Abstract: P3639

Vascular endothelial growth factor-C and mortality in patients with suspected but no history of coronary heart disease: a subanalysis of the ANOX study

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Background: The lymphatic system has been suggested to play an important role in cholesterol metabolism and cardiovascular disease. Recently, we demonstrated that serum levels of vascular endothelial growth factor-C (VEGF-C), a central player of lymphangiogenesis, are inversely and independently associated with the risk of all-cause mortality in patients with suspected or known coronary heart disease (CHD). However, the prognostic value of VEGF-C in patients with suspected but no history of CHD is still unclear.

Methods: Serum VEGF-C levels were measured in 1,717 patients with suspected but no history of CHD undergoing elective coronary angiography, enrolled in the development of novel biomarkers related to angiogenesis or oxidative stress to predict cardiovascular events (ANOX) study, and followed up for 3 years. The primary outcome was all-cause death. The secondary outcomes were cardiovascular death, and major adverse cardiovascular events (MACE) defined as a composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.

Results: During the follow-up, 161 patients died from any cause, 50 died from cardiovascular disease, and 104 developed MACE. After adjustment for established risk factors, VEGF-C levels were significantly and inversely associated with all-cause death (hazard ratio [HR] for 1-SD increase, 0.69; 95% confidence interval [CI], 0.58–0.83) and cardiovascular death (HR, 0.72; 95% CI, 0.52–0.998), but not with MACE (HR, 0.91; 95% CI, 0.74–1.13). Even after incorporation of N-terminal pro-brain natriuretic peptide, contemporary sensitive cardiac troponin-I, and high-sensitivity C-reactive protein into a model with established risk factors, the addition of VEGF-C levels further improved the prediction of all-cause death (continuous net reclassification improvement [NRI], 0.282; 95% CI, 0.121–0.443; P<0.001; integrated discrimination improvement [IDI], 0.009; 95% CI, 0.003–0.016; P=0.005), but not that of cardiovascular death (NRI, 0.178; 95% CI, -0.103–0.458; P= 0.214; IDI, 0.004; 95% CI, -0.002–0.009; P= 0.194) or MACE (NRI, 0.037; 95% CI, -0.162–0.235; P=0.717; IDI, 0.000; 95% CI, -0.0004–0.0005; P=0.872).

Conclusions: In patients with suspected but no history of CHD undergoing elective coronary angiography, a low
VEGF-C value may predict all-cause mortality independent of established risk factors and cardiovascular biomarkers.