

Vrijednost serumskog osteoprotegerina kao biomarkera u bolesnika s kalcificiranom aortnom stenozom sa ili bez zatajivanja srca

Value of serum osteoprotegerin as a biomarker in patients with calcific aortic valve stenosis with or without heart failure

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Veza između koštanog metabolizma i vaskularnih kalcifikacija potaknula je potragu za zajedničkim medijatorima koji povezuju koštani i vaskularni sustav. Od kada je prvobitno otkrivena njegova uloga ključnog regulatora koštanog metabolizma, osteoprotegerin (OPG) je postao predmetom intenzivnog istraživanja, osobito u svojoj ulozi formiranja vaskularnih i valvularnih kalcifikacija. Istraživanja in vitro te ona u animalnih modela pokazala su da OPG inhibira vaskularne kalcifikacije. Paradoksalno, klinička istraživanja pokazala su da serumska razina OPG raste u koronarnoj bolesti srca i kalcificirajućoj stenozu aortne valvule. Da istražimo navedeno, sljedeći parametri su analizirani u 51 bolesnika s teškom kalcificiranom aortalnom stenozom te 39 prema dobi i spolu usklađenih kontrolnih ispitanika, bez obstruktivne koronarne bolesti, ishemijske cerebralne bolesti, bolesti perifernih arterija te s očuvanom renalnom funkcijom: OPG, sistolička funkcija srca te razvoj srčanog zatajivanja. Vrijednost OPG je bio povišena kod bolesnika s aortnom stenozom. U zaključku, ovi podaci podupiru hipotezu o povezanosti teške aortne stenozu s promijenjenim metabolizmom OPG. Nadalje, pokazali smo da je serumski OPG značajno viši u bolesnika sa zatajivanjem srca zbog aortne stenozu u usporedbi s bolesnicima s aortnom stenozom bez zatajivanja srca. Ovi podaci ukazuju da bi se OPG mogao koristiti kao marker zatajivanja srca u ovih bolesnika, ukazujući na njihovu lošiju prognozu.

Ključne riječi: osteoprotegerin, stenozu aortne valvule, kalcifikacije, zatajivanje srca, biomarker.

Association between bone metabolism and vascular calcification has stimulated search for common mediators linking bone and vascular system. Since its initially discovered, as a key regulator in bone metabolism, osteoprotegerin (OPG) has become an object of intensive research in its role in forming vascular and valvular calcification. Studies in vitro and those in animal models have shown that osteoprotegerin inhibits vascular calcification. Paradoxically however, clinical studies have shown that serum OPG levels increases in coronary artery disease and calcific aortic valve stenosis. To further investigate the role of OPG in calcific aortic valve stenosis with and without heart failure, the following parameters were analyzed in 51 patients with severe aortic stenosis (AS) and in 39 age and gender-matched controls, without obstructive coronary artery disease, ischemic cerebral disease, ischemic peripheral artery disease and with preserved renal function: OPG, systolic heart function and development of heart failure, amongst patients with aortic stenosis. Value of OPG was elevated in patients with aortic stenosis. Furthermore, we found serum OPG levels to be significantly higher in patients with heart failure due to severe aortic stenosis, compared to its value in aortic stenosis patients, without heart failure. These data support a hypothesis connecting (severe) aortic stenosis to altered OPG, thus OPG can be used as a novel biomarker in aortic stenosis and as marker of heart failure in these patients, showing poorer prognostic function.

Keywords: osteoprotegerin, aortic valve stenosis, calcification, heart failure, biomarker.

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Table 1. Serum levels of OPG in pair-matched patients and controls.

	N	Mean OPG value	Standard deviation	t Value	p Value
Patients with AS	51	7.5243	3.71412	t=4.908	p=0.000
Controls	39	4.7964	1.22384		

*p value is significant at the 0.05 level; AS - aortic stenosis; OPG - osteoprotegerin

Table 2. Serum levels of OPG in aortic stenosis patients with or without heart failure.

AS patients	n	Mean Rank	t Value	p Value
With HF	22	37.86	$\chi^2=24.643^*$	(df=1, p=0.000)
Without HF	29	17		

*For analyses it is used nonparametrical Mann-Whitney test, for the sample is <than 30 patients; AS - aortic stenosis, HF - heart failure