Arterial function after long-term hypertension is characterized by remodeling, endothelial dysfunction and reduction of previously enhanced contractile responses. We investigated whether transient prehypertensive renin-angiotensin-aldosterone system (RAAS) blockade modifies long-term arterial function. Wistar Kyoto rats (WKY) (i) and spontaneously hypertensive rats (SHR) (ii) were prehypertensively (week 4-8) treated with losartan (iii) or spironolactone (iv) (20 and 0.5 mg/kg/day, respectively) and investigated at 8 and 72 weeks of age. Systolic blood pressure (SBP) was measured intra-arterially. In isolated mesenteric arteries, active wall stress (AWS), relaxation in response to acetylcholine and wall-to-lumen ratio (W/L) were assessed. Western blotting and immunofluorescent staining of whole-mount arterial preparations and two photon laser scanning microscopy (TPLSM) were performed to quantify endothelial nitric oxide synthase (eNOS) and analyze its intracellular distribution. In 8-week-old SHR treatments were found to have reduced SBP. Relaxation, contractile responses and vascular morphology remained unaffected irrespective of treatment. At 72 weeks, SBP was similar in all SHR groups ((i) 129±6, (ii) 222±10, (iii) 210±16, (iv) 214±9 mmHg). Relaxation and maximum AWS were enhanced after
treatments. W/L demonstrated hypertrophy (i) 0.10 +/- 0.01, (ii) 0.16 +/- 0.02, (iii) 0.15 +/- 0.01, (iv) 0.17 +/- 0.01). Untreated SHR (p<0.01), SHR treated with losartan and SHR treated with spironolactone (p<0.05) showed less eNOS as compared to WKY. In treated SHR eNOS was concentrated in a perinuclear endothelial cell compartment. In conclusion, these findings demonstrate that transient prehypertensive blockade results in a long-lasting and blood pressure independent improvement of arterial contractility and endothelium-dependent vasodilatation that persists in aging SHR. This might be associated with an intracellular redistribution of eNOS in the endothelial cell layer.