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Nomiya M[1], Miyazaki N[1], Ikegami K[1], Yamaguchi O[1]
1. *Division of Bioengineering and LUTS Research, Nihon University School of Engineering*

BLADDER OVERACTIVITY MAY PROGRESS TO BLADDER UNDERACTIVITY IN A RAT MODEL OF CHRONIC BLADDER ISCHEMIA.

Hypothesis / aims of study

It has been suggested that bladder underactivity may represent a more advanced stage in the natural history of bladder dysfunction.(1) Recently, attention has been focused on bladder ischemia which may contribute to the development as well as progression of bladder dysfunction. Pelvic arterial occlusive disease (atherosclerosis), a common clinical problem in the elderly, is an important cause of the reduction of bladder blood flow, leading to chronic bladder ischemia. We hypothesized that prolonged bladder ischemia may further aggravate bladder dysfunction with aging, resulting in bladder underactivity. Thus, the present study investigated whether bladder overactivity under ischemic condition eventually progresses to bladder underactivity in a rat model of chronic bladder ischemia.(2)

Study design, materials and methods

Adult (16-week old) male Sprague-Dawley rats were divided into arterial injury (AI) and control groups. The AI group underwent balloon endothelial injury of bilateral iliac arteries and received a 2% cholesterol diet after AI. The control group was placed on a regular diet (0.09% cholesterol) was utilized as an age-match control group. At 4, 8, 12 and 33 weeks or more (average 37 weeks), rats were performed cystometrograms (CMG) without anesthesia or restraint. Post-void residual volume (PVR) was measured after the micturition reflex by slowly evacuating the bladder through bladder catheter. After CMG, all rats from both groups were euthanized, and the iliac arteries were harvested for histological examination.

Results

In cystometry, in the control group, micturition interval (MI), bladder capacity (Bcap) and voided volume (VV) tended to increase with aging but the increases in these parameters were not significant (Table 1, Figure 2). Mean PVR was very small amount and not altered by aging within the time frames (Figure, 3). In the AI group, at 4 and 8 weeks, MI was significantly shorter, Bcap and VV were significantly less than in each age-match control group. Conversely, at 33 weeks or more, the MI was significantly longer, and the Bcap was significantly greater than the age-match controls (Table 1, Figure 2). Mean PVR in the AI group tended to increase with aging, and was greater than in each age-match control group at 8, 12 and 33 weeks or more. A significant difference was observed at 33 weeks or more (Figure 3). Baseline bladder pressure and maximum bladder pressure did not significantly differ between both groups (Table 1). Hematoxylin and eosin staining of the common iliac arteries from the AI rats showed obvious arterial wall thickening with neointimal formation compared with the control group at each time points (Figure 4). No age-related arterial wall changes were observed in the controls.

Interpretation of results

Histological study shows that arterial occlusive disease of the iliac arteries already occurred at 4 weeks after AI, and was sustained up to 33 weeks or more. This finding suggests that bladder ischemia may persist for long periods in the AI group. A prominent finding from cystometric evaluation in this model is that bladder overactivity, defined as the shortened MI and the decreased Bcap without affecting PVR, was observed in the relatively early period, whereas bladder underactivity, defined as the prolonged MI, the increased Bcap and the development of PVR, was found in the late period. Chronic bladder ischemia and repeated ischemia / reperfusion produce oxidative stress in the bladder, leading to denervation of the bladder and expression of tissue damaging molecules in the bladder wall. This may contribute to the development of bladder overactivity progressing to bladder underactivity.(3)

Concluding message

Our findings suggest that prolonged bladder ischemia may cause bladder dysfunction, which develops from bladder overactivity to bladder underactivity.

Table 1. Cystometric parameters. (*P<0.05, **P<0.01)

	Micturition Interval (min)	Bladder Capacity (ml)	Voided Volume (ml)	Baseline Pressure (cmH_2O)	Maximum Pressure (cmH_2O)	Post-void Residual (ml)
cont (n=6)	11.7±0.8	2.0±0.17	1.9±0.15	13.3±0.4	46.3±1.7	0.06±0.05
4w AI (n=7)	7.8±1.0*	1.3±018*	1.3±0.18*	14.4±0.2	46.8±3.5	0.02±0.01
cont (n=8)	12.9±0.4	2.1±0.07	2.0±0.07	15.8±1.5	55.1±5.6	0.04±0.04
8w AI (n=8)	8.6±0.7**	1.5±0.11**	1.4±0.14**	16.1±0.8	47.9±3.7	0.12±0.05
cont (n=10)	13.9±0.9	2.4±0.16	2.3±0.14	13.6±0.4	45.9±2.5	0.14±0.07
12w AI (n=17)	11.7±0.9	2.2±0.19	1.9±0.15	14.2±0.4	47.6±3.2	0.27±0.07
cont (n=11)	15.0±1.0	2.5±0.21	2.4±0.18	13.7±0.2	51.0±3.2	0.09±0.04
33w AI (n=15)	19.7±1.5*	3.9±0.41*	3.3±0.28*	13.4±0.5	47.9±2.4	0.62±0.32*

Figure 1. Typical control and AI group cystometrogram recordings (1 hour).

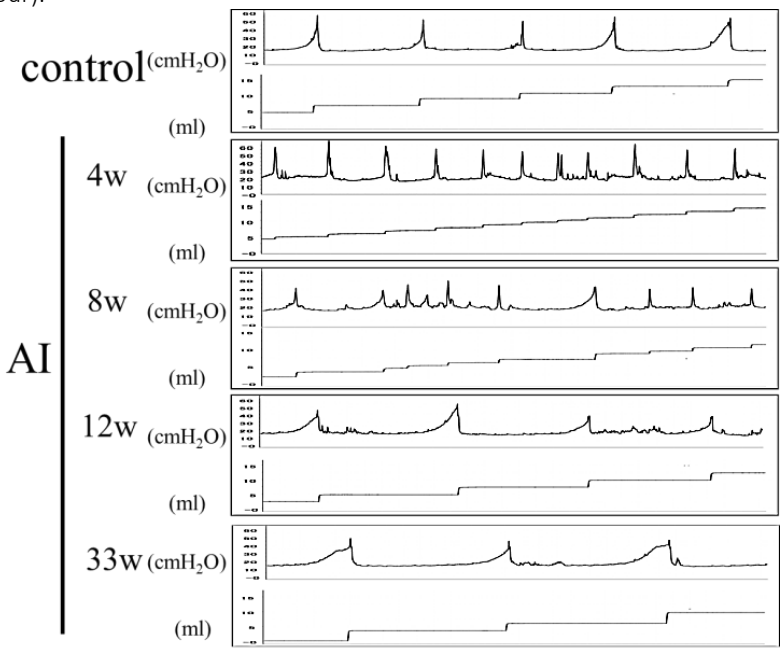


Figure 2. Micturition Interval

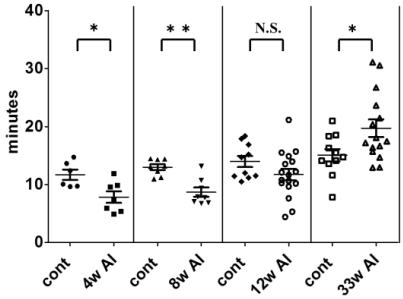


Figure 3.Post-Void Residual

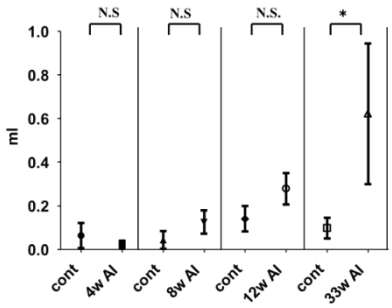
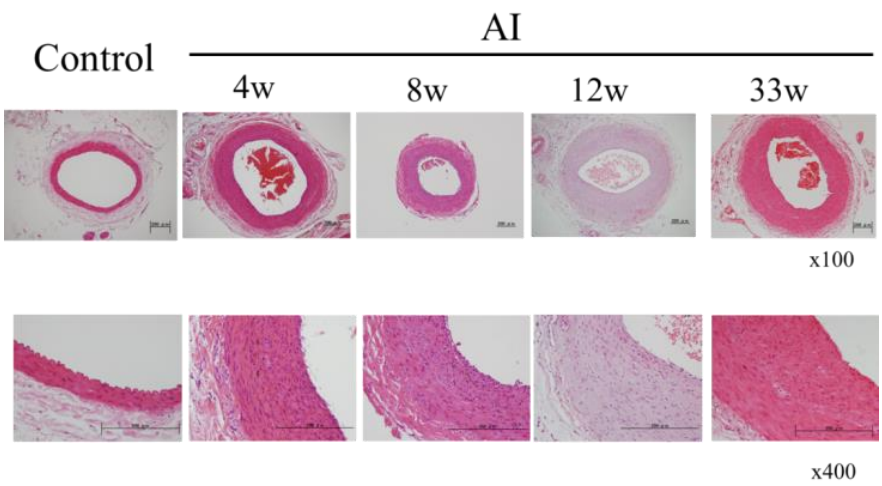
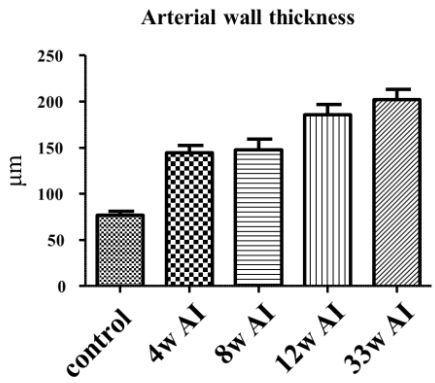


Figure 4. H&E staining of cross section of common iliac arteries in animals of control and AI groups. Scale bars indicate 200μm. Bar graph shows arterial wall thickness.





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Disclosures

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