 months in a questionnaire. NCT confirmed the CTS diagnosis. The overall prevalence of CTS was 1.1% (8 cases) on the working hand and 0.3% (2 cases) on the other. The risk of CTS was significantly increased for repetitive work with OR=1.86 (95% CI 1.06-3.19) for every 10 hours of repetitive work adjusted for forceful work and personal characteristics. Of the 8 working hand cases, 4 cases had data entry work more than 15 h/w, 2 cases had letter sorting >15 h/w, 1 case sorted bundles or parcels and 1 case lifted boxes. In all, 207 had data entry work more than 15 h/w, 104 had manual letter sorting >15 h/w, 28 sorted bundles or parcels and 73 lifted boxes. Thus the prevalence of CTS was equal in the data entry group and the letter sorting group (the data on the distribution of cases on job function were not available in the paper but are the author's comments). There were not enough cases in the data entry group to perform analyses. The annual incidence for CTS was 0.62% (4 cases) and thus no further analyses of incidence data could be made.

Nathan et al. has followed a cohort established in 1984 for 11 years (38,41). Originally, the cohort consisted of 471 participants from 4 industries representing a wide variety of hand activities collapsed into 5 groups based on on-site evaluations. One group consisted of keyboard operators with more than 4 hours of keying (n=22), the four other groups had work tasks with different levels of resistance and repetition though the classification was not obvious. The case definition at baseline was based on NCT alone. The NCT used produced very high prevalences. Thus, 28 % of the participants in the unexposed group had a positive NCT. The case definition at follow-up was based on both questionnaire symptoms and NCT. It was not stated if the at-risk population had normal NCT at baseline. Exposure data from 1984 was used. Changes in job exposure were

not considered. In 1994-95 256 participants were left in the cohort. The number of keyboard operators was not mentioned. In multivariate analyses adjusting for various potential baseline confounders, neither an effect of keyboard work nor of repetitive work was found.
In a cross sectional study by Stevens et al., or rather a mixture of a cross sectional and a case-referent study, all participants were identified as "frequent computer users" working in a medical facility (36). 256 employees participated and were divided into two groups, one group with CTS and the other without. CTS was defined as relevant symptoms in the median area reported in a questionnaire and confirmed in a clinical interview. 27 CTS cases and 222 without CTS symptoms were identified. Different characteristics were compared between the two groups but without any statistical testing. Hours of daily keyboard use and years with keyboard did not differ. However, as hours with keyboard use were more or less the same for all participants (mean 6.6 h/d, SD 1.7) then one would not expect to find differences for this variable. Mouse use was divided into no use, occasional and frequent use. Frequent mouse use was more prevalent in the CTS group (48.1% vs. 27.9%). This was not tested statistically and not further discussed. However, if the reported figures are tested with a Mantel-Haenszel chi-square test (1 df) the difference is significant (p=0.04). Participants with CTS symptoms went through an NCT. Nine (3.5%) had positive findings. The authors compared the CTS prevalence to other population based studies and concluded that it was the same as in the general population.
In another study with a case-referent approach by de Krom et al., CTS cases (n=156) were identified from a population based survey and added to cases included prospectively from an outpatient department of neurology (37). The diagnosis of CTS included relevant questionnaire symptoms confirmed by interview and a positive NCT. Referents were persons without CTS symptoms from the population based survey (n=473). Care was taken to keep the purpose of the study blinded to the participants in order to avoid information bias. Exposure information was obtained by interview. One question considered hours pr week of typing the last 5 years. It was not specified if the exposure preceded debut of symptoms. Only 7 CTS cases reported typing 1-19 hours weekly and 5 persons 20 hours or more. The relative risks were all below 1 and insignificant.
The study of Palmer et al. is not included in the table as the case definition was weak and did not include neither objective measures nor interview (42). The study is worth noting, though, because of the setting. It was a population based study including 4889 respondents (RR 58%) with main focus on hand-arm vibration and not computer work. Thus potential bias caused by subjects' health beliefs was minimized. There was one questionnaire item concerning keyboard use more than 4 hours per day. No excess risk for self reported tingling/numbness was found (PR=1.1, 95% CI 0.8-1.3), adjusted for age, smoking, headaches and tiredness/stress.
In the case-referent study by English et al. CTS cases were recruited from orthopaedic clinics (39). It is difficult to conclude from this study because no information about CTS case definition was provided and therefore the study is not included in the table. Furthermore, the exposure was defined as "finger tapping". This term may include keyboard work but this was not specified. A negative association between finger tapping and CTS was found.

Repetitive work and carpal tunnel syndrome
Four studies with a longitudinal approach focusing on the causal relationship between repetitive, low force work and CTS were found (43,44,45,46). In the study by Leclerc et al. (46) she used a positive Tinel's or Phalen's test as the only diagnostic item and that is insufficient according to known sensitivity and specificity of these clinical

signs (13,14,15,16). Thus the findings could not be interpreted in relation to CTS. Two of the four studies were based on the same population (43,44). These two studies by Werner et al. are follow-ups from a cohort of over 700 active workers. Based on NCT, 49 asymptomatic participants with an abnormal NCT and 59 with a normal NCT were followed for 17 and 70 months. Work tasks were video-filmed and categorised according to repetition rate on a scale from 1-10. The incidence of developing CTS symptoms was equal in the two groups after 17 months but significantly higher after 70 months in the group with positive NCT. Repetitive work was a risk factor for developing symptoms after 17 months (OR 1.35, 95% CI 1.03-1.77) and after 70 months (risk estimate not shown). In a well designed follow-up study by Gell et al. no association between level of repetitive hand tasks and development of CTS was found (45). The case definition included both symptoms as well as NCT. Each job was assessed and rated for ergonomic exposures. Of the original 985 subjects in the cohort, 51% were re-examined 5.4 years after baseline. There was a trend towards an association between a combination of force and repetition and developing CTS but insignificant.

One additional follow-up study was found but in this study of meatpackers it was not possible to separate the effects of force and repetition (47).

Studies of nerve involvement in computer work

Seven studies comparing median nerve function in computer users with groups without computer use were found (48,49,50,51,52,53,54). Two of the studies tested conduction velocity (52,54) whereas the other studies tested vibration sense. Vibration sense, however, is not a good indicator of CTS (55). The studies were not epidemiological in design as the selection of participants was not described and selection bias may be present.

The study of Murata et al. (52) used nerve conduction tests in two groups. One group consisted of 27 female employees in a life insurance company with 6 hours or more of data entry. The control group consisted of 24 female students. Significant differences in sensory conduction velocities (SCV) were found for measurements across the carpal tunnel whereas values proximal and distal to the tunnel did not differ. The two groups differed in symptom profile. Out of 11 symptoms the computer group reported an average of 2.8 symptoms and the control group 0.2 symptoms. The groups were comparable on the other reported characteristics (age, skin temperature, alcohol consumption, other disorders) though BMI was not reported.

The findings were in contrast to a recent study by Sandén et al. (54). Here, 82 secretaries with a median of 6 hours of daily computer work were compared to 35 nurses with very limited computer work. No differences were found between the two groups in the median nerve conduction or in the vibration threshold in t-test analyses. Furthermore, no differences were found when analyses were adjusted for pain for more than 3 months, pain during testing, age, body height, hours of duty, hours using computer and experienced intensity at work. The vibration threshold was tested before and after 4 hours of computer work and no significant differences were observed.

In the study by Doezie et al. transcriptionists with symptoms were compared to healthy controls (50). Vibration thresholds were significantly elevated in both the second and fifth finger but only for the high frequencies (125-500 Hz). Very little information about the control group was shown.

Greening et al. conducted two studies with more or less the same approach. In the study from 1998 she compared vibration sense in 29 office workers with symptoms in upper limbs and spine, 17 patients with “RSI” (repetitive strain injury) recruited from physiotherapy

practises and a control group of 27 students and teaching staff (48,49). Significantly elevated thresholds in the median area were found for both the office and the patient group compared to the control group but equally elevated in the patient group and in the office group. The authors conclude that “RSI patients have objective signs of polyneuropathy and clear changes are apparent in intensive computer use”. The study did not include a group with intensive computer use and no symptoms nor a group with symptoms and no computer use. Thus it is difficult to interpret the study findings any further than it seems that persons with upper limb disorders have higher vibration thresholds in the median area than healthy persons. In the other study by Greening, 3 groups were selected in the same way except that the office workers did not have symptoms. Again the patient group had elevated thresholds in the median and ulnar area compared to the control group (49).
A Danish study used almost the same set-up and found similar results (53). Again the patient group had significantly elevated thresholds in part of the median area and in the ulnar area compared to the asymptomatic groups. The authors concluded that persons with symptoms related to computer use had signs of nerve involvement. However, the study was not designed to show if the symptoms in the computer group was caused by the computer work.
Another Danish study used the framework of the NUDATA study to select 20 subjects with unilateral tingling and 20 asymptomatic subjects (51). The two groups had equal amounts of computer work. Vibration thresholds were increased in the symptom group for all measurements (28 comparisons) but only significantly in 2. It was concluded that tingling was not associated with impaired vibration sense. The design of the study did not allow any conclusions concerning the effect of computer use on nerve function.

Discussion

The epidemiological evidence

The epidemiological evidence of an association between computer use and CTS is inconsistent. All 5 studies identified in this review that examined the association between computer work and CTS had important limitations. Thus, a definitive study that establishes the relationship between computer use and CTS has not been conducted yet. Such a study should involve a large population with varying degrees of computer work, at least one year of follow-up, a careful exposure description and a precise CTS diagnostic procedure. A sample size of approx. 5000 participants would be needed in order to show a doubling of the risk of CTS if it is assumed that the prevalence in computer users is 2% and 1% in unexposed and approx. 30 CTS cases were needed in exposed and unexposed groups (60 cases total). Such a study would be very resourceful to carry out. Based on the studies with a CTS case definition including symptoms confirmed by interview or NCT it may be concluded that CTS is not a common disorder in computer workers with prevalences of approximately 1% though the study of Stevens et al. showed higher figures (18,19,36,40).
Based on evaluation of study design, the size of the populations and response rates, the diagnostic procedure and the exposure information the studies by Andersen et al. and Thomsen et al. were the most extensive. In both studies very intense computer work was represented (data entry, graphical work) (11,18,19). The NUDATA study found an exposure-response relationship for mouse use and CTS symptoms in the median nerve distribution area both in the cross sectional and in the follow-up analyses. The risk was gradually increased with significant findings above 20 h/w with the risk almost tripled compared to the control group. The same risk level was found in the study by Thomsen et al. None of the studies could identify a threshold limit for the use of computer.

Both studies had draw backs. The study of technical assistants was carried out at a time of intense debate on the mouse issue in Denmark (19). This may have influenced the results and thus explain why only associations with mouse and not keyboard use was found. Information bias caused by beliefs about certain associations may have very strong effects. This was shown in a study of indoor climate symptoms where reporting turned out to be dependent on the information given to the participants about the purpose of the study (56). The lack of an association could also be explained by a poor distribution of keyboard work in the population though based on self-report of keyboard use this did not seem to be the matter. However, both keyboard and mouse use was also recorded by an installed computer programme in approx. one third of the participants' computers. This was reported in another paper from the same study (57). Mean keyboard use registered by this software was 1.2 h/w (SD 1.0) whereas mean self-reported keyboard use was 8.5 h/w (SD 5.8). Registered mouse use was 6.2 h/w (SD 3.6) vs. 16.3 h/w (SD 9.3) self-reported. Therefore, it would not be possible to show an increased risk of CTS symptoms associated with keyboard use because the participants were hardly exposed. Another draw back of the NUDATA study was the lack of NCT in the diagnostic procedure. It has been shown that using this diagnostic procedure only around 25% of participants with clinically verified symptoms had a positive NCT (11). This may be even lower because the reported PPV of the case definition used was 0.25 assuming a 10% prevalence (17). The actual prevalence was much lower. Thus, the results show an association between computer work and subjective and unspecific hand symptoms more than an association with CTS. Also disturbing was the fact that a priori one would have expected that the most specific CTS case definition (including nightly symptoms) would result in the strongest associations but this was not the case.

The study by Thomsen et al. had a good CTS case definition and a good exposure description but the population was too small. The risk estimate of 1.8 was based on 8 cases only and no CTS cases in the control group. Furthermore, the interpretation was complicated by the fact that the data entry exposure was mixed with the exposure from manual letter sorting though data entry was the most frequent (11).

The study by Stevens et al. of computer users in a medical facility actually had significant positive findings on mouse use though the authors concluded otherwise (36). However, the significant finding was based on a crude analysis without adjustment for other factors, e.g. age.

The case referent study by de Krom was inconclusive. The number of exposed CTS cases in the study was very low and thus made it difficult to reach statistical significance (37). However, no pattern in the risk estimates was seen and all estimates were below 1. One of the strengths of the study was that the participants were blinded to the purpose of the study. The study by Nathan et al. had too many unclear aspects and possible bias to contribute to the overall conclusion.

Repetitive work and CTS

Computer work may be characterised as repetitive work with the use of low force. Most industrial work, however, involves more exertion of force than it is described in computer work. Two longitudinal studies were found with detailed exposure evaluation and a good diagnostic approach (43,44,45). The studies by Werner found a positive association whereas no association could be found in the other study. Thus no further evidence was added.

Peripheral nerve function

It would be further supporting evidence for an association if early signs of neurological changes could be demonstrated in computer users. The study by Murata et al. actually described an impairment of nerve conduction across the carpal tunnel but not proximally or distally in computer users with intense computer work compared to a control group (52). The interpretation of this finding, however, is influenced by the fact that the computer users also had many symptoms in the upper limbs. As in the studies of elevated vibration thresholds it is not possible to separate the effect of musculoskeletal symptoms from an effect of computer work. In a more recent and well conducted study no differences in nerve conduction and vibration thresholds were observed in computer users compared to nurses with very limited computer use (54). The results were not changed when the analyses were controlled for pain status. Thus, these studies of the median nerve did not add support to a possible effect.

Pathofysiological mechanisms

The dominating pathophysiological mechanism in the development of CTS is assumed to be increased pressure in the carpal canal. It has been shown that CTP maintained for hours at 30-40 mmHg may have an acute adverse effect on the median nerve (28,29). During mouse and keyboard work the wrist is held in 20°-30°extension and slightly ulnarly deviated. The ulnar deviation seems to be a little more pronounced in keying than when handling the mouse (11,21,22). Computer work involves very little force. The force applied when keying or clicking the mouse button is approx. 1-4 N or less than 1% of the MVC (23,24,25,27). Experiments on the effect of positions of fingers, wrist and forearm comparable to the positions common in computer use have shown that CTP increases but not to potentially harmful levels (32,33,35). Likewise, CTP measurements during experimentally induced force levels up to 10 N did not increase values beyond 20 mmHg (34). Surprisingly, mean CTP levels during actual mouse use increased to values between 28-33 mmHg when dragging or clicking with the mouse. Lower values were found with the hand static on the mouse (21). Although the experiment has never been repeated the findings indicate a possible pathophysiological mechanism. Nothing, however, is known about the long term effect of repeatedly increased pressures at this level.

Other findings

None of the identified studies addressed any possible effect of computer work on the prognosis of CTS. Thus, conclusions based on scientific evidence concerning this cannot be drawn.

Female gender was a risk factor in two of the studies (19,38). This has also been shown in other studies and also in case series (3,58,59). However, none of the studies reviewed here tested for a possible interaction between gender and computer work. Thus, no conclusions can be drawn on this point. Other non-occupational factors are known risk factors for CTS. Age, fractures of the wrist, certain medical diseases, hormonal factors, hand dominance and obesity are the best documented factors (60,61,62,63,64,65,66). These factors were included to some extent in the studies cited but not consequently. There is, however, no reason to believe that these factors should be more or less prevalent in computer users than in others.

Conclusion

The evidence of an association between computer work and CTS is inconsistent. All the 5 studies identified had limitations in either exposure, outcome, power or serious bias that made conclusions difficult. In two of the studies an exposure-response association was indicated but because of possible misclassification in exposure and outcome no firm conclusions can be drawn. Furthermore, no conclusions could be drawn concerning the effect of the duration of computer work in weeks, months or years because no data were available. The prevalence of CTS among computer users based on symptoms and NCT was approx. 1 %.

Results from studies on other kinds of repetitive, low force work and CTS did not add evidence to an association.
The main pathophysiological mechanism in the development of CTS is assumed to be increased pressure in the carpal tunnel. Mouse and keyboard work was characterised by neutral wrist positions (30° flexion-30° extension and a slight ulnar deviation) and the exertion of very low force. Measurements of CTP under these conditions showed pressure values that seemed to be below potential harmful levels. However, during actual mouse use one study showed an increase of CTP to levels where possible neurological changes were seen experimentally. These tests have not been repeated in other studies and nothing is known about the effects of prolonged or repeatedly increased pressures at this level.

Overall evaluation

There is insufficient evidence that computer work (mouse and keyboard) causes CTS.

Table 1 Epidemiological studies on carpal tunnel syndrome and use of computer mouse and keyboard. Only studies with symptoms confirmed with either nerve conduction test (NCT) or clinical interviews are included. The studies are listed chronologically according to publication year. RR=response rate, CI=confidence intervals, OR=odds ratio, BMI=body mass index.

Study	**Design, population, response rate (percent females)**	**Control group (percent females)**	**Exposure measure**	**Case definition and prevalences**	**Confounder control**	**Results**	**Strengths Weaknesses**
Andersen et al (19)	1 year follow-up study. 6943 technical assistants and machine technicians. RR at baseline 73%, follow-up 60% of baseline eligible. (62% females). Mouse and keyboard use in 5 h. exposure groups with an even distribution.	1279 participants with mouse use <2.5 hours pr. week. 532 participants with keyboard use <2.5 hours pr. week. (Percent females not shown).	Self reported hours pr week with use of mouse and keyboard	3 case definitions: 1. Tingling, numbness at least weekly in questionnaire (10.9%). 2. Def. 1 but defined to median nerve area and confirmed in interview (4.8%). 3. As def. 2 including symptoms at night (1.4%).[1] Follow-up: As def. 2. Questionnaire symptoms confirmed with interview (5.5%)[2]	Personal characteristics (11 variables), psychosocial factors (4 variables), physical work characteristics (7 variables)	Exposure groups entered as categorical variables. Baseline, mouse use: Exposure-response pattern in def. 1. and 2. Def. 3 only significant >30h/w. Keyboard use: No significant findings. Follow-up, mouse use: Significant risks and exposure-response pattern above 20 h/w. Keyboard: No significant findings.	Separate risk estimates for mouse and keyboard time presented. Indication of information bias because of the different results for mouse and keyboard use. No NCT performed.
Thomsen et al (11)	1.5 years follow-up study. 731 participants (74% females). 3 companies. RR at baseline 68-74%, at first follow-up 63% and second 50% of baseline. Mixed exposure: 1. Repetitive work tasks: Data entry (59%), letter sorting (31%), other e.g. sorting (10%) n=389 (83% females). 2. Forceful work tasks n=73 (18% females) 3. Forceful and repetitive n=28 (7% females)	Varied office work with occasional word processing, repairmen, drivers, n=219. (87% females)	Identification of job tasks by company walk through. Self reported hours per week with job tasks. Repetition and position determined with goniometer measurements.	Tingling at least once a week in the median nerve area combined with abnormal NCT. Questionnaire symptoms confirmed with interview. Prevalence 1.1% on working hand, 0.3% on the other. Annual incidence 0.62% and 0.44%, respectively.	Age, gender, seniority, BMI, forceful work	Baseline: Increased risk of CTS with OR=1.86 (95% CI 1.06-3.19) for every 10 hour increase in repetitive work Follow-up: Too few CTS cases to perform analyses. No exposure differences in cases based on questionnaires and interviews only.	Risk estimate controlled for forceful work. Diagnosis included physician interviews and NCT. Exposure characterised by objective measures. Few cases. Follow-up analyses not possible. Mixed repetitive exposure though data entry was dominant.

Nathan et al. (41,38)	11-year follow-up study. 471 participants at baseline (RR and % females not reported), 256 (54%) left at follow-up (43% females). 5 groups: 1. Very light resistance, low repetition. 2. light resistance, very high repetition (keyboard operators). 3. moderate resistance, moderate repetition 4. heavy resistance, moderate repetition. 5. very heavy, high repetition.	Group 1 (administrative, clerical work) (Percent females not shown)	Subjective evaluation of resistance and by observation. Many job functions collapsed into 27 occupations and further grouped according to level of resistance and repetition in 5 groups.	At baseline: Abnormal NCT alone. Prevalence 39%. At follow-up: Abnormal NCT and CTS symptoms or reported CTS surgery. Annual incidence 1.2%.	Baseline: Age. Follow-up: Baseline hormonal medication, endocrine disorders, menopausal status, physical activities in spare time, BMI, smoking habits.	<u>Baseline</u>: Group 2 had the lowest prevalence of positive tests (27%). Group 5 significantly higher prevalence of positive tests compared to group 1, 61% vs. 28% (p<0.001). <u>Follow-up</u>: Keyboard use OR 0.88 (95% CI 0.52-1.47). No significant work place factors except vibrations.	Only 22 keyboard operators at baseline. Baseline work tasks used with no information about job changes in follow-up period. Exposure classification unclear. Case definition at baseline based on NCT with high rate of false positive tests, no symptom reporting. Unclear if the at-risk population included baseline cases in the follow-up analyses
Stevens et al (36)	A case-referent study within a cross sectional design. 256 employees, RR 82% (97% females) at a medical facility identified as frequent computer users. Divided into a CTS group (n=27) and a group without CTS symptoms (n=222).	Participants without CTS symptoms. (97% females)	Self reported h/d of keyboard use. Years of keyboard use. No, occasional or frequent mouse use	Questionnaire symptoms combined with clinical interview confirming symptoms in median area. Prevalence 10.5%.	No adjustment.	Comparisons between CTS group and non-CTS group: <u>Mean h/d at keyboard</u> 6.6 (SD 1.7) and 6.4 (SD 2.0), respectively. <u>Mean years using keyboard</u> 8.7 (SD 5.5) and 8.8 (SD 4.8), respectively. <u>Frequent mouse use</u> 48.1% and 27.9%, respectively (p=0.04).	No statistical testing. The exposure gradient for keyboard use was small. The study actually finds a difference in mouse use but concludes that there were no differences. The difference is statistically significant if the reported figures are tested in a chisquare test. No NCT performed.
de Krom et al (37)	Case-referent study. 156 cases, 28 recruited from population, 128 consecutively from clinic RR=70% (84% females)	473 controls from general population (RR=71%, 66% females)	Weekly hours of typing in 4 groups (0, 1-7, 8-19, 20-40). Information obtained by interview.	Symptoms and abnormal NCT. Questionnaire symptoms confirmed by clinical interview. Prevalence in population sample 5.6%.	Gender, age and the interaction term gender*age. Others included in some of the analyses but not clear.	Relative risk below 1 for all groups and no pattern .	The study was presented as a general health study, thus participants were not informed about the main focus. Exposure was not related to symptom debut. Few "typing" cases (n=12)

[1] Overall prevalence in parentheses [2] One-year incidence

Abbreviations

BMI	Body mass index
CTP	Carpal tunnel pressure
CTS	Carpal tunnel syndrome
MCP	Metacarpophalangeal
N	Newton
NCT	Nerve conduction test
OR	Odds ratio
PPV	Positive predictive value
RR	Response rate
RSI	Repetitive strain injury
SD	Standard deviation
Sec	Seconds

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Appendix 1.

The Scientific Committee of the Danish Society of Occupational and Environmental Medicine.

Degree of evidence of a causal association

The following categories are used.

+++	sufficient evidence of a causal association
++	limited evidence, grade A
+	limited evidence, grade B
0	insufficient evidence of a causal association
-	evidence suggesting lack of a causal association

Description of categories:

Sufficient evidence (+++):

A causal relationship is very likely between an exposure to a specific risk factor and a specific outcome.
A positive relationship has been observed between exposure to the risk factor and the outcome in several studies in which chance, bias, and confounding could be ruled out with reasonable confidence.

Limited evidence, grade A (++):

Some convincing epidemiological evidence exists for a causal relationship between an exposure to a specific risk factor and a specific outcome.
A positive relationship has been observed between exposure to the risk factor and the outcome in several studies in which chance, bias, and confounding are not the likely explanation.

Limited evidence, grade B (+):

Some convincing epidemiological evidence exists for a causal relationship between an exposure to a specific risk factor and a specific outcome.
A positive relationship has been observed between exposure to the risk factor and the outcome, but it is not unlikely that this relationship could be explained by chance, bias, or confounding.

Insufficient evidence of a causal association (0):

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association.

Evidence suggesting lack of a causal association (-):

Several studies of sufficient quality, consistency and statistical power indicate that the specific risk factor is not causally related to the specific outcome.