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**GELSOLIN IS ASSOCIATED WITH PROGRESSION OF AORTIC ARCH CALCIFICATION IN HEMODIALYSIS PATIENTS**

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**Introduction and Aims:** Vascular calcification (VC) is a key process contributing to cardiovascular mortality in dialysis patients. Cross-sectional studies have identified several factors associated with VC, including age, diabetes, dialysis duration, markers of mineral bone metabolism, malnutrition and inflammation. Adipokines can regulate energy homeostasis and body weight, and contribute to inflammation and malnutrition in dialysis patients. Cytokines such as C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α) have been correlated with adverse clinical outcomes in ESRD patients. Gelsolin is an actin-binding protein that can modulate inflammation, and correlated inversely with HD mortality. In this report, we aim to investigate the association between aforementioned factors and progression of aortic arch calcification (AAC) in hemodialysis (HD) patients.

**Methods:** We evaluated AAC by plain chest X-ray. 184 stable prevalent HD patients were enrolled and their annual CXR in 2009 and 2013 were examined. The severity of calcification was classified (Symeondis et al. Int Angiol 2002) as grade 0 (no calcification visible), grade 1 (single thin or small spots of calcification), grade 2 (one or more areas of thick calcification, but ≤ 50% of the circular area of the aortic knob) and grade 3 (circular calcification with >50% of circular area of the aortic knob). Blood levels of gelsolin, IL-6, TNF-α, adiponectin, and leptin were measured by ELISA kits. Biographic and biochemical data at baseline were analyzed with status of AAC at baseline (2009) and in 4 years (2013).

**Results:** The characteristics of the 184 patients include: male 40%, mean age 60±11, HD vintage 61 (36-107) months. 27% had diabetes. At baseline, 110 (60%) patients had detectable AAC on plain chest X-ray. Patients with AAC had significantly lower serum albumin. They also tend to have older age, lower blood levels of gelsolin and hsCRP. Regression analysis confirmed albumin as the independent factor associated with baseline AAC. After 4 years of follow-up, 77% of the patients had AAC. 43% of those with grade 0 at baseline progressed to higher grades of aortic arch calcification. Compared to those with grade 0 at baseline, patients with grade 1 at baseline had increased risk of progression (73%, Odds ratio [OR] 2.11, 95% confidence interval [CI] 1.29-3.44, p=0.001). Furthermore, patients with grade 2 at baseline had even higher risk of progression (84%, OR 3.49, 95%CI 1.72-7.07, p<0.001). Patients with persistence or progression of AAC had significantly older age, lower blood levels of gelsolin and IL-6. They also had significantly higher prevalence of vascular disease (49% vs. 32%, p=0.046). Regression analysis confirmed baseline gelsolin as the independent factor associated with persistence and progression of AAC.

**Conclusions:** Our study demonstrated that hemodialysis patients with higher grades of aortic arch calcification are at increased risk of further progression (odds ratio 2–3). We also found lower blood levels of albumin and gelsolin associated with baseline and progressive AAC. These findings suggest that vascular calcification is a dynamic process, its progression rate is not constant, thus making the timing of effective intervention imperative. If the link between gelsolin and cardiovascular outcome can be confirmed in larger population, potential therapy involving gelsolin pathway may offer new hope for the patients.