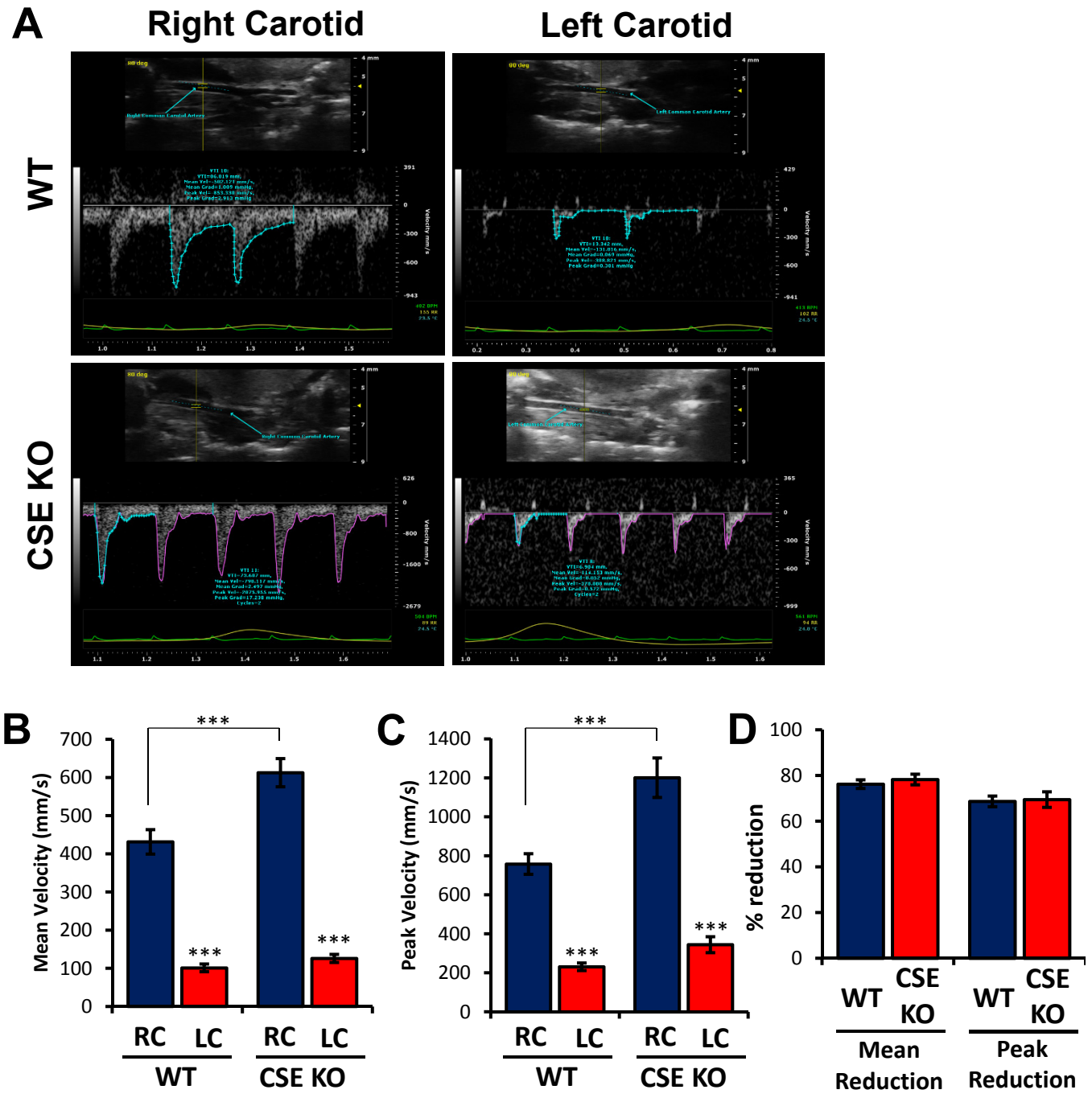
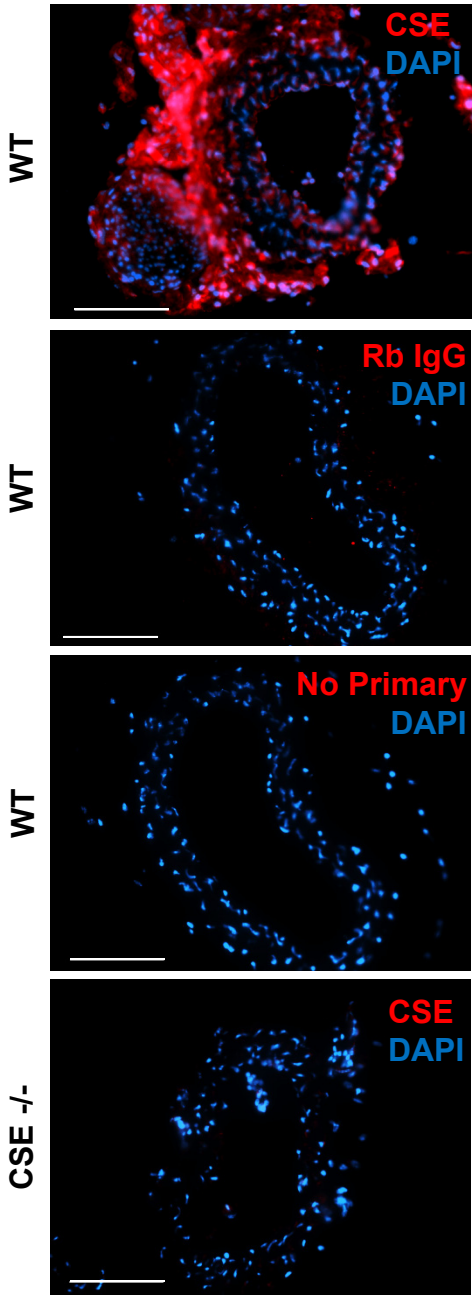
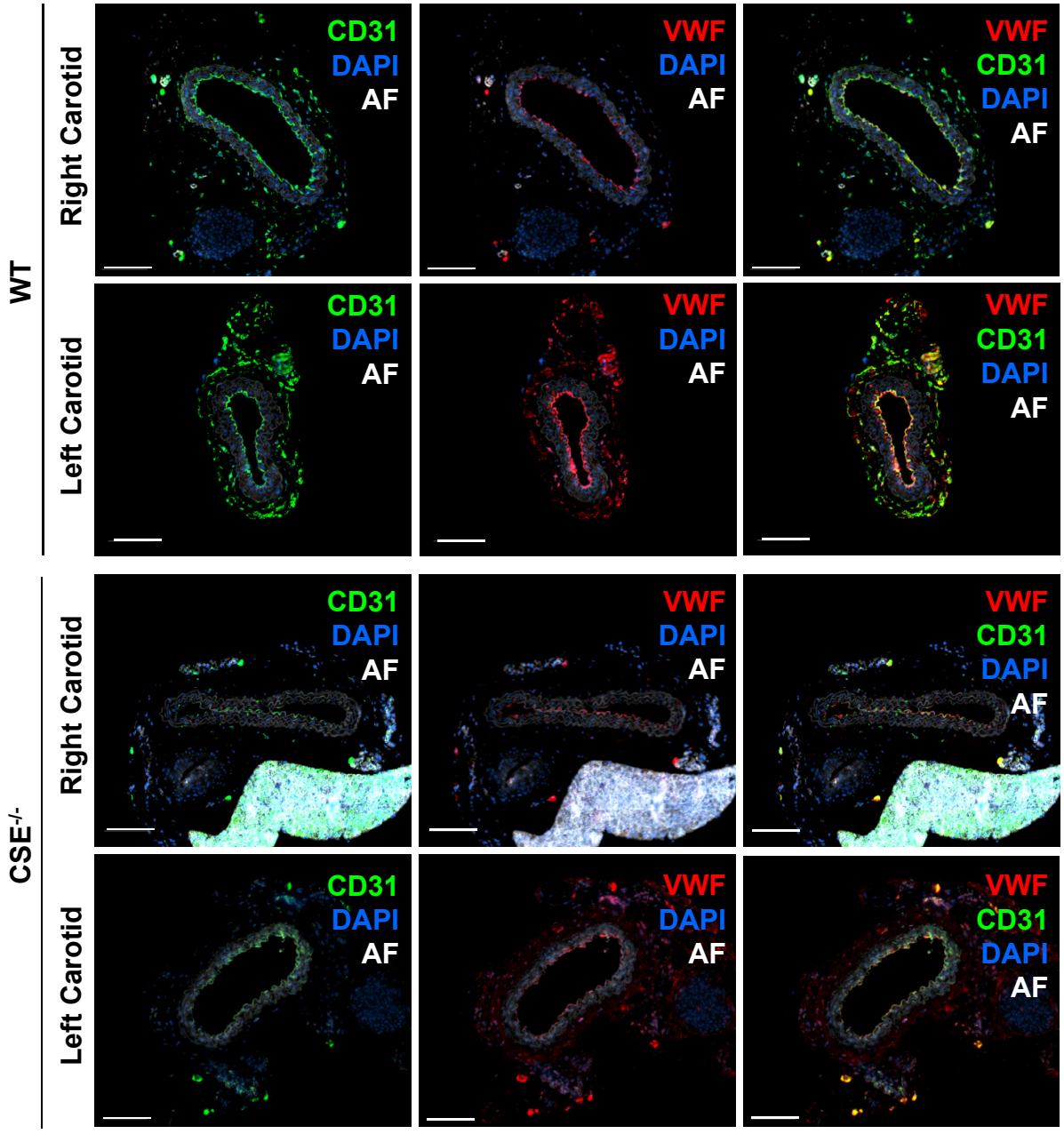
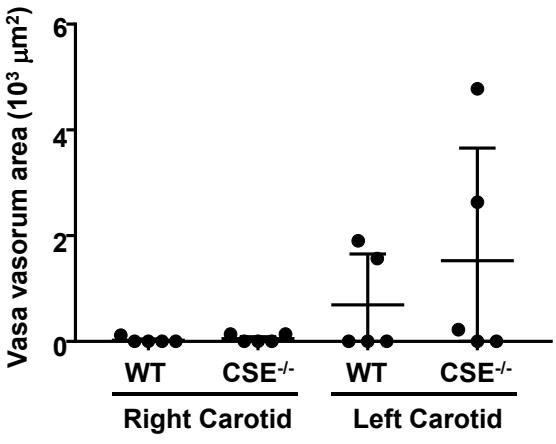


Supplementary Figure I. Ultrasound measurements after ligation. Reduction of blood flow following carotid ligation was verified by ultrasound. (A) Examples of ultrasound images taken 2 days after ligation. (B-D) Quantification of flow velocity (n=6-7, $p<0.001$ by Two-Way ANOVA).

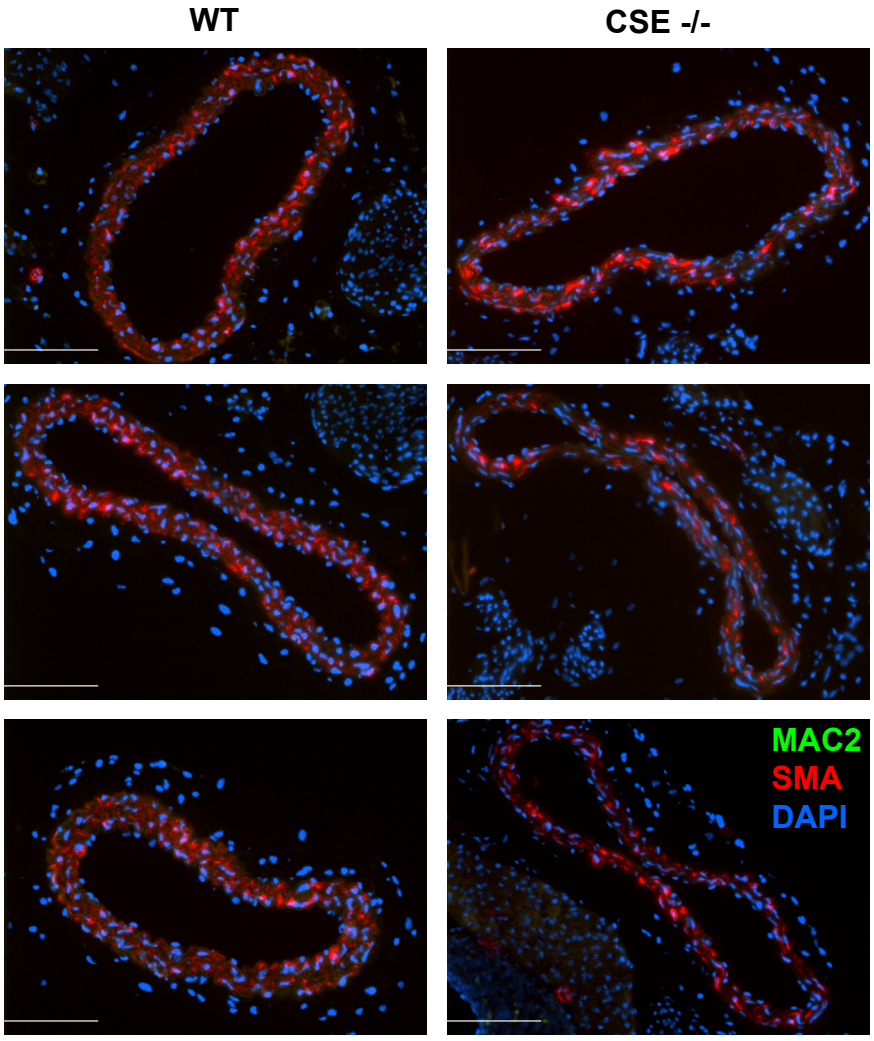


Supplementary Figure II. **CSE staining controls.** CSE staining pattern was verified using rabbit IgG and secondary antibody alone in WT vessels, and by staining for CSE in CSE-/- vessels.

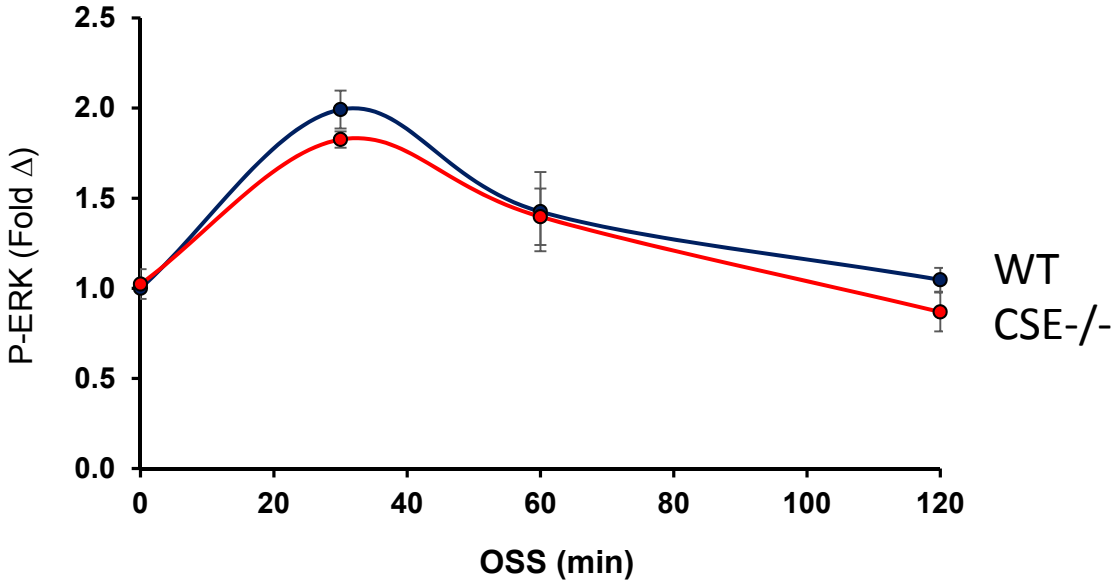




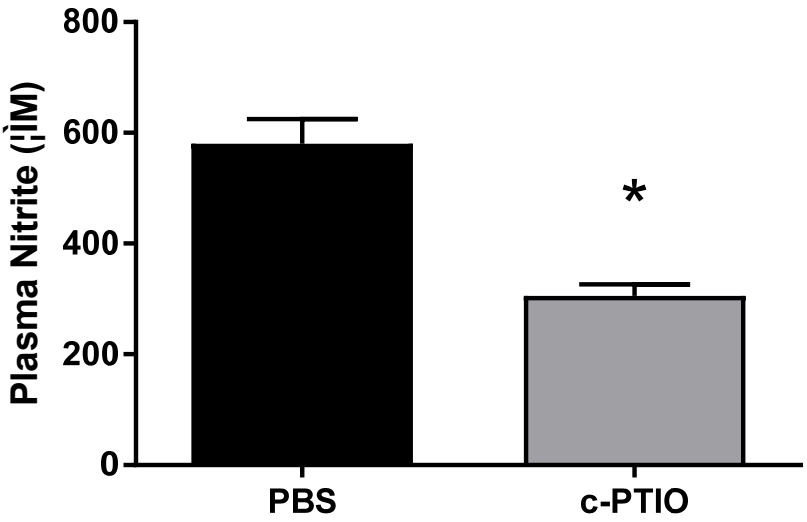
Supplementary Figure III. CSE knockout mice show no difference of vasa vasorum content in blood vessels. Right and left carotid arteries from WT and CSE$^{-/-}$ mice were stained for the endothelial cell markers CD31 (green) and vWF (red), as well as nuclei (DAPI, blue), and autoflourescence (white). Vasa vasorum areas were quantified as adventitial area positive for the endothelial markers. (scale bar = 100 μm, n=5-6, non-significant by Mann-Whitney U test).



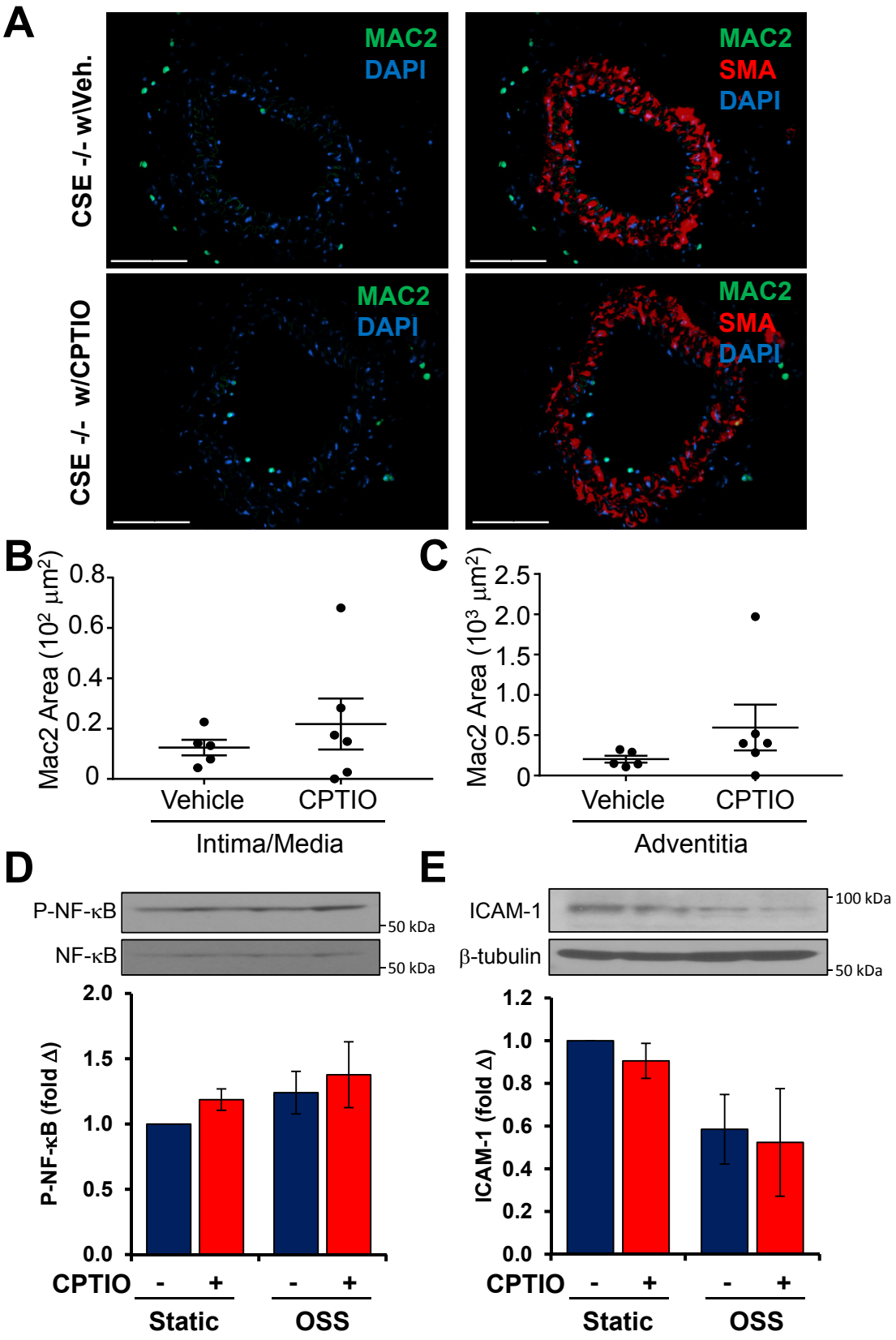
Supplementary Figure IV. Right carotid staining for vessel remodeling. Control, non-ligated right carotid arteries were stained for macrophage (Mac2, green) and smooth muscle (SMA, red) area. Three representative vessels from WT and CSE-/- mice are shown.



Supplementary Figure V. CSE ablation does not affect ERK1/2 activation by flow. Mouse aortic endothelial cells (MAECs) from Wild-type (WT) or CSE knockout (CSE-/-) mice were subjected to oscillatory flow (OSS; 0 to 120min), and p-ERK was assessed by Western Blotting. (n=4, non-significant by Two-Way ANOVA).



Supplementary Figure VI. Verification of c-PTIO effectiveness.
$CSE^{-/-}$ mice were treated with c-PTIO (1 mg/kg) for consecutive 10 days. Partial carotid ligation was performed on Day 4. Plasma was collected after another 7 days, and plasma nitrite levels were measured by triiodide chemiluminescence. n=6-8, * $p<0.05$ using Students T-test.



Supplemental Figure VII. C-PITO doesn't restore inflammation in CSE$^{-/-}$ mice. CSE$^{-/-}$ mice were treated with c-PTIO (1 mg/kg) for consecutive 10 days. Partial carotid ligation was performed on Day 4. Carotids were collected after another 7 days. (A-C) Staining for macrophages (Mac2, green) and smooth muscle cells (SMA, red) show no significant different in macrophage accumulation. (scale bar = 100 μm, n=5-6, non-significant by Mann-Whitney U test). (D/E) CSE$^{-/-}$ MAECs were exposed to 18 hrs of oscillatory shear stress in the presence or absence of CPTIO (100 μM). (n=4, $p<0.05$, Non-significant by Two Way ANOVA).