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# Does diabetes mellitus change the carpal tunnel release outcomes? Evidence from a systematic review and meta-analysis

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A B S T R A C T

*Study Design:* A systematic review and meta-analysis.
*Introduction:* Carpal tunnel syndrome (CTS) is one of the most common upper extremity conditions which mostly affect women. Management of patients suffering from both CTS and diabetes mellitus (DM) is challenging, and it was suggested that DM might affect the diagnosis as well as the outcome of surgical treatment.
*Purpose of the Study:* This meta-analysis was aimed to compare the response with CTS surgical treatment in diabetic and nondiabetic patients.
*Methods:* Electronic databases were searched to identify eligible studies comparing the symptomatic, functional, and neurophysiological outcomes between diabetic and nondiabetic patients with CTS. Pooled MDs with 95% CIs were applied to assess the level of outcome improvements.
*Results:* Ten articles with 2869 subjects were included. The sensory conduction velocities in the wrist-palm and wrist–middle finger segments showed a significantly better improvement in nondiabetic compared with diabetic patients (MD = −4.31, 95% CI = −5.89 to −2.74, $P < .001$ and MD = −2.74, 95% CI = −5.32 to −0.16, $P = .037$, respectively). However, no significant differences were found for the improvement of symptoms severity and functional status based on the Boston Carpal Tunnel Questionnaire and Quick Disabilities of the Arm, Shoulder, and Hand questionnaire as well as motor conduction velocities and distal motor latencies.
*Conclusion:* Metaresults revealed no significant difference in improvements of all various outcomes except sensory conduction velocities after CTS surgery between diabetic and nondiabetic patients. A better diabetic neuropathy care is recommended to achieve better sensory recovery after CTS surgery in diabetic patients.



## Introduction

Carpal tunnel syndrome (CTS) is one of the most common upper extremity conditions which mostly affect women.[1] Literature has proposed that various clinical conditions, including diabetes mellitus (DM), are associated with a two-fold higher risk of developing CTS.[2] It is estimated that prevalence of CTS in patients with DM without diabetic neuropathy is as high as 14%.[3] Although the underlying mechanisms of the higher incidence of CTS in diabetic patients is not fully understood but hyperglycemia, decreased blood flow and a deficiency of several neurotrophic factors make them more prone to develop neural damage.[4,5]

In some patients, CTS is benign and resolves spontaneously.[6] Conservative treatments, such as medical treatment, splinting, and local corticosteroid injection, are the first treatment of choice particularly in patients without substantial sensory or motor dysfunction.[7] However, for patients with severe CTS, or those who failed to respond well to the conservative treatments, surgical decompression is recommended.[8]

In CTS surgical decompression, in an open or endoscopic procedure, the transverse carpal ligament is cut to release the pressure

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on median nerve.[9] Previous studies have shown that surgical decompression successfully improves the functional and neurophysiological outcomes in patients with CTS.[10] The findings of a randomized controlled trial study have revealed that open surgical release in comparison with splinting alone/with local corticosteroid injection leads to better long-term improvement and can be considered superior to conservative treatments.[11]

Management of patients suffering from both CTS and DM is challenging and it was suggested that DM might affect diagnosis as well as the outcome of surgical treatment.[12,13] Although a meta-analysis of studies conducted on diabetic patients with CTS reported functional, clinical, and neurophysiological improvement in patients treated with surgical decompression, whether it is as effective as nondiabetic patients has remained controversial in different studies.[14,15] Therefore, the aim of this comprehensive meta-analysis was to systematically review the literature to characterize the difference in response to CTS surgical decompression between diabetic and nondiabetic patients.

## Methods

This systematic review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[16] PRISMA is a systematic rule which assesses the systematic review methods and guide the authors to improve the context of their systematic study.

### *Search strategy and study selection*

PubMed, Embase, and Web of Knowledge databases were searched for the relevant studies published from inception to until April 2019. The search terms including “carpal tunnel syndrome”, “CTS”, “median nerve entrapment”, “median neuropathy”, “median nerve compression”, “diabetes”, “diabetic”, “DM”, “surgery”, “surgical”, “release”, and “decompression” or their equivalents were used individually or/and in various combinations to retrieve the relevant literatures. The references list of the included studies was also manually screened to find further relevant studies. The results of the search from different databases were combined and the duplicate records were removed. To identify the relevant studies, two reviewers (A.S. and H.M.M.) independently screened the titles and abstracts of the records to select possibly relevant studies. Subsequently, they evaluated the full texts of these studies in detail to include eligible studies in the systematic review. Any disagreement was reconciled with the third reviewer (A.M.).

### *Eligibility criteria*

Studies were considered eligible if they met the following criteria: 1) Performed open or endoscopic CTS surgical decompression on both diabetic and nondiabetic patients with CTS. 2) Reported both baseline and follow-up outcomes using Boston Carpal Tunnel Questionnaire (BCTQ), Quick Disabilities of the Arm, Shoulder, and Hand (QuickDASH) Questionnaire, or evaluated nerve conduction study (NCS) variables including sensory conduction velocities (SCVs) in the wrist-palm or wrist−middle finger segments, motor conduction velocities (MCVs), or distal motor latencies (DMLs).

BCTQ consists of the symptom severity scale (SSS) containing 11 items and the functional status scale (FSS) containing 8 items. Each item is rated from 1 to 5, and the final score for each scale is calculated by dividing the sum of scores by the number of items, which generates a final score ranging from 1 to 5.[17] QuickDASH questionnaire consists of 11 items and its score is reported on a range of 0 to 100, from no disability to total disability.[18]

We included only adult patients older than 18 years. Literatures with a follow-up period less than 6 months were excluded. Furthermore, case reports, conference abstracts, letters to the editor, editorials, reviews, cadaveric studies, animal studies, non-English studies, and duplicate studies were also excluded.

### *Data extraction and quality assessment*

Two authors (A.S. and H.M.M.) independently performed the data extraction and quality assessment of the included studies. Using a predesigned spreadsheet, we recorded the following data fields for each study: first author, year of publication, country, study design, number of participants, mean age, gender ratio, follow-up duration, baseline and follow-up symptomatic, functional and neurophysiological outcomes. When the outcomes were reported for multiple follow-up durations, data of the first year of follow-up time was used for the purpose of the homogeneity of the effect sizes.

The methodological quality of the included studies was assessed using Newcastle-Ottawa Scale, which is an eight-item checklist that evaluates the risk of bias in selecting the patients, comparability of cases and controls, and measuring the outcome.[19]

### *Statistical analysis*

Comprehensive Meta-Analysis 2.2 (BioStat Inc) software was used to perform the meta-analysis. For each outcome, a meta-analysis was performed if the outcome was reported in two or more studies. The effect size of interest was the mean difference (MD) between the improvements of outcomes in diabetic compared with nondiabetic patients. By convention, we reversed the sign of the changes in BCTQ scores, QuickDASH scores, and DMLs to represent improvements. For studies that had not reported the mean and standard deviation (SD) of improvement, we calculated them using the methods described in Cochrane handbook.[20] For this purpose, the mean improvement of each outcome variable is obtained by subtracting the final mean from the baseline mean. For calculating the SD of improvements, we used the baseline and follow-up SD of the variable and assumed some degrees of correlation between the two. The correlation coefficients between the baseline and follow-up measures of each variable were calculated using the included studies that had reported SDs for improvement as well as for the baseline and final measurements.[20] Substantial heterogeneity was defined as an $I^2 > 50\%$ and a significant Cochran Q test ($P < .05$). In the case of substantial heterogeneity, random effects model was used otherwise, the fixed effects model was applied. The sensitivity analyses were performed by sequentially omitting each individual study to assess the stability of the pooled results. Egger's regression test and funnel plot were used to assess the effect of publication bias. Statistical significance was defined as $P < .05$.

## Results

### *Literature search and study characteristics*

The flow diagram of study selection strategy is shown in Figure 1. Our initial search collectively revealed 2779 records in addition to three records that were identified using the references lists of the included studies. After removing 608 duplicate records, titles and/or abstracts of the remaining 2174 records were screened, from which 37 articles were identified as possibly relevant. The full-texts of these studies were examined in detail and 27 studies were excluded based on inclusion and exclusion criteria. Of which, two studies were excluded because of containing duplicate reports with

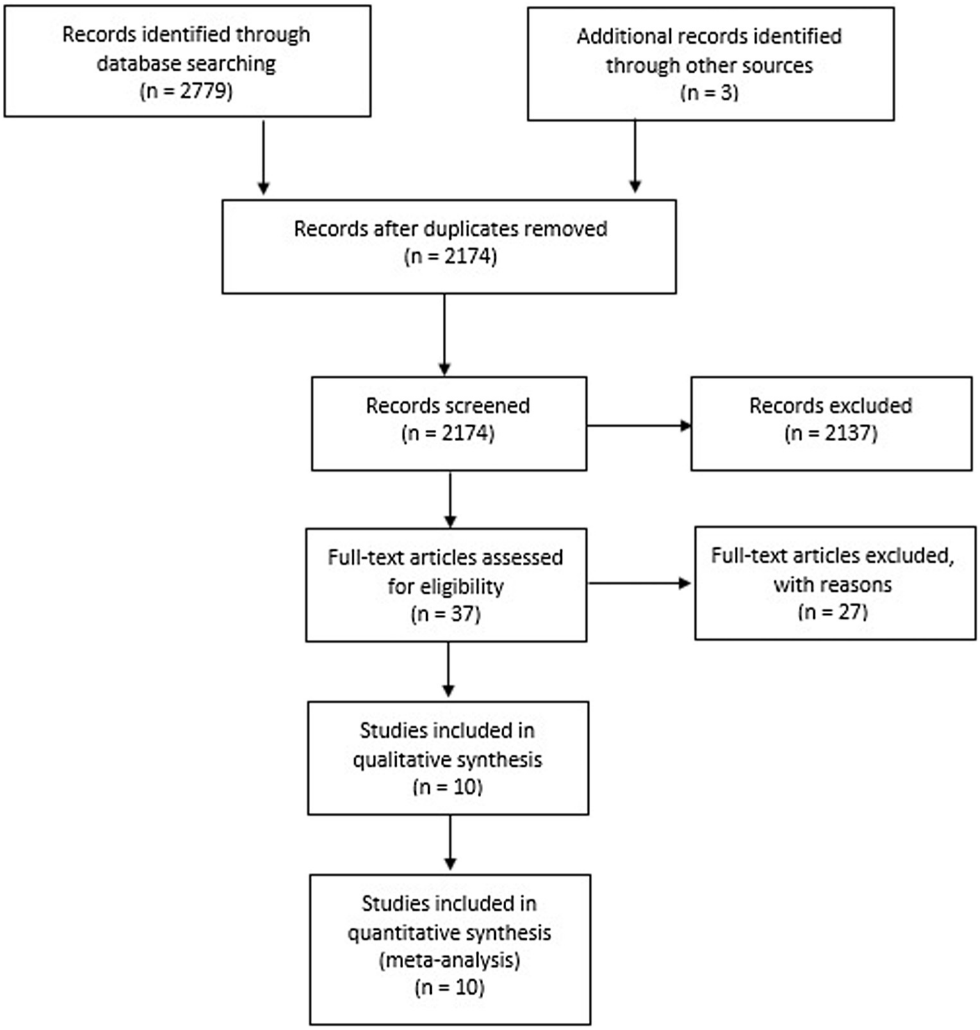


**Fig. 1.** Flowchart of study selection process.

overlapped population with another included study.[21,22] Finally, ten articles were included with 446 diabetic and 2423 nondiabetic patients with CTS treated with surgical decompression.[1,5,12,15,23-28] Those identified studies had been conducted between 2002 and 2017. Of note, the data from two articles were merged as they reported two types of outcomes for the same study population.[27,28] The mean age in diabetic and nondiabetic patients was 57.8 and 54.8, respectively. Most patients in both groups were female with 63% in diabetic and 71% in nondiabetic patients. All of the studies were cohorts, including 7 prospective and 2 retrospective studies, and no randomized controlled trial was included. The Newcastle-Ottawa Scale quality scores of the included studies

**Table 1**
Characteristics of the included studies

| First author (year) | Country | Study design | Number and gender of diabetic patients (F/M) | Number and gender of nondiabetic patients (F/M) | Mean age of the patients (diabetics/nondiabetics) | Follow-up duration | NOS quality score |
|---|---|---|---|---|---|---|---|
| Gulabi, D. (2014)[23] | Turkey | Prospective | 27 (17/10) | 42 (29/13) | 57.6/53.1 | 6 m, 10 y | 7 |
| Jenkins, P. J. (2012)[15] | UK | Prospective | 176 (107/69) | 1388 (945/443) | 58.4/54.7 | 1 y | 7 |
| Malkoc, M. (2014)[24] | Turkey | Prospective | 18 (11/7) | 21 (13/8) | 59/56.3 | 6-14 m | 6 |
| Mondelli, M. (2004)[25] | Italy | Prospective | 24 (17/7) | 72 (51/21) | 66.7/66.2 | 1 m, 6 m | 8 |
| Ozer, K. (2013)[26] | USA | Prospective | 27 (21/6) | 87 (58/29) | 50.9/46.7 | 3 m, 6 m | 6 |
| Ozkul, Y. (2002)[5] | Turkey | Prospective | 22 (19/3) | 25 (21/4) | 45.4/43.8 | 1 m, 1 y | 6 |
| Thomsen, N. O. B.[a] (2010)[28] | Sweden | Prospective | 35 (22/13) | 31 (19/12) | 53/52 | 1 y | 8 |
| Thomsen, N. O. B.[a] (2014)[27] | Sweden | Prospective | 35 (22/13) | 31 (19/12) | 53/52 | 1 y, 5 y | 7 |
| Zimmerman, M. (2017)[1] | Sweden | Retrospective | 76 (46/30) | 412 (295/117) | 59.33/55.33 | 1 y | 6 |
| Zyluk, A. (2013)[12] | Poland | Retrospective | 41 (24/17) | 345 (298/47) | 63/56 | 6 m | 6 |

NOS = Newcastle-Ottawa Scale.
[a] Thomsen, N. O. B. (2010) and Thomsen, N. O. B. (2014) used the same population in their study but they evaluated different outcomes in participants. Thomsen, N. O. B. (2010) measured the nerve conduction study (NCS) variables in the participants whereas Thomsen, N. O. B. (2014) assessed BCTQ score, sensory function, motor function and cold intolerance.

**Table 2**
The pooled analysis of mean difference in improvements after carpal tunnel surgery in diabetic and nondiabetic patients

| Variable | Number of studies | Mean difference between DM+ and DM− improvement (95% CI) | *P*-value | Heterogeneity | | |
|---|---|---|---|---|---|---|
| | | | | I2 (%) | *P*-value[a] | Model |
| BCTQ-SSS | 6 | −0.07 (−0.25 to 0.11) | .446 | 59.228 | .031 | Random |
| BCTQ-FSS | 6 | −0.1 (−0.28 to 0.08) | .266 | 56.962 | .04 | Random |
| QuickDASH score | 2 | −3.19 (−8.01 to 1.62) | .194 | 0 | .768 | Fixed |
| DML (median nerve) | 3 | −0.02 (−1.01 to 0.97) | .971 | 87.168 | <.001 | Random |
| DML (ulnar nerve) | 2 | −0.11 (−0.23 to 0.01) | .068 | 28.123 | .238 | Fixed |
| MCV (median nerve) | 2 | −0.31 (−1.51 to 0.89) | .607 | 0 | .531 | Fixed |
| MCV (ulnar nerve) | 2 | −0.17 (−1.57 to 1.23) | .812 | 0 | .535 | Fixed |
| SCV (wrist-middle finger) | 2 | −2.74 (−5.32 to −0.16)[b] | .037 | 23.675 | .252 | Fixed |
| SCV (wrist-palm) | 2 | −4.31 (−5.89 to −2.74)[b] | <.001 | 33.834 | .219 | Fixed |

DM = diabetes mellitus; BCTQ = Boston Carpal Tunnel Questionnaire; SSS = symptom severity scale; FSS = functional status scale; QuickDASH = Quick Disabilities of the Arm, Shoulder, and Hand; DML = distal motor latency; MCV = motor conduction velocity; SCV = sensory conduction velocity.
[a] *P*-value for heterogeneity within each subgroup.
[b] $P < .05$.

were in a range of 6 to 8, indicating a moderate to high quality (Table 1).

*Surgical complications*

Three of the included studies reported complications of the CTS surgery. Mondelli et al demonstrated that there is no statistically significant difference in the number of complications after CTS surgery between diabetics and nondiabetics.[25] Zyluk et al[12] reported superficial wound infection in two (4.9%) diabetics and five (1.4%) nondiabetics which were treated with oral antibiotics and rates of complications were considered too low to be statistically significant. Two (0.6%) nondiabetics with mild complex regional pain syndrome were also reported which their treatment resulted in recovery in two months.[12] Ozkul et al[5] reported one (1.9%) median nerve laceration as a complication of CTS surgery.

*QuickDASH score*

In our systematic review, two relevant studies were found using QuickDASH questionnaire (Table 2). The first study compared 76

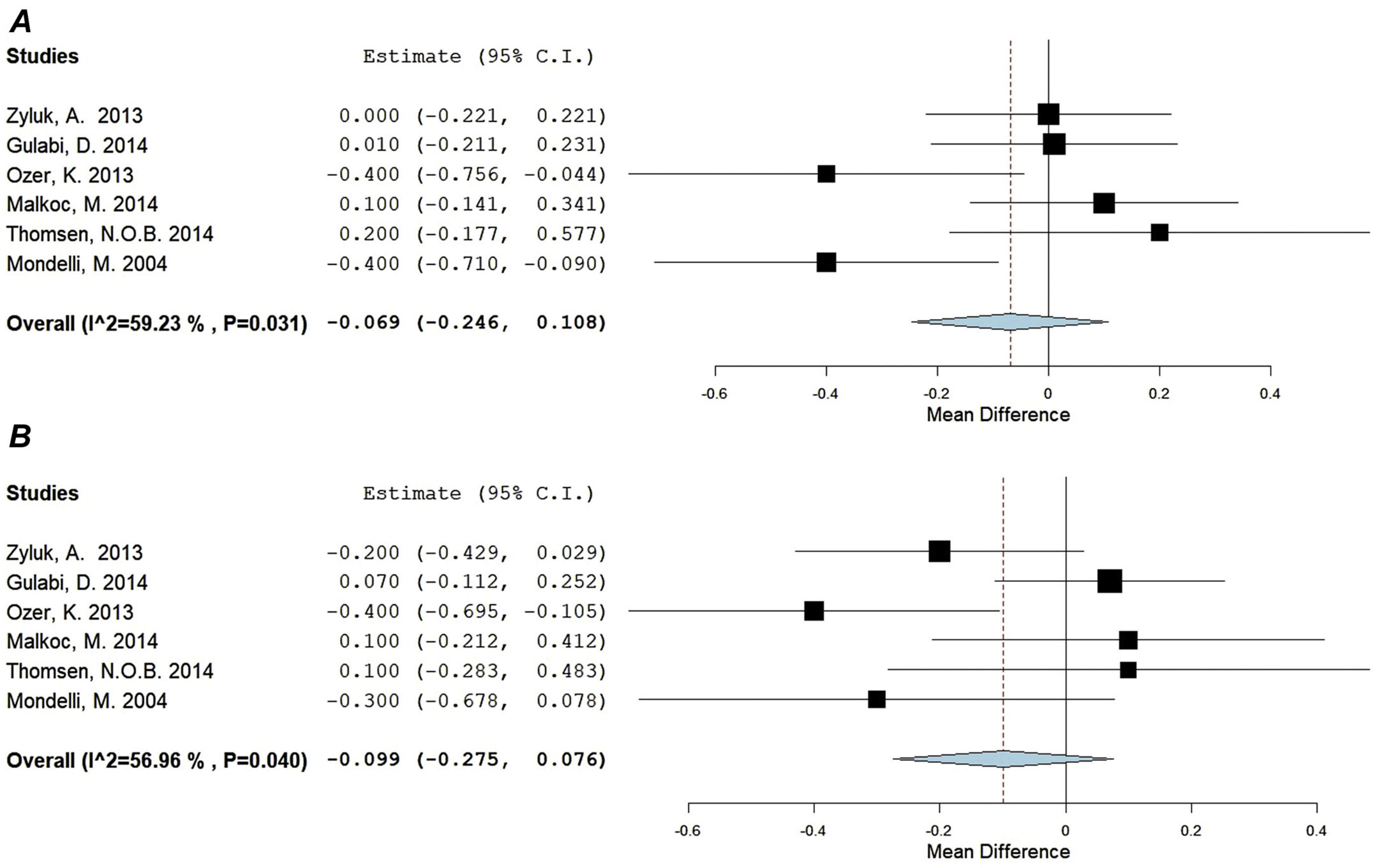


**Fig. 2.** Forest plots of mean difference in improvement of BCTQ-SSS (A) and BCTQ-FSS (B) between diabetic and nondiabetic patients with CTS. BCTQ = Boston Carpal Tunnel Questionnaire; SSS = symptom severity scale; CTS = carpal tunnel syndrome; FSS = functional status scale.

diabetic CTS with 412 nondiabetic CTS and the second study compared 176 diabetics with 1388 nondiabetics.[1,15] There was no statistically significant difference in improvements of QuickDASH score between two groups (MD = −3.19, 95% CI = −8.01 to 1.62, $P = .194$).

*BCTQ score*

Among eligible records, BCTQ was used in six studies (Table 2). Data regarding the mean and SD of improvement levels for SSS and FSS of BCTQ in six included studies were pooled to calculate the summery MD as an estimate of outcome improvement in both diabetic and nondiabetic groups. As showed in Figures 2A and 2B, our metaresults revealed no significant difference in the improvement of SSS and FSS between two study groups, indicating no difference in response to the surgical treatment (MD = −0.07, 95% CI = −0.25 to 0.11, $P = .446$ and MD = −0.1, 95% CI = −0.28 to 0.08, $P = .266$, respectively).

*Nerve conduction study*

Overall, three studies were included in the meta-analyses of NCS variables.[5,25,28] Of note, several NCS variables were reported in these studies, but we only performed the meta-analysis on variables that were reported in two or more studies, including DMLs and MCVs of median and ulnar nerves and SCVs in the wrist-palm and wrist–middle finger segments (Table 2). No significant difference in the improvement of DMLs and MCVs was observed between diabetic and nondiabetic patients. However, nondiabetic patients showed a significantly better improvement in the SCVs in the wrist-palm and wrist–middle finger segments compared with diabetic patients (MD = −4.31, 95% CI = −5.89 to −2.74, $P < .001$ and MD = −2.74, 95% CI = −5.32 to −0.16, $P = .037$, respectively).

*Sensitivity analysis and publication bias*

Sensitivity analysis regarding SSS and FSS of BCTQ revealed no significant change in the direction of the MD effects, indicating the stability and robustness of the results (Figs. 3A and 3B). Furthermore, Begg's funnel plot and Egger's regression asymmetry test were used to assess the publication bias of the meta-analysis. The effect of publication bias was not significant in the meta-analysis of SSS and FSS of BCTQ (Egger's test $P = .303$ and .26, respectively) (Figs. 4A and 4B).

**Discussion**

The effect of DM on the level of improvement after carpal tunnel surgery is still controversial and need to be clarified.[29] Therefore, a systematic review and meta-analyses of ten studies was conducted to evaluate whether the level of improvement after carpal tunnel surgery is less favorable in DM. Our meta-results revealed that, the

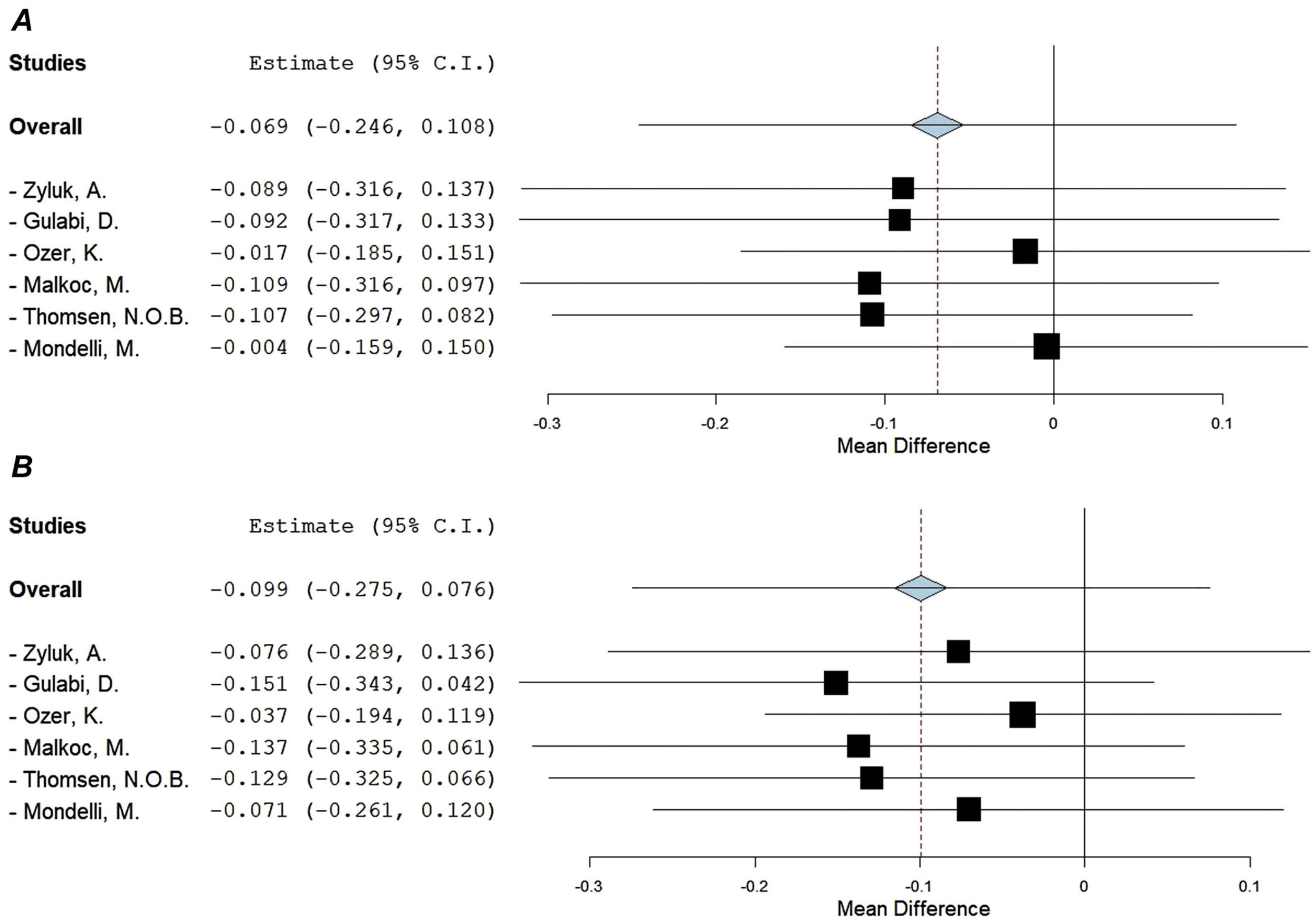


**Fig. 3.** Sensitivity analysis on the mean difference in improvement of BCTQ-SSS (A) and BCTQ-FSS (B) between diabetic and nondiabetic patients. BCTQ = Boston Carpal Tunnel Questionnaire; SSS = symptom severity scale; FSS = functional status scale.

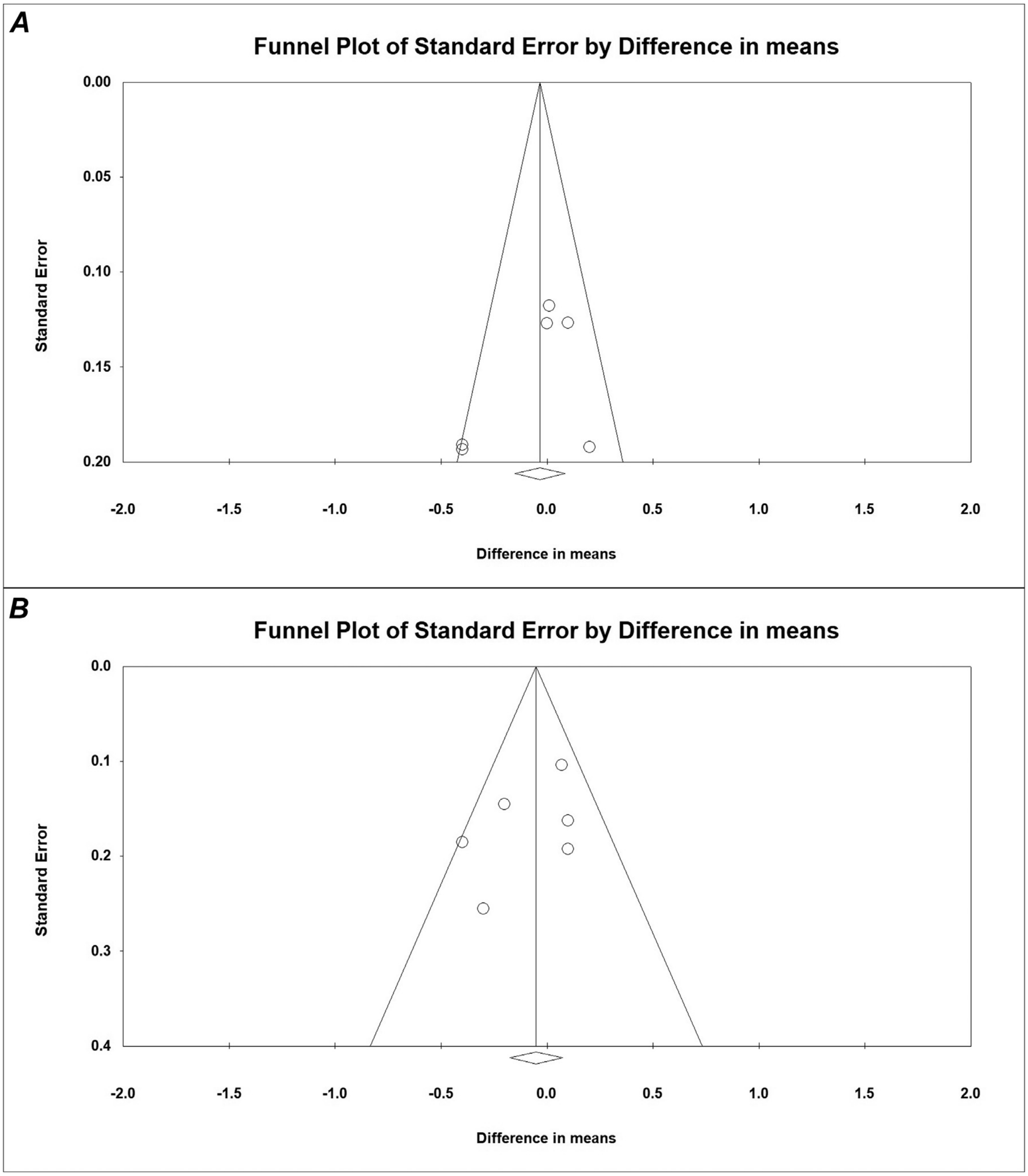


**Fig. 4.** Funnel plots of the publication bias on the mean difference in improvement of BCTQ-SSS (A) and BCTQ-FSS (B) between diabetic and nondiabetic patients. BCTQ = Boston Carpal Tunnel Questionnaire; SSS = symptom severity scale; FSS = functional status scale.

SCVs were improved significantly after CTS surgical decompression, in nondiabetic compared with diabetic patients. However, no significant differences were found for the level of improvement of MCVs and DMLs, as well as the QuickDASH score and BCTQ score between the two study groups. Furthermore, in terms of surgical complications, no significant difference was observed in both diabetic and nondiabetic patients.

Increasing evidence has considered the possible effects of DM and related treats regarding the improvement level of various outcomes after CTS surgery.[29,30] It has been proposed that the sensory dysfunction in diabetic patients with CTS might be due to a pre-existing diabetic neuropathy, which in fact is a very similar differential diagnosis to CTS.[3] Zimmerman et al suggested that diabetic patients with neuropathy have significant lesser improvement after CTS surgery than those without neuropathy.[1] In fact, the latter group had the same improvement level as nondiabetics, indicating that outcomes are affected by diabetic neuropathy, rather than diabetes itself. This highlights the importance of taking diabetic neuropathy into consideration for a more effective management of diabetic patients with CTS, by using diet, exercise and rational glycemic control.[31]

In line with our results regarding the QuickDASH score and BCTQ score, it has been shown that the recurrence rate of CTS after surgery was not significantly associated with the presence of DM.[32] A review of literatures has also concluded the same results for the effect of DM on the outcome of CTS surgery.[29] In another study, patient's satisfaction outcome after carpal tunnel release showed no significant difference between diabetic and nondiabetic patients.[33] It was also reported that while diabetic patients can experience the same degree of improvement after CTS surgery for patient satisfaction, sensory function, motor function, and pillar pain but for cold intolerance outcome represent a decreased improvement compared with nondiabetics.[34] In our previous pilot study, having the DM has been associated with a negative influence on the CTS surgical outcome in a short-term follow-up.[13] However, it was demonstrated that slower recovery in DM leads to significant difference in their improvement in a short-term follow-up but no significant difference were seen in longer follow-ups between the two groups.[35]

There are some limitations in the present meta-analysis study which have to be noticed when interpreting the conclusions. First, our included studies were all published in English which could affect pooled results. Second, among the included studies, only few of them followed the patients for more than 1 year. Therefore, we inevitably included the results from the first year of the follow-ups for the purpose of reducing the heterogeneity between the studies. Finally, more cohort studies with adequate power and long-term follow-up periods are needed to reliably assess long-term effects of DM on postsurgical outcomes.

## Conclusion

Despite the SCVs, other NCS variables and also the symptomatic and functional results of our meta-analysis revealed that both diabetics and nondiabetics can expect the same clinical benefit from carpal tunnel surgery. We suspect that significant difference in improvement of SCVs might be due to the pre-existing effects of diabetic neuropathy on sensory neurons, rather than DM itself. Nevertheless, for better sensory recovery after CTS surgery, we recommend using diet, exercise, and rational glycemic control in diabetic patients with CTS, as an adjunct to the surgical therapy. However, randomized controlled trials are needed to show if these interventions have any beneficial effects.

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