8:45

733-2 Increased Diastolic Chamber Stiffness Occurring During Supply, Demand, and Zero-Flow Ischemia Is Determined by Common Subcellular Mechanisms

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We compared mechanisms of increased diastolic chamber stiffness (↑DCS) occurring in isolated isovolumic (balloon-in-LV) blood perfused rabbit hearts during prolonged low-flow ("supply", SI), demand (DI), and zero-flow ischemia. We created i) SI by reducing coronary blood flow by 85% ii) DI by reducing coronary blood flow by 70% and superimposing tachycardia (7 Hz), and iii) global zero-flow ischemia by stopping coronary blood flow. A 5 min intracoronary infusion of butane-dione-monoxime (BDM, 5–10 mM), an agent which diminishes Ca++ activated tension, was imposed when ischemic diastolic dysfunction had occurred in SI and DI. In SI when DCS had increased, as assessed by an increase in isovolumic LVEDP of 5 mmHg (21 ± 4 min ischemia), BDM reduced LV developed pressure (DevP) from 25 ± 1 to 15 ± 2 mmHg ($n = 8$, $p < 0.001$) but did not simultaneously reduce LVEDP. Similarly in DI when LVEDP had increased 7–8 mmHg ($n = 8$, 14 ± 2 min tachycardia + ischemia) BDM reduced DevP from 35 to 25 mmHg ($p < 0.01$) but did not reduce LVEDP. We then applied a quick stretch-release (QSR) of 25% of intraventricular balloon volume to hearts during ischemic diastolic dysfunction. After zero-flow ischemia (18 ± 4 min) when LVEDP had increased 10 mmHg from a baseline of 17 mmHg (ie "classic" rigor) QSR instantly lysed increased diastolic tension (LVEDP pre-vs post-QSR 27 ± 1 vs 17 ± 1 mmHg, $p < 0.001$, $n = 6$), a response known to be characteristic of rigor. QSR similarly lysed increased diastolic tension in both SI ($n = 6$) and DI ($n = 6$) hearts when ↑DCS had occurred such that isovolumic LVEDP returned precisely to pre-contracture values. *Hence* ↑DCS occurring during both SI and DI was insensitive to BDM but was lysed by QSR similarly to contracture sustained after zero-flow ischemia. These results imply that the subcellular basis for ↑DCS was common to these ischemic states, and was a rigor, and not a Ca++ driven tension.

9:00

733-3 No Effect of Angiotensin II on Ischemic Diastolic Dysfunction in Hypertrophied and Infarcted Rat Hearts

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Pressure-overload left ventricular hypertrophy (LVH) is associated with increased diastolic dysfunction during ischemia, whereas compensatory hypertrophy following myocardial infarction is not. We tested if angiotensin II (ANG II) would exacerbate ischemia-induced diastolic dysfunction in these two models. Pressure-overload LVH (Pressure-LVH) was induced in uninephrectomized, deoxycorticosterone-salt treated rats, and infarction by ligation of the left anterior descending artery (Post-MI). Mean infarct size was 27 ± 3%. Isolated, isovolumic, red-cell perfused rat hearts were exposed to 60 min of low-flow ischemia (15% of baseline flow) followed by 30 min of reperfusion. ANG II (10^{-7} M) infusion was started at baseline and continued throughout ischemia and reperfusion. ANG II exerted a vasoconstrictive effect at baseline but did not affect LV end-diastolic pressure (LVEDP). During ischemia, diastolic dysfunction was exaggerated in untreated Pressure-LVH ($n = 5$) vs sham ($n = 5$) (ΔLVEDP 46 ± 2 vs 25 ± 3 mmHg; $p < 0.05$). ANG II treatment did not further increase LVEDP in Pressure-LVH ($n = 7$), but LVEDP tended to increase in sham ($n = 5$) (ΔLVEDP 43 ± 6 vs 40 ± 5 mmHg; ns). In untreated post-MI hearts ($n = 8$), LVEDP increased to the same extent as sham ($n = 7$) (24 ± 5 vs 35 ± 5 mmHg; ns). Again, ANG II treatment did not increase LVEDP in post-MI ($n = 7$) or sham ($n = 7$) (ΔLVEDP 31 ± 4 and 35 ± 5 mmHg; ns). During reperfusion, LVEDP remained increased in untreated Pressure-LVH but not post-MI. ANG II did not adversely affect recovery in pressure LVH or post-MI, but slightly increased LVEDP in sham. *Summary:* Diastolic dysfunction during ischemia and reperfusion is exaggerated with pressure-overload hypertrophy, but not with infarction. Extrinsic ANG II does not increase ischemic diastolic dysfunction in these animal models. *Conclusion:* ANG II has a minimal role in modulating acute ischemic diastolic dysfunction in these particular forms of LVH.

9:15

733-4 Physiologic Versus Pathologic Hypertrophy: Differences in Cardiac Rotation and Filling

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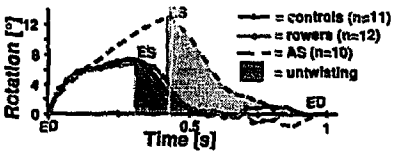
Rotational and translational motion of the heart was assessed with MR myocardial tagging in patients with physiologic and pathologic hypertrophy.

Methods: Twelve championship rowers (R), 10 patients with aortic stenosis (AS) and 11 controls (C) underwent myocardial tagging on a Philips ACS II (1.5 T) system with high temporal (35 ms) and spatial (1.4 × 1.4 mm) resolution. The left ventricle was labelled with a rectangular grid in 3 short-axis planes (base, equator, apex) and cardiac rotation was calculated from the motion of the grid crossing points:



Systolic rotation is normal in rowers but enhanced in aortic stenosis. However, diastolic untwisting is significantly prolonged in aortic stenosis but not in rowers.

Conclusions: Severe pressure overload hypertrophy is associated with enhanced systolic rotation and prolonged untwisting which overlaps diastolic filling. Thus, alterations in cardiac rotation are predominantly found during diastole in pathologic hypertrophy and may explain the occurrence of diastolic dysfunction in these patients.

9:30

733-5 Reduced Myocardial Contractile Effects of Nitric Oxide After Heart Transplantation: Implications for Diastolic Dysfunction of the Cardiac Allograft

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Diastolic left ventricular(LV) dysfunction of the cardiac allograft(CA) reduces exercise tolerance and results from decreased LV diastolic distensibility. In control subjects(C), a bicoronary(BIC) infusion (Inf) of the Nitric Oxide(NO)-donor sodium nitroprusside(SNP), induces myocardial contractile effects consisting of a fall of LV peak systolic(PS) pressure(P) and a rise of LV End-Diastolic(ED) distensibility(Dis) (= lower LVEDP at larger LVEDVolume(V)). These effects result from a direct myocardial action of NO, unrelated to systemic vasodilation, as they are not reproduced by a right atrial Inf of SNP. In the present study, the myocardial contractile effects of NO were compared in C($n = 7$) and in transplant recipients(Tx) ($n = 14$), free of rejection or graft vasculopathy, by obtaining microtip LV pressures and LV angiograms at baseline and at the end of a 5 min BIC Inf of SNP (4 μg/min). In Tx, BIC SNP caused a smaller ΔLVPSP(mmHg) (Tx: −7 ± 6; C: −16 ± 7; $p < 0.05$) and a smaller rise in LVEDD is because of smaller ΔLVEDP(mmHg) (Tx: −3 ± 3; C: −6 ± 2 $p = 0.07$) at comparable ΔLVEDV(ml) (Tx: 7 ± 7; C: 10 ± 13). In Tx, ΔLVPSP at the end of BIC SNP was inversely related to baseline LVEDP (ΔLVPSP = 0.7 LVEDP −19; $r = 0.68$; $p = 0.008$) and to baseline time constant(T) of LVPdecay (ΔLVPSP = 1.1T − 46; $r = 0.79$; $p = 0.02$). Baseline diastolic LV dysfunction of the CA therefore predicts reduced myocardial contractile response to exogenous NO. A similar deficiency in myocardial response to endothelial NO could contribute to LV diastolic dysfunction of the CA. Immune-related reactive oxidants in the CA, which bind to and inactivate NO, could explain the deficient myocardial contractile response to NO after Tx.

9:45

733-6 Inertial Nature of Pulmonary Vein Flow — Invasive and Doppler Correlation in Humans

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Previous studies have shown a relation between pulmonary vein (PV) flow velocities and LA pressure. We hypothesized that inertial forces contribute significantly to the convective component obtained from such velocity data. In 3 patients undergoing routine cardiac surgery, we measured LA and PV pressure & PV/LA gradient, while recording pulsed wave Doppler from the PV orifice. All cycles were standardized to a cycle length of 1000 ms and intervals from the Q-wave to PV Doppler S-wave, D wave and A waves and their corresponding peaks of LA/PV gradient (AccS, AccD, AccA) were measured. Inertance (M) was calculated at the onset of S-wave via — $M = (\Delta P - \frac{1}{2}\rho v^2)/dv/dt$.

Results: Nine cardiac cycles were analyzed with mean cycle length of 773 ± 53 ms. The PV/LA gradient related to the S-wave (AccS) flow preceded it by 251 ± 83 ms and had an amplitude of 1.2 ± 0.28 mmHg. AccD preceded the D-wave by 170 ± 61 ms and had an amplitude of 1.04 ± 0.44 mmHg.