OSTEOPROTEGERIN AS A MARKER OF MYOCARDIAL DAMAGE IN PATIENTS WITH TYPE 2 DIABETES AND ACUTE CORONARY SYNDROME

Anna M.Dąbrowska[1], Jerzy S.Tarach[1], Arleta Malecha-Jędraszek[2], Beata Wojtysiak-Duma[2], Anna Toruń-Jurkowska[3], Janusz Kudlicki[4], Helena Donica[2]

[1]Department of Endocrinology, [2]Department of Biochemical Diagnostics, Chair of Laboratory Diagnostics, [3]Department of Mathematics and Medical Biostatistics, [4]Department of Cardiology
Medical University, Lublin, Poland

Introduction

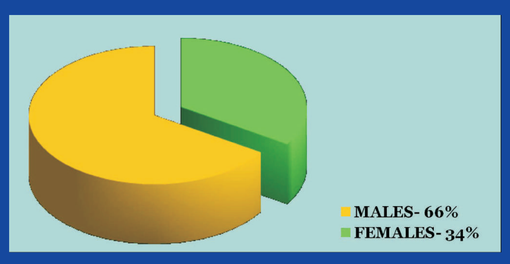
It's known that **type 2 diabetes** increases the risk of cardiovascular disease. **Silent myocardial ischaemia** occurs more frequently in diabetics and may result in more severe coronary artery disease.

Osteoprotegerin (OPG) named also as osteoclastogenesis inhibitory factor (OCIF) is a **glycoprotein** which was first reported **in rats** by **W.S. Simonet (1997)** as a protein involved in the regulation of bone density (it inhibits bone resorption).

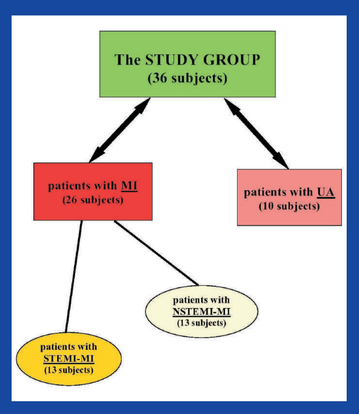
Osteoprotegerin has a molecular weight of **60 kDa** as a monomer and **120 kDa** as a disulfide-linked dimer. It belongs to the tumor necrosis factor receptor superfamily (**TNFR**) and inhibits the binding of **RANK** to **RANKL** (osteoprotegerin ligand = osteoclast differentiation factor) and thus inhibits the recruitment, proliferation and activation of osteoclasts. **Osteoprotegerin is mainly secreted** by **bone (osteoblasts)**, but is also produced by a variety of different tissues including **endothelial cells, smooth muscle cells** and **heart muscle.**

The role of OPG in the pathogenesis of:
- ☐ type 2 diabetes
- ☐ atherosclerosis
- ☐ cardiovascular complications is still studied.

Material and Methods



THE STUDY was carried out in 36 patients (12 females and 24 males) with type 2 diabetes (DM2) and acute coronary syndrome (ACS).



The STUDY GROUP was divided into subgroups:
- **26 subjects with myocardial infarction (MI)**
  - **13 patients with ST elevation (STEMI-MI)**
  - **13 patients with non-ST elevation (NSTEMI-MI)**

as well as
- **10 subjects with unstable angina (UA).**

- ☐ The material for the study was the peripheral **blood** obtained from **the ulnar vein (10ml)**.
- ☐ Serum was separated from the collected blood samples by centrifugation in standard way.
- ☐ **Serum Osteoprotegerin** concentration was determined with the use of **MicroVue OPG EIA** (an enzyme immunoassay with sensitivity of 0.4 pmol/l).

For statistical analysis of the obtained results, Statistica 8.0 StatSoft was used (test **U Mann-Whitney** and **Spearman's test** were applied).

Results

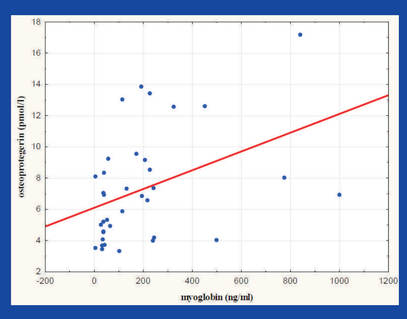
Serum levels of **OSTEOPROTEGERIN (pmol/l)** and selected **parameters in the study group**.

PARAMETERS	MEAN ± SEM
OPG (pmol/l)	**7.283 ± 3.516**
Age (years)	**70.22 ± 7.62**
BMI (kg/m2)	**29.43 ± 3.47**
HbA1C (%)	**7.21 ± 1.17**
Duration of DM2 (years)	**7.90 ± 6.34**

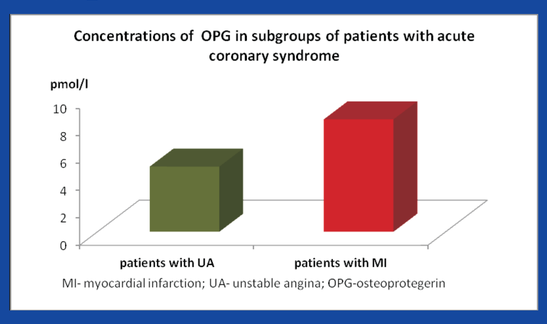
In the study group positive correlations between OPG level and troponin, CK-MB, myoglobin levels were observed.

VARIABLES	R Spearman	t(N-2)	p
CK-MB	0.463	3.046	0.004
Myoglobin	0.446	2.903	0.006
Troponin	0.484	3.225	0.003

OPG serum concentration was **positive** correlated with **myoglobin level (p=0.006),** measured few hours after MI. Patients with **higher level of myoglobin** in the blood had higher serum **OPG** concentration.

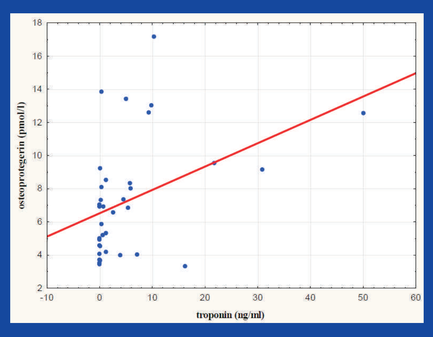


Patients with MI had increased OPG concentrations compared to subjects with UA:
8.244±3.639 pmol/l vs 4.782±1.292 pmol/l (Z=2.807; p<0.05)

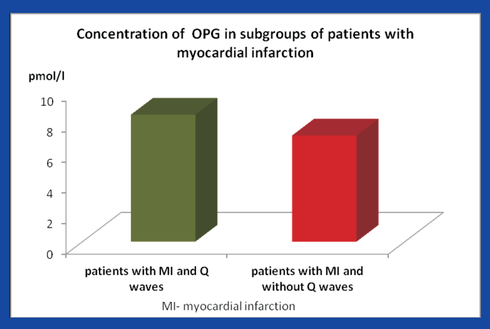


MI- myocardial infarction; UA- unstable angina; OPG-osteoprotegerin

OPG serum concentration was **positive** correlated with **troponin level (p=0.003),** measured few hours after MI. Patients with **higher troponin level** had higher concentration of **OPG** in the serum.

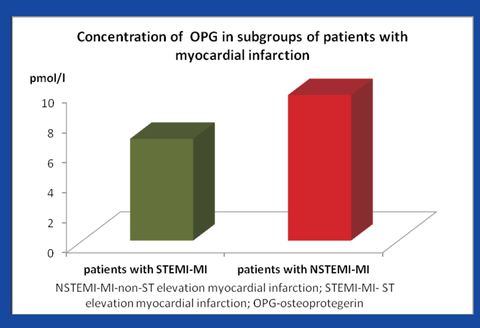


No statistically significant difference between patients with MI and Q waves and subjects with MI and without Q waves has been noted.



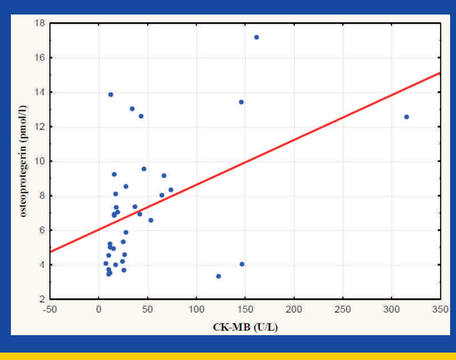
MI- myocardial infarction

In the group of patients with MI: subjects with NSTEMI-MI had *higher* serum OPG levels (9.702±4.069 pmol/l) than subjects with STEMI-MI (6.786±2.534 pmol/l) (Z=2.105; p<0.05)



NSTEMI-MI-non-ST elevation myocardial infarction; STEMI-MI- ST elevation myocardial infarction; OPG-osteoprotegerin

A **positive** correlation between **OPG** serum level and **CK-MB** concentration **(p=0.004)**, measured few hours after MI, has been observed.
Subjects with **higher CK-MB level** in the blood had higher **OPG** level in the serum.



Conclusions

Osteoprotegerin (OPG) concentration:
1. **is increased in diabetics with MI and subjects with NSTEMI-MI**
2. **correlates positively with severity of myocardial ischaemia**
3. **may be a risk factor for the progression of atherosclerosis and onset of cardiovascular disease**
4. **may predict cardiovascular events in diabetic patients**