Gelsolin and Progression of Aortic Arch Calcification in Hemodialysis patients

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OBJECTIVES

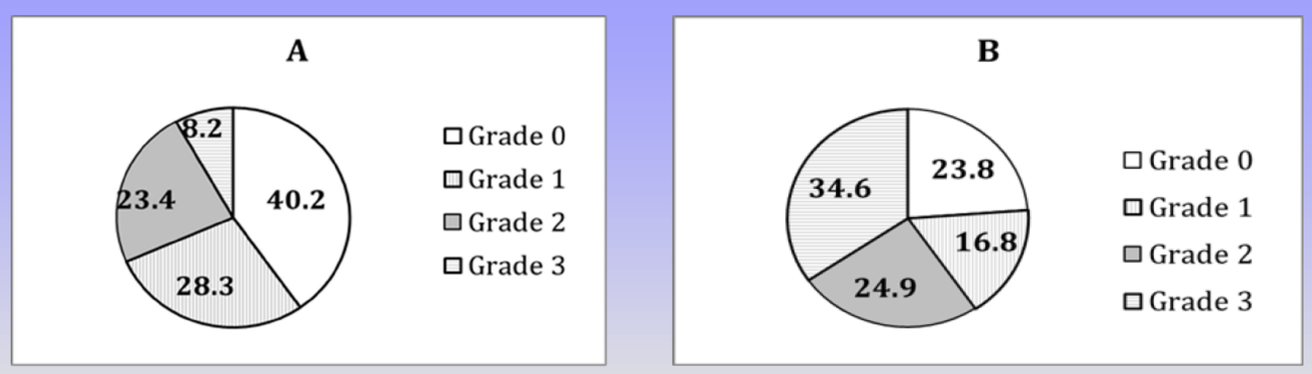
Vascular calcification (VC) is a key process contributing to cardiovascular mortality in dialysis patients. Cross-sectional studies have identified factors associated with VC, including age, diabetes, dialysis vintage, markers of mineral bone metabolism, malnutrition and inflammation. Cytokines such as C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) have been correlated with adverse clinical outcomes in dialysis 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 of aforementioned factors with aortic arch calcification (AAC) in hemodialysis (HD) patients. In addition, we characterized AAC progression over 4 years and its associated factors.

METHODS

We evaluated AAC by plain chest X-ray (CXR). 184 stable prevalent HD patients were enrolled and their annual CXR in 2009 and 2013 were examined. The severity of calcification was classified as grade 0 to 3. Blood levels of gelsolin, IL-6 and TNF-α were measured by ELISA kits. Biographic and biochemical data at baseline were analyzed with status of AAC at baseline (2009) and changes after 4 years (2013).

RESULTS

Figure 1. Distribution (in percentage %) of different grades of aortic arch calcification at (A) baseline and (B) after 4 years of follow-up.



1) The characteristics of the 184 patients include: male 40%, mean age 60±11, HD vintage 61 (36-107) months. 27% were diabetic.
2) 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).
3) 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).
4) Patients with AAC at baseline had significantly lower serum albumin. They also tend to have older age, lower handgrip strength, kt/v, gelsolin and higher hemoglobin.
5) Regression analysis confirmed HD vintage, kt/v, BMI, waist circumference, and albumin as the independent factors associated with baseline AAC.
6) Patients with persistence or progression of AAC had older age, higher mid-arm muscle area, waist circumference, IL-6, and lower gelsolin. They also had significantly higher prevalence of vascular disease (49% vs. 32%, p=0.046).
7) Regression analysis confirmed baseline gelsolin and waist circumference as the independent factors associated with persistence and progression of AAC.

CONCLUSIONS

1) Our study demonstrated that hemodialysis patients with grades 1 or 2 baseline aortic arch calcification are at increased risk of further progression (odds ratio 2~3) compared to those with grade 0 on chest X-ray.
2) Patients with AAC progression had increased chances of vascular disease.
3) In addition to the factors reported in the literature, we also found lower blood levels of gelsolin associated with progressive AAC.
4) The clinical implication is that patients with more advanced vascular calcification are at increased risk of further progression and vascular disease.
5) Therefore it is crucial to identify patients at risk and at early stage in order to administer effective intervention.
6) In addition, if the link between gelsolin and cardiovascular outcome can be confirmed in larger population, potential therapy involving gelsolin pathway may offer new hope for these patients.

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