which were unchanged (0.35 ± 0.52; p = 0.11). Thus: 1) at rest, degree of RMW abnormality correlates generally with level of RMBF and 2) RMBF response to adenosine (Ado), a measure of coronary flow reserve, correlates with RWM response to dobutamine stress which depends at least in part on augmentation of coronary flow.

10:45

704-2 Comparative Relation of Neurohormonal Activation to Hemodynamics in Primary or Precapillary Secondary Pulmonary Hypertension

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Primary (PPH) or precapillary secondary (SPH) pulmonary hypertension show similar hemodynamic abnormalities and an intense neurohormonal activation has been detected in both syndromes. Comparative analysis of the neurohormonal profile and its relation to hemodynamics of patients with PPH and SPH are not available. Plasma levels of atrial natriuretic peptide (ANP), aldosterone (ALD), renin activity (PRA), epinephrine (PE), norepinephrine (PNE) and endothelin (ET) were assessed from the antecubital vein in 12 patients with PPH and 7 patients with SPH (2 connective tissue disease, 2 chronic thromboembolic, 3 closed atrial septal defect). Hemodynamics were measured by heart catheterization. Between PPH and SPH patients no differences were assessed on cardiac index (CI) (2.2 ± 0.2 vs 2.3 ± 0.3 l/min/m^2, ns), mean pulmonary artery pressure (PAP) (55 ± 12 vs 58 ± 12 mmHg, ns), pulmonary vascular resistance (PVR) (14 ± 6 vs 14 ± 4 RU, ns) right atrial pressure (RAP) (4 ± 4 vs 8 ± 7 mmHg, p = 0.13) and mixed venous blood oxygen saturation (vSat) (62 ± 7 vs 65 ± 9%, ns). Neurohormonal parameters in patients with PPH and patients with SPH were as follows:

	ANP (pg/ml)	ALD (pg/ml)	PRA (ng/ml/h)	PE (pg/ml)	PNE (pg/ml)	ET (pg/ml)
PPH	203 ± 139	178 ± 132	1.8 ± 2.1	351 ± 420	426 ± 343	4.5 ± 3.1
SPH	210 ± 110	220 ± 262	2.5 ± 4.0	268 ± 333	637 ± 720	6.9 ± 3.7
p	ns	ns	ns	ns	ns	ns

In patients with PPH, ET was correlated to RAP (r = 0.68, p < 0.02), to CI (r = 0.66, p < 0.02) and to PVR (r = 0.65, p < 0.02). In patients with SPH, ET was correlated to RAP (r = 0.96, p < 0.01), PNE was correlated to vSat (r = −0.80, p < 0.03) and ALD was correlated to RAP (r = 0.87, p < 0.02).

Conclusions: No differences were observed on plasma levels of neurohormons between patients with PPH and SPH. In patients with PPH hemodynamic abnormalities were correlated only to ET plasma levels while in patients with SPH hemodynamics were correlated to ET, to PNE and to ALD plasma levels. Neuroendocrine activation shows a different pattern of association with hemodynamic abnormalities in patients with PPH compared to patients with SPH.

11:00

704-3 Relation of Neurohormonal Activation to Functional Class in Patients with Primary or Precapillary Secondary Pulmonary Hypertension

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Intense neurohormonal activation has been demonstrated in patients with primary or precapillary secondary pulmonary hypertension (PH) but the relation of neurohormons to functional impairment is not well known. Plasma levels of atrial natriuretic peptide (ANP), aldosterone (ALD), renin activity (PRA), epinephrine (PE), norepinephrine (PNE) and endothelin (ET) were assessed from the antecubital vein in 12 patients with primary PH, 7 patients with precapillary secondary PH (2 connective tissue disease, 2 chronic thromboembolic, 3 closed atrial septal defect) and 10 control subjects. Twelve patients were in NYHA functional class II (PH-II) and 7 in class III/IV (PH-III/IV). Mean PA pressure (PAP), cardiac index (CI), pulmonary vascular resistance (PVR) and right atrial pressure were assessed by heart catheterization:

	PAP (mmHg)	CI (l/min/m^2)	PVR (RU)	RAP (mmHg)
PH-II	53 ± 13	2.4 ± 0.4	12 ± 3	3 ± 2
PH-III/IV	61 ± 9	2.0 ± 0.5	18 ± 6	11 ± 5
p	0.17	0.07	0.009	0.0001

Neurohormons plasma levels in control subjects (C), PH-II and PH-III/IV patients were as follows:

	ANP (pg/ml)	ALD (pg/ml)	PRA (ng/ml/h)	PE (pg/ml)	PNE (pg/ml)	ET (pg/ml)
C	58 ± 18	110 ± 65	0.7 ± 0.4	33 ± 19	220 ± 101	1.7 ± 0.3
PH-II	167 ± 96*	144 ± 102	1.5 ± 2.0	298 ± 263*	420 ± 294*	3.6 ± 1.4*
PH-III/IV	276 ± 153*†	209 ± 270	3.2 ± 3.9*	462 ± 524*	820 ± 693*†	8.4 ± 3.9*°

* p < 0.05 vs C ° p < 0.001 vs PH-II † p < 0.09 vs PH-II

Conclusions: Neurohormonal activation in primary or precapillary secondary PH is detectable also in patients without overt clinical and hemodynamic signs of right heart failure (PH-II). Neurohormonal activation seems to be progressive and is more severe in functional class III/IV patients. ET shows the best statistically significant relation with functional impairment.

11:15

704-4 EDRF-mediated Increases in Conduit Artery Distensibility are Impaired in Chronic Heart Failure

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Chronic heart failure (CHF) is associated with reduced EDRF activity in resistance arteries. A similar effect in conduit arteries would reduce their distensibility and increase the load on the compromised heart. We measured pulse wave velocity (PWV), inversely related to distensibility, in the right common iliac artery (RCIA) during acetylcholine (ACh, endothelium-dependent dilator) and adenosine (Ado, endothelium-independent dilator) infusion in 6 patients with CHF (NYHA grades 2–3, EF <40%, age 50 ± 16 [SD] years, 4 men) and 9 normal subjects (N) (age 49 ± 6 years, 4 men). CHF was due to dilated cardiomyopathy (with normal blood pressure, cholesterol, glucose, and coronary angiograms). PWV, measured from the pressure pulse delay between 2 transducers 5 cm apart, was measured during infusions proximal (P) and distal (D) to the RCIA segment studied. We corrected for BP and other downstream effects by subtracting D from P effects. At baseline, PWV was similar in the two groups (CHF 8.7 ± 1.1; N 9.1 ± 1.5 ms^{-1}). ACh (10^{-7}, 10^{-6}, 10^{-5} mol/L) induced dose-dependent reductions in PWV (−5, −15, −25%) in normals but no change (+2, +2, −3%) in CHF (p = 0.0013). Ado (2 × 10^{-7}, 2 × 10^{-6}, 2 × 10^{-5} mol/L) induced similar dose-related reductions in PWV in N (−5, −12, −24%) and in CHF (−1, −12, −14%, NS). These data indicate that conduit artery distensibility is increased by ACh-stimulated EDRF activity in normal subjects but not in patients with CHF. This suggests that physiological EDRF-mediated increases in distensibility, as occur during exercise, may be impaired in CHF despite normal resting distensibility.

11:30

704-5 Adenosine Dilates Conductance and Resistance Vessels in Denervated Human Coronary Arteries and is more Potent than Dipyridamole

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Adenosine and dipyridamole are coronary vasodilators who act primarily on resistance vessels. Vascular response in the denervated heart are not well understood. To examine this question, coronary hemodynamic changes in response to standard vasodilators were assessed in eleven heart transplanted patients using simultaneously a 4.3F, 30 MHz ultrasound imaging catheter (CVIS) over a 0.014" Doppler guidewire (Cardiometrics). Measures of average peak velocity (APV) and cross-sectional area (CSA) were used to calculate volumetric flow during intravenous infusions of the endothelium independent vasodilators adenosine (140 μg/kg/min over 4 minutes) and dipyridamole (140 μg/kg/min over 4 minutes). Volumetric coronary blood flow (CBF) was calculated using the previously validated relationship CBF = 0.47 × CSA × APV. Flow reserve was assessed as a ratio of maximal pharmacologically-induced flow to steady baseline flow prior to infusion. Increase in coronary average peak velocity (261.9 vs. 194.6%, p = 0.005), lumenal area (111.8 vs 104.2%, p = 0.01), peak volumetric blood flow (515.8 vs. 317.2 cc/min, p = 0.007) and coronary flow reserve (2.93 ± 0.79 vs. 1.99 ± 0.56, p < 0.001) were higher with adenosine compared to dipyridamole. Epicardial dilation was only seen with adenosine administration (p = 0.01). Both agents caused similar decreases in systemic blood pressure and little change in heart rate.

Conclusion: Transplant recipients appear to have diminished flow velocity and flow reserve in response to endothelium-independent agents. Adenosine appears to be a more potent coronary vasodilator than dipyridamole in denervated human transplant subjects at both the epicardial and microvascular level at standard doses. Adenosine's effects in the conductance vasculature may be unique to the transplant recipient where denervation is present.

MONDAY AM