by echocardiography and the time constant of LV relaxation (Tau) was derived from the LV pressure to assess diastolic function in 94 consecutive patients with suspected cardiac disease. The sensitivity and specificity of optimal values of each peptide for detecting abnormal LV function or LVH were:

EF < 45%	sensitivity: BNP (83%) > C-ANP (79%) > N-ANP (67%) specificity: BNP (81%) > C-ANP (67%) > N-ANP (63%)
Tau > 55 ms	sensitivity: BNP (85%) > N-ANP (70%) > C-ANP (60%) specificity: BNP (74%) > C-ANP (65%) > N-ANP (61%)
LV mass index > 120 g/m^2	sensitivity: BNP (81%) > N-ANP (73%) > C-ANP (69%) specificity: BNP (90%) > N-ANP (79%) > C-ANP (67%)

By receiver-operator-characteristic (ROC) analysis, BNP was significantly more sensitive and specific than C-ANP or N-ANP for detecting abnormal EF, Tau or LV mass index with an ROC value of 0.85, 0.82, and 0.91 respectively. Sensitivity for detecting abnormal LV structure or function employing a "natriuretic peptide panel" with an abnormal BNP *or* C-ANP *or* N-ANP exceeded that of BNP alone and was for EF < 45% (96%), Tau < 55 ms (90%) and LV mass index > 120 g/m^2 (96%). *Conclusions:* BNP is the single best test to detect abnormal systolic and diastolic function and LVH in patients with suspected cardiac disease. A "natriuretic peptide panel" has very high sensitivity and may be a useful screening test in some populations.

4:15

723-2 Attenuation of B-type Natriuretic Peptide (BNP) Secreted From an Infarcted Segment Reresents the Process of Left Ventricular Remodeling After Myocardial Infarction

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As B-type natriuretic peptide (BNP) is known to be a marker for ventricular hypertrophy and/or dilatation, its measurement at the infarcted segment might be useful to evaluate infarct expansion after the onset of myocardial infarction (MI). Seventy five patients of first anterior MI without any cardiac event since their first attack were subjected to cardiac catheterization performed 18 ± 15 months (range 1 to 45 months) after the onset of MI. Hemodynamic parameters, left ventricular (LV) volumes and function on LV graphy and plasma BNP concentration (pg/ml) of aortic root (Ao) and anterior interventricular vein (AIV) were measured by radioimmunoassay. The difference of plasma BNP concentration between AIV and Ao (AIV-Ao), which reflect BNP secreted from the infarct segment, had significant correlations with EDVI (r = 0.67, p = 0.001), ESVI (r = 0.65, p = 0.001), EF (r = 0.71, p = 0.001), LVEDP (r = 0.53, p = 0.003), and the duration from the onset of MI to the cardiac catheterization (r = −0.75, p = 0.001). By multivariate analysis, however, EDVI (p = 0.003) and the duration from the onset of MI (p = 0.0021) among the variables were picked up as significant factors determining the plasma concentration of BNP at AIV-Ao. These results indicated that BNP released from the infarcted segment is enhanced by the ventricular dilatation and attenuated in the course of time after MI. These results suggested the secretion of BNP at the infarcted segment was stimulated by the infarct expansion at the early period after MI but decreased with the accomplishment of expansion during the late period.

In conclusion, BNP secreted from the infarct segment represent the process of LV remodeling after MI.

4:30

723-3 Repetitive Bolus Administration of Brain Natriuretic Peptide Reduces Cardiac Filling Pressures in Human Heart Failure

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Endogenous natriuretic peptides (NP) produce vasodilation, in response to the myocardial remodeling of congestive heart failure (CHF). Individual NP sequences of single gene origin, confer distinct cardiovascular characteristics. In this multicenter trial, we evaluated the effect of repetitive bolus administration of brain natriuretic peptide (hBNP) in patients (pts) with CHF, during hemodynamic evaluation. 28 of 29 pts were NYHA III or IV, and all had EF < 30%. hBNP was given as 5 μg Q4H (7 pts), 10 μg Q4H (6 pts), 10 μg Q6H (6 pts), with placebo groups for Q4H (6 pts) and Q6H (4 pts) intervals. For each treatment interval, pts received repetitive doses over 24 hrs. Placebo groups were pooled for statistical analysis, considering between-/within-group differences, and dosage hierarchy, p < 0.05(*) being significant. Pulmonary wedge (PWP) and right atrial (RAP) pressures:

	Placebo	5 μg Q4H	10 μg Q4H	10 μg Q6H
PWP (mmHg)				
Baseline	27 ± 7	25 ± 6	32 ± 6	27 ± 5
hBNP + 0.5 hrs	26 ± 9	16 ± 5*	19 ± 8*	12 ± 6*
hBNP + 1 hrs	27 ± 8	15 ± 6*	20 ± 7*	13 ± 6*
hBNP + 2 hrs	26 ± 5	18 ± 8*	21 ± 9*	16 ± 6*
RAP (mmHg)				
Baseline	15 ± 6	13 ± 8	12 ± 4	12 ± 7
hBNP + 0.5 hrs	15 ± 7	10 ± 8*	8 ± 6*	7 ± 5*
hBNP + 1 hrs	16 ± 7	9 ± 9*	8 ± 6*	6 ± 5*
hBNP + 2 hrs	14 ± 6	10 ± 8*	7 ± 4*	7 ± 5*

At the common time point of 12 hours, PWP (15 ± 5) and RAP (4 ± 5,) were p < 0.05 for the 10 μg Q4H interval. With the final bolus in each group, persistent response of PWP and RAP indicated no tachyphylaxis. Changes in cardiac index and systemic resistance were concordant, consistent with vasodilation. In human CHF, exogenous hBNP improves cardiac filling pressures in the setting of vasodilation, suggesting preserved hemodynamic responsiveness of the "type A" NP receptor, while reducing the atrial tension stimulus for endogenous NP release.

4:45

723-4 Exhaled Nitric Oxide as a Measure of Response to Therapy in Patients With Heart Failure

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Endogenous nitric oxide (NO) can be detected in exhaled air and increases with exercise and L-arginine administration, possibly reflecting vascular release. We hypothesized that exhaled NO would be elevated in patients with heart failure (HF) as a compensatory circulatory mechanism, and would decrease as hemodynamics improved with vasodilator and diuretic therapy. Chemiluminesence was used to measure mean mixed expired NO content of a vital capacity breath in patients with HF (n = 5) and matched controls (n = 5) during inhalation of NO-free air. Exhaled NO was higher in HF than in controls (8.4 ± 3.5 vs. 6.5 ± 2.4 ppb, p < 0.04). Serial measurements were made over of period of therapy (7.3 ± 6 days) with sodium nitroprusside (SNP) and diuresis during monitoring of pulmonary arterial pressures and cardiac output in 7 additional patients with HF breathing room air.

	Pre-therapy	SNP for 2 hrs.	Post-therapy
NO (ppb)	20.4 ± 6.2	22.8 ± 4.6	11.2 ± 1.2*
PVR (dyne-sec-cm-5)	356 ± 47	287 ± 63	147 ± 32*
CO (L/min)	3 ± 0.3	4.64 ± 0.9	4.8 ± 0.3†
PCWP (mmHg)	31 ± 3	27 ± 2	21 ± 7†

*p < 0.05 vs. baseline and SNP, †p < 0.01 vs. baseline

HF therapy improves hemodynamics and is associated with reductions in exhaled NO concentrations. Thus, elevations in exhaled NO may reflect a compensatory circulatory mechanism in HF, and exhaled NO may be an easily obtainable and quantifiable measure of clinical response to therapy in HF.

5:00

723-5 Modulation of Tumor Necrosis Factor α in Advanced Heart Failure With Cachexia Is Associated With Anabolic Effects

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Tumor Necrosis Factor (TNFα) has catabolic effects which produce cachexia in laboratory animals and humans. Indeed, patients with advanced heart failure (aHF) who demonstrate elevated levels of TNFα often suffer from cachexia, a finding characterized by reduced body fat. The purpose of this double blind, randomized, placebo-controlled study was to evaluate the impact of modulation of TNFα synthesis on alterations in body fat indices using n-3 fatty acids. 14 patients with aHF were randomly allocated to active treatment (n-3 fatty acids, 6.4 gms/d; n = 7) vs. isocaloric placebo (n = 7). TNFα production at baseline and after 18 weeks was assessed using lipopolysaccaride monocyte stimulation.

	ΔTNFα synthesis	Δ% Body Fat
n-3 Fatty Acids	−59%	+9.5%
Placebo	+44%	−4.2%

Regression analysis revealed that ΔTNFα was inversely and significantly correlated with Δ% body fat (r value = 0.60, p = 0.02). *Conclusions:* 1) N-3 fatty acid supplementation in aHF results in significant reductions in

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