Impact of soluble TWEAK, and CD163/TWEAK ratio on long-term cardiovascular mortality in patients with peripheral arterial disease

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Soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) is a potential mediator of cardiovascular disease.

We examined the associations between sTWEAK, its scavenger receptor sCD163, sCD163/sTWEAK ratio and risk for long-term all-cause and cardiovascular mortality in patients with symptomatic peripheral arterial disease (PAD).

sTWEAK and sCD163 serum levels were measured in PAD patients followed for 6.1±2.1 years (n=295). sTWEAK levels were significantly lower (672 (IQR 515; 872) vs. 814 (IQR 673; 957) pg/ml, p<0.0001), and sCD163/sTWEAK ratio significantly higher (0.91 (IQR 0.63; 1.37) vs. 0.77 (IQR 0.55; 1.12), p=0.008) in patients with critical limb ischemia (CLI) on admission compared with those with intermittent claudication (IC). During follow-up, 80 patients died, hereof 33 of cardiovascular causes. An increase of 100 pg/ml of baseline sTWEAK were associated with decreased risk for all cause [adjusted hazard ratio (HR) 0.89 (95%CI (0.80-0.99), p=0.043] and cardiovascular mortality [adjusted HR 0.83 (95%CI (0.69-0.99), p=0.038]. The patients with lower sTWEAK concentrations had a higher risk for cardiovascular death than patients in the two upper tertiles (adjusted HR=2.2, 95% CI (1.06-4.87), p=0.035). Similarly, the risk of cardiovascular death was 3-fold increased for patients in the upper tertile of sCD163/sTWEAK ratio compared to patients in two lower tertiles (adjusted HR 3.04 95% CI 1.44–6.43, p=0.004). The model including sCD163/sTWEAK ratio improves accuracy of cardiovascular death prediction (area under ROC curve 0.79 (0.72-0.86) vs. 0.84 (0.78-0.90), p=0.019).

Decreased sTWEAK concentration, and increased sCD163/sTWEAK ratio were significantly and independently associated with long-term cardiovascular mortality in patients with lower-extremity PAD.