

Supplementary Material

High Diagnostic Performance of the Indicator Plaster Neuropad for the Detection of Established Diabetic Autonomic Neuropathy

Ioanna Zografou^{1*}, Panagiotis Doukelis¹, Theocharis Koufakis¹, Evangelia Kotzakioulafi², Polykarpos Evripidou², Zisis Kontoninas², Christos Savopoulos², Michael Doulas¹, Triantafyllos Didangelos² and Konstantinos Kantartzis^{3,4}

Supplementary Table S1. Stratified analysis Neuropad

	Not established DAN (N=95) Group B		Established DAN (n=85) Group A			p
Abnormal CARTs	No	1 abnormal	Mild DAN (2 abnormal)	Moderate DAN (3 abnormal)	Severe DAN (4 abnormal)	
N	57	38	51	24	10	
Gender (M/F)	35/22	16/22	18/32	13/11	5/5	0.107
Age (y)	39.9±15.4	52.5±15.4	53.2±13.4	55.5±13.6	60.1±15.3	<0.001
Diabetes type (1/2)	37/20	14/24	20/31	8/16	3/7	0.011
Diabetes duration (y)	13.8±6.6	17.1±6.6	17.7±7.1	22.7±9.8	20.6±3.1	<0.001
Alcohol (Y/N)	5/52	7/31	3/48	2/22	0/10	0.227
Smoking (Y/N)	44/13	32/6	46/5	22/2	8/2	0.335
Hypertension (Y/N)	51/6	26/12	34/17	12/12	6/4	<0.001
Neuropad (Y/N)	5/52	15/23	42/9	22/2	10/0	<0.001
HbA1c (%)	7.16±1.2	7.5±1.5	7.7±1.3	7.5±1.5	8±0.8	0.081
B12 (pg/mL)	515.9±121.2	511.8±113.6	533.6±148.9	566.2±136.8	523.4±185.7	0.545
MCR	57.8±25.8	19.5±13.4	14.8±7.4	10.9±7.6	9.3±7.5	<0.001
Sd	84.7±48.9	29.5±18.8	25.7±12.3	19.4±12.1	14±12.2	<0.001
Valsalva	1.4±0.2	1.3±0.1	1.22±0.1	1.17±0.1	1.2±0.1	<0.001
Postural index	1.16±0.1	1.09±0.1	1.06±0.1	1.04±0	1.02±0.03	<0.001
Orthostatic hypotension	0.79±2.9	3.6±9	17.9±7.7	26.3±8.8	32.5±11.4	<0.001

P value is from one way ANOVA among the abnormal CARTs. Post hoc tests were performed with Bonferroni correction.

The following tables depict the post hoc test with Bonferroni correction. Significant results are presented in bold.

Supplementary Table S2. Comparisons between abnormal CARTs (0 abnormal vs 1,2,3,4 abnormal CARTs)

	Not established DAN (N=95) Group B			Established DAN (n=85) Group A								
Abnormal CARTs	No	1 abnormal	p	No	Mild DAN (2 abnormal)	p	No	Moderate DAN (3 abnormal)	p	No	Severe DAN (4 abnormal)	p
N	57	38		57	51		57	24		57	10	
Gender (M/F)	35/22	16/22	0.02	35/22	18/32	0.48	35/22	13/11	0.036	35/22	5/5	0.55
Age (y)	39.9±15.4	52.5±15.4	<0.001	39.9±15.4	53.2±13.4	<0.001	39.9±15.4	55.5±13.6	<0.001	39.9±15.4	60.1±15.3	0.001
Diabetes type (1/2)	37/20	14/24	0.00047	37/20	20/31	0.00047	37/20	8/16	0.00047	37/20	3/7	0.00047
Diabetes duration (y)	13.8±6.6	17.1±6.6	0.224	13.8±6.6	17.7±7.1	0.047	13.8±6.6	22.7±9.8	<0.001	13.8±6.6	20.6±3.1	0.062
Alcohol (Y/N)	5/52	7/31	0.841	5/52	3/48	0.841	5/52	2/22	0.841	5/52	0/10	0.841
Smoking (Y/N)	44/13	32/6	0.071	44/13	46/5	0.071	44/13	22/2	0.071	44/13	8/2	0.071
Hypertension (Y/N)	51/6	26/12	0.00047	51/6	34/17	0.00047	51/6	12/12	0.00047	51/6	6/4	0.00047
Neuropad (Y/N)	5/52	15/23	<0.001	5/52	42/9	<0.001	5/52	22/2	<0.001	5/52	10/0	<0.001
HbA1c (%)	7.16±1.2	7.5±1.5	1.000	7.16±1.2	7.7±1.3	0.268	7.16±1.2	7.5±1.5	1.000	7.16±1.2	8±0.8	0.696
B12 (pg/mL)	515.9±121.2	511.8±113.6	1.000	515.9±121.2	533.6±148.9	1.000	515.9±121.2	566.2±136.8	1.000	515.9±121.2	523.4±185.7	1.000
MCR	57.8±25.8	19.5±13.4	<0.001	57.8±25.8	14.8±7.4	<0.001	57.8±25.8	10.9±7.6	<0.001	57.8±25.8	9.3±7.5	<0.001
Sd	84.7±48.9	29.5±18.8	<0.001	84.7±48.9	25.7±12.3	<0.001	84.7±48.9	19.4±12.1	<0.001	84.7±48.9	14±12.2	<0.001
Valsalva	1.4±0.2	1.3±0.1	<0.001	1.4±0.2	1.22±0.1	<0.001	1.4±0.2	1.17±0.1	<0.001	1.4±0.2	1.2±0.1	<0.001
Postural index	1.16±0.1	1.09±0.1	<0.001	1.16±0.1	1.06±0.1	<0.001	1.16±0.1	1.04±0	<0.001	1.16±0.1	1.02±0.03	<0.001
Orthostatic hypotension	0.79±2.9	3.6±9	<0.001	0.79±2.9	17.9±7.7	<0.001	0.79±2.9	26.3±8.8	<0.001	0.79±2.9	32.5±11.4	<0.001

Supplementary Table S3: Comparison between abnormal CARTs (1 abnormal vs 2,3,4 abnormal CARTs)

Abnormal CARTs	1 abnormal	Mild DAN (2 abnormal)	p	1 abnormal	Moderate DAN (3 abnormal)	p	1 abnormal	Severe DAN (4 abnormal)	p
N	38	51		38	24		38	10	
Gender (M/F)	16/22	18/32	0.48	16/22	13/11	0.48	16/22	5/5	0.01
Age (y)	52.5±15.4	53.2±13.4	1.000	52.5±15.4	55.5±13.6	1.000	52.5±15.4	60.1±15.3	1.000
Diabetes type (1/2)	14/24	20/31	0.317	14/24	8/16	0.317	14/24	3/7	0.317
Diabetes duration (y)	17.1±6.6	17.7±7.1	1.000	17.1±6.6	22.7±9.8	0.028	17.1±6.6	20.6±3.1	1.000
Alcohol (Y/N)	7/31	3/48	0.035	7/31	2/22	0.035	7/31	0/10	0.035
Smoking (Y/N)	32/6	46/5	1.000	32/6	22/2	1.000	32/6	8/2	0.689
Hypertension (Y/N)	26/12	34/17	0.920	26/12	12/12	0.230	26/12	6/4	0.009
Neuropad (Y/N)	15/23	42/9	0.057	15/23	22/2	0.057	15/23	10/0	0.057
HbA1c (%)	7.5±1.5	7.7±1.3	1.000	7.5±1.5	7.5±1.5	1.000	7.5±1.5	8±0.8	1.000
B12 (pg/mL)	511.8±113.6	533.6±148.9	1.000	511.8±113.6	566.2±136.8	1.000	511.8±113.6	523.4±185.7	1.000
MCR	19.5±13.4	14.8±7.4	1.000	19.5±13.4	10.9±7.6	0.679	19.5±13.4	9.3±7.5	0.952
Sd	29.5±18.8	25.7±12.3	1.000	29.5±18.8	19.4±12.1	1.000	29.5±18.8	14±12.2	1.000
Valsalva	1.3±0.1	1.22±0.1	0.019	1.3±0.1	1.17±0.1	<0.001	1.3±0.1	1.2±0.1	0.225
Postural index	1.09±0.1	1.06±0.1	0.104	1.09±0.1	1.04±0	0.004	1.09±0.1	1.02±0.03	0.006
Orthostatic hypotension	3.6±9	17.9±7.7	<0.001	3.6±9	26.3±8.8	<0.001	3.6±9	32.5±11.4	<0.001

Supplementary Table S4: Comparison between abnormal CARTs (2 abnormal vs 3,4 abnormal CARTs and 3 vs 4)

Abnormal CARTs	Mild DAN (2 abnormal)	Moderate DAN (3 abnormal)	p	Mild DAN (2 abnormal)	Severe DAN (4 abnormal)	p	Moderate DAN (3 abnormal)	Severe DAN (4 abnormal)	p
N	51	24		51	10		24	10	
Gender (M/F)	18/32	13/11		18/32	5/5		13/11	5/5	
Age (y)	53.2±13.4	55.5±13.6	1.000	53.2±13.4	60.1±15.3	1.000	55.5±13.6	60.1±15.3	1.000
Diabetes type (1/2)	20/31	8/16	0.194	20/31	3/7	0.194	8/16	3/7	0.317
Diabetes duration (y)	17.7±7.1	22.7±9.8	0.050	17.7±7.1	20.6±3.1	1.000	22.7±9.8	20.6±3.1	1.000
Alcohol (Y/N)	3/48	2/22	0.841	3/48	0/10	0.841	2/22	0/10	0.271
Smoking (Y/N)	46/5	22/2	0.193	46/5	8/2	0.193	22/2	8/2	0.689
Hypertension (Y/N)	34/17	12/12	0.009	34/17	6/4	0.009	12/12	6/4	0.368
Neuropad (Y/N)	42/9	22/2	<0.001	42/9	10/0	<0.001	22/2	10/0	0.002
HbA1c (%)	7.7±1.3	7.5±1.5	1.000	7.7±1.3	8±0.8	1.000	7.5±1.5	8±0.8	1.000
B12 (pg/mL)	533.6±148.9	566.2±136.8	1.000	533.6±148.9	523.4±185.7	1.000	566.2±136.8	523.4±185.7	1.000
MCR	14.8±7.4	10.9±7.6	1.000	14.8±7.4	9.3±7.5	1.000	10.9±7.6	9.3±7.5	1.000
Sd	25.7±12.3	19.4±12.1	1.000	25.7±12.3	14±12.2	1.000	19.4±12.1	14±12.2	1.000
Valsalva	1.22±0.1	1.17±0.1	1.000	1.22±0.1	1.2±0.1	1.000	1.17±0.1	1.2±0.1	1.000
Postural index	1.06±0.1	1.04±0	1.000	1.06±0.1	1.02±0.03	0.544	1.04±0	1.02±0.03	1.000
Orthostatic hypotension	17.9±7.7	26.3±8.8	<0.001	17.9±7.7	32.5±11.4	<0.001	26.3±8.8	32.5±11.4	0.239