

CORRELATION BETWEEN CARDIOVASCULAR AUTONOMIC NEUROPATHY AND DISTAL SYMMETRIC POLYNEUROPATHY IN TYPE 2 DIABETES

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ABSTRACT

Objective: To study whether HR variability might be impaired before the clinician becomes aware for the presence of PNP and to define the correlation between CAN and PNP in type 2 diabetes.

Patients and method: 212 type 2 diabetic patients were examined by 5 autonomic reflex tests: 1. deep breathing test 2. Valsalva test; 3. heart rate response during stand test; 4. orthostatic blood pressure response; 5. diastolic blood pressure response during isometric exercise. PNP was diagnosed Michigan screening test.

Results: More than half the patients without evidence of PNP were diagnosed as subclinical CAN and almost 3/4 of patients with evidence of PNP had autonomic impairment.

We found a good correlation between CAN and PNP ($p=0.0017$).

Conclusion:

1. CAN may develop first and independent from PNP in type 2 diabetes.
2. Evidence of one type of neuropathy increases the risk for the other type of neuropathy.
3. Periodical survey of neurological involvement should include autonomic function testing besides the well known practice of screening for somatic neuropathy in diabetes.

Key words: diabetic autonomic neuropathy, cardiovascular autonomic neuropathy, chronic distal symmetric polyneuropathy, autonomic function tests

BACKGROUND

Chronic sensory-motor distal symmetric polyneuropathy (PNP) and autonomic neuropathy are the most common forms of involvement of peripheral nervous system in diabetes (1). Early recognition of PNP may result in a reduced incidence of foot ulceration and consequently amputation (2), and its annual screening by examining pinprick, temperature and vibration perception and ankle reflexes is already a well-known practice. Diabetic autonomic neuropathy (DAN), particularly cardiovascular autonomic neuropathy (CAN), substantially increases morbidity and mortality in diabetic patients (3,4,5). As patient's history and physical examination are ineffective for early detection of

CAN, noninvasive tests that have demonstrated efficacy are required. Patients should be screened for signs of autonomic dysfunction at the time of diagnosis in type 2 diabetes and within 5 years after diagnosis in type 1 diabetes (unless an individual has symptoms suggestive of autonomic dysfunction earlier) (6). The obtained values serve as baseline and autonomic function testing should be regularly done afterwards, enabling early detection of CAN and therapeutic interventions. It was demonstrated that tight metabolic control, lowering body weight, regular physical exercise results in improving the results of autonomic function tests (7) in early stages of involvement. Medication (aldose reductase-inhibitors (8), beta-blockers (9), ACE inhibitors (10) may also improve heart rate variability.

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Several studies report that worsening of autonomic function tests was not correlated with electrophysiology of somatic fibers (11), postulating that the 2 forms of neuropathy follow different pathways. Other authors, Weinberg and Pfeiffer (12) report that presence of DAN has a predictive value for somatic neuropathy.

The objective of this study was to explore whether HR variability might be impaired before the clinician becomes aware for the presence of PNP and to define the correlation between CAN and PNP in type 2 diabetes.

PATIENTS AND METHOD

Two hundred twelve type 2 diabetic patients (49% men), ages 20-80 years (mean age: 52+-5.10 years), diabetes duration 0-33 years (mean duration: 7.26 years, SD=6.45) were examined by 5 autonomic reflex tests: 1.deep breathing test 2.Val-salva test; 3.heart rate response during stand test; 4.orthostatic blood pressure response; 5.dyastolic blood pressure response during isometric exercise. PNP was diagnosed by examining pinprick, temperature, a 10 g monofilament pressure sensation at

the distal halluces, vibration perception (by using a 128 Hz tuning-fork), and ankle reflexes. Nondiabetic causes of neuropathy were excluded. A conventional value of 0/0.5/1 was given to an anormal/ borderline/abnormal value for each test. CAN was defined as a total vegetative score ≥ 2 .

RESULTS

There was an equal distribution according to gender and a normal distribution according to age in the group of type 2 diabetic subjects, Table 1 and Figure 1.

Both CAN and PNP had a high prevalence in type 2 diabetes. Clinical signs of PNP were present in 75.38% cases, Figure 2, and 62.26% patients had impairment of autonomic function tests, Figure 3.

More than half (51,85%) the patients without PNP scored ≥ 2 at autonomic function testing. Regarding the patients who already had evidence of PNP, the prevalence of CAN was higher, 72.45%, Figure 4.

We found a good correlation between CAN and PNP ($p=0.0017$), Table 2.

Table 1. Distribution of cases according to age

Age group	Men		Women		Total	
	No. cases	%	No.cases	%	No.cases	%
<20	0	0	2	1.49	2	0.77
20-30	2	1.59	4	2.99	6	2.31
31-40	20	15.87	4	2.99	24	9.23
41-50	34	26.98	40	29.85	74	28.46
51-60	44	34.92	56	41.79	100	38.46
61-70	22	17.46	26	19.40	48	18.46
71-80	4	3.17	2	1.49	6	2.31
Total	126	100.00	134	100.00	260	100.00

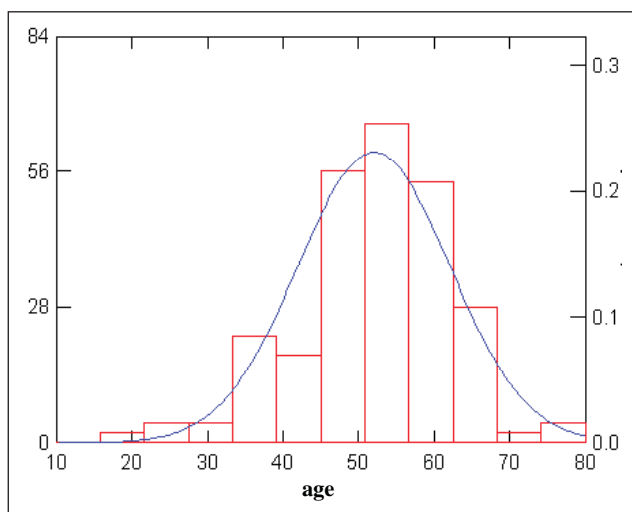


Figure 1. Prevalence of PNP in type 2 diabetes

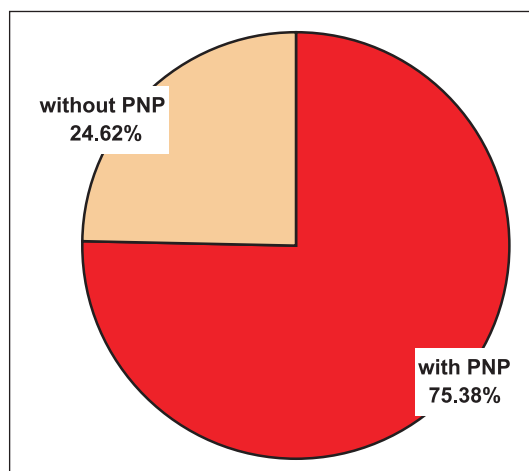


Figure 2. Prevalence of different stages of CAN in type 2 diabetes

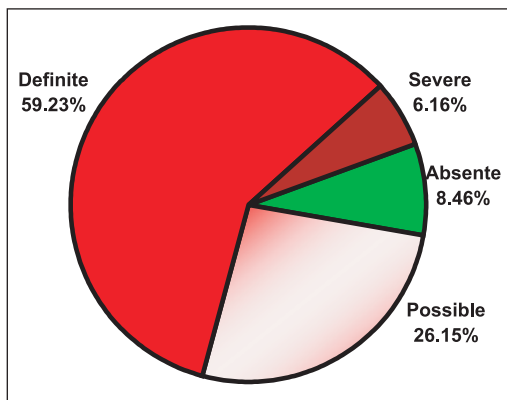


Figure 3. Prevalence of CAN according to the presence of DPN

Table 2

Tested association	PNP – CAN (score ≥ 2) in type 2 diabetes	
test	χ^2	
liberty grades	1	
$\alpha = 0.05$	$\chi^2_{\alpha} = 3.81$	
χ^2	9.8002	
p	0.0017	
OR	2.7	
CI 95% for OR	Min	1.4339
	Max	5.0841
Conclusion	Positive correlation	

DISCUSSION

Our findings are according to studies that report that parasympathetic neuropathy may develop independently from somatic neuropathy (13). We reported a lower prevalence of CAN (51.85%) in patients without PNP, comparatively to other studies (66.7%) (11), but we highlight the important find-

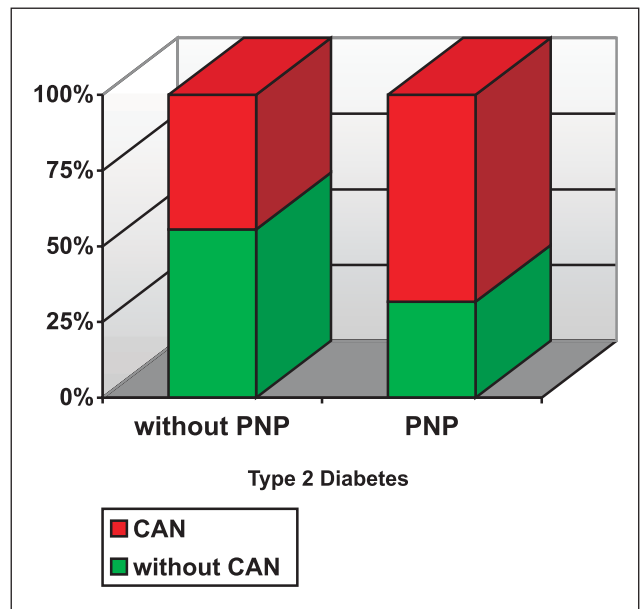


Figure 4. Prevalence of PNP according to different stages of CAN

ing that an important number of patients without clinical evidence of PNP had subclinical impairment of autonomic function.

CONCLUSION

1. CAN may develop first and independent from PNP in type 2 diabetes.
2. Evidence of one type of neuropathy increases the risk for the other type of neuropathy.
3. Periodical survey of neurological involvement should include autonomic function testing besides the well known practice of screening for somatic neuropathy in diabetes.

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