

# Vascular Calcification of the Pudendal is a Sentinel for Elevated Aortic Pulse Wave Velocity



Queen's UNIVERSITY

Paul S Jeronimo, Cynthia M Pruss, Kristin M McCabe, Navid Shobeiri, Tina Maio Twofoot, Jason GE Zelt, Bruno Svajger, Mandy Turner, Kim Laverty, Michael A Adams, Rachel M Holden  
Department of Biomedical and Molecular Sciences and Department of Medicine, Queen's University, Kingston ON, Canada

## Introduction and Background

The leading cause of mortality in chronic kidney disease (CKD) is cardiovascular disease<sup>1</sup>. Impaired kidney function leads to altered mineral handling in CKD<sup>2</sup>. Calcium-phosphate crystals deposit in arterial walls causing vascular calcification (VC), a common manifestation of cardiovascular disease in CKD. VC of the aorta, necessarily including the thoracic segment, results in elevated pulse wave velocity (PWV), an indicator of decreased arterial compliance and a predictor of mortality<sup>3</sup>. Our recent research indicates that peripheral blood vessels (e.g. internal pudendal artery) have a distinctive susceptibility to hydroxyapatite formation (Figure 1).

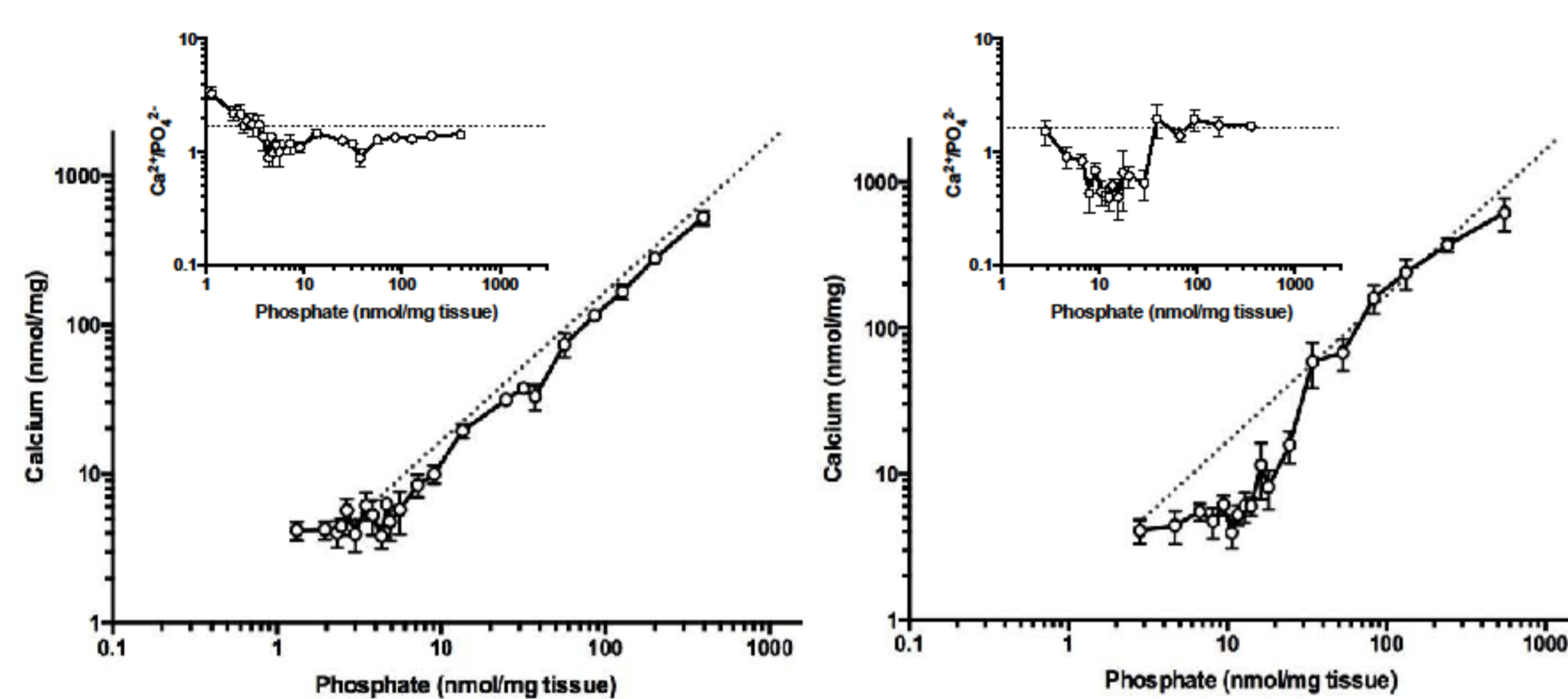


Figure 1: Calcium and phosphate accrual in the pudendal artery (A) and the renal artery (B). The dotted line represents the calcium and phosphate values of hydroxyapatite.

## Objectives

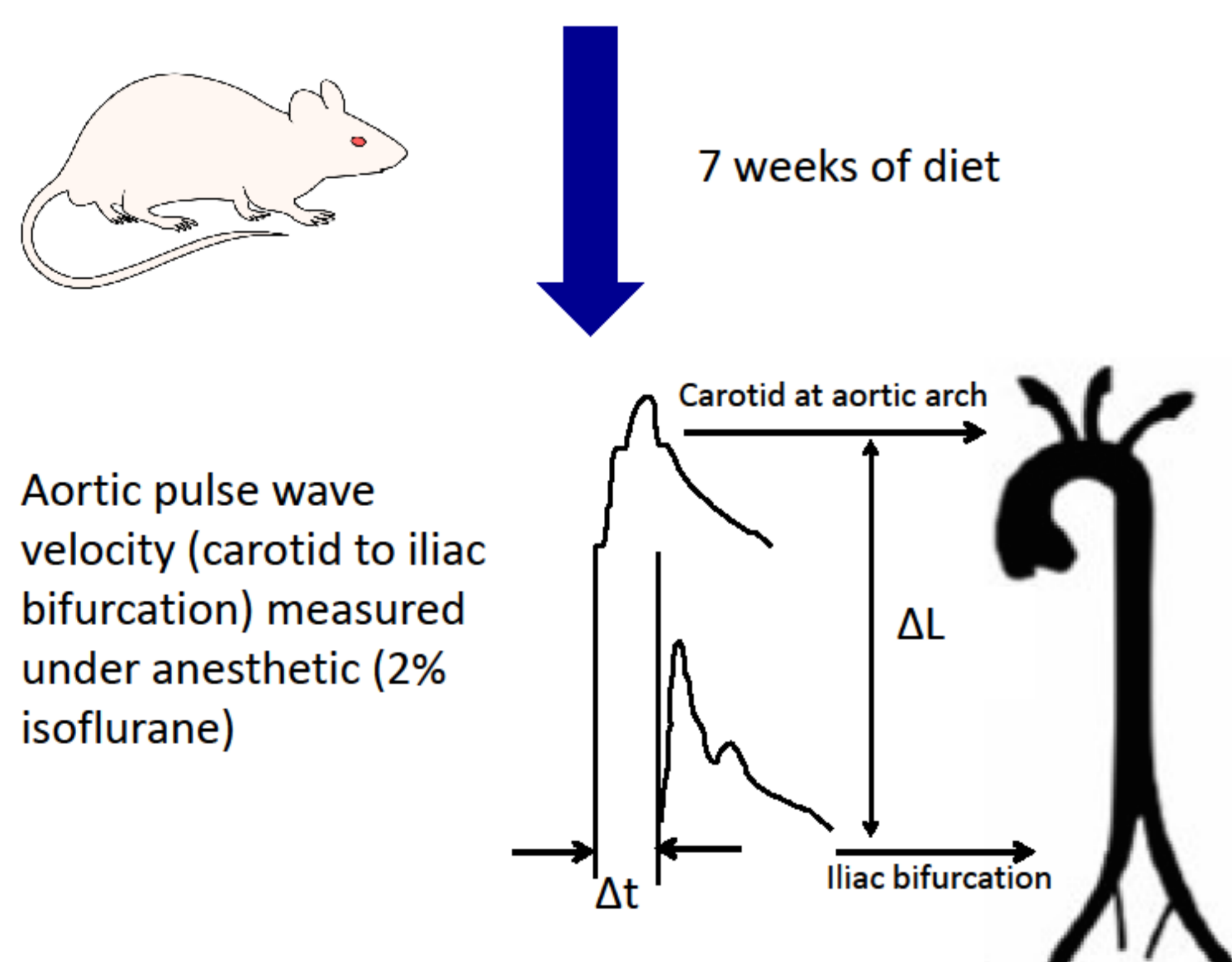
To evaluate whether mineral accumulation in the pudendal artery in an adenine-induced rat model of CKD is a sentinel for calcification of the thoracic aorta and resulting alterations in PWV.

## Methods

14 week old male Sprague Dawley Rats

**Control**  
Standard Rat Chow  
n=61

**CKD**  
0.25% Adenine Diet  
n=145



- Aortic pulse wave velocity (carotid to iliac bifurcation) measured under anesthetic (2% isoflurane)
- Serum creatinine assessed as a measure of kidney function
- Calcium and phosphate content measured in various central and peripheral blood vessels
- Contractility of the pudendal assessed via myograph

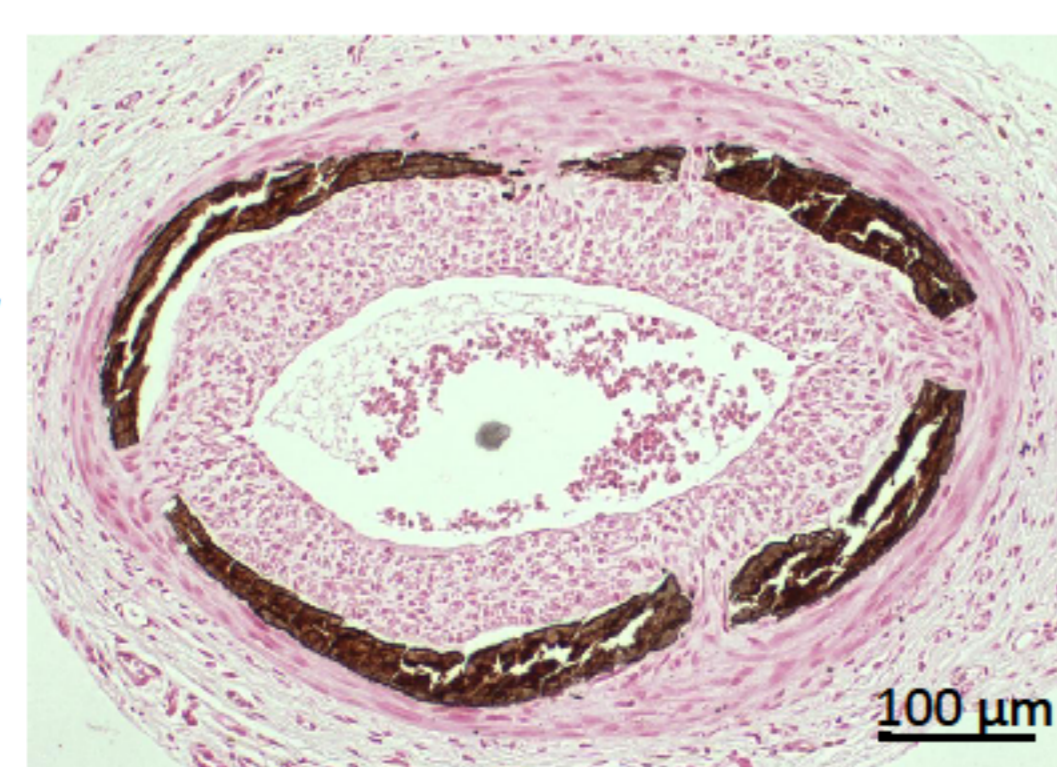


Figure 2: Von Kossa stain of severely calcified pudendal artery

## Conclusions

- Progressive vascular calcification is particularly severe in the pudendal artery
- Vascular calcification of the pudendal artery occurs prior to calcification of the thoracic aorta and systemic changes
- Pudendal artery calcification appears to be an early sentinel for alterations in central hemodynamic parameters, including PWV, and further vascular calcification

## Results

- Pulse wave velocity is not correlated with severity of CKD

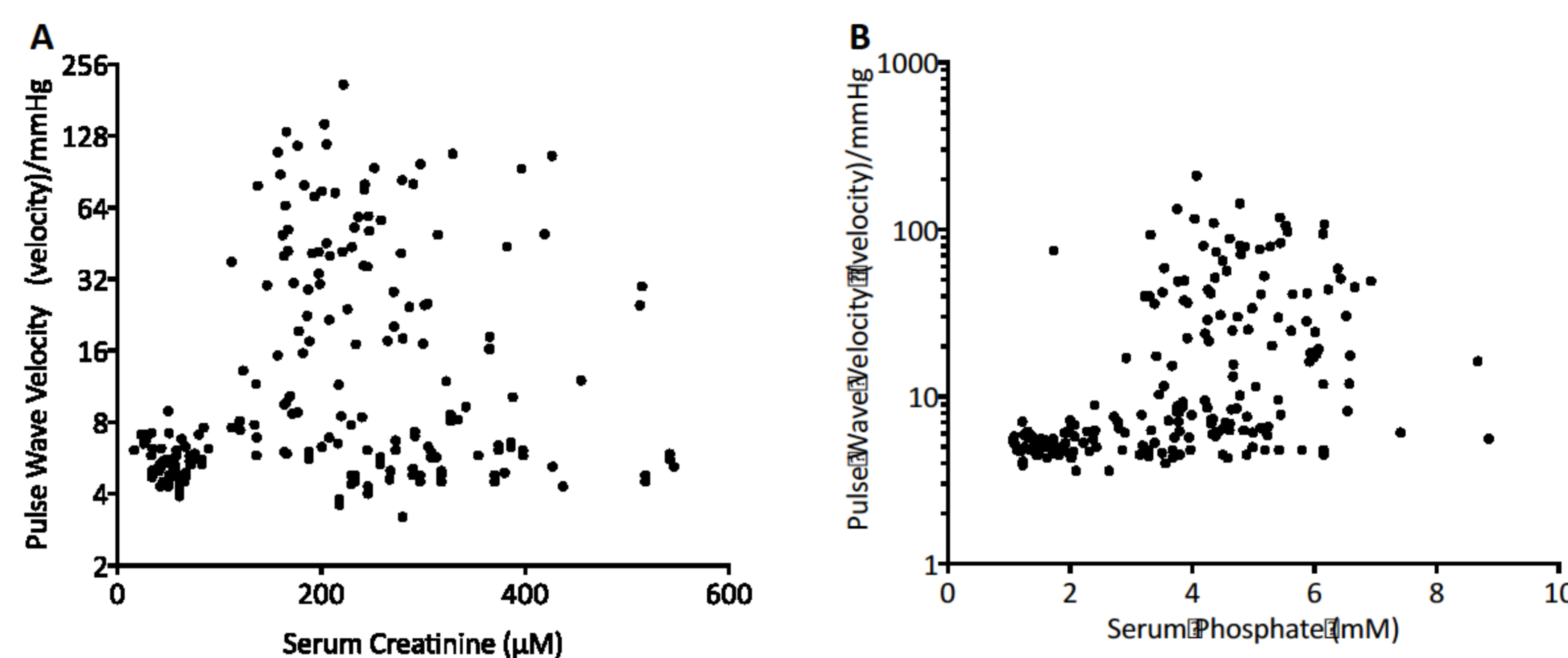


Figure 3: Pulse wave velocity, normalized to mean arterial pressure, does not correlate to serum creatinine (A) or serum phosphate (B).

- Elevated pulse wave velocity requires calcification of the thoracic aorta

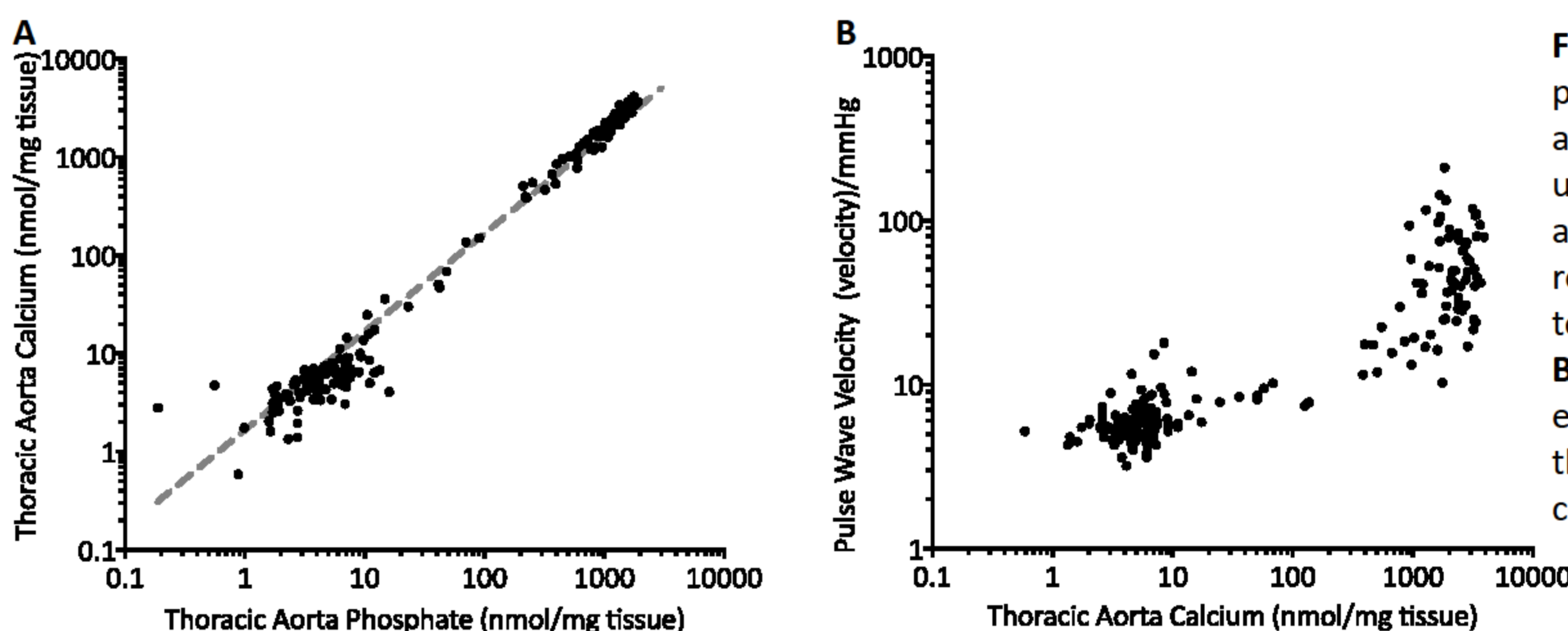


Figure 4: A - Calcium and phosphate of the thoracic aorta showing dichotomy of uncalcified and calcified aortas. The dotted line represents 10:6 ratio of Ca<sup>2+</sup> to PO<sub>4</sub><sup>3-</sup> in hydroxyapatite. B - Pulse wave velocity elevated in rats with high thoracic aorta calcium content.

- Vascular calcification of the pudendal artery precedes that of the thoracic aorta

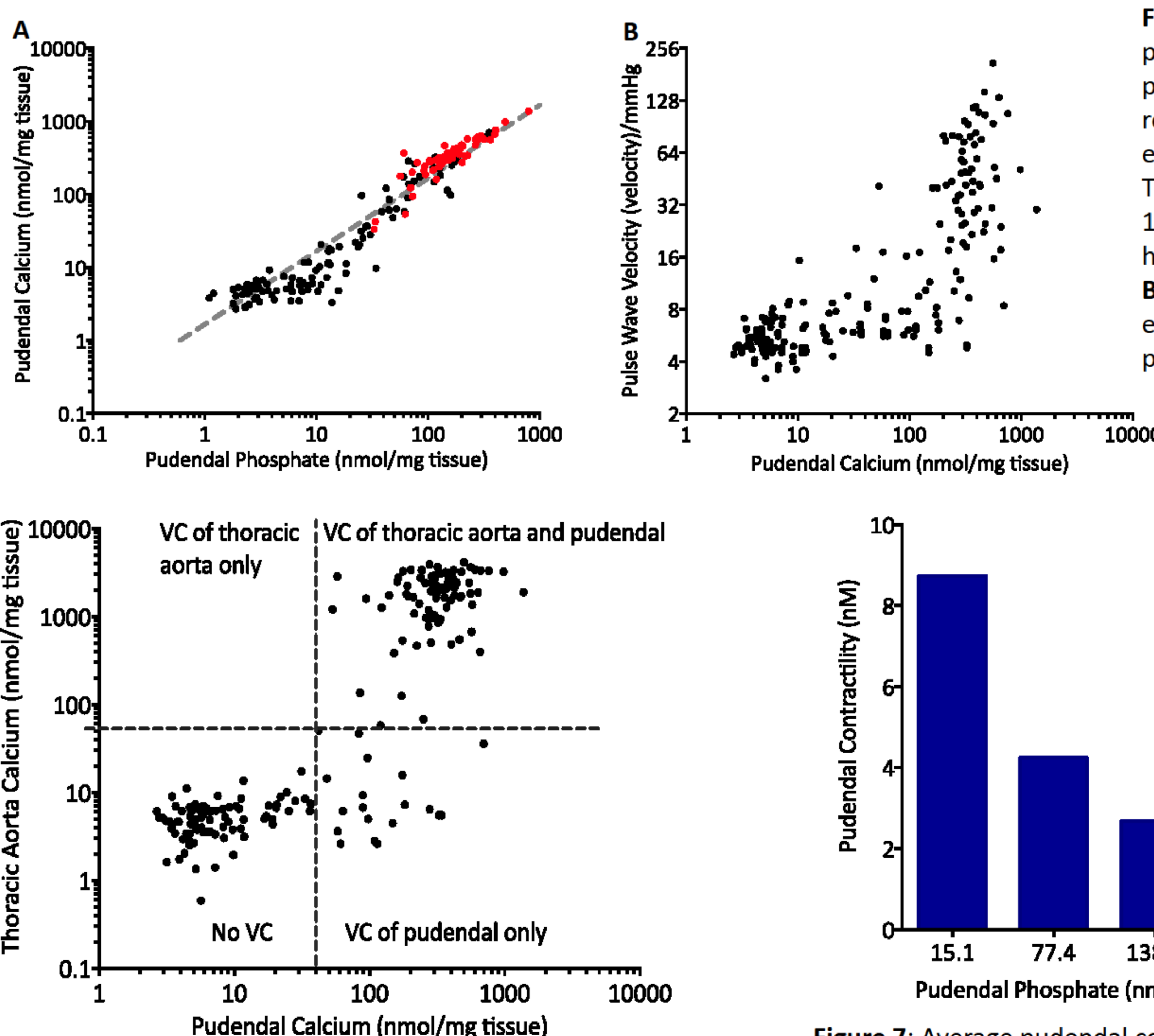


Figure 5: A - Calcium and phosphate contents of the pudendal artery. Black and red points have normal and elevated PWV, respectively. The dotted line represents 10:6 ratio of Ca<sup>2+</sup> to PO<sub>4</sub><sup>3-</sup> in hydroxyapatite. B - PWV not necessarily elevated in rats with high pudendal calcium content.

Figure 6: Thoracic aorta and pudendal calcium accrual. VC of the pudendal without VC of the thoracic aorta occurs but not VC of the thoracic aorta alone.

## Acknowledgements



## References

- Go, A. S., Chertow, G. M., Fan, D., McCulloch, C. E. & Hsu, C. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. *N. Engl. J. Med.* 351, 1296-1305 (2004).
- Sigrist, M. K., Taal, M. W., Bungay, P. & McIntyre, C. W. Progressive Vascular Calcification over 2 Years Is Associated with Arterial Stiffening and Increased Mortality in Patients with Stages 4 and 5 Chronic Kidney Disease. *Clin. J. Am. Soc. Nephrol.* 2, 1241-1248 (2007).
- Schlieper, G., Schurgers, L., Brandenburg, V., Reutlingsperger, C. & Floege, J. Vascular calcification in chronic kidney disease: an update. *Nephrol. Dial. Transplant.* 31, 31-39 (2016).

