Serum osteoprotegerin as a marker of left ventricle hypertrophy in stable kidney transplant recipients

Jerzy Chudek[1,2], Aureliusz Kolonko[1], Magdalena Szotowska[1], Piotr Kuczera[1], Andrzej Więcek[1]

[1]Department of Nephrology, Endocrinology and Metabolic Diseases, [2]Department of Pathophysiology; Medical University of Silesia, Katowice, Poland

BACKGROUND: Osteoprotegerin (OPG) is an important physiological regulator of osteoclastogenesis and marker of atherosclerosis. Increased serum OPG levels were reported in patients with chronic kidney disease and severe vascular calcifications, which are a well-known factor participating in the development of left ventricle hypertrophy (LVH). This cross-sectional study aimed to evaluate whether OPG is a marker of LVH in stable kidney transplant recipients.

PATIENTS AND METHODS: Echocardiography, carotid ultrasound (intima media thickness - IMT) and pulse wave velocity (PWV) were performed in 112 kidney transplant recipients with a mean time after transplant of 8.0 ± 1.8 years. OPG, parathormone (PTH), inflammatory markers, adhesion molecules and N-terminal prohormone of the brain natriuretic peptide (NT-proBNP) concentrations were measured. LVH was diagnosed in patients with left ventricle mass index (LVMI) >110 g/m^2 for women and >134 g/m^2 for men.

RESULTS: In 64 patients (57%) LVH was diagnosed. Patients with LVH were older by roughly 3 years, had 10 months longer dialysis vintage, greater IMT and more frequent carotid plaques. They also had slightly higher systolic BP and more frequent MACE in anamnesis. Moreover, they had higher serum PTH, hsCRP, OPG, and NT-proBNP concentrations, but lower eGFR and HDL. Serum OPG level was significantly related to LVMI (r=0.280, p=0.005) (Fig. 1) and NT-proBNP (r=0.226, p=0.02) (Fig. 2), but not to eGFR. Additionaly, serum NT-proBNP concentration was proportional to LVMI (r=0.416, p<0.001) and inversely related to eGFR (r=-0.251, p=0.01). In backward stepwise multivariate regression analysis, the LVMI variability was independently explained by NT-proBNP (β=0.358), OPG (β=0.203) and eGFR (β=-0.104). <u>Receiver operating curve (ROC) analysis showed that OPG over 4.8 pmol/l is more sensitive marker of LVH than NT-proBNP over 429 pg/ml (78.1% vs. 62.5%), however with lower specificity (47.9% vs. 66.7%).</u>

CONCLUSION: The assessement of OPG in addition to NT-proBNP improves the prediction of LVH in stable kidney transplant recipients, however its usefulness in clinical practice requires further studies.

Table 1 — Patients characteristics

|	LVH (+) n=64	LVH (-) n=48	ANOVA
Age [years]	52 (49-55)	49 (45-52)	NS
Gender [M/F]	45/19	24/24	0.05
BMI [kg/m^2]	27.7 (26.4-29.0)	26.7 (25.3-28.1)	NS
Duration of dialysis [mo]	38 (30-46)	28 (20-35)	NS
Time after transplantation [y]	7 (4-9)	8 (7-9)	NS
Hypertension [%]	92.2	89.6	NS
Diabetes n[%]	19 (29.7)	14 (29.2)	NS
Coronary artery disease n[%]	6 (9.4)	2 (4.2)	NS
MACE n[%]	19 (29.7)	4 (8.3)	0.01
Systolic BP [mmHg]	139 (135-144)	137 (132-143)	0.02
Diastolic BP [mmHg]	85 (83-87)	86 (84-87)	NS
eGFR [ml/min/1.73m^2]	46 (41-51)	56 (48-63)	0.03
hsCRP [mg/L]	5.9 (3.8-8.0)	3.3 (2.3-4.2)	0.04
Calcium [mmol/L]	2.38 (2.32-2.44)	2.39 (2.36-2.42)	NS
Phosphate [mmol/L]	1.10 (1.03-1.16)	1.10 (1.03-1.16)	NS
Parathormon [pg/mL]	243 (166-319)	144 (112-176)	0.03
Cholesterol [mmol/L]	5.4 (5.1-5.7)	5.4 (5.1-5.8)	NS
HDL [mmol/L]	1.1 (1.0-1.2)	1.3 (1.2-1.5)	0.004
Triglicerydes [mmol/L]	1.8 (1.6-2.1)	1.6 (1.4-1.9)	NS
LDL [mmol/L]	3.5 (3.2-3.8)	3.3 (3.0-3.7)	NS
PWV [m/s]	13.2 (12.0-14.5)	12.8 (10.9-14.7)	NS
IMT [nm]	0.7 (0.66-0.74)	0.6 (0.56-0.63)	<0.001
LVMI [g/m^2]	171 (160-182)	105 (100-110)	<0.001
Carotid plaques n(%)	29 (45)	12 (25)	0.04
NT-proBNP [pg/mL]*	2566 (1077-4055)	732 (336-1127)	0.04**
OPG [pmol/L]	6.4 (5.8-7.1)	5.5 (4.9-6.0)	0.04

Data shown as means ± 95% CI or frequencies, *median and quartiles, ** Kruskal-Wallis test. LVH: left ventricular hypertrophy,, BMI: body mass index, MACE: major adverse cardiac events, BP: blood pressure, eGFR - MDRD: estimated glomerular filtration rate based on Modification of Diet in Renal Disease Study formula, CRP: C-reactive protein, HDL: high-density cholesterol, LDL: low-density cholesterol, PWV: pulse wave velocity, IMT: carotid intima media thickness, LVMI: left ventricular mass index, NT-proBNP: N-terminal prohormone for brain natriuretic peptide, OPG: osteoprotegerin.

Fig. 1

r=0.280; p=0.004
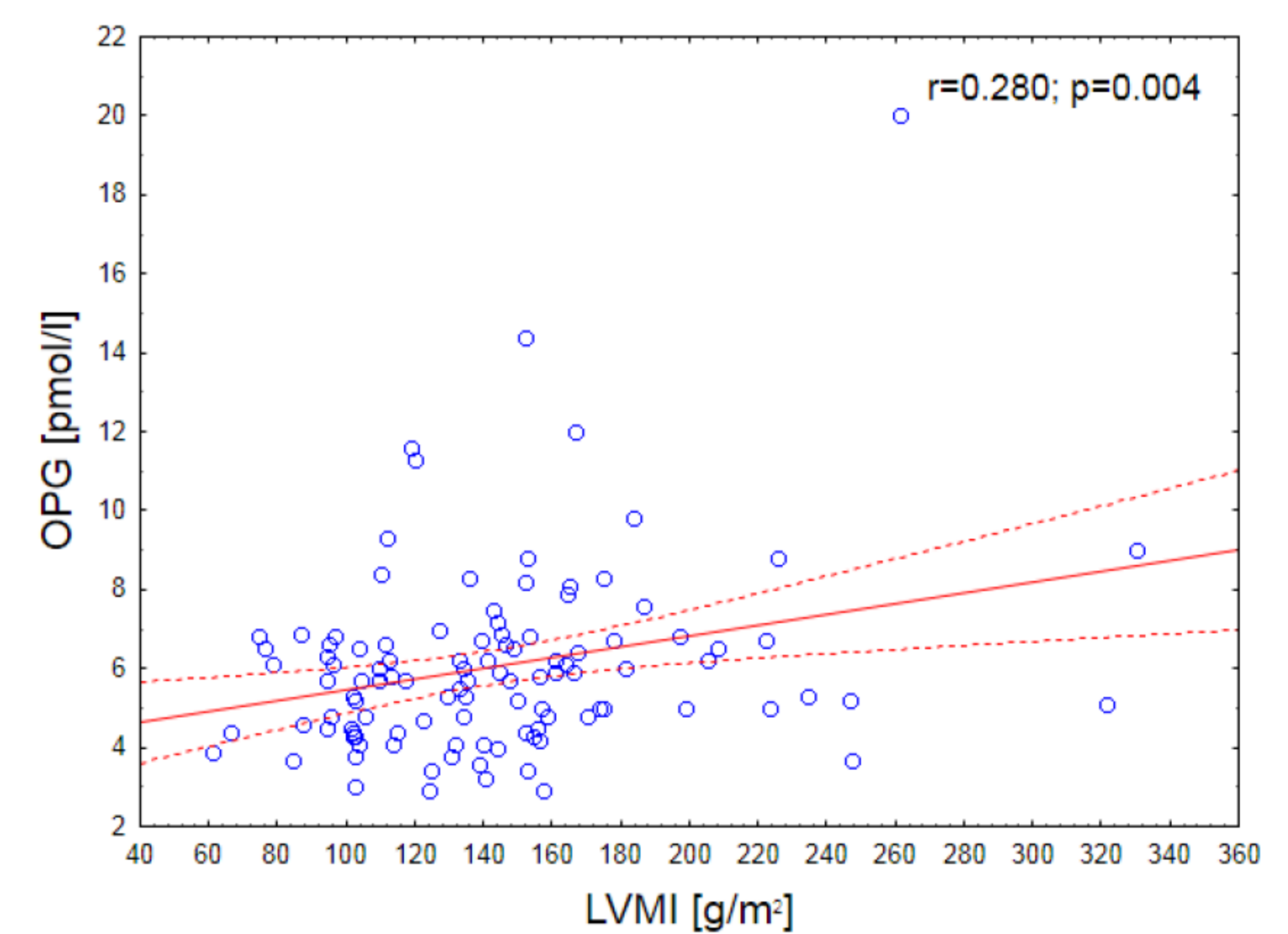
The univariate correlation between osteoprotegerin (OPG) and left ventricular mass index (LVMI)

Fig. 2

r=0.226; p=0.02
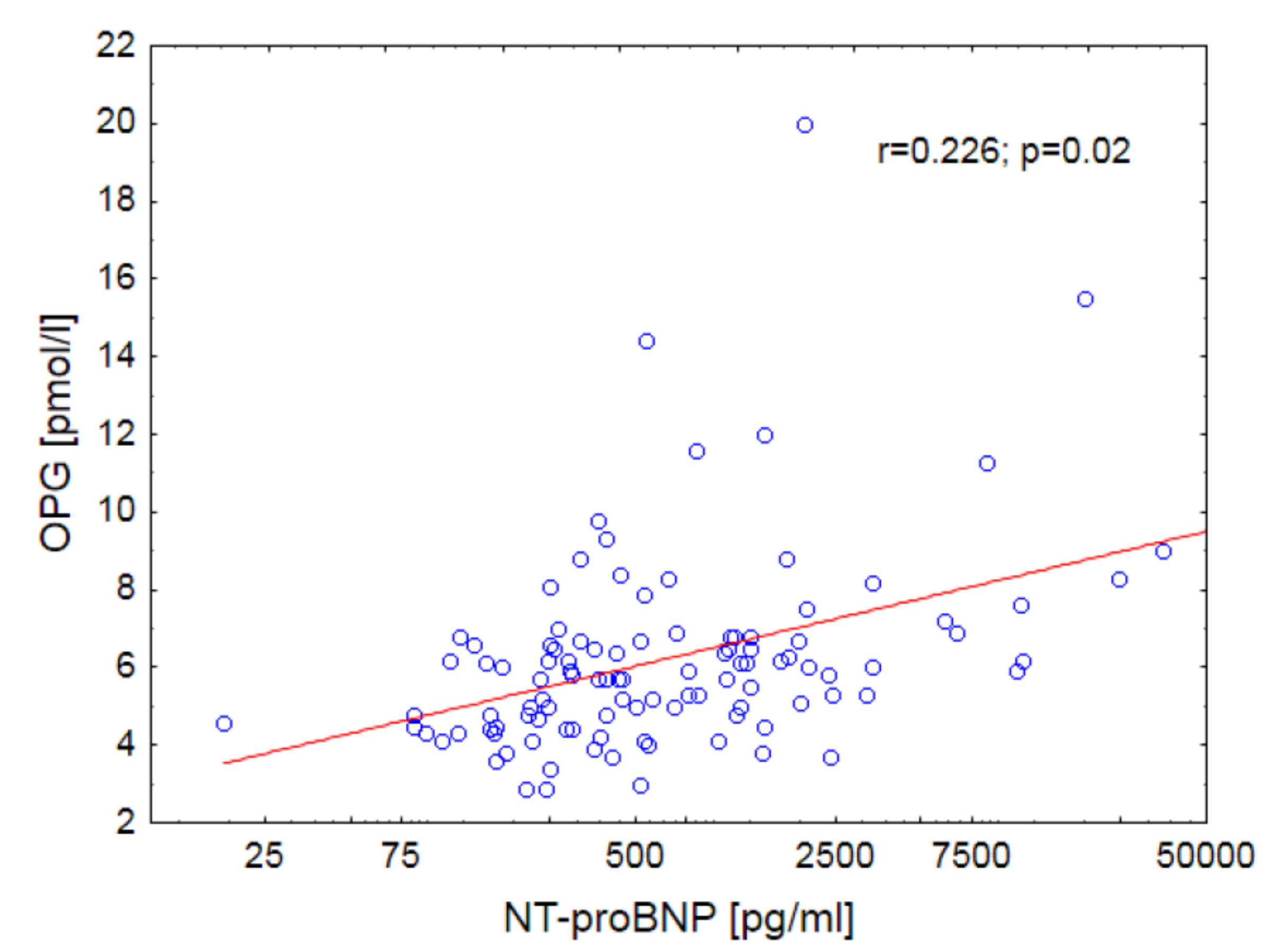
The univariate correlation between osteoprotegerin (OPG) and N-terminal prohormone for brain natriuretic index (NT-proBNP).

Table 2

The results of backward stepwise multivariate regression analysis for LVH

Independent variable	β	p
NT-proBNP [per 1 pg/mL]	0.358 (0.183-0.533)	<0.001
OPG [per 1 pmol/l]	0.203 (0.028-0.378)	0.04
eGFR [per 1 ml/min/1.73m^2]	-0.104 (-0.279- 0.071)	0.11

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N) Renal Transplantation. N2) Clinical epidemiology of renal transplantation.
Jerzy Chudek

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