

Variable	Missing values, %	All, n=67	T2D, n=11	T2D+MASLD, n=33	T2D+MASLD+F, n=23	p value	Test
<i>General characteristics</i>							
Age (years)	0.0	59.8 ± 8.3	59.6 ± 8.7	59.4 ± 8.1	60.7 ± 8.7	0.851	ANOVA
Sex (F/M, %)	0.0	56.7/43.3	63.6 /36.4	60.6/39.4	47.8/52.2	0.560	Chi squared
CAP (dB/m)	0.0	319.5 ± 57.4	225.3 ± 34.3	332.3 ± 38.6	346.3 ± 42.0	0.000	Kruskal-Wallis
Stiffness (Kpa)	0.0	6.1 [4.8 - 7.9]	5 [4.35 - 5.8]	5.2 [4.4 - 6]	9.7 [7.9 - 11.9]	0.000	Kruskal-Wallis
T2D duration (years)	5.97	6.0 [2.0 - 10.0]	5.0 [2.5 - 10.5]	6.0 [3.0 - 9.5]	6.0 [0.0 - 10]	0.864	Kruskal-Wallis
<i>Glucose homeostasis</i>							
Glucose (mg/dL)	1.49	118 [107 - 133]	115 [105 - 129]	120 [108 - 129]	116 [109 - 144]	0.788	Kruskal-Wallis
HbA1c (%)	1.49	6.2 [5.8 - 6.9]	6 [5.6 - 6.9]	6.2 [5.9 - 6.5]	6.4 [5.8 - 6.9]	0.852	Kruskal-Wallis
Insulin (uU/mL)	17.9	20.8 ± 11.8	13.9 ± 4.8	19.0 ± 12.0	26.2 ± 11.8	0.017	ANOVA
HOMA-IR	17.9	4.9 [3.8 - 7.0]	3.97 [3.3 - 4.4]	4.6 [3.5 - 6.8]	6.6 [4.6 - 10.9]	0.005	Kruskal-Wallis
HOMA-B	17.9	132.9 ± 72.9	115.7 ± 54.2	111.1 ± 52.3	169.0 ± 90.2	0.018	ANOVA
<i>Lipid homeostasis</i>							
Triglycerides (mg/dL)	2.99	140 [93 - 191]	94 [79 - 123]	146 [89 - 191]	153 [105 - 217]	0.149	Kruskal-Wallis
Total-Cho (mg/dL)	1.49	184.7 ± 35.0	179.2 ± 41.8	185.9 ± 32.8	185.7 ± 36.1	0.853	ANOVA
VLDL-Cho (mg/dL)	10.5	26.5 [18.8 - 38.0]	19.0 [16.0 - 24.5]	29.0 [18.0 - 38.0]	29.5 [20.8 - 36.3]	0.193	Kruskal-Wallis
HDL-Cho (mg/dL)	7.46	50.6 ± 11.3	58.6 ± 14.6	50.6 ± 10.3	46.4 ± 8.8	0.013	ANOVA
LDL-Cho (mg/dL)	8.96	105.4 ± 32.5	97.2 ± 30.1	106.6 ± 30.8	108.1 ± 36.6	0.647	ANOVA
Remnant-Cho	8.96	27 [19 - 38]	19 [16 - 25]	29 [18 - 38]	31 [21 - 43]	0.128	Kruskal-Wallis
<i>Liver parameters</i>							
Bilirubin (mg/dL)	10.4	0,53 ± 0,30	0,61 ± 0,39	0,47 ± 0,34	0,60 ± 0,18	0.231	ANOVA
Alkaline phosphatase, ALP (U/L)	16.4	69,7 ± 20,5	71,7 ± 27,3	69,3 ± 18,0	69,4 ± 21,3	0.953	ANOVA
<i>Treatments</i>							
DPP4	0.0	17 (25.4)	2 (18.2)	10 (30.3)	5 (21.7)	0.643	Chi squared
GLP1	0.0	12 (17.9)	1 (9.1)	7 (21.2)	4 (17.4)	0.660	Chi squared

Metformin	0.0	42 (62.7)	6 (54.5)	22 (66.6)	14 (60.9)	0.753	Chi squared
SGLT2	0.0	11 (16.4)	3 (27.3)	4 (12.1)	4 (17.4)	0.496	Chi squared
<i>Anthropometric parameters</i>							
BMI (kg/m ²)	0.0	33.1 ± 4.0	31.1 ± 4.1	33.3 ± 4.1	33.6 ± 3.6	0.194	ANOVA
Waist circumference (cm)	2.99	106.3 ± 10.8	100.6 ± 13.5	106.2 ± 9.5	109.4 ± 10.4	0.087	ANOVA
Body round index	2.99	6.6 [5.5 - 7.7]	6.1 [4.9 - 7.6]	6.4 [5.6 - 7.1]	6.9 [5.8 - 8.0]	0.326	Kruskal-Wallis
Phase angel (degree)	1.49	5.6 ± 0.8	5.4 ± 0.5	5.6 ± 0.8	5.9 ± 0.8	0.144	ANOVA
Fat mass (%)	0.0	35.9 ± 7	34.2 ± 8.3	36.3 ± 6.9	36.0 ± 6.6	0.688	ANOVA
Fat free mass (%)	0.0	64.0 ± 7.0	65.8 ± 8.3	63.5 ± 7	64.0 ± 6.6	0.652	ANOVA
Muscle mass (%)	0.0	60.8 ± 6.7	62.5 ± 7.9	60.3 ± 6.7	60.8 ± 6.3	0.654	ANOVA
Total Body Water (%)	0.0	44.6 ± 5.8	46.3 ± 5.8	43.9 ± 6.6	45.0 ± 4.4	0.4798	ANOVA
Extracelullar Body Water (%)	1.49	18.9 (1.5)	19.3 (2.0)	18.8 (1.4)	18.867 (1.256)	0.6681	ANOVA
Intracelullar Body Water (%)	1.49	22.9 (3.3)	23.1 (3.9)	22.6 (3.4)	23.153 (2.996)	0.8381	ANOVA
<i>Biochemical variables</i>							
Prothrombin activity (%)	16.4	102.0 (14.0)	99.2 (23.3)	105.1 (8.2)	98.6 (15.0)	0.390	Kruskal-Wallis
Albumin (g/dL)	10.4	4.6 (0.3)	4.5 (0.2)	4.6 (0.3)	4.7 (0.3)	0.266	ANOVA
Creatinine (mg/dL)	10.4	0.81 (0.21)	0.72 (0.11)	0.81 (0.27)	0.85 (0.14)	0.333	ANOVA
Platelets (x10 ⁹ cells/L)	10.4	245.3 (58.2)	236.9 (38.2)	249.4 (60.8)	242.9 (63.1)	0.836	ANOVA
Potassium (mmol/L)	11.9	4.4 (0.3)	4.4 (0.3)	4.4 (0.3)	4.4 (0.3)	0.869	ANOVA
<i>Immunological parameters</i>							
Basophils (%)	10.4	0.69 (0.28)	0.7 (0.32)	0.64 (0.26)	0.77 (0.30)	0.3159	ANOVA
Basophils (x10 ³ cells/mm ³)	10.4	0.049 (0.024)	0.043 (0.022)	0.045 (0.016)	0.058 (0.032)	0.1163	ANOVA
Eosinophils (%)	10.4	3.03 (1.99)	3.16 (1.87)	2.92 (2.17)	3.12 (1.86)	0.5289	Kruskal-Wallis
Eosinophils (x10 ³ cells/mm ³)	10.4	0.22 (0.20)	0.20 (0.15)	0.22 (0.21)	0.24 (0.21)	0.5048	Kruskal-Wallis
Immature granulocytes (%)	10.4	0.39 (0.30)	0.34 (0.24)	0.36 (0.17)	0.46 (0.43)	0.5887	Kruskal-Wallis

Leukocytes (x10 ³ cells/mm ³)	10.4	7.04 (1.65)	6.15 (0.95)	7.15 (1.36)	7.25 (2.14)	0.2149	ANOVA
Lymphocytes (%)	10.4	30.09 (6.48)	32.98 (6.0)	29.43 (6.17)	29.81 (7.06)	0.3488	ANOVA
Lymphocytes (x10 ³ cells/mm ³)	10.4	2.09 (0.56)	2.02 (0.44)	2.08 (0.50)	2.13 (0.70)	0.897	ANOVA
Monocytes (%)	10.4	8.18 (1.95)	7.63 (1.43)	7.94 (2.06)	8.75 (1.9)	0.2261	ANOVA
Monocytes (x10 ³ cells/mm ³)	10.4	0.57 (0.16)	0.47 (0.09)	0.57 (0.19)	0.62 (0.20)	0.1083	ANOVA
Neutrophils (%)	10.4	57.61 (6.75)	55.19 (5.8)	58.70 (6.97)	57.09 (6.75)	0.3612	ANOVA
Neutrophils (x10 ³ cells/mm ³)	10.4	4.08 (1.14)	3.40 (0.62)	4.21 (0.98)	4.17 (1.43)	0.1525	ANOVA
<i>Hematological variables</i>							
Mean corpuscular hemoglobin concentration (MCHC, g/dL)	10.4	29.8 (1.7)	29.2 (2.2)	29.8 (1.4)	30.0 (1.9)	0.499	ANOVA
Hemoglobine (g/dL)	10.4	15.0 (1.3)	14.6 (1.0)	14.7 (1.1)	15.2 (1.7)	0.316	ANOVA
Red cells distribution width (RDW, %)	11.9	13.5 (1.1)	14.0 (1.2)	13.1 (0.6)	13.8 (1.4)	0.122	Kruskal-Wallis
<i>Cardiovascular parameters</i>							
sBP (mmHg)	0.0	139 [128 - 150]	132 [126 - 137]	140 [127 - 150]	140 [132 - 151]	0.200	Kruskal-Wallis
dBp (mmHg)	0.0	80 ± 11	77 ± 9	81 ± 12	81 ± 10	0.474	ANOVA
<i>Comorbilities</i>							
Cardiopathy: Related to T2D	14.9	4 (6.1)	1 (9.1)	1 (3.0)	2 (8.7)	0.797	Chi squared
Cardiopathy: Non-related to T2D	14.9	3 (4.6)	0 (0)	2 (6.1)	1 (4.3)	0.797	Chi squared
Nephropathy: Related to T2D	14.9	1 (1.5)	0 (0)	1 (3.0)	0 (0)	0.393	Chi squared
Nephropathy: Non-related to T2D	14.9	4 (6.1)	0 (0)	1 (3.0)	3 (13.0)	0.393	Chi squared
Retinopathy: Related to T2D	0.0	2 (3.0)	0 (0)	1 (3.0)	1 (4.3)	0.784	Chi squared

Nutritional status							
Calcium (mg/dL)	38.8	9.6 [9.4 - 9.9]	9.5 [9.25 - 10]	9.6 [9.4 - 9.8]	9.7 [9.5 - 10.1]	0.283	ANOVA
Vitamin B9 (nmol/L)	34.3	7.5 [5.4 - 10.6]	9.7 [6.9 - 12.2]	6.5 [5.1 - 9.8]	7.8 [5.4 - 10.5]	0.778	ANOVA
Vitamin B12 (pmol/L)	35.8	348 [275 - 431]	292 [250 - 408]	310 [264 - 423]	399 [325 - 431]	0.418	ANOVA
<i>Mediterranean Diet Adherence *</i>							
Do you use olive oil as the principal source of fat for cooking?	0.0	61 (91.0)	11 (100)	29 (87.9)	21 (91.3)	0.475	Chi squared
How much olive oil do you consume per day (including that used in frying, salads, meals eaten away from home, etc.)? ≥4 ts/day	0.0	61 (91.0)	10 (90.9)	31 (93.9)	20 (87.0)	0.667	Chi squared
How many servings of vegetables do you consume per day? ≥2 s/day or ≥1 garnish and side	0.0	27 (40.3)	6 (54.5)	17 (51.5)	4 (17.4)	0.026	Chi squared
How many pieces of fruit (including fresh-squeezed juice) do you consume per day? ≥3 s/day	0.0	27 (40.3)	54 (36.4)	14 (42.4)	9 (39.1)	0.930	Chi squared
How many servings of red meat, hamburger, or sausages do you consume per day? A full serving is 100–150 g, <1 s/day	0.0	43 (64.2)	10 (90.9)	20 (60.6)	13 (56.5)	0.123	Chi squared
How many servings (12 g) of butter, margarine, or cream do you consume per day? <1 s/day	0.0	59 (88.1)	10 (90.9)	30 (90.9)	19 (82.6)	0.610	Chi squared

How many carbonated and/or sugar-sweetened beverages do you consume per day? <1 s/day	0.0	59 (88.1)	10 (90.9)	30 (90.9)	19 (82.6)	0.610	Chi squared
Do you drink wine? How much do you consume per week? ≥7cups/week	0.0	14 (20.9)	2 (18.2)	6 (18.2)	6 (26.1)	0.752	Chi squared
How many servings (150 g) of legumees do you consume per week? ≥3s/week	0.0	15 (22.4)	5 (45.4)	6 (18.2)	4 (17.4)	0.133	Chi squared
How many servings of fish/seafood do you consume per week? 100–150 g of fish, 4–5 pieces or 200 g of seafood, ≥3s/week	0.0	31 (46.3)	6 (54.5)	15 (45.5)	10 (43.5)	0.825	Chi squared
How many times do you consume commercial (not homemade) pastry such as cookies or cake per week? <2s/week	0.0	41 (61.2)	6 (54.5)	20 (60.6)	15 (65.2)	0.833	Chi squared
How many times do you consume nuts per week? 1 s = 30g, ≥3s/week	0.0	36 (53.7)	6 (54.5)	20 (60.6)	10 (43.5)	0.449	Chi squared
Do you prefer to eat chicken, turkey or rabbit instead of beef, pork, hamburgers, or sausages?	0.0	46 (68.7)	10 (90.9)	24 (72.7)	12 (52.2)	0.058	Chi squared
How many times per week do you consume boiled vegetables, pasta, rice, or	0.0	34 (50.8)	5 (45.4)	16 (48.5)	13 (56.5)	0.780	Chi squared

other dishes with a sauce of tomato, garlic, onion, or leeks sautéed in olive oil (sofrito)? ≥2 s/week							
SCORE HIGH VS LOW	0.0	40 (59.7)	10 (90.9)	19 (57.6)	11 (47.8)	0.053	Chi squared
<i>Smoking habit</i>							
Smoking: never	1.5	30 (45.5)	7 (63.6)	17 (51.5)	6 (26.1)	0.109	Chi squared
Smoking: former	1.5	6 (9.1)	0 (0.0)	4 (12.1)	2 (8.7)	0.109	Chi squared
Smoking: current	1.5	30 (45.5)	4 (36.4)	11 (33.3)	15 (65.2)	0.109	Chi squared
Cigarettes: never	1.5	30 (52.6)	7 (70.0)	17 (65.4)	6 (28.5)	0.093	Chi squared
Cigarettes: light (1–10 cigarettes per day)	1.5	7 (12.3)	1 (10.0)	3 (11.5)	3 (14.3)	0.093	Chi squared
Cigarettes: Moderate (11–19 cigarettes per day)	1.5	3 (5.3)	0 (0.0)	0 (0.0)	3 (14.3)	0.093	Chi squared
Cigarettes: Heavy (≥20 cigarettes per day)	1.5	17 (29.8)	2 (20.0)	6 (23.1)	9 (42.9)	0.093	Chi squared
Exposed vs. never exposed	1.5	45.45 / 54.55	57.14 / 63.64	46.88 / 53.12	73.91 / 26.09	0.058	Chi squared
<i>Physical activity</i>							
During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling? (days)	0.0	0: 95.55% / 2: 2.99% / 7: 1.49%	0: 90.91% / 2: 9.09% / 7: 0%	0: 96.97% / 2: 3.03% / 0%	0: 95.65% / 2: 0% / 7: 4.35%	Not applied	
How much time did you usually spend doing vigorous physical activities on one of those days? (min)	0.0	30 min: 1.49%	0	0	30 min : 4.35%		

During the last 7 days, on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking (days)	0.0	0: 58.21% / 1: 5.97% / 2: 16.42% / 3: 5.97% / 4: 1.49% / 5: 7.46% / 6: 1.49% / 7: 2.99%	0: 54.55% / 1: 9.09% / 2: 18.18% / 4: 9.09% / 5: 9.09%	0: 57.58% / 1: 3.03% / 2: 21.21% / 5: 9.09% / 6: 3.03% / 7: 6.06%	0: 60.87% / 1: 8.70% / 2: 8.70% / 3: 17.39% / 5: 4.35%	
How much time did you usually spend doing moderate physical activities on one of those days? (min)	0.0	NA: 95.52 / 30 min: 4.48%	0	30 min : 3.03%	30 min: 8.70%	
During the last 7 days, on how many days did you walk for at least 10 minutes at a time? (days)	0.0	0 : 14.92% / 1: 8.95% / 2: 7.46% / 3: 4.48% / 4: 2.99% / 5: 13.43% / 6: 4.48% / 7: 43.28%	0 : 18.18% / 1: 9.09% / 3: 9.09% / 4: 9.09% / 5: 9.09% / 7: 45.45%	0 : 12.12% / 1: 6.06% / 2: 15.15% / 5: 24.24% / 6: 3.03% / 7: 45.45%	0 : 17.39% / 1: 13.04% / 2: 8.70% / 3: 8.70% / 4: 4.35% / 6: 8.70% / 7: 39.13%	
How much time did you usually spend walking on one of those days? (min)	0.0	15 min: 10% / 20 min: 5% / 30 min: 80% / 45 min: 5%	15 min: 18.18%	15 min: 3.03% / 30 min: 24.24%	15 min: 4.35% / 20 min: 4.35% / 30 min: 80% / 45 min: 26.09%	
During the last 7 days, how much time did you spend sitting on a week day? (hours: <=8h / >8h)	0.0	82.09% / 17.91%	100% / 0%	78.79% / 21.21%	78.26% / 21.74%	
METs/week	0.0	990 [636 - 1455]	693 [339 - 1794]	990 [742 - 1470]	876 [489 - 1288.2]	0.479 Kruskal-Wallis
Sedentary (sitting minutes/day)	0.0	300 [180-450]	240 [120 - 360]	300 [180 - 420]	360 [240 - 480]	0.123 Kruskal-Wallis

Table S1. Characterization of patients with T2D. Mean (standard deviation) / mean \pm standard deviation. Median [interquartile range]. ALT, alanine aminotransferase; APRI, AST to Platelet Ratio Index; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; dBP, diastolic blood pressure; F, fibrosis; FIB-4, Fibrosis-4 index; GGT, gamma-glutamyl transferase; GM, gut microbiota; HbA1c, hemoglobin A1c; HDL-Cho, high-density lipoprotein cholesterol; HOMA-B, homeostatic model assessment of insulin secretion; HOMA-IR, homeostatic model assessment of insulin resistance; IQR, interquartile range; IR, insulin resistance; IPAQ, International Physical Activity Questionnaire; LDL-Cho, low-density lipoprotein cholesterol; LSM, liver stiffness measurement; MASLD, metabolic dysfunction-associated steatotic liver disease; MedDiet, Mediterranean diet; MEDAS, Mediterranean Diet adherence screener; METs, Metabolic Equivalent Task; n, number; NFS, NAFLD fibrosis score; PA, physical activity; Remnant-Cho, remnant cholesterol; s, serving; sBP, systolic blood pressure; T2D, type 2 diabetes; Total-Cho, total cholesterol; ts, tablespoon; VLDL-Cho, very-low-density lipoprotein cholesterol; vs., versus.

Variables	T2D vs T2D+MASLD	T2D vs T2D+MASLD+F	T2D+MASLD vs T2D+MASLD+F	Test
<i>Glucose homeostasis</i>				
HOMA-IR	0.093	0.005	0.073	Dunn + Holm
HOMA-B	0.811	0.327	0.085	Dunn + Holm
<i>Biochemical parameters</i>				
HDL-Cho	0.249	0.057	0.269	Games-Howell
<i>Anthropometry</i>				
Waist circumference	0.429	0.173	0.497	Games-Howell
<i>Transaminases</i>				
GGT	0.261	0.001	0.002	Dunn + Holm
ALT	0.198	0.002	0.006	Dunn + Holm
AST	0.355	0.004	0.004	Dunn + Holm
<i>Non-invasive algorithms</i>				
FIB-4	0.566	0.748	0.198	Dunn + Holm
APRI	0.608	0.010	0.005	Dunn + Holm
NFS	1.00	1.00	1.00	Dunn + Holm
<i>Lifestyle habits</i>				
MedDiet adherence, high vs. low	0.134	0.071	0.588	Fisher + Bonferroni
Vegetables, ≥ 2 s/day or ≥ 1 garnish and side	1.00	0.004	0.089	Fisher + Bonferroni
White meat preference over red meat	0.408	0.158	0.316	Fisher + Bonferroni
Smoking exposure, exposed vs. never exposed	0.728	0.089	0.089	Fisher + Bonferroni
<i>GM</i>				
Chao1	0.880	0.910	0.450	Mann-Whitney U test
Shannon	0.860	0.830	0.880	Mann-Whitney U test
Simpson	1.00	0.860	0.500	Mann-Whitney U test

Table S2. Adjusted p values from cohort characterization. ALT, alanine aminotransferase; APRI, AST to Platelet Ratio Index; AST, aspartate aminotransferase; F, fibrosis; FIB-4, Fibrosis-4 index; GGT, gamma-glutamyl transferase; GM, gut microbiota; HDL-Cho, high-density lipoprotein cholesterol; HOMA-B, homeostatic model assessment of insulin secretion; HOMA-IR, homeostatic model assessment of insulin resistance; IQR, interquartile range; IR, insulin resistance; MASLD, metabolic dysfunction-associated steatotic liver disease; MedDiet, Mediterranean diet; n, number; NFS, NAFLD fibrosis score; T2D, type 2 diabetes; vs., versus.

Cohort description (N=152)					
F/M (%)	Weight (kg)	Height (m)	Age (years)	BMI (kg/m ²)	Obesity (BMI ≥30 kg/m ²) (%)
46.7/53.3	73.0 (15.0)	1.70 (0.08)	46.0(8.2)	25.1 (4.2)	10.5

Table S3. Controls from non-T2D cohort. BMI: body mass index; F: female; M=male.

Variables	β	Std. Error	Z value	p-value
Smoking exposure	-0.208	1.056	-0.197	n.s
Vegetables consumption	1.076	1.147	0.939	n.s
White meat preference	-1.567	1.342	-1.168	n.s
MedDiet adherence	-1.812	1.601	-.1131	n.s
<i>Megasphaera massiliensis</i>	0.001	0.002	0.344	n.s
<i>Clostridium saudiense</i>	0.003	0.003	1.070	n.s
ALT	0.040	0.053	0.753	n.s
HOMA-IR	0.690	0.477	1.447	n.s
HDL-Cho	-0.072	0.045	-1.587	n.s

Table S4. Logistic regression model T2D vs. T2D+MASLD. ALT = alanine aminotransferase; AST = aspartate aminotransferase; HDL-Cho = high-density lipoprotein cholesterol; HOMA-IR = homeostatic model assessment of insulin resistance. P-values ≤ 0.1 were considered statistically significant. P-values ≤ 0.1 were considered statistically significant.