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RESEARCH ARTICLE

Influence of Risk Factors and Diabetic Complications on Peripheral Nerve Function in Type 2 Diabetes Mellitus

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Objective: The aim of this study was to evaluate the impact of age, diabetes duration, glycaemic control, existence of cardiac autonomic neuropathy (CAN), retinopathy and of macroangiopathy on the peripheral nerve function in patients with type 2 diabetes.
Methods: One hundred forty-nine type 2 diabetes mellitus patients were assessed with peripheral motor and sensory nerve conduction tests and cardiovascular reflex tests, as well as being evaluated for retinopathy, common carotid artery intimal-media-thickness (IMT) and ankle-brachial index (ABI).
Results: The duration of diabetes has the strongest effect in the reduction of the amplitude of motor response in the peroneal nerve and of the sensory amplitude in the sural nerve. The strongest correlations were found between glycaemic control and decreasing motor amplitude in the median nerve and sensory amplitude in the sural nerve, respectively. The motor and sensory nerve action potential amplitudes were significantly affected in the group of patients with CAN. According to multivariate logistic regression analysis, duration of diabetes and presence of CAN were the most important factors that influenced the motor and sensory nerve function.
Conclusion: The presence of CAN together with diabetes duration and poor glycaemic control were associated with impaired peripheral nerve function, while macroangiopathy does not seem to be associated with the impairment of these electrophysiological parameters.

Keywords: electrophysiological parameters, motor and sensory nerve function, cardiac autonomic neuropathy, glycaemic control, diabetes duration, macroangiopathy

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Introduction

Neuropathy is one of the earliest and most common chronic complications of diabetes. Diabetic neuropathy is a complex disorder, as it is associated with a large spectrum of clinical abnormalities reflecting the variable damage of small and large fibres. Most common among the diabetic neuropathies are diabetic sensorimotor polyneuropathy (DSPN) and autonomic neuropathies. Cardiovascular autonomic neuropathy (CAN) is one of the most ignored of all serious complications of diabetes [1,2,3].

Different neurophysiological tests are required to identify dysfunction of different nerve fibers in diabetes. For assessing large myelinated fibres function, nerve conduction studies (NCS) are considered as an early and reliable indicator of the presence and severity of nerve damage in diabetes. Damage to small thinly unmyelinated nerves or autonomic fibres (Aδ and C fibres) can be assessed by cardiac autonomic testing [4].

Conclusive clinical evidence from randomized prospective trials supports a central role for hyperglycaemia in the pathogenesis of CAN and DSPN, although other metabolic and vascular factors contribute to the disease state [5].

Despite the long-recognized association between clinical features of DSPN and CAN in diabetic patients, there is still controversy regarding the relationship between somatic and autonomic nerve damage in this type of patient. Given the increasing number of patients with diabetic complications worldwide, there is no doubt that a better understanding of these complications is very important for improving the diagnosis of and treatment strategies for these patients.

The purpose of this study was to determine the influence of age, diabetes duration, glycaemic control, the existence of CAN, retinopathy (marker of microvascular complications) and of macrovascular complications on the electrophysiological parameters of motor and sensory nerve fiber in type 2 diabetic patients. So far the potential association between the existence of cardiac autonomic damage and the electrophysiological parameters assessing the function of motor and sensory fibres has not been extensively investigated.

Material and methods

This was a prospective study on 149 consecutive patients with type 2 diabetes mellitus from Diabetes and Neurology Department's of the Mures University Hospital (Tîrgu Mures, Romania). All study subjects presented the American Diabetes Association (ADA) criteria for definition of type 2 diabetes. Patients with other ethiologies of neuropathy or presenting cardiac arrhythmia, clinically manifest coronary artery disease, thyroid diseases (hypo- or hyper-

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thyroidism), hypo- or hyperglycaemia in the previous 24h, any kind of acute illness, severe systemic disease such as cardiac, pulmonary or kidney insufficiency and patients who were on medication with effects the autonomic nervous system, were eexcluded from the study group [3]. This study protocol was approved by the University of Medicine and Pharmacy Targu Mures Review Board, and all participants gave their written informed consent.

All patients were evaluated with a complete physical and neurological examination. High-performance liquid chromatography technique was used for assessing the levels of glycated haemoglobin (HbA1c), using a reference rage of 4.1-6.0 for non-diabetic patients.

An independent ophthalmologist assessed the presence and severity of diabetic retinopathy and we classified without retinopathy those patients with normal fundoscopy and pre-proliferative retinopathy, and with retinopathy patients with proliferative retinopathy.

An electroneurographic protocol was used for NCS, and standard techniques were used for assessment of nerve conduction, measurements being performed bilaterally on the median, ulnar, peroneal, tibial and sural nerves, based on conventional NCS methods with surface electrodes [6, 7]. In the motor nerves we assessed the motor nerve conduction velocities (MNCV), compound muscle action potential amplitudes (CMAP), and distal motor latencies (DML), the amplitudes of the responses being measured from baseline to the negative peak of the CMAPs, while in the sensory nerves we assessed conduction velocities (SNCV), sensory nerve action potential amplitudes (SNAP) and distal sensory latencies (DSL), the amplitudes of the responses being measured from peak to peak of the SNAPs. Latencies and amplitude values were read from the equipment after accurate cursor placement was ensured. A supramaximal stimulation of 0.1 ms duration was delivered for all the motor NCS. The SNAPs were recorded by antidromic techniques, using 0.1 ms stimulus duration. NCS were typically performed bilaterally with mean values used in statistical analyses [7].

Assessment of CAN was performed according to Ewing's method, based on a complex of five non-invasive autonomic tests: the blood pressure response to postural change from lying to standing and to sustained handgrip and the heart rate variation in response to slow deep breathing, to Valsalva maneuver or to a postural change from lying to standing [8]. Heart rate variation was analysed using an ELI 250 electrocardiograph system (Research Technology Inc.) and was based on determination of R-R intervals on surface Electrocardiogram. The results of the deep-breathing test were interpreted according to normal age-related values [9, 10]. In the context of at least two abnormal standard tests the patients were classified as CAN+ [11].

The common carotid artery intima-media thickness (CCA-IMT) was assessed using carotid ultrasonography (Siemens Accuson Antares Ultrasound System) on both common carotid arteries with a linear array 5-mHz transducer as reported previously [12], and the ankle-brachial index (ABI) was assessed using a hand-held 5-mHz Doppler device (HI Dop Vascular Doppler set) in all patients.

Statistical analyses were performed using MedCalc Software (Version 12.3.0 bvba, Mariakerke, Belgium). Data were considered as nominal or quantitative variables. Nominal variables were characterized using frequencies. Quantitative variables were tested for normality of distribution using Kolmogorov–Smirnov test and were characterized by median and percentiles (25–75%) or by mean and standard deviation (SD), when appropriate. Student's t-tests were used to assess differences between continuous variables (expressed as mean ± SD). The correlation between quantitative variables was assessed using Pearson correlation. Multivariate analysis was carried out using linear regressions. We used electrophysiological parameters as a dependent variable. A significance level of 0.05 was used for all analyses, and all p values reported are two-tailed.

Results

From 149 patients, 80 were female (53.7%) and 69 (46.3%) were male. *Table I* summarizes the clinical characteristics of the patient group.

Table I. Characteristics of the patient group

	N	Minimum	Maximum	Mean	Std. Deviation
Age of patients (years)	149	33	77	58,32	8,392
Age at DM diagnosis (years)	149	22	74	50,09	9,491
Duration of diabetes (years)	149	0	37	8,22	6,964
HbA1c (%)	149	5,6	14,0	8,357	1,4605
ABI	149	0,65	1,45	0,9589	0,1328
CCA-IMT (mm)	149	0,6	1,5	0,913	0,1965

Influence of patient's age, duration of diabetes and glycemic control

The relationship between electrophysiological parameters and examined risk factors was first investigated by univariate correlation analysis. From all 21 electrophysiological parameters of motor and sensory conduction studied, we found that there was a significant negative correlation between duration of diabetes and amplitude of motor and sensory action potential in all investigated nerves. The most important correlations were found between the duration of diabetes and CMAP in the peroneal nerve (r^2= -0.67, p-0.0001) for motor nerves, and between the duration of diabetes and SNAP in the sural nerve (r^2= -0.59, p-0.0001) for sensory nerves (*Table II*).

Nerve conduction velocities were significantly negative correlated with diabetes duration only in the tibial nerve (r= -0.51, p-0.0001) and in the sensory ulnar nerve (r= -0.47, p-0.0001).

Table II. Univariate correlations of the electrophysiological parameters with age and duration of diabetes

Electrophysiological Parameters		Age of patients		Diabetes Duration	
		Correlation coefficient r	P value	Correlation coefficient r	P value
Median nerve (motor)	DL (msec)	0.09	0,23	0,41	0,0001
	CMAP(mV)	-0,08	0,30	-0,55	0,0001
	MNCV(m/sec)	-0,07	0,37	-0,25	0,001
Ulnar nerve (motor)	DL(msec)	0,12	0,11	0,23	0,004
	CMAP (mV)	-0,11	0,18	- 0,58	0,0001
	MNCV(m/sec)	-0,08	0,30	- 0,42	0,0001
Peroneal nerve	DL(msec)	0,14	0,08	0,21	0,009
	CMAP (mV)	-0,17	0,03	- 0,67	0,0001
	MNCV(m/sec)	-0,04	0,62	- 0,30	0,0002
Tibial nerve	DL(msec)	0,02	0,71	- 0,18	0,02
	CMAP (mV)	-0,17	0,02	- 0,56	0,0001
	MNCV(m/sec)	-0,08	0,33	- 0,51	0,0001
Median nerve (sensory)	DL(msec)	0,13	0,10	0,41	0,0001
	SNAP (μV)	-0,14	0,07	- 0,52	0,0001
	SNCV(m/sec)	-0,12	0,13	- 0,29	0,0001
Ulnar nerve (sensory)	DL(msec)	0,03	0,70	0,13	0,07
	SNAP (μV)	-0,13	0,10	- 0,58	0,0001
	SNCV(m/sec)	-0,17	0,03	- 0,47	0,0001
Sural nerve	DL(msec)	0,01	0,89	0,15	0,07
	SNAP (μV)	-0,04	0,57	-0,59	0,0001
	SNCV(m/sec)	-0,03	0,7	-0,19	0,02

Table III. Multivariate regression analysis of electrophysiological parameters with diabetes duration, age, gender and glycaemic control

Electrophysiological Parameters		Diabetes Duration p-value	Age p-value	Gender p-value	HbA1c p-value
Median nerve (motor)	DL (msec)	<0,0001*	0,86	0,55	0,54
	CMAP (mV)	<0,0001	0,93	0,3	0,007
	MNCV(m/sec)	0,002	0,55	0,62	0,04
Ulnar nerve (motor)	DL (msec)	0,01	0,26	0,51	0,63
	CMAP (mV)	<0,0001	0,88	0,04	0,13
	MNCV (m/sec)	<0,0001	0,72	0,52	0,007
Peroneal nerve	DL (msec)	0,03	0,18	0,83	0,23
	CMAP (mV)	<0,0001	0,32	0,12	0,02
	MNCV (m/sec)	0,0001	0,68	0,69	0,11
Tibial nerve	DL (msec)	0,02	0,54	0,96	0,72
	CMAP (mV)	<0,0001	0,12	0,02	0,01
	MNCV (m/sec)	<0,0001	0,92	0,96	0,001
Median nerve (sensory)	DL (msec)	<0,0001	0,43	0,99	0,03
	SNAP (μV)	<0,0001	0,42	0,32	0,0002
	SNCV (m/sec)	0,21	0,54	0,28	0,0001
Ulnar nerve (sensory)	DL (msec)	0,16	0,87	0,32	0,27
	SNAP (μV)	<0,0001	0,42	0,17	0,0003
	SNCV(m/sec)	<0,0001	0,23	0,22	0,41
Sural nerve	DL (msec)	0,11	0,99	0,7	0,03
	SNAP (μV)	<0,0001	0,77	0,18	0,0001
	SNCV (m/sec)	<0,02	0,83	0,76	0,11

Multivariate analyses: When gender, age, duration of diabetes and glycaemic control were introduced into the model as independent variables, and electrophysiological parameters (DL, NCV, CMAP and SNAP) as dependent variables, we found that 18 electrophysiological parameters correlated significantly with diabetes duration, 12 with glycaemic control, only 2 with gender of patients and none with age of patients. CMAP and SNAP in all nerves were correlated significantly with diabetes duration, but the most important correlation was found for CMAP in the peroneal nerve (r^2=0,47, p<0,0001) and for SNAP in the sural nerve (r^2=0.45, p<0.0001).

The amplitude of motor response in median, tibial and peroneal motor nerves were significantly correlated with glycaemic control, but the most important correlation was with CMAP in the median nerve (r^2=0,43, p-0,007). The amplitude of sensory response in all investigated nerves was significantly correlated with glycaemic control, but the most important correlation was found between glycaemic control and SNAP in the sural nerve (r^2=0.45, p-0.0001) (*Table III*).

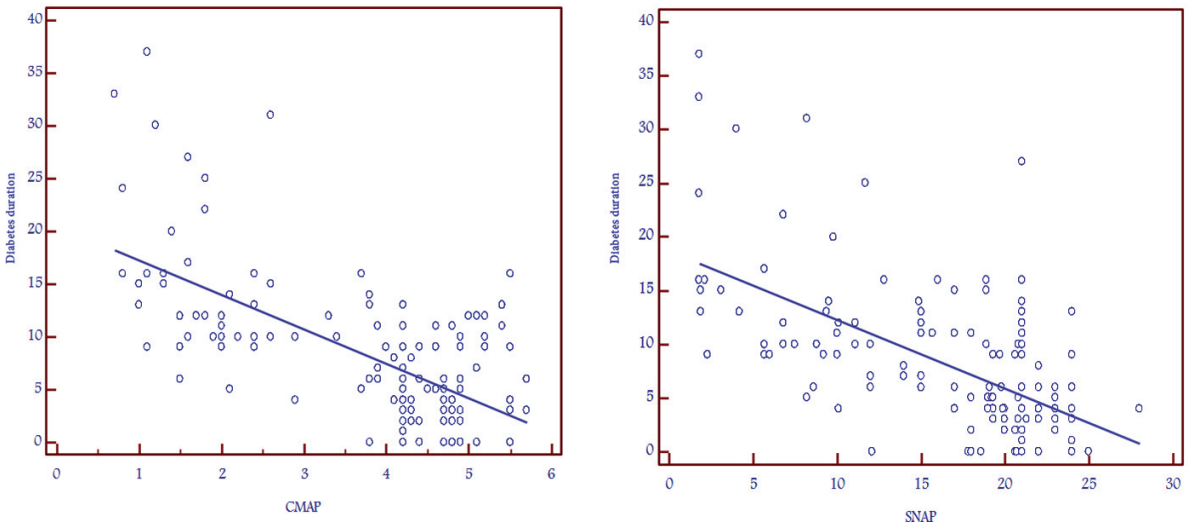

Fig. 1. Correlation between duration of diabetes and CMAP on peroneal nerve (left) and SNAP on sural nerve (right)

Influence of the presence of diabetic complications

The relationship between electrophysiological parameters of motor and sensory nerve function and the existence of CAN was investigated by univariate analysis. CMAP in all motor nerves and SNAP in all sensory nerves were significantly affected in the group of patients with CAN (p-0.0001). MNCV and SNCV were significantly low in all motor nerves and sensory nerves (except in the sural nerve) in the patients group with CAN (*Table IV*).

Multivariate analyses When duration of diabetes, CCA-IMT, ABI, presence of retinopathy and CAN were introduced into a model as independent variables, and electrophysiological parameters of motor and sensory conduction as dependent variables, we found that duration of diabetes and presence of CAN were independent predictors for impairment of nerve conduction in patients with type 2 diabetes. Among electrophysiological parameters only CMAP and SNAP in all nerves correlated significantly with duration of diabetes and with presence of CAN. The most important association for motor nerves was found between CMAP in the peroneal nerve and the presence of CAN (r^2=0.51, p<0.0001), and between SNAP in all sensory nerves and the presence of CAN (p<0.0001).

There was no significant correlation between electrophysiological parameters and ABI, IMT (markers of macroangiopathy) and retinopathy (marker of microangiopathy) (*Table V*).

Table IV. A comparison of electrophysiological parameters in patients with and without cardiac autonomic neuropathy

Electrophysiological Parameters		With CAN Mean ±SD	Without CAN Mean ±SD	Difference between average	p- value
Motor median nerve	DL(msec)	3,8±0,37	3,3±0,59	0,48	0,0001
	CMAP(mV)	5,2±1,36	8,3±2,1	3,06	0,0001
	MNCV(m/sec)	50,1±4,5	52,04±3,2	1,9	0,003
Motor ulnar Nerve	DL(msec)	2,9±0,5	2,7±0,43	0,21	0,007
	CMAP(mV)	5,7±1,3	8,8±1,7	3,01	0,0001
	MNCV(m/sec)	51,5±2,2	54,5±3,6	3,02	0,0001
Peroneal nerve	DL(msec)	4,3±0,29	4,1±0,35	0,27	0,0001
	CMAP(mV)	2,4±0,46	4,5±0,66	2,1	0,0001
	MNCV(m/sec)	41,2±2,9	43,3±1,7	2,1	0,0001
Tibial nerve	DL(msec)	4,9±0,44	5,1±0,17	0,12	0,01
	CMAP (mV)	5,2±2,3	9,4±2,3	4,12	0,0001
	MNCV(m/sec)	41,9±3,5	45,1±2,3	3,2	0,0001
Sensory median nerve	DL(msec)	2,9±0,61	2,4±0,63	0,55	0,0001
	SNAP(μV)	10,6±4,9	19,9±3,2	9,32	0,0001
	SNCV(m/sec)	47,8±6,2	51,8±4,1	4,02	0,0001
Sensory ulnar nerve	DL(msec)	2,7±1,1	2,3±0,58	0,42	0,003
	SNAP(μV)	10,15±3,6	16,1±2,7	5,9	0,0001
	SNCV(m/sec)	50,9±3,16	53,3±2,4	2,3	0,0001
Sural nerve	DL(msec)	2,46±0,25	2,31±0,33	0,14	0,009
	SNAP(μV)	5,2±1,9	11,5±3,66	6,2	0,0001
	SNCV(m/sec)	42,8±2,3	43,5±2,7	0,65	0,16

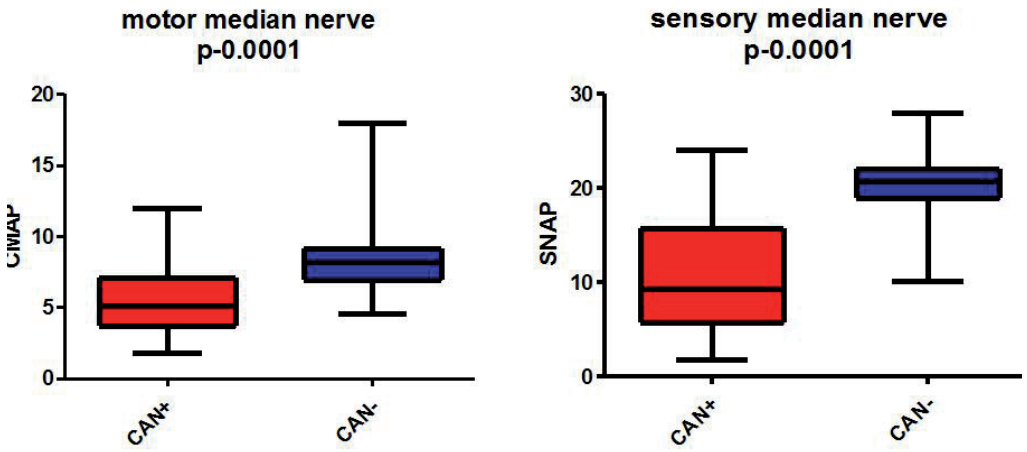

Fig. 2. Relation between CAN and CMAP /SNAP on median nerve

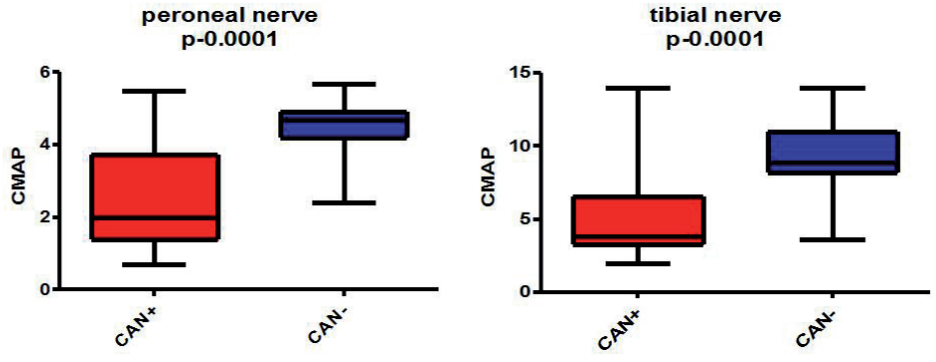

Fig. 3. Relation between CAN and CMAP on peroneal nerve and tibial nerve

Table V. Multivariate regression analysis of electrophysiological parameters with duration of diabetes, retinopathy, CAN, ABI and CCA-IMT.

Electrophysiological Parameters		Diabetes duration	Retino-pathy	CAN	ABI	CCA-IMT
Motor median nerve	DL(msec)	0,05	0,6	0,05	0,62	0,9
	CMAP(mV)	0,007	0,35	0,006	0,33	0,84
	MNCV(m/sec)	0,35	0,48	0,52	0,89	0,37
Motor ulnar nerve	DL(msec)	0,32	0,22	0,21	0,7	0,45
	CMAP(mV)	0,002	0,49	<0,0001	0,07	0,19
	MNCV(m/sec)	0,11	0,89	0,1	0,02	0,17
Pero-neal nerve	DL(msec)	0,1	0,35	0,05	0,63	0,77
	CMAP(mV)	0,0002	0,62	<0,0001	0,07	0,63
	MNCV(m/sec)	0,14	0,38	0,04	0,08	0,87
Tibial nerve	DL(msec)	0,13	0,66	0,15	0,67	0,08
	CMAP (mV)	0,01	0,38	0,002	0,26	0,29
	MNCV(m/sec)	0,0003	0,31	0,26	0,15	0,4
Sensory median nerve	DL(msec)	0,03	0,3	0,13	0,96	0,75
	SNAP(μV)	0,0007	0,22	<0,0001	0,36	0,06
	SNCV(m/sec)	0,47	0,15	0,11	0,94	0,58
Sensory ulnar nerve	DL(msec)	0,73	0,62	0,03	0,42	0,82
	SNAP(μV)	0,001	0,75	<0,0001	0,06	0,19
	SNCV(m/sec)	0,0005	0,62	0,47	0,08	0,97
Sural nerve	DL(msec)	0,87	0,65	0,17	0,14	0,9
	SNAP(μV)	0,007	0,7	<0,0001	0,62	0,58
	SNCV(m/sec)	0,06	0,3	0,34	0,94	0,09

Data are means ±SD.
ABI: Ankle-Brachial Index, CCA-IMT: common carotid artery intima-media thickness

Discussion

Diabetic neuropathy is the most common and troublesome complication of diabetes mellitus, leading to great morbidity and mortality among these patients. Diabetic distal symmetric polyneuropathy (DSPN) is the most common form of diabetic neuropathy. Nerve conduction studies (NCS) represent the gold standard for diagnosing diabetic neuropathy, because is known to be a sensitive, objective and quantitative indicator regarding the presence and severity of sensory and motor nerve damage in patients with diabetes. Electrophysiological test results provide the most accurate diagnosis of DSPN and are the most consistent indicator of subclinical neuropathy. Expert panels for the definition of DSPN recommend evaluation of NCS as a diagnostic criteria for DSPN [2, 11, 13, 14].

The purpose of this study was to determine the association between peripheral nerve function and age of patients, risk factors for the development of neuropathy (glycaemic control and diabetes duration), existence of retinopathy and cardiac autonomic neuropathy (as indicators of microangiopathy) and CCA-IMT, ABI (as indicators of macroangiopathy).

Our observations that the motor and sensory nerves of the lower extremities are most affected in patients with type 2 diabetes are supported by previous data [15]. Our data shows that among all electrophysiological parameters, the amplitude of motor response in the peroneal nerve and the amplitude of sensory response in the sural nerve were the most affected by the duration of diabetes. This confirmed that DSPN is a distal axonopathy of the dying-back type and the dysfunction is correlated with the length of these nerves. The fact that the amplitudes of nerve responses were the most affected electrophysiological parameter suggests that the axonal degeneration and failure of axonal regeneration is the primary mechanism for nerve damage in diabetes [14, 16].

This study demonstrates that impairment of sensory and motor electrophysiological parameters correlated with the duration of type 2 diabetes, and multivariate analysis showed that duration of diabetes and glycaemic control were independent predictors for the impairment of nerve conduction parameters. Duration of diabetes was a stronger predictor for impairment of electrophysiological parameters than glycaemic control (18 parameters affected versus 12 parameters affected). Pirart, in a study on 4400 diabetic patients followed up for 25 years, demonstrated that prevalence of neuropathy was dependent on the duration of diabetes and on the quality of diabetes control, independent of the age of the patients [17]. Our results are in line with those reported by other authors, namely that the severity of diabetic neuropathy expressed by electrophysiological parameters was significantly related with duration of diabetes mellitus and with metabolic control [18, 19, 20].

The UK Prospective Diabetes Study (UKPDS) confirmed that the progression of neuropathy was dependent on glycaemic control and the thight metabolic control can reduce the prevalence of neuropathy [21]. Longitudinal data from follow-up studies suggest that duration of diabetes and severity of hyperglycaemia correlated with the severity of neuropathy. The subsequent analysis of data from the UKPDS study showed that even minor reductions of HbA1c levels are beneficial in reducing the risk of microvascular complications, including neuropathy [5, 22, 23, 24].

Increased levels of blood glucose in the past increased the risk of subsequent diabetic complications. So, if glycaemic control was poor in the early years of diabetes, despite later adequate metabolic control, the rate of diabetic complications will not decrease [25]. The difference observed in our study with regards to the fact that the duration of diabetes had a greater influence on impaired electrophysiological parameters than glycaemic control assessed by HbA1c levels, can be explained by the fact that at the time of diagnosis of type 2 diabetes, hyperglycaemia has already been present for a long time without causing signs and symptoms, and consequently has not been recognized and treated. This asymptomatic period may create the basis for subsequent damage of peripheral nerves. This phenomenon is known as 'hyperglycaemic memory' or 'metabolic memory' and explains by epigenetic changes why poor metabolic control has long-term effects [26].

There are few data in the literature regarding the association between electrophysiological parameters assessing motor and sensory fibres function and cardiovascular autonomic neuropathy in diabetes. In our study we observed that there was a significant difference between the means of electrophysiological parameters in the group with CAN in comparison to the group without CAN. This concomitant damage of the somatic and autonomic nerve fibers suggests that there is a common pathophysiological mechanism of damage to these different types of fibers. Duration of diabetes and degree of metabolic control are considered as risk factors for the development of both autonomic and distal neural damage in diabetic polyneuropathy. These results contradict those reported by Toyry et al, who described that the development of the somatic and autonomic neuropathy is divergent in type 2 diabetes, suggesting the existence of a different pathophysiological mechanism, but Toyry included only newly diagnosed non-insulin-dependent diabetic patients [27].

The multivariate analysis of our data demonstrated an independent association between the presence of CAN and impaired sensitive and motor electrophysiological parameters. A close association was observed between the SNAP in all investigated sensory nerves and the presence of CAN. This relationship suggests that the sensory axonal damage correlates with impaired cardiovascular autonomic function, both manifestations of diabetic microangiopathy. Our results support the idea that there is no difference in the vulnerability of autonomic and somatic nerve fibres to hyperglycaemia in patients with diabetes, and there are likely similar susceptibilities of the autonomic (small, less myelinated) and somatic (large, myelinated) nerve fibers to hyperglycaemia.

The results from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study demonstrated at a level of medicine-based evidence that cardiac autonomic dysfunction and neuropathy are powerful predictors of risk of mortality, and that patients with cardiac and somatic neuropathy represent a high-risk group in which aggressive diabetes treatment strategies have to be weighed against the mortality risk [28, 29] . In light of these results, identification of the presence of neuropathy (somatic and autonomic) should become a priority. Because functional changes in the peripheral large myelinated and in cardiac autonomic fibres are already detectable in asymptomatic patients it becomes extremely important to conduct an electrophysiological evaluation in order to diagnose these complications.

There was not a significant relationship between impairment of peripheral nerve function and ABI, respectively CCA-IMT, as indicators of macroangiopathy in type 2 diabetes. These data are not consistent with those reported by Valensi et al. [19]. Microangiopathy and macroangiopathy frequently coexist in diabetes mellitus, because both are vascular complications which share the same risk factors. Papanas et al. demonstrated that ABI was significantly lower in diabetics with microvascular complications [30]. Diabetes induces not only structural changes in the arterial wall, such as increased IMT and accelerated atherosclerosis, but also functional changes such as arterial stiffness. Arterial stiffness can cause inversely increased ABI values due to incompressible vessels [31]. In this study we did not exclude patients with medial artery calcification (ABI ≥1.3) from the statistical analysis, and this could be a possible explication of the insufficient strength of our statistical data. Carotid IMT is accepted as a marker of early atherosclerosis [32]. Functional disturbances rather than structural processes within the vascular system can explain why the early phase of atherosclerotic changes does not correlate with the impairment of peripheral nerve function in patients with type 2 diabetes.

Conclusions

This study showed that in this group of patients with type 2 diabetes, the duration of diabetes and glycaemic control in addition to the presence of cardiac autonomic dysfunction are associated with impaired electrophysiological parameters of sensory and motor fibers. This finding supports that there is a high degree of coexistence of somatic and cardiac autonomic neuropathy in diabetes, implying that a combined assessment of the two different types of peripheral nerve damage in diabetes is necessary. In order to reduce mortality and to use correct treatment strategies with these patients both these complications must be diagnosed, even in asymptomatic patients.

Competing interests

The authors declare that they have no competing interests.

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