Author's response to reviews

Title: Type 2 diabetes seems not to be a risk factor for the carpal tunnel syndrome

Authors:

Steven H Hendriks (s.hendriks@isala.nl)
Peter R van Dijk (pe.van.dijk@isala.nl)
Klaas H Groenier (k.h.groenier@med.umcg.nl)
Peter Houpt (p.houpt@isala.nl)
Henk JG Bilo (H.J.G.Bilo@isala.nl)
Nanne Kleefstra (n.kleefstra@isala.nl)

Version: 4
Date: 7 July 2014

Author's response to reviews: see over
Author’s response to reviews

Title: Type 2 diabetes is not a risk factor for the carpal tunnel syndrome

Authors:
Steven H Hendriks (s.hendriks@isala.nl)
Peter R van Dijk (p.r.van.dijk@isala.nl)
Klaas H Groenier (k.h.groenier@umcg.nl)
Peter Houpt (p.houpt@isala.nl)
Henk JG Bilo (h.j.g.bilo@isala.nl)
Nanne Kleefstra (n.kleefstra@isala.nl)

Version: 4 Date: 08 July 2014
Comments from the Associate Editor (Mauro Mondelli)

Dear authors, you have improved the manuscript, but it needs further corrections. I ask you to pay particular attention to the comments of the referee n. 2.

Dear dr. Mondelli,

First of all, we want to thank you for the constructive suggestions and the opportunity to submit a revised version. We also thank the reviewers again for their constructive comments and suggestions.

In the document below, we provided a point-by-point reply to your, and the reviewers', comments.

I recommend including at the end of the discussion few brief sentences summarizing the bias in the enrolment of cases and controls:
1) cases and controls were enrolled in a secondary care setting, they are the most severe (because they required surgery). All cases and controls less severe, treated by general practitioners with conservative therapy, were lost.
2) taking into account the prevalence of diabetes type II and of CTS in general population, the sample size of this study is quite small in respect of the population at risk and the number of patients potentially affected by CTS and by diabetes in this population. The authors should underline, as reported in the cover letter to my previous comments, that they captured only 1% of diabetics and 12% of CTS patients in the population at risk.
3) the type of controls may be inadequate and therefore be responsible for the lack of association between CTS and diabetes.

Thank you for the suggestions for the discussion. We added the following sentences to the discussion section:

(page 8, line 195) “Several limitations should be mentioned. First, cases and controls were only enrolled in a secondary care setting and thereby mostly severe cases were included. Thus, less severe CTS patients treated with conservative treatment by general practitioners did not participate in the current study. Therefore, the generalizability of our results is limited to secondary care. In addition, external validity is also limited due to the fact that the studied population consisted of only ~1% of the DM and ~11% of the CTS patients of the total amount of DM and CTS patients in our region.”

And:

(page 9, line 204) “Additionally, as overweight is identified as a risk factor for the occurrence of lumbar disc herniation, and overweight is also a major risk factor for T2DM, this could have resulted in a higher prevalence of DM in the HNP population compared with the general population (15,16). Therefore, shared risk factors, such as BMI, should be taken into account when interpreting the results of our study. Third, it should be noticed that, due to the amount of missing data any relevant relationships cannot be excluded based on the present study.”

Furthermore we summarized these limitations at the end of the discussion section:

(page 9, line 220) “Taken together, it could be hypothesized that BMI and age, both well known risk factors for T2DM, are important risk factors for CTS as well, and may explain the relationship found between T2DM and CTS in other studies. Despite the limitations of the present study, i.e. choice of control group, limited generalizability due to the secondary setting, magnitude of missing data and small sample size, this is a hypothesis worth further testing.”

Minor change
At page 3, line 65, delete “[Aroori]?” or change to “[1].”

We changed [Aroori] into [1].
Reviewer 1

Title: Type 2 diabetes is not a risk factor for the carpal tunnel syndrome
Version: 3 Date: 14 June 2014
Reviewer: Russell Gelfman

Reviewer’s report:

The authors have responded to most of the concerns. The following issues remain:

Essential Revisions

Methods, line 90 – sensible, consider using sensory.

Methods, line 95 – electrophysiological, consider using electrophysiologically.

Data Sources, line 112 – specialism, consider using specialty

Major Compulsory Revisions


I would recommend a more detailed critique of these relationships, not just on the possible relationship between DM and HNP.

We want to thank the reviewer for his valuable comments.

Concerning the choice of control group, we fully acknowledge the drawbacks of choosing a population of HNP patients. We agree with the reviewer that it is, at least, conceivable that the choice for HNP patients as a control group could have introduced several confounders (e.g. BMI) that could well have influenced the findings of our study. We did our utmost best to comment upon this in the following sentences of the discussion section:

(page 9, line 201) “Second, the choice to use surgery-treated HNP patients as a control population is a topic for debate. Smaller studies have described a relationship between DM and HNP, so although inconclusive, the prevalence of T2DM could be higher among these persons than in the general population [14]. Additionally, as overweight is identified as a risk factor for the occurrence of lumbar disc herniation, and overweight is also a major risk factor for T2DM, this could have resulted in a higher prevalence of DM in the HNP population compared with the general population (15,16). Therefore, shared risk factors, such as BMI, should be taken into account when interpreting the results of our study.”

And:
“Taken together, it could be hypothesized that BMI and age, both well known risk factors for T2DM, are important risk factors for CTS as well, and may explain the relationship found between T2DM and CTS in other studies. Despite the limitations of the present study, i.e. choice of control group, limited generalizability due to the secondary setting, magnitude of missing data and small sample size, this is a hypothesis worth further testing.”

Taking into account the choice of the control group, the title of our manuscript is probably a bit too strong. Therefore we changed the tone of the title of our paper:

“Type 2 diabetes seems not to be a risk factor for the carpal tunnel syndrome.”

Reviewer 2

**Title:** Type 2 diabetes is not a risk factor for the carpal tunnel syndrome  
**Version:** 3  
**Date:** 19 June 2014  
**Reviewer:** Jeferson Becker

**Reviewer’s report:**

The authors have carried out the requested modifications, which have made a marked improvement to the manuscript. However, there are still a couple of things to be corrected.

**Major Compulsory Revisions**

1. The control group does not allow the authors to reach their conclusions. They may say that ‘Although type 2 diabetes was more frequently diagnosed among patients with carpal tunnel syndrome, it could not be identified as an independent risk factor.’ It was actually written in the abstract conclusions, but it is not that clear in the discussion and in the manuscript conclusion. Moreover, the title seems a bit too strong. The authors cannot extend their conclusion to the entire population so it would be better to say that ‘Type 2 diabetes seems not to be a risk factor for carpal tunnel syndrome’ or something similar.

We want to thank the reviewer for his valuable comments.

Concerning the choice of control group, we fully acknowledge the drawbacks of choosing a population of HNP patients. We did our utmost best to comment upon this in the discussion of the manuscript:

“Second, the choice to use surgery-treated HNP patients as a control population is a topic for debate. Smaller studies have described a relationship between DM and HNP, so although inconclusive, the prevalence of T2DM could be higher among these persons than in the general population [14]. Additionally, as overweight is identified as a risk factor for the occurrence of lumbar disc herniation, and overweight is also a major risk factor for T2DM, this could have resulted in a higher prevalence of DM in the HNP population compared with the general population (15,16). Therefore, shared risk factors, such as BMI, should be taken into account when interpreting the results of our study.”

Furthermore, the conclusion in our abstract is indeed described more clearly compared to our conclusion of the manuscript. Therefore we repeated our abstract conclusion in the manuscript conclusion:

“Although type 2 diabetes was more frequently diagnosed among patients with carpal tunnel syndrome, it could not be identified as an independent risk factor.”

Taking into account the choice of the control group, we agree with the reviewer that the title of our manuscript is a bit too strong. Therefore we changed the tone of the title of our paper:

“Type 2 diabetes seems not to be a risk factor for the carpal tunnel syndrome.”
Minor essential revision

2. Details of which EMG machine was used to perform the examinations should be included and if the hand temperature was controlled.

   We used the synergy system from Viasys Healthcare for the nerve conduction studies. We did not control for hand temperature during the NCS. According to a neurophysiologist from our hospital, it is not necessary to control for hand temperature because of the fact that we do not use absolute latency measurements in our hospital which could be influenced by temperature.

   We added the following sentence to the methods section of the paper:

   (page 4, line 94) “All nerve conduction studies were performed with a Synergy system (Viasys Healthcare, 2005) without controlling for the hand temperature.”

3. Everything else was corrected.

Reviewer 3

Title: Type 2 diabetes is not a risk factor for the carpal tunnel syndrome
Version: 3 Date: 4 June 2014
Reviewer: Elisabeth Chroni

Reviewer’s report:

Thank for asking to review this manuscript after revision. The manuscript is much improved. The main limitation of this work i.e. lack of healthy controls, remains but it is now clearly stated and justified in the discussion section.

The idea to examine whether diabetes mellitus is, or is not, predispose factor for carpal tunnel syndrome has been expressed before. The authors acknowledge previous work on the topic. All in all, I think that this manuscript deserve to be published since, the topic is clinical relevant, it refers to two common medical conditions and it confirms the initial hypothesis by fair statistical analysis. No further revisions are required.

We want to thank the reviewer for her critique on our manuscript. We agree with the fact that the lack of healthy controls is the main limitation. In this current (revised) version of the manuscript we emphasized this in the discussion.