Association of the *PPARG2 Pro12Ala*, *TNFα G(-308)A* and *G(2-38)A*, *LIPC C(-514)T*, *ACE I/D*, *SLCO1B1 Val174Ala* polymorphism with endothelial function and atorvastatin response in type 2 diabetic patients

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Introduction and objectives :

The endothelial dysfunction (ED) is the early marker of macrovascular diseases. Statin therapy improves macrovascular outcomes in patients with type 2 diabetes (T2D). To assess the association of the endothelial dysfunction (ED) parameters and the lipid-lowering response to atorvastatin therapy in patients with type 2 diabetes (T2D) with potential genetic markers

Methods

Research design

Patients: with T2D
Research design: prospective open study
Included: 122 patients with T2D and dyslipidemia
Drug: atorvastatin 10/20 mg (N=49 /N=48)
Treatment period: 52 2 weeks

Lipid profile before and after treatment

pulse wave analysis with reactive hyperemia before and after treatment

genetic markers

Candidate genes of atherosclerosis development and progression

PPARG2 gene - It encodes a nuclear receptor, which is regulated by fatty acid synthesis, TNF-α, resistin, adiponectin, adipogenesis factors

TNF-α gene - It encodes proinflammatory cytokine α, its polymorphisms are associated with obesity and insulin resistance

LIPC gene – It's responsible for the hepatic lipase synthesis and LDL-C, HDL-C remodeling

ACE gene - It encodes angiotensin converting enzyme catalyzes the cleavage of angiotensin I to angiotensin II

SLCO1B1 gene - It encodes the ATP-binding proteins translocators drugs

Statistic analysis was evaluated using the Mann-Whitney, Wilcoxon tests, p <0,05

Results

Table 1. Clinical characteristics of completed the study protocol patients (n = 97) before statin treatment

Clinical parameters	Value
Gender (male%/female%)	23/77
BMI, kg /m^2	32,0 [28;33,7][1]
Age, years	64 [55;69]
The duration of T2D, years	9 [7,5;13]
HbA1c, %	8,2 [7,1;10,2]
Smoking,%	13,8
Cardiovascular heredity, %	35
Hypertension, %	84,5
Hypertension duration, years	7 [3;15]
Systolic blood pressure, mm Hg	146 [130;150]
Diastolic blood pressure, mmHg	85 [75;90]
Drugs therapy that block the RAS, %	86,9
Therapy of ACE-ingibitors %/ blockers of the RAS%	52/48

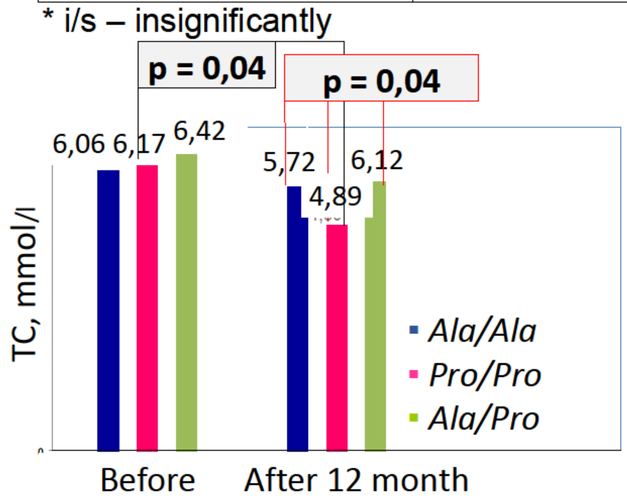
[1] Data are presented: Me [25 percentile; 75 percentile]%

Results

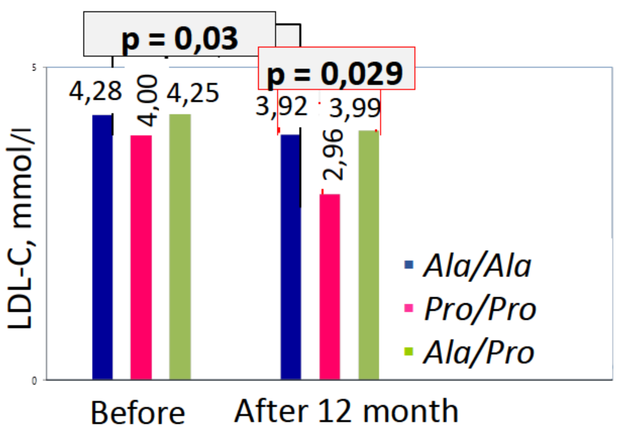
Table 2. Dynamics of lipid spectrum and HbA1c before and after 12 months statin therapy, n = 97

Clinical parameters	Before	after 12 months	p
HbA1c, %	8,2 [7,1;10,2]	8,0 [6,9;10,0]	i/s
Cholesterol (TC), mmol/l	5,88 [4,6;6,30]	5,25 [4,55; 6,30]	< 0,05
LDL-C, mmol/l	3,78 [2,8; 4]	3,09 [2,80; 2,58]	i/s
Triglycerides, mmol/l	2,12 [1,6;3,5]	1,63 [1,60; 1,18]	< 0,05
HDL-C, mmol/l	1,05 [0,88; 1,3]	1,16 [0,88; 0,88]	i/s

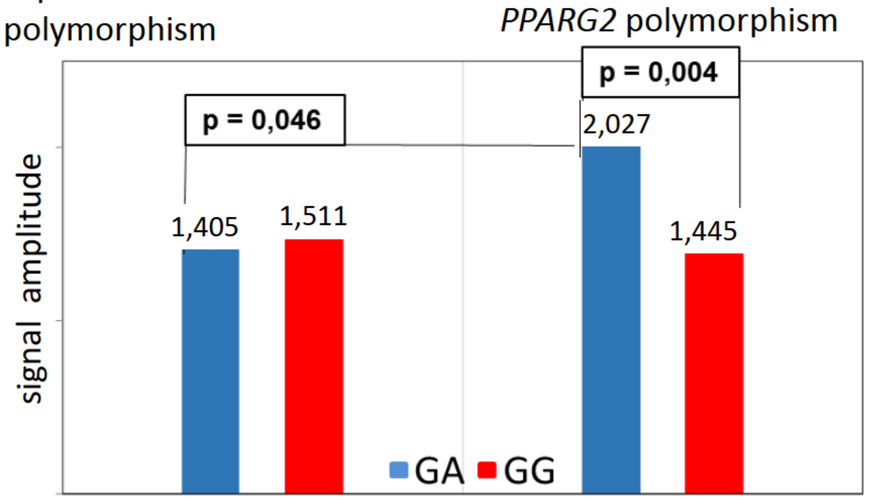
* i/s – insignificantly



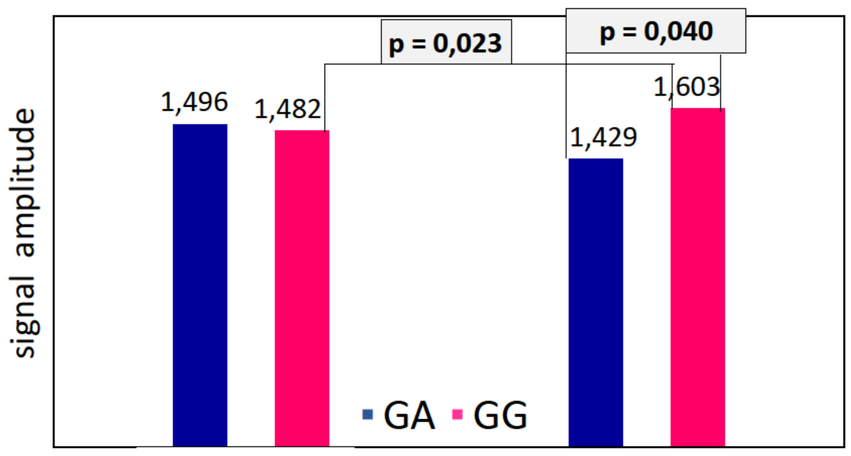
Pic.1. Dynamics of TC on statin therapy depends on the *Pro12Ala PPARG2* polymorphism



Pic.2. Dynamics of LDL-C on statin therapy depends on the *Pro12Ala PPARG2* polymorphism



Pic.3. ED dynamics on statin therapy depends on the *TNFα G (308) A* polymorphism



Pic.4. ED dynamics on statin therapy depends on the *TNFα G (238) A* polymorphism

Conclusion

- *PPARG2 Pro12Ala* polymorphism accounts for interindividual variability of response to statin therapy in patients with T2D.
- Significant association of *TNF-α* gene polymorphism with ED in T2D suggests an important role of inflammation in the genesis of macrovascular diseases.

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