

**Serum levels of osteoprotegerin are raised in diabetic peripheral neuropathy and are significantly correlated with peripheral arterial calcification**

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The osteoprotegerin (OPG) signalling pathway has been linked with diabetic neuropathy. The aim was to measure serum OPG in diabetic patients with and without neuropathy and to investigate its possible association with vibration perception threshold as a marker of large fibre neuropathy and with the presence of peripheral arterial calcification on foot and ankle radiographs. **Methods:** We studied 45 patients with diabetic neuropathy, 88 patients without neuropathy and 22 healthy controls. Serum levels of osteoprotegerin were measured using ELISA (Biomedica, Austria). All patients had palpable foot pulses. Large fibre neuropathy was assessed by measuring vibration perception threshold (VPT) at the apex of the hallux and the mean of both feet was calculated. A subset of 38 patients was also assessed for the presence of peripheral arterial calcification on foot and ankle x-rays. **Results:** Serum OPG was significantly raised in patients with diabetic neuropathy compared with patients without neuropathy (5.1 pmol/l [3.8-6.1] versus 3.9 pmol/l [3.0-4.9],  $p=0.005$ ; median [25<sup>th</sup>-75<sup>th</sup> percentile]) and also compared with healthy controls (5.1 pmol/l [3.8-6.1] versus 2.9 pmol/l [2.6-3.8],  $p<0.001$ ). Overall, serum OPG levels were positively correlated with the mean VPT ( $r=0.262$ ,  $p=0.009$ ). In the subset of 38 patients, serum OPG was significantly correlated with the presence of peripheral arterial calcification ( $r=0.445$ ,  $p=0.005$ ) as well as the mean VPT ( $r=0.253$ ,  $p=0.012$ ). Serum OPG was raised in both type 1 and type 2 diabetic neuropathic patients. In type 1 diabetes, serum OPG was significantly raised in patients with neuropathy compared with patients without neuropathy (5.0 pmol/l [3.9-5.7] versus 3.8 pmol/l [2.9-4.6],  $p=0.042$ ) and also compared with healthy controls (5.0 pmol/l [3.9-5.7] versus 2.9 pmol/l [2.6-3.8],  $p<0.001$ ). Furthermore, in type 2 diabetes serum OPG was raised in patients with neuropathy compared with patients without neuropathy (5.5 pmol/l [3.4-6.6] versus 4.0 pmol/l [3.2-4.9],  $p=0.05$ ) and also compared with healthy controls (5.5 pmol/l [3.4-6.6] versus 2.9 pmol/l [2.6-3.8],  $p<0.001$ ). **Conclusions:** Serum OPG is raised in both type 1 and type 2 diabetic patients with neuropathy. Furthermore, serum OPG is significantly correlated with peripheral neuropathy and peripheral arterial calcification.