

RESEARCH: COMPLICATIONS

Vibrotactile sense 5 years after carpal tunnel release in people with diabetes: A prospective study with matched controls

Niels O. B. Thomsen^{1,2}  | Lars B. Dahlin^{1,2}

¹Department of Hand Surgery, Skåne University Hospital, Malmö, Sweden

²Department of Translational Medicine – Hand Surgery, Lund University, Malmö, Sweden

Correspondence

Niels O. B. Thomsen, Department of Hand Surgery, Skåne University Hospital, SE-205 02 Malmö, Sweden.
Email: niels.thomsen@med.lu.se

Funding information

Supported by grants from the Swedish Research Council (Medicine), Svenska Diabetesförbundet, Diabetesföreningen Malmö, Konsul Thure Carlsson Fund for Medical Research, Stiftelsen Sigurd och Elsa Goljes Minne, Region Skåne and Funds from the University Hospital Malmö, Sweden.

Abstract

Aim: To compare vibrotactile sense, 5 years after carpal tunnel release in people with and without diabetes.

Methods: Out of 35 people with diabetes and carpal tunnel syndrome, age- and gender-matched with 31 people without diabetes but with idiopathic carpal tunnel syndrome, 27 and 30 people, respectively, participated in this prolonged follow-up. Vibration perception threshold of the index and little finger (median and ulnar nerve, respectively), 5 years after surgery, was measured at seven different frequencies (8, 16, 32, 64, 125, 250 and 500 Hz).

Results: Significant improvement of vibration perception threshold from 1 to 5 years after carpal tunnel release was found at 64 Hz for people with diabetes, while improvement for people without diabetes was demonstrated at several frequencies (64–250 Hz). However, both groups demonstrated a significant decrease in vibration perception threshold for the low frequencies (8–16 Hz). At 5 years, people with diabetes had significantly impaired vibration perception threshold at the index finger for high frequencies (125–500 Hz), and for nearly all frequencies (16 Hz, 64–500 Hz) at the little finger, compared to people without diabetes.

Conclusion: After carpal tunnel release, significant mid-term improvement of vibrotactile sense appears limited for people with diabetes, compared to a continuous improvement for people without diabetes. In addition, a decline in low-frequency vibrotactile sense occurs for the median as well as the ulnar nerve innervated fingers. Clinical Trial Registration NCT01201109

KEY WORDS

carpal tunnel syndrome, diabetes mellitus, entrapment neuropathy, vibration perception threshold, vibrotactile sense

Prior presentation: Vibration perception threshold data before and 1 year after carpal tunnel release has previously been published in *Diabet Med.* 2011 **28**:1401–1406. [Correction added on 17 December 2020, after first online publication: The title was incorrect and was amended in this version.]

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2020 The Authors. *Diabetic Medicine* published by John Wiley & Sons Ltd on behalf of Diabetes UK

1 | INTRODUCTION

Distal symmetric polyneuropathy represents the most common form of diabetic neuropathy.¹ For assessment of large fibre function in distal symmetric polyneuropathy, clinical testing of vibrotactile sense using a 128 Hz tuning fork as well as the 10 g monofilament test is recommended.² Elevated vibration perception threshold, reflecting large myelinated A α and A β -fibre dysfunction, is found early-on in type 1 diabetes.³ In elderly men with type 2 diabetes, vibrotactile sense of the hand has been found impaired, predominantly in the ulnar nerve innervated fingers.⁴

In nerve entrapment such as carpal tunnel syndrome, large myelinated nerve fibres are recognised as more susceptible to pressure/ischaemia than unmyelinated nerve fibres.⁵ Nerve conduction studies are the most commonly used objective diagnostic tool for assessment of large fibre function in nerve entrapment. However, impaired vibrotactile sense at 256 Hz has been demonstrated as an early sign of acute peripheral nerve compression, which develops before an increase in static two-point discrimination (2-PD) can be measured.⁶

Using multifrequency vibrometry, in the same group of participants as studied here, we previously demonstrated improvement of vibrotactile sense 1 year after carpal tunnel release, but with significant impairment in people with diabetes before and after surgery, compared to people without diabetes.⁷

The purpose of this study is to prolong our previously published clinical trial to compare vibration perception thresholds, 5 years after carpal tunnel release in people with and without diabetes.

2 | PARTICIPANTS AND METHODS

Between 2004 and 2007, consecutive individuals with type 1 and type 2 diabetes referred to our outpatient clinic, with symptomatic carpal tunnel syndrome lasting for at least 6 months, as well as inadequate symptomatic relief to 6 weeks treatment with a wrist splint, were asked to participate in the study. The diagnosis of carpal tunnel syndrome was based on characteristic clinical history, symptoms and nerve conduction study verification (antidromic wrist to palm sensory conduction velocity <44 m/s and distal motor latency >4.1 ms). We allowed a maximum age difference of 5 years, in our effort to age- and gender-matched people with diabetes and carpal tunnel syndrome with a control group of people with idiopathic carpal tunnel syndrome. Inclusion criteria and the surgical procedure for open carpal tunnel release have previously been described in detail.⁸ In the current prolonged study, participants were evaluated at least 5 years after the carpal tunnel release.

What is new?

- Upper extremity vibrotactile sense is impaired in people with diabetes and carpal tunnel syndrome. However, significant recovery of vibration perception thresholds has been demonstrated to occur early-on after nerve decompression.
- Our findings, 5 years after carpal tunnel release, suggests a continuous improvement of vibrotactile sense at higher frequencies, but mainly among people without diabetes. Oppositely, a long-term decline in low frequencies are found for the median and ulnar nerve innervated fingers for both people with and without diabetes.
- For people with diabetes, vibrotactile sense in the hand can be expected to improve after carpal tunnel release, however, to a smaller degree than for people without diabetes.

For the initial study, 35 people with diabetes and carpal tunnel syndrome were individually age- and gender-matched with 31 people without diabetes who had idiopathic carpal tunnel syndrome. For the current prolonged follow-up, eight people with diabetes and one person without diabetes were not able to participate for various reasons. Thus, the study population consists of 27 people with diabetes and carpal tunnel syndrome, and the control group comprises of 30 people without diabetes who have idiopathic carpal tunnel syndrome.

2.1 | Outcome measures

The primary outcome was improvement of vibration perception threshold from 1 to 5 years after carpal tunnel release. The secondary outcomes were differences in vibration perception threshold improvement between (1) people with diabetes versus people without diabetes, (2) subgroups of people with type 1 diabetes versus type 2 diabetes and (3) those with peripheral neuropathy versus those without signs of peripheral neuropathy. Finally, to investigate whether changes in vibration perception threshold correlates with age, HbA_{1c} level and previously published nerve conduction study results.

2.2 | Vibration perception thresholds

As previously described, vibration perception thresholds were obtained on the pulp of the index and little finger, representing median and ulnar nerve function, respectively.⁷ Seven frequencies were recorded (8, 16, 32, 64, 125, 250 and 500 Hz) using a VibroSense Meter (VibroSense Dynamics

AB). Seated in a separate room with constant temperature, the participants were equipped with hearing protectors to maintain a calm and quiet environment. They were instructed to let the centre of the finger pulp in question, rest passively on the probe of the tactilometer. The vibration perception threshold was determined by the method of limits, to register at which amplitude the vibratory sensation is first perceived and again when it disappears.^{9,10} To ensure homogeneity, all investigations were performed independently by the same technician. The vibration perception threshold values are expressed in decibel (dB), where a high value indicates more impaired vibrotactile sense.

2.3 | Statistics

Data on characteristics of the participants are given as median (range) unless otherwise stated, while results from the vibration perception threshold analyses are reported as median [IQR].

We tested for differences of continuous variables between groups using non-parametric Mann–Whitney U-test and within groups by Wilcoxon signed rank test. Correlations were performed using Spearman rank sum test and expressed as a coefficient (r_s) with a level of significance. $p < 0.05$ was considered statistically significant. Statistical analysis was performed using SPSS 26.0 for Windows (SPSS Inc.).

2.4 | Ethics

The Regional Ethical Review Board at Lund University approved the study (LU 508-03), and all patients gave informed consent to participate.

3 | RESULTS

The study population characteristics are shown in Table 1. The group of people with diabetes included 13 with type 1 diabetes and 14 with type 2 diabetes. Peripheral neuropathy was based on detection of abnormal nerve conduction values in both the sural (sensory conduction velocity and sensory nerve action potential) and the peroneal nerve (compound muscle action potential).¹¹ With these criteria, we found neurophysiologic signs of peripheral neuropathy in 10 of the 27 people with diabetes. None of the people without diabetes had peripheral neuropathy. Z-scores from the nerve conduction values were calculated as standard deviation (SD) from mean of the patients without diabetes ([value of patients with diabetes–the mean value of patients without diabetes]/SD of patients without diabetes), indicating mild peripheral neuropathy among the people with diabetes (data not shown).¹²

3.1 | Vibration perception thresholds

At 5 years, people with diabetes had significantly impaired vibration perception thresholds at the median nerve innervated index finger for the high frequencies (125–500 Hz) and for nearly all frequencies, (16 Hz, 64–500 Hz) at the ulnar nerve innervated little finger compared to the people without diabetes. No differences between groups were found at 32 Hz. Significant improvement of vibration perception thresholds (index and little finger) from 1 to 5 years after carpal tunnel release was only demonstrated at 64 Hz for people with diabetes, whereas improvement for people without diabetes was found at several frequencies (64–250 Hz). However, a significant decrease in vibration perception threshold (index and

TABLE 1 Participant characteristics, at 5-year follow-up after carpal tunnel release

Characteristics	People with diabetes (<i>n</i> = 27)	People without diabetes (<i>n</i> = 30)
Age, (years)	61 (36–79)	57 (40–83)
Female/Male (<i>n</i>) [%]	16/11 [59/41]	19/11 [63/37]
Duration of CTS (months)	27 (8–96)	48 (12–180)
Duration of diabetes (years)	17 (1–43)	—
BMI (kg/m ²)	28.7 (17–38.1)	25.7 (20.4–0.8)
HbA _{1c} (mmol/mol)	[53 (38–91)]	[35 (23–49)]
HbA _{1c} (%)	7.0 (5.6–10.5)	5.4 (4.3–6.6)
Follow-up after surgery (months)	68 (59–82)	64 (59–69)
Nerve conduction study on the median nerve		
SCV before surgery (m/s)	18.4 (14.0–22.8)	24.1 (20.2–28.0)
SCV at 5 years follow-up (m/s)	37.5 (34.8–40.2)	44.0 (41.4–46.6)

Data are median (range) unless otherwise stated.

HbA_{1c}, glycosylated haemoglobin; SCV, sensory conduction velocity at the carpal tunnel segment (normal value >44 m/s).

TABLE 2 Vibration perception thresholds in the index and little finger of people with and without diabetes, before and after carpal tunnel release

	People with diabetes					People without diabetes				
	Preoperative (N = 35, p value) ^a	1 year (N = 35; p value) ^a	5 year (N = 27; p value) ^a	Pre vs 1 year (p value) ^b	1 vs 5 years (p value) ^b	Preoperative (N = 31)	1 year (N = 31)	5 years (N = 30)	Pre vs 1 year ^b (p value)	1 vs 5 years ^b (p value)
Index finger										
8 Hz	105 [8] (0.424)	102 [8] (0.015)	107 [7] (0.962)	0.001	0.001	103 [6]	105 [6]	108 [6]	0.248	0.029
16 Hz	115 [7] (0.024)	111 [7] (0.557)	115 [6] (0.742)	0.002	0.019	112 [8]	113 [7]	114 [6]	0.875	0.096
32 Hz	121 [8] (0.007)	118 [6] (0.094)	117 [9] (0.317)	0.005	0.971	115 [9]	117 [7]	116 [7]	0.557	0.566
64 Hz	118 [12] (0.009)	116 [9] (0.031)	110 [10] (0.068)	0.270	0.001	111 [10]	112 [8]	107 [8]	0.456	0.001
125 Hz	117 [16] (0.025)	114 [8] (0.036)	112 [8] (0.021)	0.015	0.077	110 [14]	110 [6]	106 [9]	0.732	0.013
250 Hz	127 [19] (0.006)	122 [17] (0.015)	124 [15] (0.001)	0.001	0.790	121 [13]	115 [11]	111 [12]	0.003	0.023
500 Hz	143 [17] (0.152)	139 [16] (0.025)	139 [18] (0.002)	0.002	0.509	139 [14]	132 [11]	129 [14]	0.001	0.279
Little finger										
8 Hz	103 [8] (0.549)	102 [7] (0.403)	107 [6] (0.169)	0.242	0.001	102 [8]	104 [7]	106 [5]	0.367	0.029
16 Hz	113 [7] (0.055)	111 [8] (0.475)	115 [7] (0.049)	0.031	0.001	110 [8]	111 [5]	112 [5]	0.875	0.023
32 Hz	120 [9] (0.005)	118 [6] (0.007)	120 [7] (0.081)	0.061	0.073	116 [7]	116 [7]	118 [5]	0.784	0.082
64 Hz	119 [10] (0.019)	116 [9] (0.064)	114 [10] (0.010)	0.114	0.025	113 [10]	114 [8]	108 [9]	0.906	0.001
125 Hz	115 [10] (0.025)	114 [9] (0.027)	114 [8] (0.001)	0.343	0.454	109 [13]	110 [8]	107 [9]	0.318	0.003
250 Hz	124 [15] (0.006)	122 [14] (0.001)	119 [11] (0.005)	0.013	0.667	117 [12]	115 [12]	113 [12]	0.001	0.721
500 Hz	140 [16] (0.097)	135 [17] (0.007)	138 [16] (0.012)	0.048	0.943	134 [16]	128 [16]	128 [14]	0.001	0.705

Results are median [IQR]. Significant improvement is marked in bold and significant decrease in bold italic. Preoperative and 1-year follow-up data have previously been published.⁷

^ap values are differences between people with and people without diabetes. p values < 0.05 are indicated in bold.

^bp values are preoperative results versus 1-year follow-up, and 1-year versus 5-year follow-up.

TABLE 3 Vibration perception thresholds in the index and little finger of people with type 1 diabetes and people with type 2 diabetes, before and after carpal tunnel release

	People with type 1 diabetes					People with type 2 diabetes				
	Preoperative (N = 15; p value) ^a	1 year (N = 15; p value) ^a	5 years (N = 13 ^b ; p value) ^b	Pre vs 1 year (P value) ^b	1 vs 5 years c(p value) ^b	Preoperative (N = 20)	1 year (N = 20)	5 years (N = 14)	Pre vs 1 year (p value) ^b	1 vs 5 years (p value) ^b
Index finger										
8 Hz	104 [11] (0.681)	100 [8] (0.240)	106 [5] (0.905)	0.002	0.004	105 [6]	102 [7]	108 [10]	0.147	0.019
16 Hz	116 [6] (0.584)	111 [7] (0.521)	114 [7] (0.280)	0.008	0.086	114 [7]	112 [6]	117 [7]	0.084	0.074
32 Hz	117 [12] (0.256)	118 [8] (0.780)	118 [9] (0.867)	0.222	0.990	121 [8]	118 [5]	116 [9]	0.013	0.975
64 Hz	115 [9] (0.111)	116 [9] (0.657)	108 [7] (0.038)	0.865	0.003	121 [12]	116 [12]	112 [10]	0.006	0.019
125 Hz	113 [17] (0.271)	111 [9] (0.099)	108 [11] (0.155)	0.064	0.108	118 [15]	116 [11]	113 [12]	0.117	0.363
250 Hz	134 ± 14 (0.945)	117 [19] (0.149)	124 [16] (0.830)	0.001	0.505	125 ± 10	124 [15]	121 [16]	0.044	0.272
500 Hz	147 [24] (0.758)	137 [18] (0.283)	142 [21] (0.550)	0.015	0.117	142 [13]	141 [13]	137 [17]	0.049	0.433
Little finger										
8 Hz	106 [10] (0.493)	100 [10] (0.438)	107 [6] (0.302)	0.112	0.009	103 [7]	103 [6]	110 [7]	0.968	0.002
16 Hz	115 [6] (0.391)	109 [9] (0.521)	113 [6] (0.259)	0.023	0.064	112 [9]	111 [6]	117 [7]	0.421	0.002
32 Hz	122 [7] (0.811)	117 [8] (0.980)	120 [7] (0.302)	0.156	0.388	119 [11]	119 [6]	122 [8]	0.212	0.125
64 Hz	118 [11] (0.837)	116 [11] (0.347)	113 [12] (0.094)	0.156	0.039	119 [12]	117 [11]	117 [10]	0.421	0.272
125 Hz	115 [15] (0.973)	112 [11] (0.059)	112 [5] (0.061)	0.088	0.937	115 [11]	118 [9]	118 [9]	0.872	0.331
250 Hz	125 [17] (0.864)	118 [13] (0.314)	119 [11] (0.702)	0.020	0.556	122 [14]	123 [17]	121 [13]	0.171	0.972
500 Hz	142 [20] (0.758)	130 [13] (0.149)	134 [18] (0.650)	0.020	0.382	139 [13]	139 [15]	139 [15]	0.546	0.363

Results are median [IQR]. Significant improvement is marked in bold and significant decrease in bold italic.

^ap values are differences between people with type 1 diabetes and people with type 2 diabetes. p < 0.05 are indicated in bold.

^bp values are preoperative results versus 1-year follow-up, and 1-year versus 5-year follow-up.

TABLE 4 Vibration perception thresholds in the index and little finger of people with diabetes having peripheral neuropathy and people with diabetes without peripheral neuropathy, before and after carpal tunnel release

	People with diabetes and neuropathy				People with diabetes without neuropathy					
	Preoperative $N = 14$ (p value) ^a	1 year $N = 14$ (p value) ^a	5 years $N = 10$ (p value) ^a	Pre vs 1 year (p value) ^b	1 vs 5 years (p value) ^b	Preoperative ($N = 21$)	1 year ($N = 21$)	5 years ($N = 17$)	Pre vs 1 year. (p value) ^b	1 vs 5 years (p value) ^b
Index finger										
8 Hz	107 [9] (0.396)	102 [7] (0.702)	108 [4] (0.414)	0.019	0.028	105 [8]	101 [8]	106 [10]	0.028	0.002
16 Hz	116 [11] (0.616)	113 [5] (0.175)	116 [4] (0.675)	0.124	0.283	114 [6]	110 [6]	113 [9]	0.003	0.044
32 Hz	120 [11] (0.959)	120 [5] (0.018)	120 [7] (0.170)	0.594	0.540	121 [7]	116 [7]	115 [9]	0.002	0.723
64 Hz	118 [9] (0.904)	118 [8] (0.077)	109 [6] (0.786)	0.510	0.005	118 [13]	114 [10]	110 [12]	0.126	0.013
125 Hz	118 [14] (0.478)	115 ±[8] (0.293)	113 [7] (0.204)	0.140	0.126	113 [18]	111 [12]	110 [12]	0.530	0.210
250 Hz	135 [24] (0.097)	130 [15] (0.077)	128 [14] (0.066)	0.009	0.906	122 [14]	119 [15]	117 [15]	0.004	0.619
500 Hz	151 [16] (0.083)	143 [11] (0.210)	148 [17] (0.066)	0.056	0.086	140 [12]	136 [17]	135 [14]	0.015	0.687
Little finger										
8 Hz	107 [7] (0.056)	103 [8] (0.235)	108 [4] (0.473)	0.331	0.059	101 [9]	102 [8]	107 [8]	0.550	0.001
16 Hz	115 [5] (0.071)	113 [6] (0.083)	115 [8] (0.204)	0.096	0.169	111 [9]	110 [8]	113 [8]	0.145	0.001
32 Hz	123 [9] (0.396)	119 [7] (0.083)	123 [7] (0.204)	0.245	0.086	119 [8]	117 [7]	120 [10]	0.135	0.266
64 Hz	117 [6] (0.306)	119 [7] (0.474)	114 [11] (0.824)	0.683	0.139	121 [13]	115 [12]	114 [12]	0.021	0.620
125 Hz	115 [10] (0.666)	115 [9] (0.630)	112 [9] (0.902)	0.730	0.767	111 [11]	113 [13]	115 [11]	0.391	0.523
250 Hz	126 [13] (0.192)	126 [17] (0.154)	121 [10] (0.359)	0.300	0.813	122 [15]	119 [12]	119 [14]	0.019	0.679
500 Hz	143 [17] (0.259)	140 [19] (0.198)	138 [19] (0.414)	0.300	0.878	137 [15]	135 [15]	138 [17]	0.057	0.943

Results are median [IQR]. Significant improvement is marked in bold and significant decrease in bold italic.

^a p values are differences between people with diabetes having peripheral and people with diabetes without peripheral neuropathy. p values < 0.05 are indicated in bold.

^b p values are preoperative results versus 1-year follow-up, and 1-year versus 5-year follow-up.

little finger) for both participant groups was demonstrated at the low frequencies (8–16Hz; Table 2).

We were unable to demonstrate any meaningful differences in improvement of vibrotactile sense for subgroups of people with type 1 diabetes and type 2 diabetes, nor those with and without peripheral neuropathy (Tables 3 and 4).

3.2 | Correlations

Significant negative correlation between improvement of vibration perception threshold and HbA_{1c} level was found among people with diabetes, but for the little finger only (8Hz [$r_s = -0.43$, $p < 0.03$], and 500Hz [$r_s = -0.46$ to 0.47 , $p < 0.02$]).

We found that changes in vibration perception threshold correlated with age for people with diabetes only (index finger at 8–16 and 125–500 Hz [$r_s = 0.44$ – 0.53 , $p < 0.02$], little finger at 8 and 125–500 Hz [$r_s = 0.42$ – 0.59 , $P < 0.03$]).

Our results could not demonstrate any correlation between the changes in vibration perception threshold from 1 to 5 years after surgery, and previously published significant recovery of median nerve sensory conduction velocity over the carpal tunnel segment for people with and without diabetes.¹³

In the subgroups of people with diabetes, with and without peripheral neuropathy, no correlation was found between recovery of vibration perception thresholds, and changes in nerve conduction study results for the sural and peroneal nerves.

4 | DISCUSSION

This is the first report to provide a mid-term follow-up on vibrotactile sense after carpal tunnel release, which furthermore encompasses a matched group of people with and without diabetes. Previously, 1 year after carpal tunnel release, we were able to demonstrate a significant recovery of vibration perception threshold at several frequencies among the people with diabetes. Still, vibration perception threshold was significantly impaired in people with diabetes compared to people without diabetes.⁷ In the present study, 5 years after surgery, our findings suggest a continuous improvement of vibration perception threshold at higher frequencies, but mainly among people without diabetes. At low frequencies (8–16Hz), a decrease in vibration perception threshold is demonstrated for all participants and applies to the median nerve innervated index finger as well as for the ulnar nerve innervated little finger. While our results indicate that diabetes has a negative impact on improvement of vibration tactile sense, the impact due to type of diabetes or peripheral neuropathy seems insignificant.

The vibrotactile sense depends on the function of rapidly adapting mechanoreceptive Meissner and Pacinian corpuscles. Meissner corpuscles located in the dermal papillae are sensitive to low-frequency vibration between 5 and 50 Hz, while Pacinian corpuscles located in the deep dermis or subcutaneous tissue, respond to high frequencies above 50 Hz with a probable maximum sensitivity around 250 Hz.¹⁴ The density of mechanoreceptors increases in the direction from the palm to the finger pulp, with Meissner corpuscles being more abundant than Pacinian corpuscles.¹⁵

With carpal tunnel syndrome, the myelinated nerve fibres at the compression site can be characterised by metabolic conduction block, and in persistent cases development of segmental demyelination and ultimately Wallerian degeneration of myelinated nerve fibres.¹⁶ If axonal loss is not predominant, a significant improvement of vibration perception threshold may be found just a few months after nerve decompression.¹⁷ Based on biopsies of the uncompressed posterior interosseous nerve at the distal forearm, obtained at the time of carpal tunnel release, we have previously demonstrated more advanced endoneurial microangiopathy, and a significant reduction in myelinated nerve fibre density for people with diabetes compared to people without diabetes.^{18,19} As vibratory sensation is conveyed from the mechanoreceptors via large myelinated nerve fibres to the dorsal root ganglia, neuropathy with a reduction in myelinated fibre density may contribute to the impairment, and lesser improvement of vibration perception threshold, as demonstrated for the people with diabetes. Noteworthy, and of potential impact for improvement of vibration perception threshold, is the morphologic finding in type 1 diabetes of regenerative nerve fibre clusters in between a degenerative morphology represented by segmental demyelination and axonal loss.²⁰

From 1- to the 5-year follow-up, both patient groups demonstrated a deterioration of vibration perception thresholds at the low frequencies (8 and 16 Hz), involving the index as well as the little finger. The density of Meissner corpuscles in the hand is likely not to be affected by local nerve entrapment such as carpal tunnel syndrome.²¹ However, a decrease in Meissner corpuscles has been identified from finger skin biopsies in people with diabetes, which may be of importance for the demonstrated impairment of low-frequency vibration perception thresholds.²² With age, there is a significant decline of the vibrotactile sense.²³ However, its relevance in this study seems uncertain as a follow-up period of 5 years may be too short for an age-related decline to manifest itself. A decrease in lower-frequency vibration perception threshold has previously been demonstrated for the upper extremity, as well as for the lower extremity, among people with type 1 diabetes. Here, a strong association was found between impaired vibration perception threshold, neuropathic symptoms, and the risk for development of diabetic foot ulcers.^{24,25}

Although not proven, it would seem reasonable that a reduction in Pacinian corpuscles would occur in diabetes, as demonstrated for the Meissner corpuscles. If so, it would, together with the significant nerve fibre and endoneurial capillary pathology described from posterior interosseous nerve biopsies, support the larger improvement of vibration perception thresholds among higher frequencies, for the people without diabetes compared to the people with diabetes.¹⁸

On the same people with diabetes as studied here, we have previously demonstrated significant improvement of neurophysiological parameters at 5 years after carpal tunnel release.¹³ However, in this study, significant improvement of vibration perception thresholds among people with diabetes was limited to vibration sense at 64 Hz, only. While nerve decompression can recover myelinated nerve fibre function and improve nerve conduction velocity, the dying back phenomenon and reduction in mechanoreceptive corpuscles among people with diabetes remains. It may explain why the mid-term improvement of vibration perception threshold seems less and do not correlate to the previously reported recovery of nerve conduction parameters.

We found postoperative changes in vibration perception threshold at the ulnar nerve innervated little finger, to parallel the pattern of changes demonstrated for the median nerve innervated index finger. This was somewhat unexpected as we carefully had excluded patients with clinical and neurophysiological signs of ulnar nerve entrapment. Anatomically, the carpal tunnel and Guyon's canal are connected, because the deep antebrachial fascia at wrist level represents the volar bound of the carpal tunnel as well as the dorsal bound of Guyon's canal. Thereby, an ulnar nerve vulnerability could be relevant as morphologic and pressure changes in Guyon's canal have been shown to coexist with carpal tunnel syndrome.²⁶ Furthermore, after carpal tunnel release, ultrasonography has demonstrated a near normalisation of the ulnar nerve cross section area, and neurophysiological improvement of ulnar sensory nerve conduction velocity are known to occur.²⁷ Tourniquet studies with occlusion of the brachial artery suggests that the ulnar nerve is more sensible to ischemia than the median nerve.²⁸ A general ulnar nerve susceptibility to ischaemia would have an immediate influence on diabetes, where microangiopathy are known to enhance endoneurial hypoxia.^{1,19} An impact of diabetes on the ulnar nerve is supported by a negative correlation between improvement in vibration perception thresholds and HbA_{1c} for the little finger.

The role of vibrotactile perception threshold testing in recovery after nerve decompression has not been established. Previously, for the same people with and without diabetes as studied here, we demonstrated a significant sensory recovery for the index finger at 1 year post-surgery. It was

followed by a non-significant decline at 5 years which was most evident for people with diabetes. At 5 years, none of the participants demonstrated recurrent symptoms in terms of numbness and paresthesia, in the median nerve innervated fingers. In addition, no relationship has been demonstrated between post-surgical improvement of vibrotactile sense, and patients' self-assessment of functional limitations or symptom severity.^{7,29}

A strength of our study is the prospective, 5-year follow-up of age- and gender-matched participants. In addition, the vibration perception threshold examinations were done by the same experienced technicians which secures consistency of measurements. A limitation of our study is the relatively low sample size that limits the statistical power when evaluating subgroups based on type of diabetes or the presence of peripheral neuropathy. Also, although we had an overall attendance rate of 86% at the 5-year follow-up, the majority of dropouts were among the people with diabetes. Lastly, in the search for correlations between variables, multiple testing is involved, which is why these results should be interpreted with caution.

In conclusion, our study provides new knowledge on upper extremity vibrotactile sense in diabetes as well as its potential for recovery after carpal tunnel release. After the significant recovery of vibrotactile sense 1 year after nerve decompression, a further progress at 5 years seems limited for people with diabetes, compared to the continuous improvement for people without diabetes. In addition, a mid-term decline in low-frequency vibrotactile sense occurs for the median as well as the ulnar nerve innervated fingers. The latter finding warrants further investigation.

ACKNOWLEDGEMENTS

We thank Ingrid Hallberg for performing the vibration perception threshold measurements.

CONFLICT OF INTEREST

None declared.

ORCID

Niels O. B. Thomsen  <https://orcid.org/0000-0003-2522-4804>

REFERENCES

1. Feldman EL, Callaghan BC, Pop-Busui R, et al. Diabetic neuropathy. *Nat Rev Dis Primers*. 2019;5:41.
2. Pop-Busui R, Boulton AJM, Feldman EL, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes Care*. 2017;40:136–154.
3. Ising E, Dahlin LB, Elding LH. Impaired vibrotactile sense in children and adolescents with type 1 diabetes – signs of peripheral neuropathy. *PLoS One*. 2018;13:e0196243.
4. Dahlin LB, Thrainsdottir S, Cederlund R, et al. Vibrotactile sense in median and ulnar nerve innervated fingers of men with type

- 2 diabetes, normal or impaired glucose tolerance. *Diabet Med.* 2008;25:543–549.
5. Dahlin LB, Shyu BC, Danielsen N, Andersson SA. Effects of nerve compression or ischaemia on conduction properties of myelinated and non-myelinated nerve fibres. An experimental study in the rabbit common peroneal nerve. *Acta Physiol Scand.* 1989;136:97–105.
 6. Szabo RM, Gelberman RH, Williamson RV, Dellon AL, Yaru NC, Dimick MP. Vibratory sensory testing in acute peripheral nerve compression. *J Hand Surg.* 1984;9A:104–109.
 7. Thomsen NO, Cederlund R, Speidel T, Dahlin LB. Vibrotactile sense in patients with diabetes and carpal tunnel syndrome. *Diabet Med.* 2011;28:1401–1406.
 8. Thomsen NO, Cederlund R, Rosen I, Bjork J, Dahlin LB. Clinical outcomes of surgical release among diabetic patients with carpal tunnel syndrome: prospective follow-up with matched controls. *J Hand Surg Am.* 2009;34:1177–1187.
 9. Goldberg JM, Lindblom U. Standardised method of determining vibratory perception thresholds for diagnosis and screening in neurological investigation. *J Neurol Neurosurg Psychiatry.* 1979;42:793–803.
 10. Lundborg G, Lie-Stenstrom AK, Sollerman C, Stromberg T, Pyykko I. Digital vibrogram: a new diagnostic tool for sensory testing in compression neuropathy. *J Hand Surg.* 1986;11:693–699.
 11. England JD, Gronseth GS, Franklin G, et al. Distal symmetric polyneuropathy: a definition for clinical research: report of the American Academy of Neurology, the American Association of Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. *Neurology.* 2005;64:199–207.
 12. Tankisi H, Pugdahl K, Fuglsang-Frederiksen A, et al. Pathophysiology inferred from electrodiagnostic nerve tests and classification of polyneuropathies. Suggested guidelines. *Clin Neurophysiol.* 2005;116:1571–1580.
 13. Thomsen NOB, Andersson GS, Bjork J, Dahlin LB. Neurophysiological recovery 5 years after carpal tunnel release in patients with diabetes. *Muscle Nerve.* 2017;56:E59–E64.
 14. Lundstrom RJ. Responses of mechanoreceptive afferent units in the glabrous skin of the human hand to vibration. *Scand J Work Environ Health.* 1986;12:413–416.
 15. Johansson RS, Vallbo AB. Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *J Physiol.* 1979;286:283–300.
 16. Rempel D, Dahlin L, Lundborg G. Pathophysiology of nerve compression syndromes: response of peripheral nerves to loading. *J Bone Joint Surg Am.* 1999;81:1600–1610.
 17. Lang E, Spitzer A, Pfanmuller D, Claus D, Handwerker HO, Neundorfer B. Function of thick and thin nerve fibers in carpal tunnel syndrome before and after surgical treatment. *Muscle Nerve.* 1995;18:207–215.
 18. Thomsen NO, Mojaddidi M, Malik RA, Dahlin LB. Reduced myelinated nerve fibre and endoneurial capillary densities in the forearm of diabetic and non-diabetic patients with carpal tunnel syndrome. *Acta Neuropathol.* 2009;118:785–791.
 19. Mojaddidi MA, Ahmed MS, Ali R, et al. Molecular and pathological studies in the posterior interosseous nerve of diabetic and non-diabetic patients with carpal tunnel syndrome. *Diabetologia.* 2014;57:1711–1719.
 20. Dahlin LB, Rix KR, Dahl VA, et al. Three-dimensional architecture of human diabetic peripheral nerves revealed by X-ray phase contrast holographic nanotomography. *Sci Rep.* 2020;10:7592.
 21. Schmid AB, Bland JD, Bhat MA, Bennett DL. The relationship of nerve fibre pathology to sensory function in entrapment neuropathy. *Brain.* 2014;137:3186–3199.
 22. Peltier AC, Myers MI, Artibee KJ, et al. Evaluation of dermal myelinated nerve fibers in diabetes mellitus. *J Peripher Nerv Syst.* 2013;18:162–167.
 23. Lin YH, Hsieh SC, Chao CC, Chang YC, Hsieh ST. Influence of aging on thermal and vibratory thresholds of quantitative sensory testing. *J Peripher Nerv Syst.* 2005;10:269–281.
 24. Dahlin E, Ekholm E, Gottsater A, Speidel T, Dahlin LB. Impaired vibrotactile sense at low frequencies in fingers in autoantibody positive and negative diabetes. *Diabetes Res Clin Pract.* 2013;100:e46–50.
 25. Lindholm E, Londahl M, Fagher K, Apelqvist J, Dahlin LB. Strong association between vibration perception thresholds at low frequencies (4 and 8 Hz), neuropathic symptoms and diabetic foot ulcers. *PLoS One.* 2019;14:e0212921.
 26. Ablove RH, Moy OJ, Peimer CA, Wheeler DR, Diao E. Pressure changes in Guyon's canal after carpal tunnel release. *J Hand Surg Br.* 1996;21:664–665.
 27. Ginanneschi F, Filippou G, Reale F, Scarselli C, Galeazzi M, Rossi A. Ultrasonographic and functional changes of the ulnar nerve at Guyon's canal after carpal tunnel release. *Clin Neurophysiol.* 2010;121:208–213.
 28. Swenson JD, Hutchinson DT, Bromberg M, Pace NL. Rapid onset of ulnar nerve dysfunction during transient occlusion of the brachial artery. *Anesth Analg.* 1998;87:677–680.
 29. Thomsen NO, Cederlund RI, Andersson GS, Rosen I, Bjork J, Dahlin LB. Carpal tunnel release in patients with diabetes: a 5-year follow-up with matched controls. *J Hand Surg Am.* 2014;39:713–720.

How to cite this article: Thomsen NO, Dahlin LB. Vibrotactile sense 5 years after carpal tunnel release in people with diabetes: A prospective study with matched controls. *Diabet Med.* 2021;38:e14453. <https://doi.org/10.1111/dme.14453>