

HIGH GLUCOSE DOES NOT MODULATE THE FORMATION OF VASCULAR CALCIFICATION IN EXPERIMENTAL UREMIC RATS

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OBJECTIVES

Vascular calcification is often seen in patients with chronic kidney disease and diabetes and is associated with increased mortality, myocardial infarction, stroke, and limb amputation. Results of previous studies by our laboratory and others showed that high phosphate-induced phenotypic switching of vascular smooth muscle cells (SMCs) into osteogenic cells plays an important role in the calcification process. In the present studies, we examined if glucose concentration affected high phosphate-induced SMC phenotypic switching and vascular calcification in experimental animal models and in cultured SMCs.

METHODS

(1) Cultured rat aortic SMCs were incubated in the medium with various concentrations of phosphate (0.9, 1.8, 2.7, and 4.5 mmol/L) and glucose (5, 25, and 50 mmol/L) for 6 and 8 days, and calcium deposition was measured.

(2) Male Sprague-Dawley rats were divided into 4 groups: adenine-fed uremic group; streptozotocin (STZ)-injected hyperglycemic group; adenine-fed and STZ-injected uremic/hyperglycemic group; and controls. Vascular calcification in the aorta of these rats was analyzed.

RESULTS

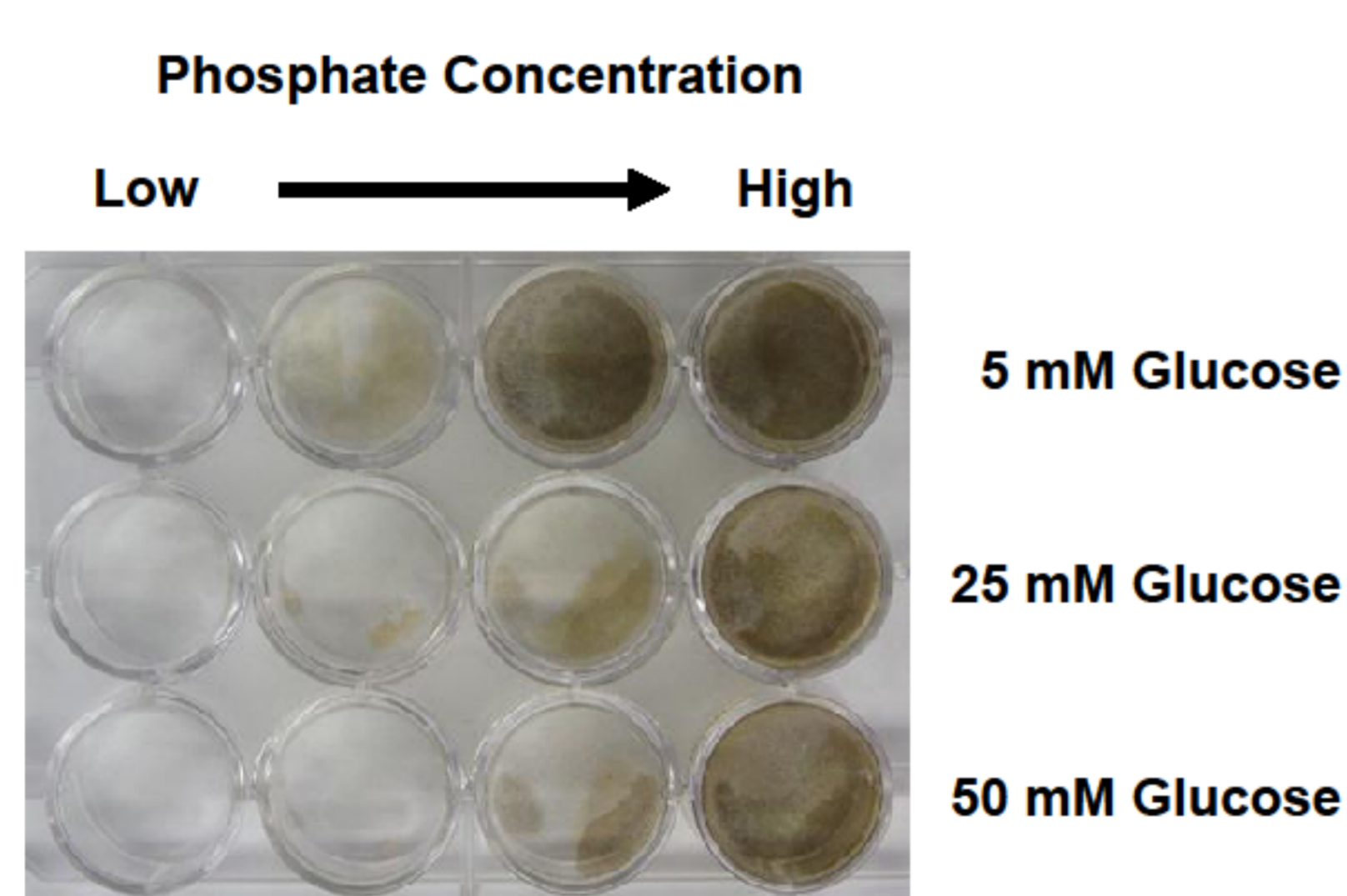


Figure 1. High phosphate, but not high glucose, induced calcification in cultured SMCs. SMC calcification was examined by von Kossa staining after 8-day incubation with various concentrations of phosphate and glucose.

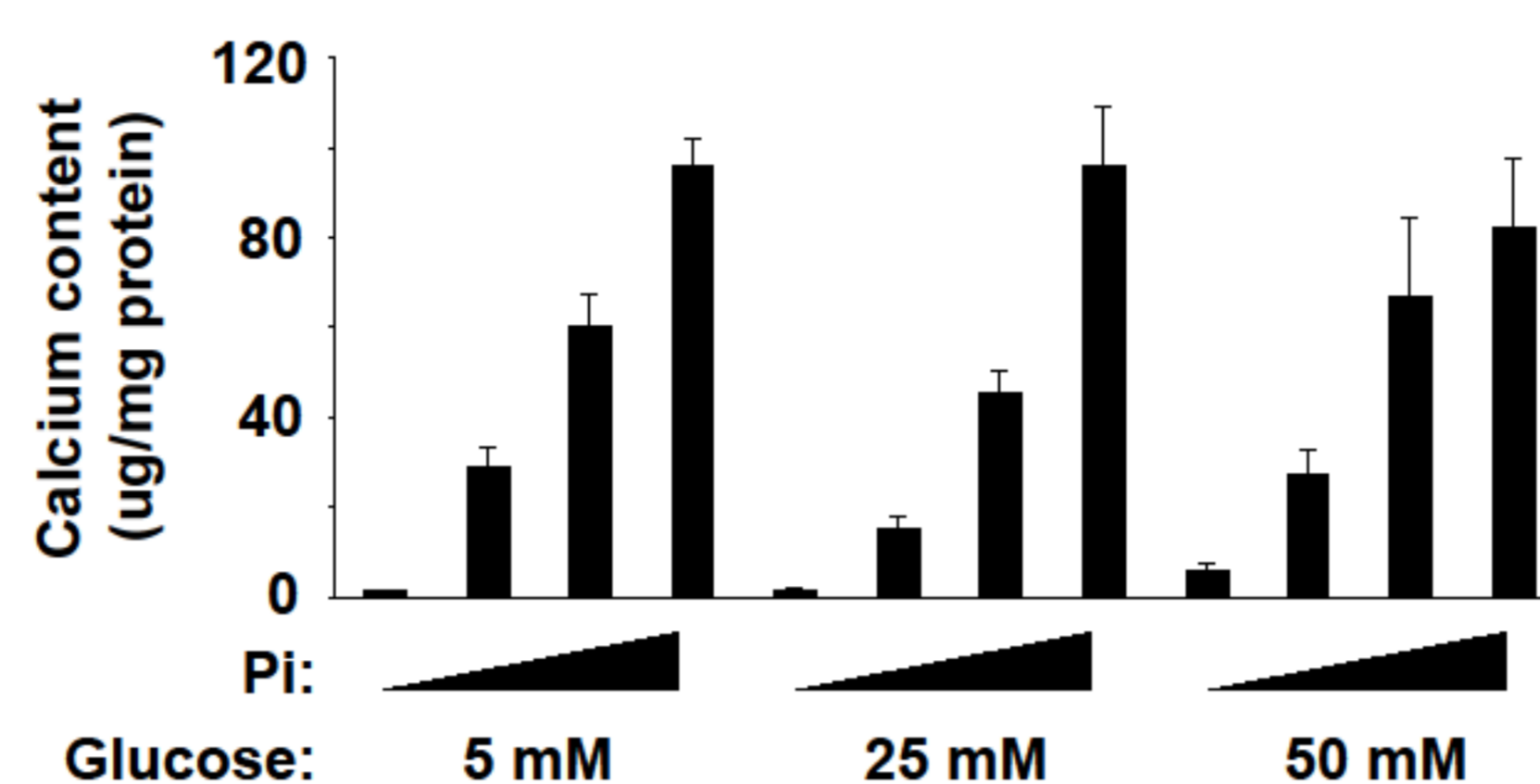


Figure 2. High phosphate, but not high glucose, induced calcification in cultured SMCs. Calcium content was measured after 6-day incubation with various concentrations of phosphate and glucose.

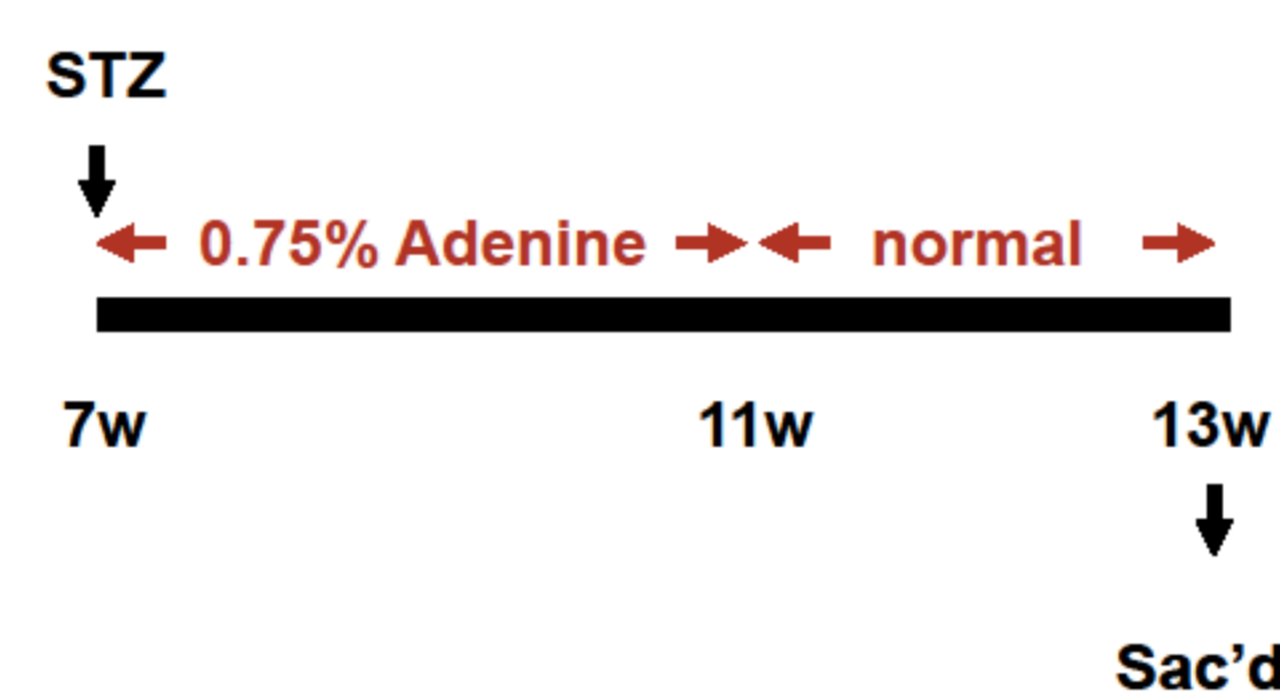


Figure 3. A: A schematic protocol for adenine-induced uremic rats and STZ-induced hyperglycemic rats.

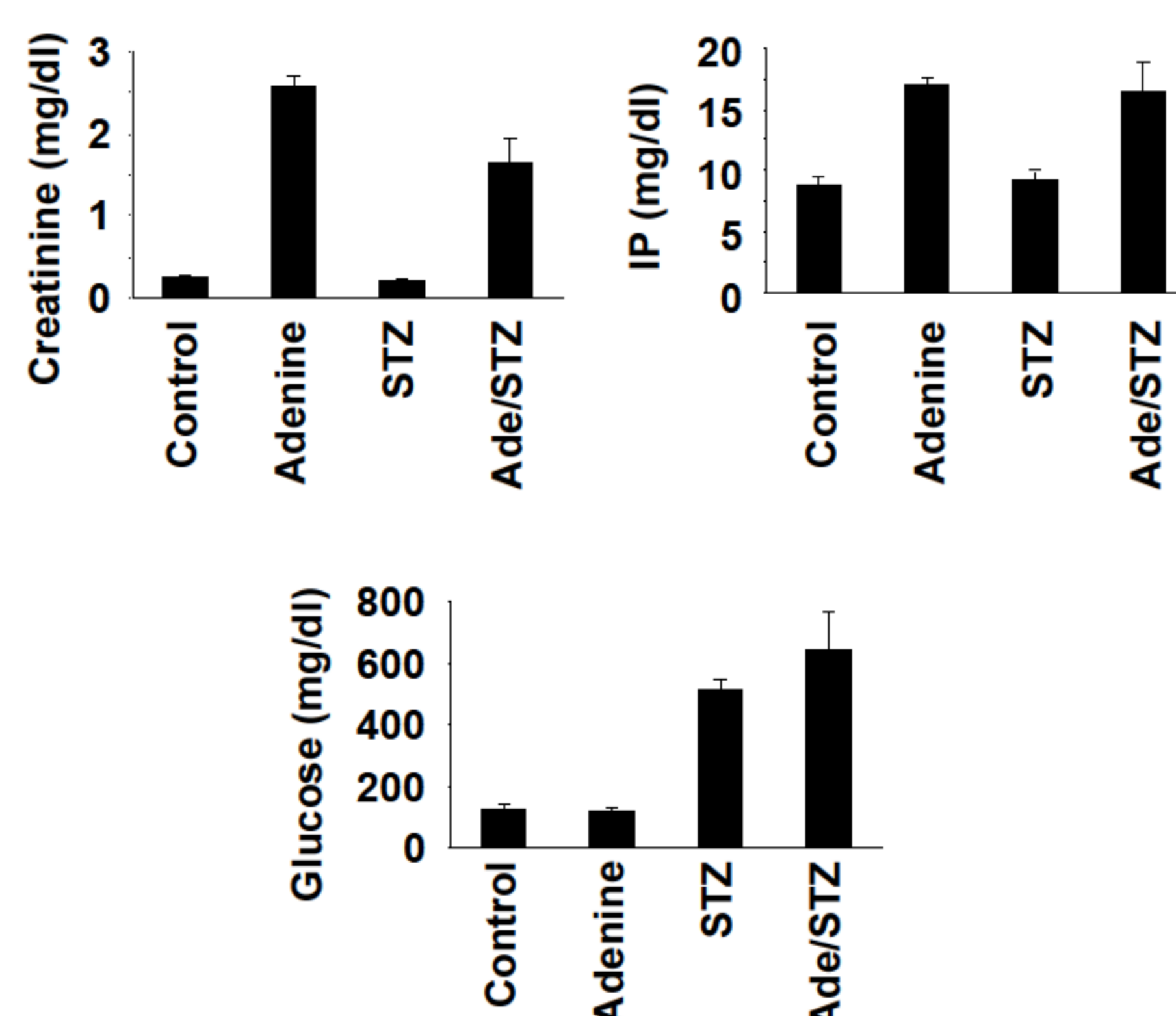


Figure 4. Serum concentrations of creatinine, phosphate, and glucose in adenine-induced uremic rats, adenine-induced/STZ-injected uremic/hyperglycemic rats, STZ-injected hyperglycemic rats, and control rats.

RESULTS

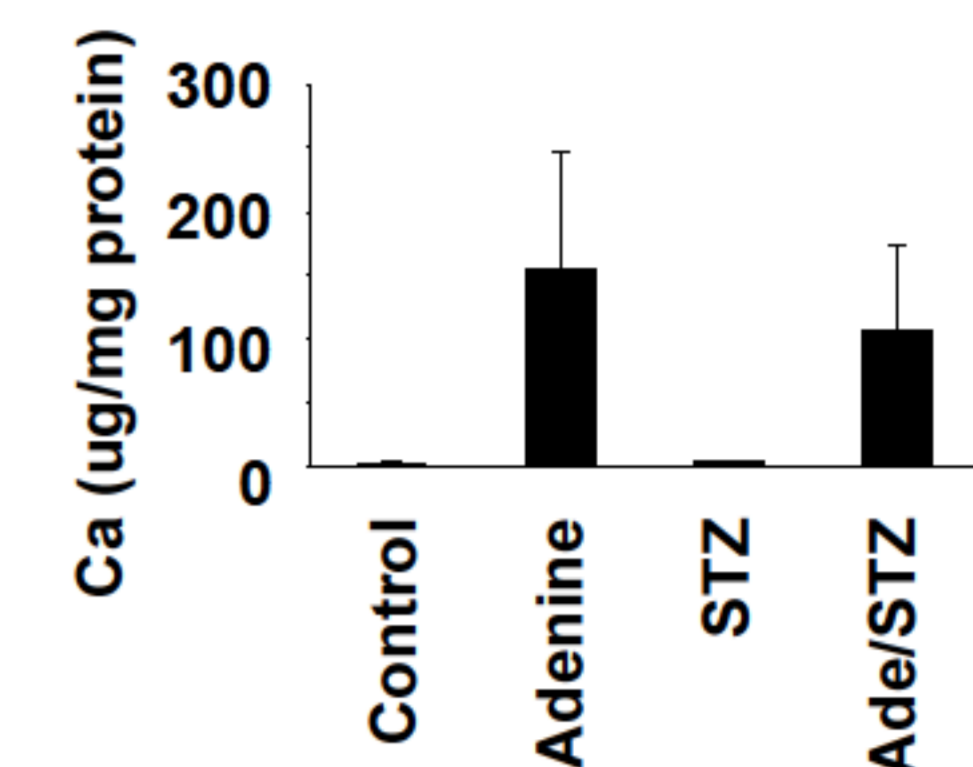


Figure 5. Aortic calcium deposition was increased in uremic rats and uremic/hyperglycemic rats.

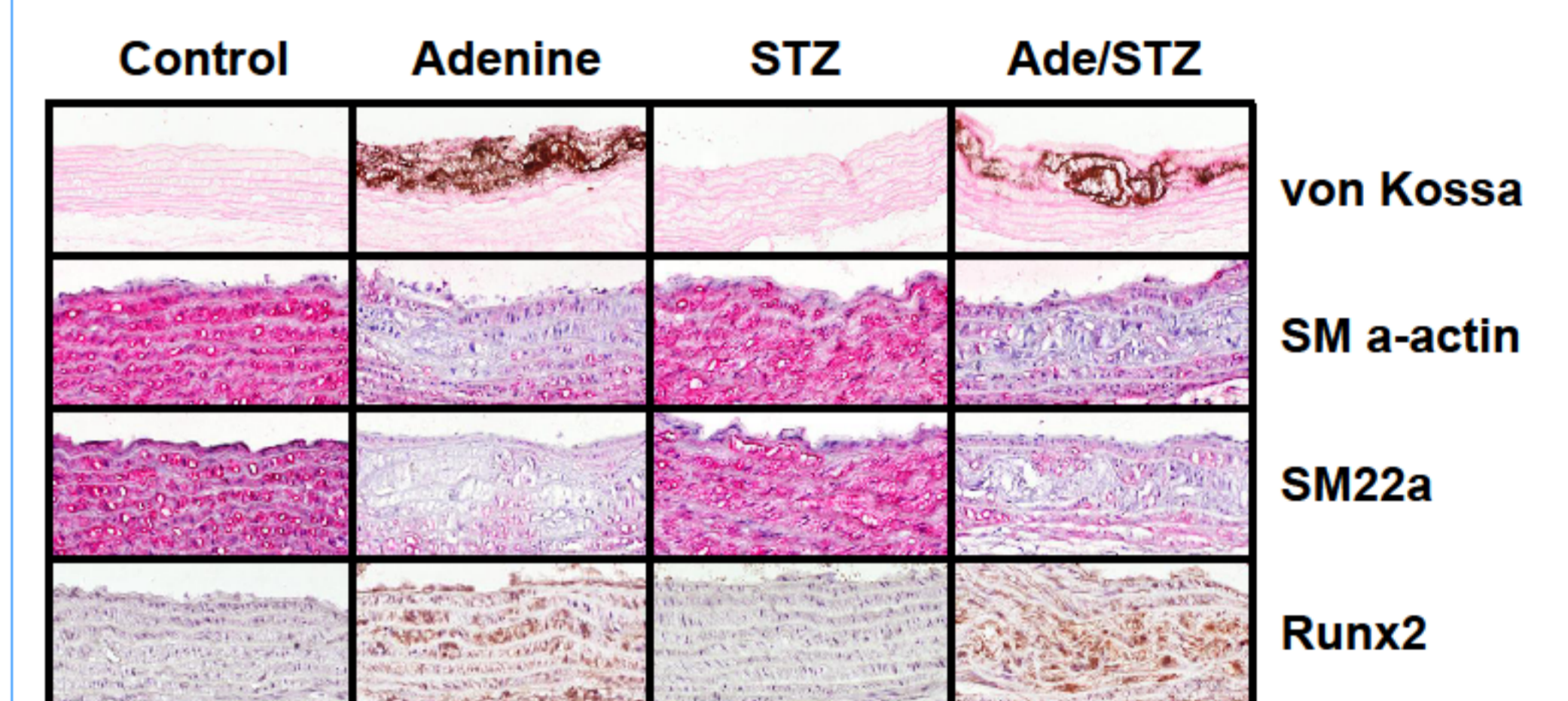


Figure 6. Vascular calcification and SMC phenotypic switching were induced in uremic rats and uremic/hyperglycemic rats.

SUMMARY

1. High phosphate concentration increased calcification in cultured SMCs. However, glucose concentration did not affect high-phosphate-induced calcification of SMCs.
2. Adenine-induced uremic rats exhibited severe aortic calcification. However, streptozotocin-induced hyperglycemic condition did not affect vascular calcification in adenine-induced uremic rats and control rats.

CONCLUSIONS

Results suggest that high glucose does not directly modulate high phosphate-induced calcification in experimental uremic rats and in cultured SMCs.

