Non-Alcoholic Fatty Liver Disease Is not Related to the Prevalence of Diabetic Polyneuropathy in Type 2 Diabetes

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INTRODUCTION. Nonalcoholic fatty liver disease (NAFLD) has been suggested as independent predictor for kidney disease and proliferative retinopathy in patients with type 2 diabetes (T2D), while the association with diabetic polyneuropathy (DPN) is debated. The **AIM** of this study is to evaluate the association between DPN and predictive tools of NAFLD and liver fibrosis and ultrasonography (US) diagnosis of steatosis.

Table 1. Clinical characteristics of T2DM subjects according to the presence of DPN.

	DPN $^-$ (n = 21)	DPN $^+$ (n = 21)	p
General and anthropometric characteristics			
Male (%)	52,4	66,7	0,346
Age (years)	53,71 ± 11,67	63,19 ± 10,41	***0,008***
Duration of diabetes (years)	5,52 ± 6,57	10,79 ± 8,80	***0,034***
Body weight (Kg)	94,71 ± 25,09	86,37 ± 19,12	0,233
BMI (Kg/m²)	34,30 ± 9,28	30,95 ± 5,68	0,167
With obesity (%)	61,9	57,1	0,753
Waist circumference (cm)	109,64 ± 17,79	106,76 ± 14.38	0,577
Hip circumference (cm)	116,52 ± 17,37	107,98 ± 15,36	0,099
Smoking (%)	81	61,9	0,172
Physical activity (%)	28,6	14,3	0,259
Biochemical evaluations			
Fasting glucose (mg/dl)	150,09 ± 41,17	172,19 ± 54,80	0,148
HbA1c (mmol/mol)	59,90 ± 16,06	59,62 ± 13,32	0,950
Uric acid (mg/dl)	6,04 ± 1,37	5,77 ± 1,50	0,600
AST-GOT (U/L)	28,67 ± 19,11	32,81 ± 26,09	0,561
ALP-GPT (U/L)	32,81 ± 21,61	30,29 ± 14,47	0,659
γ-GT (U/L)	39,19 ±38,14	45,19 ± 41,68	0,629
Total cholesterol (mg/dl)	165,38 ± 49,48	158,52 ± 47,62	0,650
HDL (mg/dl)	46,81 ± 13,90	44,86 ± 12,78	0,638
LDL (mg/dl)	102,58 ± 35,80	91,00 ± 39,37	0,357
Triglycerides (mg/dl)	140,38 ± 58,67	162,62 ± 102,58	0,395
Complications and comorbidities			
With diabetic retinopathy (%)	0	15,8	0,071
With albuminuria (%)	9,5	42,1	***0,017***
With hypertension (%)	66,7	90,5	0,060
With dyslipidemia (%)	76,2	95,2	0,078
With ischemic heart disease (%)	23,8	42,9	0,190
With heart failure (%)	9,5	33,3	0,060
With cerebrovascular disease (%)	9,5	14,3	0,634
With peripheral vascular disease (%)	18,8	47,5	0,085
With chronic kidney disease (%)	9,5	28,6	0,116
With US-liver steatosis (%)	90	94,4	0,612
With US-liver steatosis+ AST/ALT alteration (%)	33,3	23,8	0,513
Therapy			
With antihypertensive therapy (%)	63,2	90,5	***0,014***
With antidyslipidemic therapy (%)	61,9	95,2	***0,008***
With non-insulin antidiabetic therapy (%)	76,2	76,2	0,147
With mixed antidiabetic therapy (%)	9,5	23,8	0,214
With insulin therapy (%)	4,8	9,5	0,549

Table 2. Non-invasive biomarkers of liver steatosis and fibrosis scores of T2DM subjects according to the presence of DPN.

	DPN $^-$ (n = 21)	DPN $^+$ (n = 21)	p
Non-invasive biomarkers of liver steatosis			
HIS score (mean ± SD)	46,17 ± 10,67	42,44 ± 7,79	0,204
HIS high-risk score (%)	85,7	85,7	1
FLI score (mean ± SD)	73,62 ± 29,51	71,02 ± 27,71	0,769
FLI high risk score (%)	76,2	66,7	0,733
Non-invasive biomarkers of fibrosis			
FIB-4 score (mean ± SD)	1,18 ± 0,51	1,75 ± 0,94	***0,022***
FIB-4 high risk score (%)	0	14,3	0,072
NAFLD Fibrosis score (mean ± SD)	1,74 ± 0,94	2,38 ± 0,88	0,128
NAFLD Fibrosis high risk score (%)	85,7	95,2	0,599
AST/ALT ratio (mean ± SD)	0,91 ± 0,28	1,10 ± 0,70	0,252
AST/ALT ratio high risk score (%)	4,8	9,5	1
APRI score (mean ± SD)	0,32 ± 0,20	0,40 ± 0,25	0,252
APRI high risk score (%)	19,0	23,8	1

METHODS. Forty-two T2DM subjects (mean age 58,45 ± 11,93 years, duration 8,15 ± 8,12 years, HbA1c 59,76 ± 14,58 mmol/mol, 25 males), underwent clinical evaluation of DPN by Michigan Neuropathy Screening Instrument (MNSI), Michigan Diabetic Neuropathy Score (MDNS) and Diabetic Neuropathy Index (DNI). NAFLD was evaluated by predictive tools: Fatty Liver Index (FLI) and Hepatic Steatosis Index (HIS), and confirmed by liver ultrasonography. Liver fibrosis was evaluated by scores Fibrosis-4 (FIB-4), NAFLD Fibrosis, aspartate aminotransferase to alanine aminotransferase (AST/ALT) ratio, aspartate aminotransferase to platelet ratio index (APRI).

RESULTS. **Table 1.** DPN$^+$ patients were older (p=0.08), with longer diabetes duration (p=0.034) and characterized by higher prevalence of impaired urinary albumin excretion (p=0.017), hypertension (p=0.014) and dyslipidemia (p=0.098). No difference in the prevalence of US-liver steatosis was found. **Table 2**. Considering NAFLD risk, no differences in DPN$^-$ and DPN$^+$ were detected. Among fibrosis scores, FIB-4 score was higher in DPN$^+$ vs DPN$^-$ (p=0,022) (**Figure 1**).
Figure 2. Correlation between the value of NAFLD Fibrosis score and neuropathic deficits was observed.

Figure 1. FIB-4 score in DPN$^-$ and DPN$^+$ subjects.

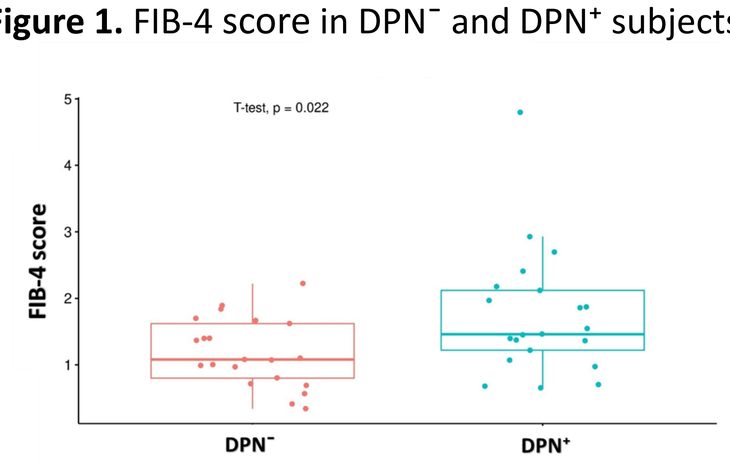
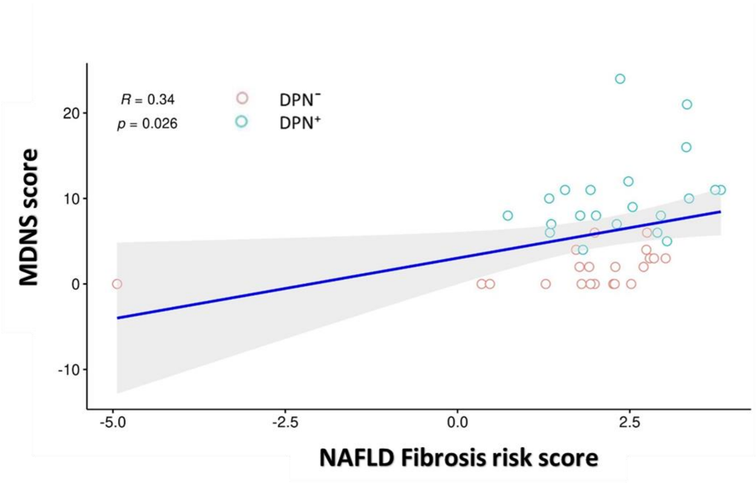


Figure 2. Correlation between NAFLD Fibrosis score and MDNS score.



CONCLUSIONS. Although in a small sample of T2D subjects, liver steatosis is not independently associated with clinical diagnosis of DPN. Relation between DPN and risk of liver fibrosis has been documented; this finding requires validation in larger studies and considering elastographic or biopsy gold standard diagnosis.
Strengths: well characterized T2D population.
Limitations: only tertiary level hospital, limited elastography data, no data of autonomic neuropathy and small fibers nerve.

References
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