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The Role of Apoptosis in Phosphate Induced Rat Aortic Valve Interstitial Cells Calcification

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Background:
The mechanisms involved in the initiation of valvular calcification are unknown, but apoptotic bodies may serve an important role in this process. Hyperphosphatemia was shown to stimulate vascular smooth muscle cell and endothelial cell apoptosis, a process that may initiate valvular calcification in patients with chronic kidney disease. In the present study, we investigated the role of apoptosis in phosphate induced AVICs calcification.

Methods:
Valve Interstitial cells (ICs) were isolated from valve leaflets of Sprague–Dawley rats. Calcification was induced by incubating the cells with phosphate 3.5 mM for 7 days. To assess the role of apoptosis, the cells were exposed to phosphate as well as Caspase inhibitor (zvad). We evaluated mineralization of cells using von -kossa staining and ca quantification by cresophthalein method. Osteoblast related proteins (Runx-2, osteopontin and osteocalcin) were evaluated using immunostaining, real time PCR and western blot.

Results:
Inhibition of apoptosis with the caspase inhibitor didn't reduce the calcification. The RNA level of osteopontin and the protein level of osteocalcin were also remained unchanged; however pre-treatment with caspase inhibitor decreased Runx-2 expression.

Conclusions:
Our result suggests that apoptosis inhibition does not modify calcification in valve interstitial cells. However, one of osteoblast marker level was reduced as result of apoptosis inhibition. We conclude that apoptosis may play a role in osteoblast features during calcification; however it does not affect directly the mineralization process.