

Effect of semaglutide on subclinical atherosclerosis and cardiometabolic compensation: a real-world study in patients with type 2 diabetes

SUPPLEMENTARY MATERIAL

Supplementary Table S1: Baseline demographics and clinical characteristics of patients stratified according to the disease duration.			
Variables	Early diabetes (n=12)	Medium diabetes (n=9)	Late diabetes (n=19)
Age (years)	61 ± 11	66 ± 10	69 ± 8
Male	10 (83)	4 (44)	12 (63)
Disease duration (years)	3 ± 2	11 ± 1	23 ± 7
Smoking status:			
• Yes	• 7 (58)	• 2 (22)	• 4 (21)
• Ex-smoker	• 2 (17)	• 5 (56)	• 9 (47)
Familiarity with CV diseases	8 (67)	5 (56)	10 (53)
Comorbidities:			
• Hypertension	• 10 (83)	• 9 (100)	• 15 (79)
• Dyslipidemia	• 8 (66)	• 9 (100)	• 15 (79)
• Obesity	• 9 (75)	• 6 (67)	• 13 (68)
• Diabetes complications	• 2 (16)	• 2 (22)	• 7 (37)
Concomitant therapies:			
• β-blockers	• 3 (25)	• 4 (44)	• 11 (58)
• ACE inhibitors	• 5 (41)	• 5 (56)	• 3 (16)
• Calcium antagonists	• 3 (25)	• 3 (33)	• 5 (26)
• Diuretics	• 4 (33)	• 2 (22)	• 9 (47)
• AT1R blockers	• 5 (41)	• 4 (44)	• 11 (58)
Lipid-lowering drugs:			
• Statins	• 6 (50)	• 9 (100)	• 15 (79)

**Supplementary Material**

<ul style="list-style-type: none"> <li>Fibrates</li> <li>Omega-3</li> </ul>	<ul style="list-style-type: none"> <li>1 (8)</li> <li>–</li> </ul>	<ul style="list-style-type: none"> <li>–</li> <li>3 (33)</li> </ul>	<ul style="list-style-type: none"> <li>1 (5)</li> <li>3 (16)</li> </ul>
Aspirin use	7 (58)	5 (56)	13 (68)
Data are presented as mean ± SD or n (%).			
ACE: Angiotensin-converting enzyme; CV: Cardiovascular; SD: Standard deviation.			

<b>Supplementary Table S2: The effect of 4-month semaglutide therapy on patients with early diabetes (n=12).</b>			
<b>Variables</b>	<b>Baseline (mean ± SD)</b>	<b>4 months (mean ± SD)</b>	<b>p-value</b>
<b><i>Anthropometric parameters</i></b>			
Weight (kg)	90 ± 14	84 ± 10	0.006
Waist (cm)	102 ± 9	97 ± 7	0.001
BMI (kg/m <sup>2</sup> )	31 ± 3	29 ± 3	0.003
<b><i>Glycemic parameters</i></b>			
Glycemia (mg/dL)	170 ± 50	118 ± 25	0.007
HbA1c (%)	9±2	7±1	<0.001
<b><i>Plasma lipids</i></b>			
Total CHO (mg/dL)	177 ± 37	158 ± 26	0.024
TG (mg/dL)	133 ± 40	129 ± 47	0.808
LDL CHO (mg/dL)	109 ± 33	88 ± 22	0.006
HDL CHO (mg/dL)	42 ± 8	44 ± 6	0.137
<b><i>Hepatic parameters</i></b>			
Alkaline phosphatase (U/l)	99 ± 66	77 ± 31	0.074
GGT (UI/L)	51 ± 32	41 ± 18	0.067
AST (UI/L)	24 ± 10	20 ± 6	0.058

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ALT (UI/L)	30 ± 19	24 ± 11	0.054
<b>Carotid IMT</b> (mm)	1 ± 0.1	0.9 ± 0.1	0.003
SD: standard deviation; TG: triglycerides; CHO: cholesterol; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase.			

<b>Supplementary Table S3. The effect of 4-month semaglutide therapy on patients with medium diabetes (n=9).</b>			
<b>Variables</b>	<b>Baseline (mean ± SD)</b>	<b>4 months (mean ± SD)</b>	<b>p-value</b>
<b><i>Anthropometric parameters</i></b>			
Weight (kg)	84 ± 17	81 ± 17	0.009
Waist (cm)	98 ± 11	94 ± 11	0.024
BMI (kg/m <sup>2</sup> )	31 ± 8	30 ± 8	0.008
<b><i>Glycemic parameters</i></b>			
Glycemia (mg/dL)	177 ± 115	121 ± 16	0.133
HbA1c (%)	9±3	7±1	0.009
<b><i>Plasma lipids</i></b>			
Total CHO (mg/dL)	187 ± 60	152 ± 23	0.122
TG (mg/dL)	191 ± 122	131 ± 39	0.101
LDL CHO (mg/dL)	108 ± 54	82 ± 21	0.183
HDL CHO (mg/dL)	46 ± 14	46 ± 12	0.728
<b><i>Hepatic parameters</i></b>			
Alkaline phosphatase (U/l)	70 ± 42	59 ± 24	0.195
GGT (UI/L)	38 ± 20	34 ± 18	0.054
AST (UI/L)	25 ± 22	22 ± 12	0.418
ALT (UI/L)	30 ± 27	24 ± 15	0.190
<b>Carotid IMT</b>	1 ± 0.2	0.9 ± 0.2	<0.001
SD: standard deviation; TG: triglycerides; CHO: cholesterol; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase.			

Supplementary Table S4. The effect of 4-month semaglutide therapy on patients with late diabetes (n=19).			
Variables	Baseline (mean $\pm$ SD)	4 months (mean $\pm$ SD)	p-value
<b><i>Anthropometric parameters</i></b>			
Weight (kg)	89 $\pm$ 18	83 $\pm$ 15	<0.001
Waist (cm)	102 $\pm$ 12	98 $\pm$ 11	0.002
BMI (kg/m <sup>2</sup> )	33 $\pm$ 4	30 $\pm$ 4	<0.001
<b><i>Glycemic parameters</i></b>			
Glycemia (mg/dL)	179 $\pm$ 68	124 $\pm$ 23	<0.001
HbA1c (%)	9 $\pm$ 2	7 $\pm$ 0.7	<0.001
<b><i>Plasma lipids</i></b>			
Total CHO (mg/dL)	176 $\pm$ 37	155 $\pm$ 34	<0.001
TG (mg/dL)	155 $\pm$ 94	131 $\pm$ 47	0.086
LDL CHO (mg/dL)	104 $\pm$ 40	89 $\pm$ 35	0.004
HDL CHO (mg/dL)	41 $\pm$ 11	39 $\pm$ 8	0.300
<b><i>Hepatic parameters</i></b>			
Alkaline phosphatase (U/l)	69 $\pm$ 22	63 $\pm$ 21	0.013
GGT (UI/L)	31 $\pm$ 17	29 $\pm$ 14	0.347
AST (UI/L)	19 $\pm$ 6	19 $\pm$ 5	0.777
ALT (UI/L)	27 $\pm$ 13	24 $\pm$ 10	0.015
<b><i>Carotid IMT</i></b>	1 $\pm$ 0.1	0.9 $\pm$ 0.08	<0.001
SD: standard deviation; TG: triglycerides; CHO: cholesterol; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase.			

Supplementary Table S5: Anthropometric, glycemic, hepatic parameters and plasma lipids variation according to diabetes duration				
Variables	Delta			p-value
	Early diabetes (n=12)	Medium diabetes (n=9)	Late diabetes (n=19)	
<b>Anthropometric parameters</b>				
Weight (kg)	-5.5 (5.5)	-3.5 (3.1)	-5.9 (5.0)	0.472
Waist (cm)	-4.7 (3.2)	-3.3 (3.6)	-3.3 (4.0)	0.603
BMI (kg/m²)	-1.8 (1.6)	-1.2 (1.1)	-2.3 (2.1)	0.351
<b>Glycemic parameters</b>				
Glycemia (mg/dL)	-52 (54)	-56 (100)	-55 (57)	0.986
<b>Plasma lipids</b>				
Total CHO (mg/dL)	-19 (25)	-34 (59)	-21 (21)	0.548
TG (mg/dL)	-4 (53)	-60 (98)	-24 (58)	0.175
LDL CHO (mg/dL)	-21 (22)	-26 (50)	-14 (19)	0.600
HDL CHO (mg/dL)	+3.1 (6.7)	+0.7 (5.5)	-1.8 (7.5)	0.163
<b>Hepatic parameters</b>				
Alkaline phosphatase (U/l)	-22.0 (38)	-10.8 (22.8)	-6.5 (7.5)	0.243
GGT (UI/L)	-9.7 (16.5)	-4.4 (5.9)	-1.9 (8.6)	0.179
AST (UI/L)	-4.0 (6.6)	-3.2 (11.3)	-0.2 (3.2)	0.273
ALT (UI/L)	-5.4 (8.7)	-6.3 (13.3)	-3.1 (5.0)	0.594
SD: standard deviation; TG: triglycerides; CHO: cholesterol; AST: aspartate aminotransferase; ALT: alanine aminotransferase; GGT: gamma-glutamyl transferase.				

Supplementary Table S6: Correlation between hepatic steatosis markers (FLI, HSI), hepatic fibrosis markers (AST/ALT ratio, BARD score) and triglyceride glucose (TyG) index and changes in cIMT and HbA1c				
Univariate analysis of variance	Dependent variable: cIMT		Dependent variable: HbA1c	
	F	p-value	F	p-value
FLI	0.838	0.367	2.426	0.129
HSI	2.161	0.151	0.817	0.373
AST/ALT ratio	0.958	0.335	1.274	0.267
BARD score	0.162	0.690	0.052	0.821
TyG index	0.000	0.985	4.187	<b>0.049</b>
cIMT: carotid intima-media thickness; HbA1c: hemoglobin A1c; FLI: Fatty Liver Index; HSI: Hepatic Steatosis Index; TyG: triglyceride-glucose index. Bold values represent statistically significant p-value.				

Supplementary Table S7: Correlation between anthropometric, glycemic, hepatic parameters and plasma lipids and changes in cIMT and HbA1c.				
Univariate analysis of variance	Dependent variable: cIMT		Dependent variable: HbA1c	
	F	p-value	F	p-value
Total CHO	0.784	0.382	1.638	0.209
TG	0.927	0.324	2.053	0.161
LDL CHO	0.315	0.578	1.545	0.222
Alkaline phosphatase	0.085	0.73	0.821	0.371
GGT	0.937	0.340	0.571	0.455
AST	0.100	0.754	0.889	0.352
ALT	0.001	0.969	0.071	0.792
cIMT: carotid intima-media thickness; HbA1c: hemoglobin A1c; TG: triglycerides; CHO: cholesterol; GGT: gamma-glutamyl transferase; AST: aspartate aminotransferase; ALT: alanine aminotransferase;				