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TOPIC:

7. Hypertension, Atherosclerosis and Aneurysm

TITLE:

Systolic augmentation in mice estimated from high precision invasive blood pressure recordings

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TEXT:

Objectives: Systolic augmentation is the contribution of reflected pressure waves to the arterial systolic pressure, and is normally presented as augmentation index, AIx. Elevated AIx is a significant risk factor for premature CV disease. We developed a technique to estimate AIx in mice.

Methods: A Samba Preclin pressure transducer (0.42/0.25 mm od) was introduced into the aortic arch via carotid artery in isofluran anesthetized mice. Pressure was recorded at 2 kHz. Pulse wave analysis (PWA) was used to measure diastolic pressure (Pdiast) and two systolic peaks, Psyst and Paug, the second representing the systolic augmented pressure. The incisura and a reflected peak occurring in diastole were also analyzed. AIx was measured as $(\text{Paug} - \text{Psyst}) / (\text{Paug} - \text{Pdiast}) * 100$

Results: The pressure measurements with the Samba Sensor allowed for identification of Pdiast, Psyst and Paug. In young C57/B6 mice, Pdiast was 86 ± 4.7 mmHg, Psyst was 106 ± 6 mmHg and Paug 116 ± 7 mmHg. AIx was 33 %, i.e. the reflected pressure accounted for approx 33 % of the pulse pressure. The incisura (indicating aortic valve closure) could be detected, and the ejection period estimated (42 ± 4 % of the cardiac cycle). A diastolic reflected wave was often found. ApoE(-/-) mice kept on a western diet for 4 mo had significantly increased peak/augmented systolic pressure (134 ± 6 mmHg) and AIx, but not diastolic pressure (93 ± 6 mmHg). In 15 mo old apoE(-/-) mice on chow diet, blood pressure and AIx were significantly elevated, as was pulse wave propagation rate.

Conclusion: Aortic pressure recordings in mice allowing PWA can be obtained with the Samba Preclin system. There is considerable AIx in young healthy mice. With age and atherosclerosis there was a marked increase in AIx and pulse wave propagation rate, as a result of arterial stiffening. Increased reflection can explain most of the increased pulse pressure in old atherosclerotic mice.

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TITLE:

Endothelium mediated dilatation and systolic augmentation in normal and atherosclerotic mice in vivo.

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TEXT:

Objectives: Endothelial dysfunction is associated to hypertension and atherosclerosis, and contributes to increased reflection of pulse pressure/systolic augmentation (AIx) in man. As there are many mouse vascular disease models, we developed a technique to study endothelium mediated dilatation (EMD) in vivo in mice.

Methods: High precision aortic pressure recordings were obtained from isoflurane anaesthetized mice with a Samba Preclin pressure system. We measured diastolic (Pdiast), systolic (Psyst) and augmented systolic pressures, and used pulse wave analysis (PWA) to calculate AIx in isoflurane anaesthetized mice. Measurements were made before and after injection of 3 µg metacholine (Mch) i.p. to trigger EMD. L-NAME was used to block eNOS.

Results: Blood pressure was reduced from 116 ± 7/86 ± 5 mmHg (syst/diast) to 105 ± 5/80 ± 2 mmHg by 3 µg metacholine in healthy B6 mice. AIx was reduced from 34 to 13 %, and the reduced pressure reflection thus explained most of the reduction in systolic pressure by Mch. Mch also lowered pulse wave propagation rate. L-NAME significantly increased blood pressure and antagonized the effect of Mch. ApoE(-/-) mice kept on a western diet for 4 mo had significantly increased systolic pressure (134 ± 6 mmHg) and AIx, but not diastolic pressure (93 ± 6 mmHg). The response to Mch was significantly blunted.

Conclusion: Mch caused endothelium mediated reductions in aortic pressure in mice, systolic reductions were larger than diastolic. This difference was due to reduced systolic reflection as evaluated by PWA. The technique was used to investigate disease related changes in vascular reactivity. Atherosclerotic mice have higher pulse and systolic pressure than normal mice, and endothelium mediated dilatation is blunted. The aortic atherosclerosis led to increased stiffness and systolic reflection, which explained the elevated systolic pressure. PWA can be used to assess vascular reactivity in anaesthetized mice.