Enabling meta-analysis in systematic reviews on carpal tunnel syndrome

Gerritsen, A.A.M.; de Vet, H.C.W.; Scholten, R.J.P.M.; van Tulder, M.W.; Bouter, L.M.

published in
Journal of Hand Surgery (American Volume)
2002

DOI (link to publisher)
10.1053/jhsu.2002.35074

document version
Publisher's PDF, also known as Version of record

Enabling Meta-Analysis in Systematic Reviews on Carpal Tunnel Syndrome

Annette A.M. Gerritsen, PhD, Henrica C.W. de Vet, PhD, Rob J.P.M. Scholten, MD, PhD, Maurits W. van Tulder, PhD, Lex M. Bouter, PhD, *Amsterdam, The Netherlands*

Possible solutions to the problems of clinical heterogeneity of outcome measures and inadequate reporting of results for randomized controlled trials (RCTs) on carpal tunnel syndrome (CTS) are presented. Meta-analysis was impeded by these problems in 2 systematic reviews concerning conservative and surgical treatment options for CTS. A solution to the problem of inadequate data presentation is to add explicit information on minimal requirements with regard to data presentation to guidelines for the reporting of studies. To resolve the problem of clinical heterogeneity of the outcomes there should be consensus on the (validated) outcomes that should be used in RCTs. For CTS there is little evidence available on the reliability, validity, and responsiveness to change of the commonly used outcomes in RCTs. Resolving both problems will increase the comparability of RCTs, enabling the calculation of a pooled estimate of effect in a meta-analysis. (J Hand Surg 2002;27A:828–832. Copyright © 2002 by the American Society for Surgery of the Hand.)

Key words: Carpal tunnel syndrome, review, randomized controlled trial, data reporting, outcome measures.

Systematic reviews of high-quality, randomized controlled trials (RCTs) are considered to be the highest level of evidence in research concerning medical interventions.[1] To quantify the effect of the various treatment options, preferably a meta-analysis is performed. By combining individual study results a precise estimate of the magnitude of the treatment effect can be obtained. Meta-analysis is, therefore, an important part of a systematic review. Meta-analysis is only feasible if RCTs are clinically homogeneous, that is, if the patients, interventions, comparisons, outcomes, and timing of follow-up measurements are sufficiently similar.[2] Randomized controlled trials, however, may use a range of different outcome measures.[3,4] Another prerequisite for combining study results is adequate and uniform data presentation. Reporting of results in biomedical journals is often inadequate.[5,6]

This article presents possible solutions to the problems of clinical heterogeneity of the outcome measures and inadequate reporting of results for RCTs on carpal tunnel syndrome (CTS). First we show, however, that meta-analysis was impeded by these problems in 2 systematic reviews concerning conservative and surgical treatment options for CTS.[7,8]

From the Institute for Research in Extramural Medicine, and the Department of Clinical Epidemiology and Biostatistics, Vrije Universiteit Medical Centre; and the Dutch Cochrane Centre/Department of Clinical Epidemiology and Biostatistics, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands.

Received for publication November 12, 2001; accepted in revised form May 7, 2002.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

Supported by the Health Care Insurance Council of the Netherlands.

Reprints requests: Annette A.M. Gerritsen, PhD, Institute for Research in Extramural Medicine, Vrije Universiteit Medical Centre, Van der Boechorststraat 7, 1081 BT Amsterdam, The Netherlands.

0363-5023/02/27A05-0010$35.00/0
doi:10.1053/jhsu.2002.35074

Systematic Reviews

Methods

To identify publications, a search was performed with Medline (January 1966–March 2000), Embase

(January 1988–February 2000), and the Cochrane Controlled Trials Register (2000, issue 1), together with reference checking. A generic search for RCTs[9] was combined with a specific search for CTS (by using the key words carpal tunnel syndrome, carpal tunnel, carpal syndrome, and tunnel syndrome). To be included, a study had to meet the following criteria: (1) the study population consisted of patients with CTS; (2) the efficacy of one or more conservative treatment options was evaluated or different surgical techniques were compared; (3) the study was designed as an RCT; and (4) the results were published as a full report, written in Dutch, English, French, or German. Studies were selected by 2 reviewers independently and disagreements were discussed to reach a consensus.

Data from the articles were extracted independently by 2 reviewers and recorded on a standardized form. Discrepancies were identified and resolved after discussion. Information was collected on patients, interventions, outcomes, timing of follow-up measurements, and results. Outcome measures were considered to be clinically homogeneous if the definitions and measurement scales were sufficiently similar in the opinion of the reviewers. Reporting of the results was considered to be adequate if any of the following data were presented for each treatment group, next to the number of patients per group: the mean and SD; the median and (interquartile) range of the outcome measure (continuous outcomes); the number of patients with the outcome of interest (dichotomous outcomes); and the frequency distribution of the outcome measure (ordinal outcomes). The feasibility of combining individual study results was investigated based on both the similarity of outcome measures and adequacy of reporting of the results.

Results

Regarding the conservative treatment options there were 2 studies available for each of the following contrasts of interventions: steroid injections versus placebo,[10,11] ultrasound versus placebo,[12,13] pyridoxine versus placebo,[14,15] diuretics versus placebo,[16,17] and oral steroids versus placebo.[16,18] Of the RCTs on surgical techniques 7 RCTs compared endoscopic carpal tunnel release with open carpal tunnel release (OCTR),[19–26] 3 RCTs evaluated the effect of OCTR with a new incision technique versus OCTR with a standard incision,[27–30] and 3 RCTs compared OCTR with additional internal neurolysis with OCTR alone.[31–34]

Data presentation in the RCTs concerning conservative treatment options for CTS was generally adequate. The most commonly used outcome measures were those related to symptoms of CTS. A wide variety of those measures were used including the following: specific descriptions of symptoms (eg, pain, paraesthesias),[11,13] more general expressions (eg, night discomfort or just symptoms),[10,14] combinations of symptoms (eg, night/day pain/paraesthesias, global symptom score),[13,16,18] measures relating to improvement of symptoms (eg, symptoms improved/changed/worsened),[15] or severity of symptoms (eg, main complaints: no complaints at all [0] to the most intense complaints I can imagine [10]).[12] Because pooling of heterogeneous outcomes will lead to an uninterpretable and misleading pooled estimate, meta-analysis is not feasible. Only the 2 trials concerning the efficacy of oral steroids[16,18] used the same outcome measure, but unfortunately only one[16] adequately reported means and SDs. Two of the other outcome measures (distal motor latency and distal sensory latency) were considered to be sufficiently similar, but this was only a very small subset of all outcomes used and in our opinion not the most important ones. In general, pooling of a subset of outcome measures may be misleading.

The RCTs concerning surgical treatment options for CTS also used many different types of outcomes related to symptoms, but the other commonly used outcome measures (such as grip and pinch strength, manual muscle testing, 2-point discrimination, Semmes-Weinstein monofilament testing, nerve conduction studies, and return to work) were considered to be sufficiently similar. Data presentation, however, was often inadequate and combining individual study results is therefore not possible. Most articles reported both pre- and postoperative data but did not add change scores. In most cases dichotomous data were reported correctly. For continuous data, however, many articles failed to report the standard deviation of the outcome[23,25,26,28,29,31] and/or the total number of patients in each group.[19,26,27,33,34] Sometimes data had to be estimated from graphs, which is often very inaccurate because of the unclear scales used on the vertical axes.[23,28–30] Furthermore in some studies data for a particular outcome were presented as dichotomous data, whereas in other studies they were presented as continuous data or, for example, as percentage change from baseline.[26,28,29]

Because pooling of the data was not possible in both systematic reviews on CTS, qualitative analyses were performed instead by using a rating system consisting of 4 levels of evidence.[35]

Enabling Meta-Analysis

The aim of this article was to present possible solutions to the problems of clinical heterogeneity of the outcome measures and inadequate reporting of results for RCTs on CTS. This will increase the comparability of the RCTs, enabling the calculation of a pooled estimate of effect in a meta-analysis, in addition to estimating the strength of the evidence in a qualitative analysis. Other aspects of clinical homogeneity, that is, similarity of the patients, interventions, comparisons, and timing of follow-up measurements are not addressed.

Outcome Measures

To resolve the problem of clinical heterogeneity of the outcome measures in a particular field of research, for example, CTS research, the outcomes and the instruments used to measure these outcomes should be standardized. In addition to this set of standard outcomes, researchers could add outcome measures of their own choice. A good example of efforts to standardize outcome measures is the Outcome Measures in Rheumatoid Arthritis Clinical Trials project, the mission of which was to develop consensus on a core set of outcomes for rheumatoid arthritis (and other major musculoskeletal conditions).[36] Another recent example is the proposal for standardized use of outcome measures for low back pain research.[37] Also for CTS research and research in other fields efforts should be made to achieve international consensus on the use of outcomes in RCTs, similar to the efforts that resulted in consensus criteria for the classification of CTS in epidemiologic studies.[38]

Outcome measures selected for standardized use should be relevant to patient health status and should preferably be validated (ie, evaluated with regard to reliability, validity, and responsiveness to change), otherwise invalid outcomes might be combined, providing a precise estimate of the wrong results. There is little evidence available, however, on the reliability, validity, and responsiveness to change of the commonly used outcome measures in CTS studies and more research is therefore needed. In 1993 a self-administered questionnaire for CTS was introduced, consisting of a scale for the assessment of severity of symptoms and a scale for the assessment of functional status.[39] These scales have been reported to be reproducible, internally consistent, valid, and responsive to clinical change[39,40] and have subsequently been used in several studies.[24,41,42] Four of the 9 studies on conservative treatment options started including patients after the publication of this questionnaire but unfortunately did not include it as an outcome measure.[9,12,13,16]

Reporting of Results

The problem of inadequate reporting of the results can easily be resolved. There clearly has to be a standardized format for the presentation of data that includes the key elements needed for pooling. For dichotomous outcomes the number of patients with the outcome of interest and the total number of patients should be presented for each treatment group to enable calculation of a pooled estimate of effect (eg, odds ratio, risk ratio, or risk difference). For continuous outcomes, the mean and SD of the outcome measure and the total number of patients should be presented for each treatment group to enable calculation of a mean difference or a standardized mean difference (effect size). These values should be presented for both follow-up data and change scores. Presentation of the median and (interquartile) range is appropriate for reporting if the outcome is not normally distributed, but methods to pool these data have not yet been developed.

Many journals have already adopted guidelines for the reporting of studies. Since 1988 the Uniform Requirements for Manuscripts Submitted to Biomedical Journals includes a section on the presentation of statistical aspects.[43] This section is quite brief: "When possible, quantify findings and present them with appropriate indicators of measurement error or uncertainty (such as confidence intervals)," "Give numbers of observations," and "Identify statistical measures of variation such as standard deviation and standard error of the mean." In 1997 these uniform requirements were accepted by more than 500 journals.[44]

An important recent example is the Consolidated Standards of Reporting Trials (CONSORT) statement published in 1996.[45] By the end of 1997 this guideline was adopted by more than 70 journals.[46] In these guidelines the section on presentation of the data is rather concise: "State estimated effect of intervention on primary and secondary outcome measures, including a point estimate and measure of precision (confidence interval)," "State results in absolute numbers when feasible (eg, 10/20 not 50%)," and "Present summary data and appropriate descriptive and inferential statistics in sufficient detail to permit alternative analyses and replication."

Most studies included in the systematic review

concerning surgical treatment options for CTS were published before the introduction of the CONSORT statement. Moreover, only one of the journals in which these RCTs were published has endorsed the statement (Nederlands Tijdschrift voor Geneeskunde). Some of the other journals have included guidelines on data presentation in their instructions for authors, but none of them states that studies should be reported in accordance with the Uniform Requirements.

A possible solution to the problem of inadequate data presentation would be to add explicit information to a revised CONSORT statement on minimal requirements with regard to data presentation including the key elements needed for pooling. To overcome the problem of inadequate data presentation in a systematic review, additional information could be requested from the researchers of the original studies. This may not be feasible in many reviews, however, because of a lack of time and resources. Furthermore data of trials published at least 5 years previously might no longer be available, or it might be difficult to find the researchers of old trials.

The authors thank Dick van Geldere and Sandra Struijs for performing the data extraction.

References

1. Sackett DL, Straus SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine. How to practice and teach EBM. vol 7. Guidelines. New York: Churchill Livingstone, 1997:169–182.
2. Thompson SG. Why sources of heterogeneity in meta-analysis should be investigated. BMJ 1994;309:1351–1355.
3. White KP, Harth M. An analytical review of 24 controlled clinical trials for fibromyalgia syndrome (FMS). Pain 1996;64:211–219.
4. Felson DT. Choosing a core set of disease activity measures for rheumatoid arthritis clinical trials. J Rheumatol 1993;20:531–534.
5. Altman DG. Statistical reviewing for medical journals. Stat Med 1998;17:2661–2674.
6. Murray GD. The task of a statistical referee. Br J Surg 1988;75:664–667.
7. Gerritsen AAM, de Krom MCTFM, Struijs MA, Scholten RJPM, de Vet HCW, Bouter LM. Conservative treatment options for carpal tunnel syndrome: a systematic review of randomised controlled trials. J Neurol 2002;249:272–280.
8. Gerritsen AAM, Uitdehaag BMJ, van Geldere D, Scholten RJPM, de Vet HCW, Bouter LM. Systematic review of randomized clinical trials of surgical treatment for carpal tunnel syndrome. Br J Surg 2001;88:1285–1295.
9. Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. BMJ 1994;309:1286–1291.
10. Dammers JWHH, Veering MM, Vermeulen M. Injection with methylprednisolone proximal to the carpal tunnel: randomised double blind trial. BMJ 1999;319:884–886.
11. Girlanda P, Dattola R, Venuto C, Mangiapane R, Nicolosi C, Messina C. Local steroid treatment in idiopathic carpal tunnel syndrome: short- and long-term efficacy. J Neurol 1993;240:187–190.
12. Ebenbichler GR, Resch KL, Nicolakis P, Wiesinger GF, Uhl F, Ghanem A-H, Fialka V. Ultrasound treatment for treating the carpal tunnel syndrome: randomised "sham" controlled trial. BMJ 1998;316:731–735.
13. Oztas O, Turan B, Bora I, Karakaya MK. Ultrasound therapy effect in carpal tunnel syndrome. Arch Phys Med Rehabil 1998;79:1540–1544.
14. Spooner GR, Desai HB, Angel JF, Reeder BA, Donat JR. Using pyridoxine to treat carpal tunnel syndrome. Randomized control trial. Can Fam Physician 1993;39:2122–2127.
15. Stransky M, Rubin A, Lava NS, Lazaro RP. Treatment of carpal tunnel syndrome with vitamin B_6: a double-blind study. South Med J 1989;82:841–842.
16. Chang M-H, Chiang H-T, Lee SS-J, Ger L-P, Lo Y-K. Oral drug of choice in carpal tunnel syndrome. Neurology 1998;51:390–393.
17. Pal B, Mangion P, Hossain MA, Wallace AS, Diffey BL. Should diuretics be prescribed for idiopathic carpal tunnel syndrome? Results of a controlled trial. Clin Rehabil 1988;2:299–301.
18. Herskovitz S, Berger AR, Lipton RB. Low-dose, short-term oral prednisone in the treatment of carpal tunnel syndrome. Neurology 1995;45:1923–1925.
19. Brown RA, Gelberman RH, Seiler JG III, Abrahamsson S-O, Weiland AJ, Urbaniak JR, Schoenfeld DA, Furcolo D. Carpal tunnel release. A prospective, randomized assessment of open and endoscopic methods. J Bone Joint Surg 1993;75A:1265-1275.
20. Benedetti RB, Sennwald G. Endoskopische dekompression des N. medianus nach *agee*: prospektive studie mit vergleich zur offenen dekompression. Handchir Mikrochir Plast Chir 1996;28:151–155.
21. Sennwald GR, Benedetti R. The value of one-portal endoscopic carpal tunnel release: a prospective randomized study. Knee Surg Sports Traumatol Arthrosc 1995;3:113–116.
22. Jacobsen MB, Rahme H. A prospective, randomized study with an independent observer comparing open carpal tunnel release with endoscopic carpal tunnel release. J Hand Surg 1996;21B:202–204.
23. Erdmann MWH. Endoscopic carpal tunnel decompression. J Hand Surg 1994;19B:5–13.
24. Hoefnagels WAJ, van Kleef JGF, Mastenbroek GGA, de Blok JA, Breukelman AJ, de Krom MCTFM. Operatieve behandeling wegens carpaletunnelsyndroom: endoscopisch of klassiek (open)? Een prospectief gerandomiseerd onderzoek. Ned Tijdschr Geneeskd 1997;141:878–882.
25. Stark B, Engkvist-Löfmark C. Endoskopische operation oder konventionelle offene Operationstechnik bei karpaltunnelsyndrom: eine prospektive, vergleichende studie. Handchir Mikrochir Plast Chir 1996;28:128–132.
26. Foucher G, Buch N, Van Overstraeten L, Gautherie M,

Jesel M. Le canal carpien. Peut-il être encore sujet de controverse? Chirurgie 1993–1994;119:80–84.
27. Nakamichi K-I, Tachibana S. Ultrasonographically assisted carpal tunnel release. J Hand Surg 1997;22A:853–862.
28. Brüser P, Richter M, Larkin G, Lefering R. The operative treatment of carpal tunnel syndrome and its relevance to endoscopic release. Eur J Plast Surg 1999;22:80–84.
29. Richter M, Brüser P. Die operative behandlung des karpaltunnelsyndroms: ein vergleich zwischen langer und kurzer schnittführung sowie endoskopischer spaltung. Handchir Mikrochir Plast Chir 1996;28:160–166.
30. Citron ND, Bendall SP. Local symptoms after carpal tunnel release. A randomized prospective trial of two incisions. J Hand Surg 1997;22B:317–321.
31. Mackinnon SE, McCabe S, Murray JF, Szalai JP, Kelly L, Novak C, Kin B, Burke GM. Internal neurolysis fails to improve the results of primary carpal tunnel decompression. J Hand Surg 1991;16A:211–218.
32. Lowry WE Jr, Follender AB. Interfascicular neurolysis in the severe carpal tunnel syndrome. A prospective, randomized, double-blind, controlled study. Clin Orthop 1988; 227:251–254.
33. Holmgren-Larsson H, Leszniewski W, Lindén U, Rabow L, Thorling J. Internal neurolysis or ligament division only in carpal tunnel syndrome—results of a randomized study. Acta Neurochir 1985;74:118–121.
34. Holmgren H, Rabow L. Internal neurolysis or ligament division only in carpal tunnel syndrome II. A 3 year follow-up with an evaluation of various neurophysiological parameters for diagnosis. Acta Neurochir 1987;87:44–47.
35. van Tulder MW, Esmail R, Bombardier C, Koes BW. Back schools for non-specific low back pain (Cochrane Review). In: The Cochrane Library, Issue 4. Oxford: Update Software, 2000.
36. Felson DT. Choosing a core set of disease activity measures for rheumatoid arthritis clinical trials. J Rheumatol 1993;20:531–534.
37. Deyo RA, Battie M, Beurskens AJ, Bombardier C, Croft P, Koes B, Malmivaara A, Roland M, von Korff M, Waddell G. Outcome measures for low back pain research. A proposal for standardized use. Spine 1998;23:2003–2013.
38. Rempel D, Evanoff B, Amadio PC, de Krom M, Franklin G, Franzblau A, Gray R, Gerr F, Hagberg M, Hales T, Katz JN, Pransky G. Consensus criteria for the classification of carpal tunnel syndrome in epidemiologic studies. Am J Public Health 1998;88:1447–1451.
39. Levine DW, Simmons BP, Koris MJ, Daltroy LH, Hohl GG, Fossel AH, Katz JN. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. J Bone Joint Surg 1993;75A:1585–1592.
40. Atroshi I, Johnsson R, Sprinchorn A. Self-administered outcome instrument in carpal tunnel syndrome. Reliability, validity and responsiveness evaluated in 102 patients. Acta Orthop Scand 1998;69:82–88.
41. Katz JN, Keller RB, Fossel AH, Punnett L, Bessette L, Simmons BP, Mooney N. Predictors of return to work following carpal tunnel release. Am J Ind Med 1997;31: 85–91.
42. Padua L, Padua R, LoMonaco M, Romanini E, Tonali P for the Italian CTS Study Group. Italian multicentre study of carpal tunnel syndrome: study design. Ital J Neurol Sci 1998;19:285–289.
43. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. Ann Intern Med 1988;108:258–265.
44. International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. JAMA 1997;277:927–934.
45. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, Pitkin R, Rennie D, Schulz KF, Simel D, Stroup DF. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. JAMA 1996;276: 637–639.
46. Moher D. CONSORT: an evolving tool to help improve the quality of reports of randomized controlled trials. JAMA 1998;279:1489–1491.