High prevalence of cardiac autonomic neuropathy in patients with diabetic foot disease attending a university hospital diabetic foot clinic.

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Diabetic cardiac autonomic neuropathy (CAN)

- Diabetic CAN is defined as the impairment of autonomic control of the cardiovascular system in diabetes.
- Prevalence of confirmed CAN in unselected people with type 1 and type 2 diabetes is approximately 20%
- Prevalence rates increase (~50-60%) with age and duration of diabetes

V Spallone et al *Diabetes Metab Res Rev 2011*

Clinical manifestations of CAN

- ✓ Sinus tachycardia
- ✓ Reduced exercise tolerance
- ✓ Orthostatic hypotension
- ✓ Silent myocardial ischemia
- ✓ Intraoperative cardiovascular lability

- Presence of CAN increases mortality by 2-3 fold.[2]

- Intensive diabetes therapy/ multifactorial cardiovascular risk intervention retards CAN development in type 1 and type 2 DM respectively[3].

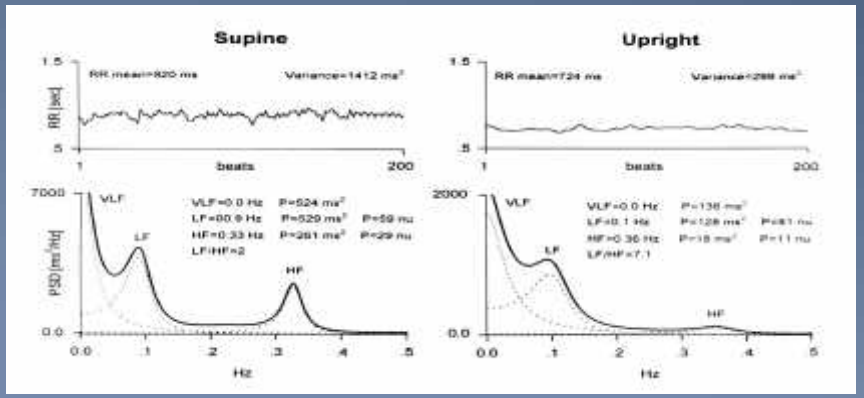
1.Vinik AI et al *Diabetes Care 2003*
2.Maser RE et al *Diabetes Care 2003*
3.Gaede P. Et al NEJM 2008

Cardiovascular autonomic reflex tests (CARTs) assess cardiovascular autonomic function by measuring end-organ response to provocative physiological manoeuvres.

TABLE II—*Normal, borderline, and abnormal values in tests of cardiovascular autonomic function*

	Normal	Borderline	Abnormal
Tests reflecting parasympathetic function			
Heart-rate response to Valsalva manoeuvre (Valsalva ratio)	⩾1·21	1·11–1·20	⩽1·10
Heart-rate (R-R interval) variation during deep breathing (maximum-minimum heart rate)	⩾15 beats/min	11–14 beats/min	⩽10 beats/min
Immediate heart-rate response to standing (30:15 ratio)	⩾1·04	1·01–1·03	⩽1·00
Tests reflecting sympathetic function			
Blood-pressure response to standing (fall in systolic blood pressure)	⩽10 mm Hg	11–29 mm Hg	⩾30 mm Hg
Blood-pressure response to sustained handgrip (increase in diastolic blood pressure)	⩾16 mm Hg	11–15 mm Hg	⩽10 mm Hg

Heart rate variability (HRV) provides information regarding autonomic balance of the cardiovascular system



Background

- Patients with peripheral neuropathy are at enhanced risk of CVD, which is magnified in patients with diabetic foot disease
- Drugs used for the treatment of diabetic foot disease (e.g. anti-biotics,anti-depressants, analgesics for neuropathy) may adversely impact on autonomic state.
- The prevalence of cardiac autonomic dysfunction in patients with diabetic foot disease and variables associated with cardiac autonomic dysfunction is unknown.

Aim

To assess the prevalence of autonomic dysfunction in patients with diabetic foot disease

To determine the clinical/biochemical variables associated with autonomic dysfunction in this cohort of patients

Methods

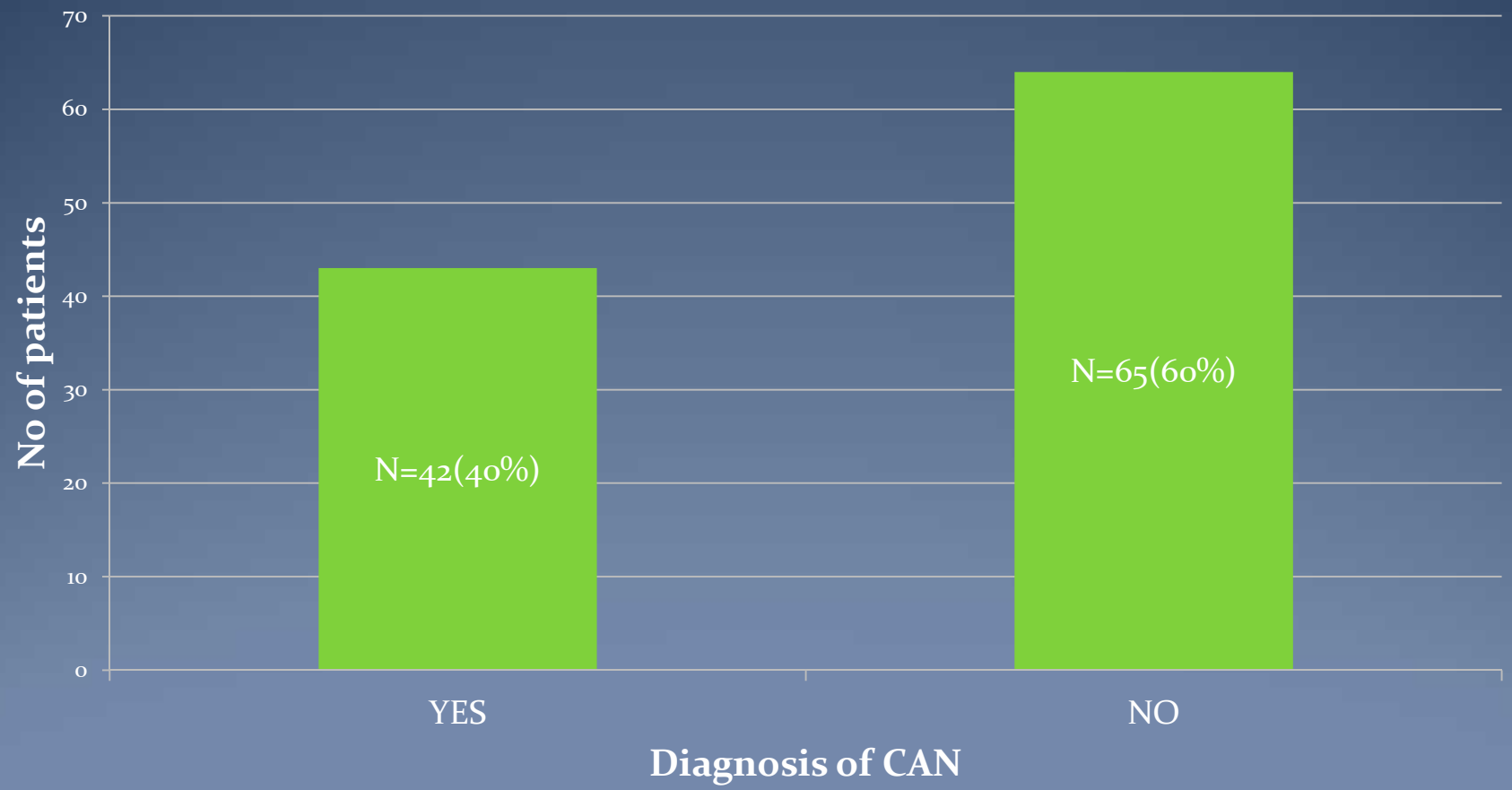
- Cross-sectional study of 107 consecutive patients with diabetes and foot disease (88% active or history of ulcer) attending the specialist foot clinic at Guy's and St Thomas' Hospital, London.
- Cardiovascular autonomic function assessed using the 4 standard CART tests.
- Short-term time-/ frequency-domain measures of HRV were calculated (DiCAN ,Medicore Co,Ltd).
- CAN diagnosis was defined as the presence of at least two abnormal cardiovagal results on CARTs.

Demographic,clinical and biochemical characteristics of the cohort

Variable	n=107
Male	77 (72%)
Age (years)	59 ± 14
T1DM /T2DM	27%/73%
Duration of diabetes (years)	17.7 ± 10
Insulin (T2DM)	33 (66%)
Body mass index (kg/m^2)	29.3 ± 6
SBP (mmHg)	135.5 ± 19.7
DBP (mmHg)	75.3 ± 11
HbA1c (%)	8.5 ± 2
Cholesterol (mmol/l)	4 ± 1
eGFR(ml/min)	77±44
ACR	5.3 (1.6-28.3)

- Values are expressed as mean±SD or IQ range
- ACR=albumin-creatinine-ratio,SBP=systolic blood pressure,DBP=diastolic blood pressure,e-GFR=estimated glomerular filtration rate

Prevalence of CAN in our cohort of patients with diabetic foot disease



- When HRV measures were used for diagnosis prevalence of CAN increased to 55%

Demographic and biochemical characteristics of patients with and without CAN

Variable	CAN+ (42)	CAN- (65)	P value
Male Female	30 (72%) 12 (28%)	30 (78.9%) 8 (21.1%)	0.9
Age (years)	56.5± 14	61 ± 13.7	0.1
T1DM T2DM	13 (31%) 29 (69%)	12 (18%) 53 (82%)	0.47
Duration of diabetes (years)	17.4 ± 10	17.9 ± 11	0.8
Insulin	23 (46%)	27 (54%)	0.68
Body mass index (kg/m^2)	29.1 ± 6.5	29.4± 5.8	0.77
SBP (mmHg)	135 ± 22	135 ± 20	0.95
HbA1c	8.9 ± 2	8.3 ± 1.9	0.15
Cholesterol	4.2± 1.2	3.9 ± 1	0.2
eGFR	72 ± 45	80±44	0.4
Urine ACR	4.6 (1.7-34.3)	5.2 (2.3-22.8)	0.66

SBP=systolic blood pressure,eGFR =estimated glomerular filtration rate, ACR=albumin-creatinine ratio
mean ± SD shown or median (IQ range)

Clinical characteristics of patients with and without CAN

Variable	CAN+ (42)	CAN- (65)	P value
Retinopathy	29 (69)	40 (61)	0.42
Nephropathy	22 (75.9)	23 (60.5)	0.185
Ulcer present	26 (62)	44 (68)	0.13
Amputation	15 (35)	35 (55.3)	0.06
Foot infection	6(14)	14 (22)	0.32
CVD	11 (26)	24(37)	0.25
HTN	23 (55)	44 (67)	0.17
PVD	11 (37.9)	28 (43)	0.13
Dyslipidaemia	15 (35)	28 (43)	0.44

CVD=cardiovascular disease,HTN=hypertension,PVD=peripheral vascular disease
Values expressed as n(%)

Time-domain measures of heart rate variability are associated with insulin and b-blocker use in T2DM patients(n=82)*

Variable	Standard. Beta coefficient	p - value
Age	-0.32	0.023
Gender	-0.13	0.26
Diabetes duration	-0.05	0.71
SBP	-0.27	0.03
HbA1c	0.23	0.1
eGFR	-0.02	0.85
Insulin use	-0.38	0.005
B-blocker use	0.46	0.000

*Multiple linear regression analysis with log-transformed SDNN as dependent variable
Results for r MSSD were similar

Conclusions

- There is a high prevalence of cardiac autonomic neuropathy in patients with diabetic foot disease attending a tertiary referral foot clinic
- There were no significant clinical or biochemical differences between patients with or without CAN.
- CAN is not associated with traditional risk markers.
- Screening for CAN should be considered in these high risk patients.

Thank You for your attention!