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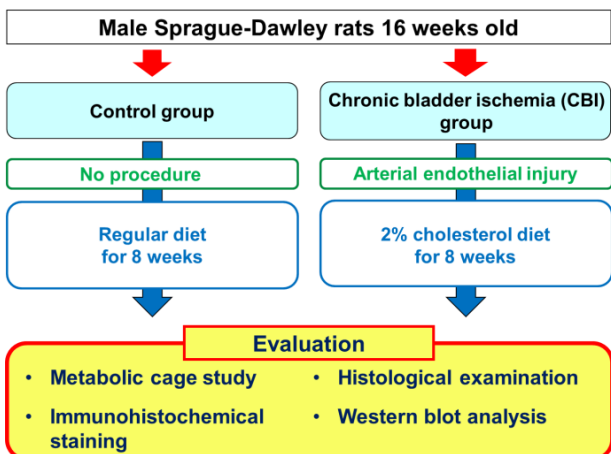
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**Aims of study**

Uroplakin (UP) Ia, UP Ib, UP II, and UP III are well known to be critical to normal urothelial barrier function<sup>1</sup>. Recent studies have suggested that UPs play a role in the homeostasis of urinary bladder mucosa and UP defects lead to abnormal voiding patterns<sup>2</sup>. On the other hand, chronic ischemia induced by occlusive disease in pelvic arteries plays a key role in the development of lower urinary tract symptom. However, the mechanisms underlying the changes in bladder function caused by chronic ischemia have not been completely elucidated. Whether arterial occlusive disease-related chronic ischemia affects UPs in the bladder has not been established. This study aimed to investigate the effects of arterial occlusive disease-related chronic ischemia on UPs in the bladder using a rat model of chronic bladder ischemia (CBI).

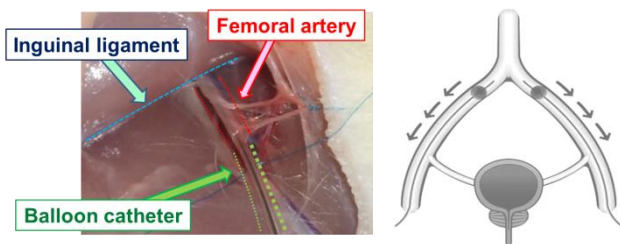
**Materials and methods**

**Study design**



**Iliac arterial endothelial injury**

A balloon catheter was passed through the femoral artery into the common iliac artery. The balloon was inflated and then withdrawn from the common iliac artery to the femoral artery to induce endothelial injury in the common iliac arteries. The maneuver was repeated 10 times on each side.



**Metabolic cage study**

For 24 hr over 3 consecutive days each rat was placed in an individual metabolic cage with a 12/12 hr dark/light cycle. Urine output was monitored for a further 24 hr using a digital balance below the metabolic cage.

**Histological examination**

Common iliac arterial wall thickness was determined by averaging wall thickness at four distinct location in each sample

**Western blot analysis**

We used western blotting to measure the expression of UP Ia, UP Ib, UP II, UP III and HIF1α, which was oxidative stress marker, in the bladders of the rats.

**Immunohistochemical staining**

Immunohistochemical staining was performed on formalin-fixed Paraffin-embedded tissue sections. The percentage of positive tumor cells was used to evaluate the expressions of UP.

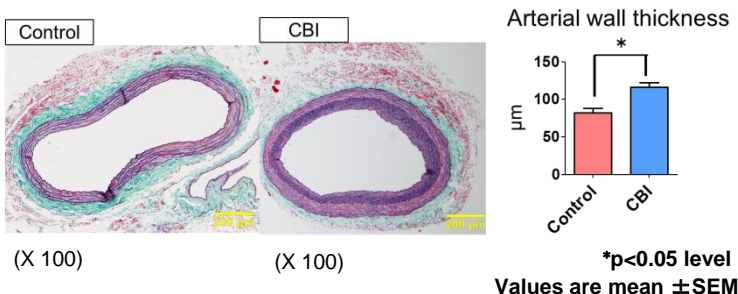
**Statistical analysis**

All values were expressed as mean ± standard deviation. An unpaired t test was used for analysis of categorical variables, and linear regression analysis was used for continuous variables. P-values of <0.05 were considered to be statistically significant.

**Results**

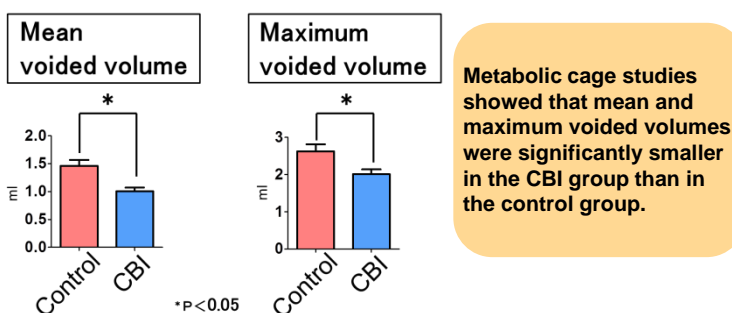
The body weight and bladder wet weight were not significantly different between groups (data is not shown).

**Figure.1. Elastica Masson staining of cross-section of common iliac arteries**



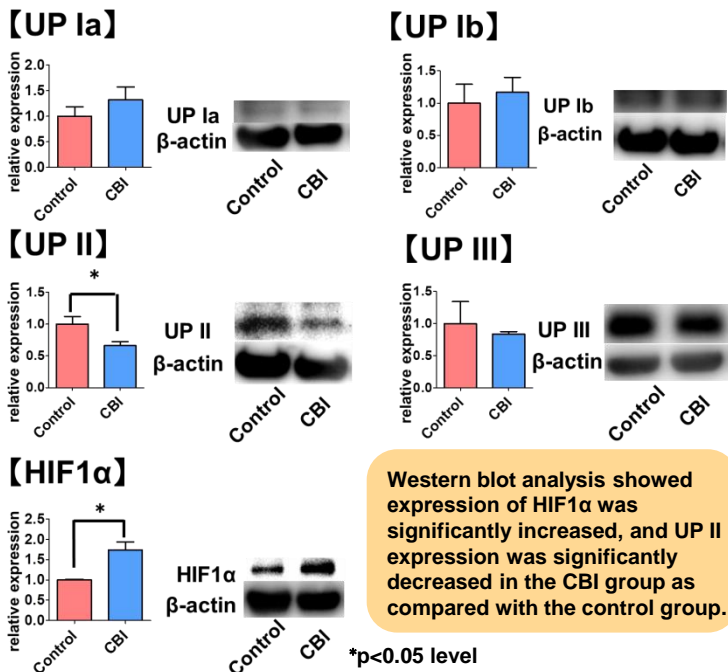
Mean arterial wall thickness was significantly greater in the CBI group than in the control group

**Figure.2. Metabolic cage study**



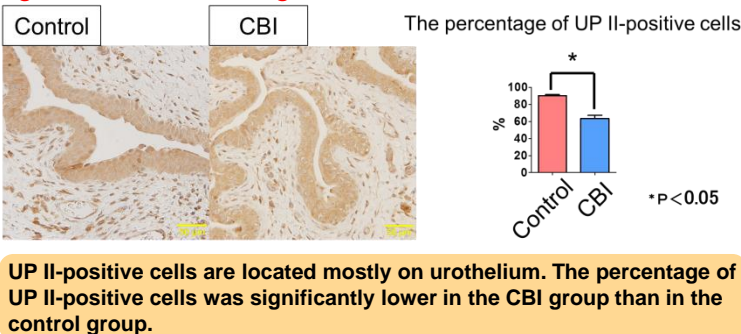
Metabolic cage studies showed that mean and maximum voided volumes were significantly smaller in the CBI group than in the control group.

**Figure.3. Expression of uroplakin (UP) and HIF1α at the protein level**



Western blot analysis showed expression of HIF1α was significantly increased, and UP II expression was significantly decreased in the CBI group as compared with the control group.

**Figure.4. Immunohistological examination**



UP II-positive cells are located mostly on urothelium. The percentage of UP II-positive cells was significantly lower in the CBI group than in the control group.

**Conclusions**

Our results suggest that pelvic arterial occlusive disease causes uroplakin II deficiency in the bladder of this rat model. uroplakin II deficiency might be one cause of chronic ischemia-related bladder dysfunction.

**References**

1) Hu P, et al: Role of membrane proteins in permeability barrier function: uroplakin ablation elevates urothelial permeability. Am J Physiol Renal Physiol 2002;283:F1200-7.  
2) Aboushwareb T, et al: Alterations in bladder function associated with urothelial defects in uroplakin II and IIIa knockout mice. NeuroUrol Urodyn. 2009;28(8):1028-33