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Non-Alcoholic Fatty Liver Disease Is not Related to the Prevalence of Diabetic Polyneuropathy in Diabetes / Greco, Carla; Boni, Stefano; Coluccia, Silvia; Colzani, Massimiliano; Santi, Daniele; Simoni, Manuela. - (2022). (Intervento presentato al convegno 32nd Neurodiab Annual Meeting tenutosi a Bergen, Norway nel 15-18 Settembre 2022).

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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 <sup>-</sup> (n = 21)	DPN <sup>+</sup> (n = 21)	p
<i>General and anthropometric characteristics</i>			
Male (%)	52,4	66,7	0,346
Age (years)	53,71 ± 11,67	63,19 ± 10,41	<b>0,008</b>
Duration of diabetes (years)	5,52 ± 6,57	10,79 ± 8,80	<b>0,034</b>
Body weight (Kg)	94,71 ± 25,09	86,37 ± 19,12	0,233
BMI (Kg/m <sup>2</sup> )	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
<i>Biochemical evaluations</i>			
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
<i>Complications and comorbidities</i>			
With diabetic retinopathy (%)	0	15,8	0,071
With albuminuria (%)	9,5	42,1	<b>0,017</b>
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
<i>Therapy</i>			
With antihypertensive therapy (%)	63,2	90,5	<b>0,014</b>
With antidyslipidemic therapy (%)	61,9	95,2	<b>0,008</b>
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

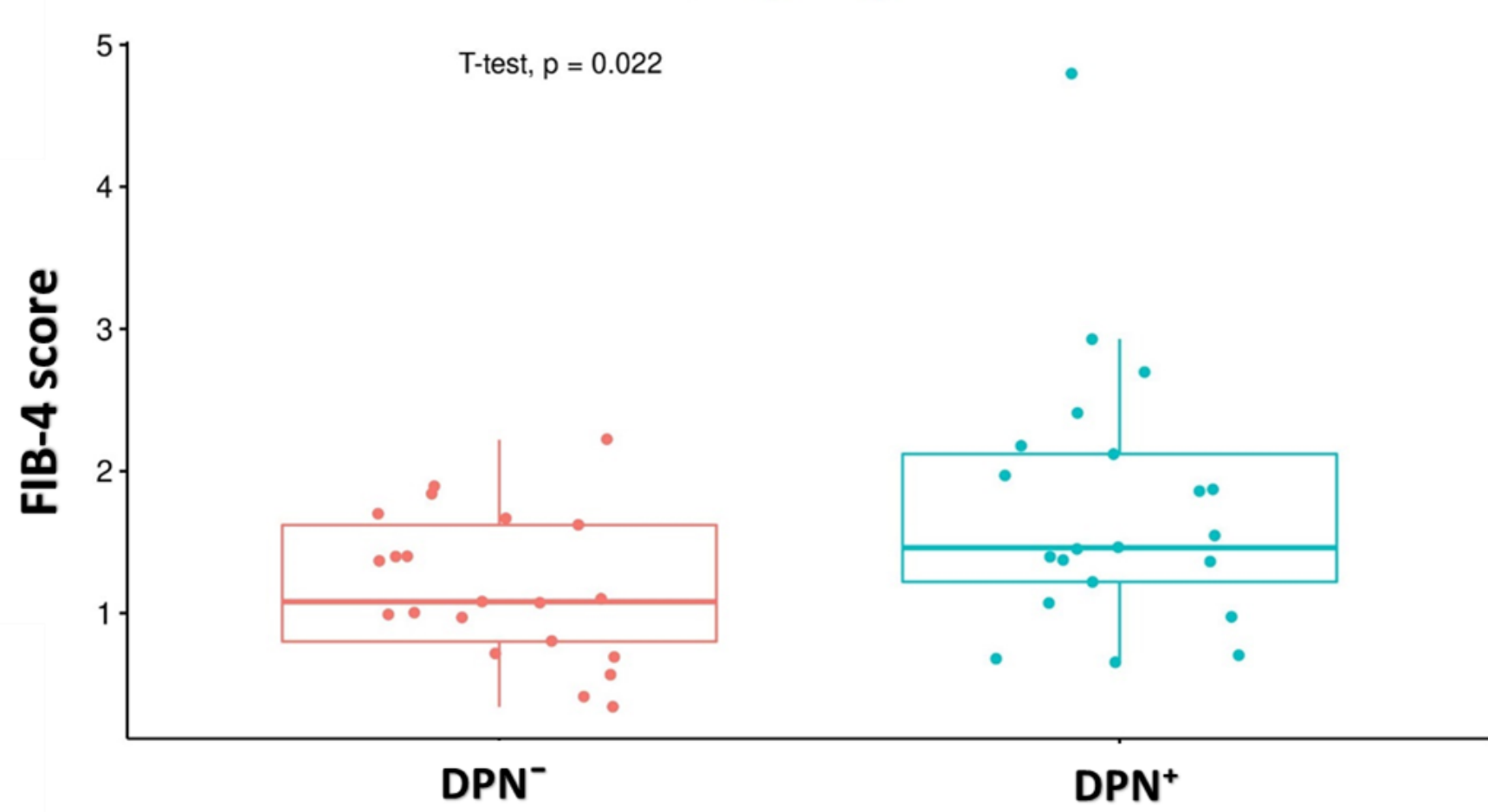
**Table 2.** Non-invasive biomarkers of liver steatosis and fibrosis scores of T2DM subjects according to the presence of DPN.

	DPN <sup>-</sup> (n = 21)	DPN <sup>+</sup> (n = 21)	p
<i>Non-invasive biomarkers of liver steatosis</i>			
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
<i>Non-invasive biomarkers of fibrosis</i>			
FIB-4 score (mean ± SD)	1,18 ± 0,51	1,75 ± 0,94	<b>0,022</b>
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

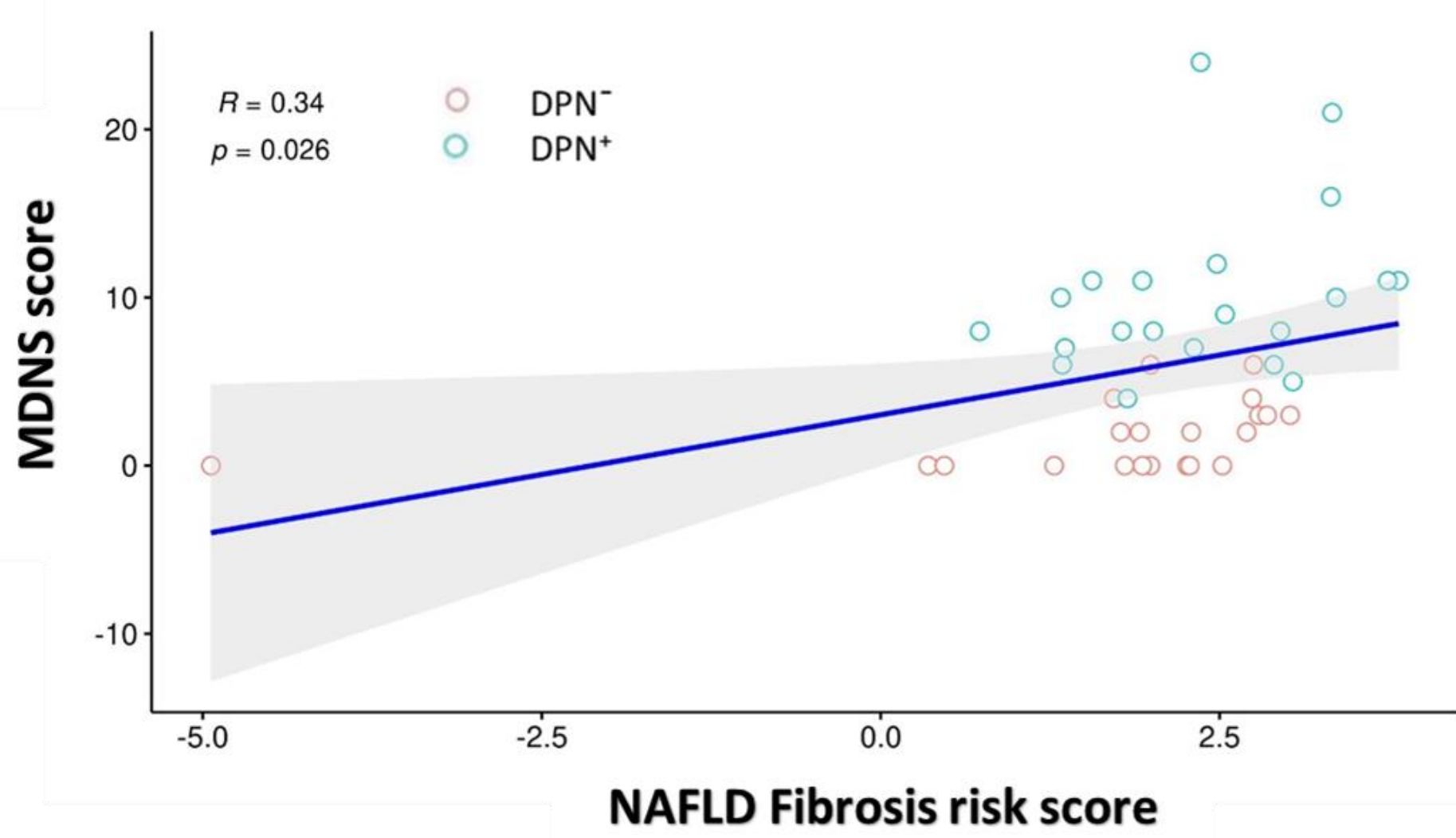
**METHODS.** Forty-two T2DM subjects (mean age 58,45 ± 11,93 years, duration 8,15 ± 8,12 years, HbA1c 59,76 ± 14,58 mmol/mol, 25 males), underwent clinical evaluation of DPN by Michigan Neuropathy Screening Instrument (MNSI), Michigan Diabetic Neuropathy Score (MDNS) and Diabetic Neuropathy Index (DNI). 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<sup>+</sup> 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<sup>-</sup> and DPN<sup>+</sup> were detected. Among fibrosis scores, FIB-4 score was higher in DPN<sup>+</sup> vs DPN<sup>-</sup> (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<sup>-</sup> and DPN<sup>+</sup> 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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