with increased polyamine levels in the heart to lead to this dramatic phenotype.

LB37

Sildenafil (Viagra) Induces Delayed Preconditioning Through iNOS-Dependent Pathway in Mouse Heart

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Sildenafil citrate (Viagra) is the most widely used drug for treating erectile dysfunction in men. We recently demonstrated that it induces potent protective effects against ischemia-reperfusion (I-R) injury in rabbit hearts through opening of mitoKATP channels (Am J Physiol 2002;283:H1263). In the present study, we investigated the role of nitric oxide (NO)-dependent signaling pathway in the delayed cardioprotection by sildenafil. Adult male ICR mice were treated with Saline or Sildenafil (0.7 mg/kg, i.p.) 24 hours before global I-R in Langendorff mode. Infarct size reduced from 27.6Â±3.3% in saline controls to 6.9Â±1.2% in sildenafil-treated mice (meansÂ±SEM, P<0.05) without compromising cardiac function. RT-PCR revealed a transient increase in endothelial and inducible NO synthases (eNOS and iNOS) mRNA in sildenafil-treated mice, peaking at 45 min (eNOS) and 2 hours (iNOS) after sildenafil injection. The magnitude of mRNA surge was more pronounced for iNOS than eNOS. In addition, a significant increase in both iNOS and eNOS protein was detected 24 hours after sildenafil treatment. Selective inhibitor of iNOS, 1400W (10 mg/kg, i.p. given 30 min before I-R) abolished sildenafil-induced protection (23.7Â±2.8%, P<0.05 vs. Sildenafil). These data suggest that induction of NOS is an essential component of signaling mechanism for sildenafil-induced delayed preconditioning. However, iNOS appears to be the primary isoform that mediates the robust cardioprotection.

LB38

Arterial Wall Tissue Content of Cholesterol Directly Correlates with the Extent of Arterial Thrombosis After an Acute Vascular Event

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Serum cholesterol has been shown to be an independent marker for acute coronary events, however cholesterol content in arterial wall tissue has not been studied in relationship to such events. 24 NZW rabbits were used in this study. Atherosclerosis was induced in 20 rabbits by balloon endothelial debridement and feeding cholesterol enriched diet for 6 months. Plaque disruption and thrombosis was then triggered by histamine and Russell's viper venom as has been previously described. Group (Gp) I (n=4) were non-triggered controls; Gp II (n=4) were non-triggered atherosclerotic controls; Gp III (n=8) were triggered atherosclerotic rabbits; Gp IV (n=8) were triggered atherosclerotic rabbits pretreated with β-carotene. Tissue cholesterol and protein content were assayed from the thoracic and abdominal aorta. The findings were then correlated to postmortem thrombi number and surface areas. There was a strong correlation between thrombus surface area and number of thrombi on arterial wall with arterial tissue cholesterol content in Gp III (r=0.98; p=0.003, r=0.93; p=0.0001) and Gp IV (r=0.54; p=0.006, r=0.74; p=0.001). β-carotene reduced the extent of thrombosis but this was not statistically significant.

The amount of total tissue cholesterol in atherosclerotic arteries was strongly correlated with the extent of thrombosis following triggering in the model of plaque disruption and thrombosis.

Gp	Surface Area of Aorta (mm^2)	Weight of Aorta (g)	Thrombus Area(m^2)	Thrombus Number	Tissue Protein (mg/g)	Tissue Cholesterol (µg/)
I	1550±181	1.62±0.6	0	0	10.4±1.7	458±83
II	1881±233	3.92±0.3	0	0	10.0±2.0	2479±283
III	1664±285	3.48±0.2	78.6±39	5.0±4.3	11.0±1.1	2855±256
IV	1545±193	3.76±0.5	50.3±26	2.3±1.3	9.1 ±1.1	2854±365

LB39

Epicardial Pacing Is Not Necessary After Human Myocardial Ischemia-Reperfusion Injury

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Background: Temporary epicardial pacing wires are routinely placed following human myocardial ischemia-reperfusion injury (cardio-pulmonary bypass surgery) for treatment of post-op arrhythmias. In addition to financial costs, there are also finite clinical risks, such as bleeding and pericardial tamponade, associated with wire removal. **Methods:** Fifty-eight pts, who underwent CABG (70.7%), valve surgery (13.8%), combination valve surgery and CABG (5.2%), aneurysm repair (3.4 %), or left atrial mass excision (1.7%), were evaluated for use of post-op epicardial pacing wires. A forward stepwise logistic regression model was constructed to determine possible predictors of pacing during hospitalization. **Results:** The mean age was 61 ± 11 years, and 60% of pts were male. Within the study population, 69% had hyperlipidemia, 81% were hypertensive, 46.6% had DM, and 65.5% used tobacco. Over 1/3 of pts had a prior MI or CHF. Nine pts (15.5%) required pacing. Out of 17 possible predictors, use of digoxin was the only statistically significant variable for necessity of pacing (Wald χ^2=5.622, p= 0.018). The single predictor model had a R^2 of 0.164. **Conclusions:** Pacing wires are commonly placed during cardiac surgery, despite lack of conclusive evidence to support this practice. Our data suggests that pacing wires do not need to be routinely placed in all adult cardiac surgery pts, and should only be used selectively in pt populations at increased risk.

LB40

14,15-Epoxyeicosatrienoic acid activates store-operated calcium channels in rat pulmonary microvascular endothelial cells

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The P 450 monooxygenase-derived arachidonic acid metabolite, 14,15-epoxyeicosatrienoic acid (14,15-EET), and the Ca^{2+} ATPase blocker thapsigargin (TG) increase endothelial cell permeability measured by the filtration coefficient (K_f) in isolated, perfused rat lungs. Cytosolic Ca^{2+} concentration ($[Ca^{2+}]_i$) is known to play an important role in control of pulmonary vascular endothelial cell (PMVEC) barrier function. To test whether 14,15-EET (methyl ester) increases $[Ca^{2+}]_i$ in PMVEC from rats, and if this increase is due to Ca^{2+} entry via store-operated channels (SOC), we measured $[Ca^{2+}]_i$ by fura 2 fluorescence. Changes in $[Ca^{2+}]_i$ were expressed by the fluorescence ratio of the Ca^{2+}-bound (340 nm) to Ca^{2+}-unbound (380 nm) at emission wavelength 510 nm. 14,15-EET induced a dose-dependent (1, 3 and 10 µM, n = 4, 7 and 11, respectively) increase in $[Ca^{2+}]_i$ that was reversed by application of the Ca^{2+} chelator EGTA (ethylene glycol tetraacetic acid) (5mM, n = 4). There was no further increase in $[Ca^{2+}]_i$ when TG (1µM) was applied following the response to 14,15-EET (3µM, n = 4) or when 14,15-EET (n = 8) was applied following the TG-induced increase in $[Ca^{2+}]_i$. These results demonstrate that 14,15-EET induces a dose-dependent increase in $[Ca^{2+}]_i$ and additionally indicate that the 14,15-EET induced Ca^{2+} entry is linked to activation of the SOC in rat PMVEC. Supported by The Research Council of Norway and HL61955.