a 16-segment construct for both ECHO and g-SPECT. The motion in each segment was graded from 1 (normal) to 4 (dyskinetic).

The correlations between g-SPECT- and ECHO regarding the end-systolic volume (ESV), end-diastolic volume (EDV) and LV ejection fraction (EF) were good: 0.821, 0.787, and 0.768, respectively (for all correlations, $p < 0.0001$). Absolute values were similar withg-SPECT and ECHO with respect to ESV (76 ± 60 ml vs 70 ± 42 ml, p = 0.52), EDV (127 ± 67 ml vs 131 ± 38 ml, p = 0.74) and LV-EF (46 ± 16% vs 51 ± 17%, p = 0.08). Agreement between g-SPECT and ECHO with respect to normal vs abnormal wall motion was 82%; exact agreement for wall motion scores was 72%.

Thus, g-SPECT is an accurate technique for the evaluation of global and regional LV function and volumes, when compared to ECHO.

1180-146 Global Left Ventricular Function Assessment Using Gated SPECT-201: Comparison With Echocardiography

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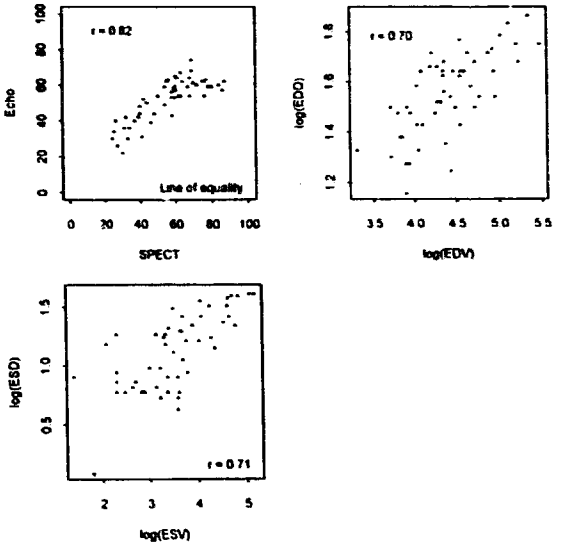
Background: Quantitative measures of left ventricular (LV) function such as ejection fraction (EF) and volume (V) at end diastole (ED) and end systole (ES) are helpful in managing patients with known or suspected CAD. These parameters are routinely measurable from gated SPECT Tl-201 myocardial perfusion studies, but have not been validated against 2D echo, commonly used for this.

Methods: We compared LVEF, EDV and ESV from resting gated SPECT Tl-201 with LVEF, ED and ES dimensions (D) by echo in 52 patients (both tests ≤30 days). SPECT measures were from 10–15° acquisitions using a multi-headed detector, weight-adjusted (3–4.5 mCi) Tl-201 dosage, LEAP collimators, 8 frames/cycle, no beat rejection, and a commercially available software program (QGS®). Echocardiograms were acquired using a 2.5/2.0 mHz HP transducer; LVEF was by biplane Simpson's Rule. There were 35 males; 20 patients had prior MI; none had atrial fibrillation.

Results: SPECT LVEF was 55 ± 17 (range 24–87), and echo LVEF was 53 ± 12 (range 23–75) (P = NS). Mean difference (SPECT-Echo) was 2.6 with 95% CI −0.2, 5.4 ($p \geq 0.07$). Regression analysis using logarithmic scale showed R = 0.7 for both EDV (D) and ESV (D).



Conclusion: Gated SPECT Tl-201 and 2D echo quantitative measurements of LVEF, ED and ES are highly comparable over a broad range from highly abnormal to normal.

1180-147 Correlation of Angiographic Coronary Anatomy With Tc99m Sestamibi SPECT Imaging Using a Balloon Occlusion Model in Patients Undergoing Coronary Angioplasty

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SPECT perfusion imaging uses a standard bulls-eye plot with assignment of vascular territory to predict the "culprit" coronary artery in the evaluation of myocardial ischemia. Because of the interpatient variability in coronary anatomy this inflexible model may not be accurate. To evaluate this model, 18 patients undergoing balloon coronary angioplasty were injected with 10–15 mCi Tc-99m sestamibi during the final balloon inflation thus inducing single vessel ischemia. SPECT imaging was begun within 90 minutes of injection. Nuclear imaging was interpreted by 3 readers, without knowledge of the interventional vessel, using a standard 17-segment model. Two systems were used to assign segments to each of the 3 coronary arteries: 1) the standard model and 2) an angiographically-directed assignment whereby each segment was assigned to a coronary artery based on the distribution of the artery in each patient.

Results: SPECT imaging revealed defects in all patients. Nuclear interpretation using the standard model correctly identified single vessel ischemia in only 3/18 (17%) patients (predicted 2 vessel ischemia in 8 patients, 3 vessel ischemia 7 patients); using the angiographic-directed assignment, SPECT imaging correctly identified single vessel ischemia in 16/18 (89%) patients. Using this model, only 2 pts had nuclear defects in segments that did not subtend the intervention vessel.

Conclusion: In a balloon occlusion ischemia model, SPECT imaging accurately identifies ischemic myocardial regions; however, standard nuclear assignment frequently overestimates the number of vascular territories affected. This may have implications the interpretation of stress imaging.

1180-148 Incremental Prognostic Value of Gated SPECT Ejection Fraction in Patients Undergoing Dual-Isotope Exercise or Adenosine Stress SPECT

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Background: The evaluation of new technology in a cost-containing environment demands validation of technology in the context of existing modalities. With this in mind, we sought to evaluate the incremental prognostic value of post-stress gated SPECT ejection fraction (gSPECT EF) over the information yielded by perfusion SPECT alone.

Methods: We followed-up 1032 consecutive patients (pts) who underwent stress sestamibi/rest thallium SPECT with post-stress gated SPECT (62% exercise stress, mean age = 67 ± 11; 65% male; mean follow-up 1.7 ± 0.3 yrs) who were found to have 32 hard events (HE; MI or cardiac death; 3.6% HE rate). Scans were interpreted using visual assessment of 20 myocardial segments (seg) and a 5-point scale (0 = nl, 4 = absent tracer uptake). The summed stress score (SSS) was defined as the sum of the 20 segmental scores. Pts who underwent revascularization early after SPECT (<60 days) were excluded (n = 130) leaving a study population of 902 pts. Multivariable Cox proportional hazards analysis (CPH) was used to predict the added prognostic value of gSPECT EF over SPECT perfusion data.

Results: CPH revealed a significant increase in χ^2 with the addition of EF to SSS adjusting for type of stress performed (global χ^2: 34 to 43, $p < 0.0001$). Pts with abnl scans (SSS >3) were stratified by the EF result (EF ≤50% = 2.0%/yr, EF >50% = 5.8%/year; $p < 0.05$.

Conclusion: Gated SPECT yields incremental prognostic value and furthers risk stratification of pts with abnormal SPECT.

1180-166 Clinical Course of Reverse Redistribution on Thallium-210 Myocardial SPECT in Patients With Myocardial Infarction

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Background: Reverse redistribution (RRD) on thallium-201 myocardial scintigraphy is thought to be a manifestation of reperfusion therapy. Wall motion abnormality is observed in the RRD segments, but the mechanism associated with wall motion abnormality in the RRD segments is yet to be defined. We assessed the clinical significance of RRD on rest thallium-201 myocardial scintigraphy in the acute phase of myocardial infarction (MI).

Methods: Thallium-201 and iodine-123-BMIPP myocardial SPECT were analyzed in 26 patients with one-vessel disease and successful percutaneous transluminal coronary angioplasty 7 to 13 days after the onset of MI (acute phase) and one month after (follow-up phase). Tomographic image of the left ventricle were divided into 11 segments. The segments with RRD on thallium-201 SPECT in the acute phase were assessed by iodine-123-BMIPP uptake and two-dimensional echocardiography.

Results: Seventy-two segments showed RRD on thallium-201 SPECT; 69 segments (96%) had suppressed BMIPP uptake in the acute phase. None of the patients had restenosis in the artery supplying the myocardial segment exhibiting RRD at one month after the onset. In the follow-up phase, 37 of 72 RRD segments become normal, and BMIPP uptake normalized in all 37 segmets. In the acute phase, 70 of 72 segments with RRD exhibited wall motion abnormality. Wall motion of all the 72 segments improved in the follow-up phase.

Conclusions: The majority of RRD segments on thallium-201 had suppressed fatty-acid metabolism with wall motion abnormality in the acute phase, but wall motion abnormality of the RRD segments improved with recovery of fatty-acid metabolism in the follow-up phase.

1181 Risk Factor Modification and Endothelial Function

Wednesday, April 1, 1998, 9:00 a.m.–11:00 a.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 10:00 a.m.–11:00 a.m.

1181-47 Fibrinolytic Potentiation by Estrogen Therapy at Conventional Dosage in Postmenopausal Women is Independent of Coagulation Pathway Activation

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Estrogen use in general has been associated with increased risk of venous thromboemboli and has been shown to activate dose-dependently coagulation pathways. We have recently shown that oral estrogen therapy at conventional dosage potentiates fibrinolysis in postmenopausal women, a process that could be a consequence of primary estrogen-induced coagulation activation. To assess the mechanism of estrogen-induced fibrinolysis, we measured parameters of coagulation activation [prothrombin fragment$_{1+2}$ (F_{1+2}), thrombin-antithrombin (TAT) complexes] and parameters of fibrinolysis potentiation [tissue-type plasminogen activator (t-PA) and plasminogen activator inhibitor (PAI-1) activities] at baseline and following 1 month of conjugated equine estrogen (CEE) 0.625 mg administered to 9 postmenopausal women.

Results: (data = mean ± SD): CEE marginally increased F_{1+2} by 18 ± 31% (P = 0.14) and nonsignificantly increased TAT by 6 ± 50% (P = 1.00). CEE reduced PAI-1 activity by 38 ± 30% (P = 0.03) and increased t-PA activity by 68 ± 85% (P = 0.09). There was no association between %ΔTAT and %Δt-PA (r = 0.05), and the associations between %ΔTAT and %ΔPAI-1 (r = 0.393), %ΔF_{1+2} and Δt-PA (r = −0.60), or %ΔF_{1+2} and %ΔPAI-1 (r = 0.527) were directionally opposite anticipated correlations if potentiation of fibrinolysis was a result of coagulation activation. We conclude that potentiation of fibrinolysis is a primary effect of CEE at the dosage used in our study and likely accounts for the low risk of venous thromboemboli in postmenopausal women taking at conventional dosage of this preparation.

1181-48 The L-Arginine: Nitric Oxide Pathway Contributes to the Acute Release of Tissue Plasminogen Activator *in vivo* in Man

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Background: Effective endogenous fibrinolysis requires rapid release of endothelial tissue plasminogen activator (t-PA). Using the nitric oxide synthase inhibitor, L-N^G-monomethylarginine (L-NMMA), we examined the contribution of endogenous nitric oxide to substance P induced t-PA release *in vivo* in man.

Methods: Blood flow and plasma fibrinolytic and hemostatic factors were measured in both forearms of 8 healthy male volunteers who received unilateral brachial artery infusions of substance P (2–8 pmol/min) and L-NMMA (1–4 μg/min).

Results: Substance P caused dose-dependent increases in blood flow ($p < 0.001$) and plasma t-PA antigen ($p = 0.04$) and activity ($p < 0.001$) concentrations confined to the infused forearm but had no effect on plasminogen activator inhibitor type 1 (PAI-1) or von Willebrand factor concentrations. In the presence of L-NMMA, substance P again caused significant increases in blood flow ($p < 0.001$) and t-PA antigen ($p = 0.003$) and activity ($p < 0.001$) concentrations but these increases were significantly less than with substance P alone ($p < 0.001$, $p = 0.05$ and $p < 0.01$ respectively). L-NMMA alone significantly reduced blood flow in the infused arm, but had no measureable effect on t-PA or PAI-1 concentrations.

Conclusions: The L-arginine:nitric oxide pathway contributes to substance P induced t-PA release *in vivo* in man. This provides an important potential mechanism whereby endothelial dysfunction increases the risk of atherothrombosis through a reduction in the acute fibrinolytic capacity.

1181-49 The Estrogen Receptor Agonist/antagonist Tamoxifen Improves Endothelial Function in Postmenopausal Women

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Previous breast cancer treatment trials using tamoxifen, have reported significant reduction of cardiovascular events. Since endothelial dysfunction is an early sign of atherosclerosis, we assessed endothelial function in 13 postmenopausal women receiving tamoxifen as monotherapy for breast cancer (mean daily dose 21 ± 3 mgr, duration of treatment 30 ± 21 months, age 51 ± 9 years). No patient was diabetic or smoker. Cholesterol was 217 ± 28 mg/dl, Triglycerides 187 ± 70 mg/dl and HDL chol 50 ± 20 mg/dl. Brachial artery diameter in response to hyperemic flow (endothelium-dependent stimulus) and to sublingual nitroglycerin (endothelium-independent vasodilator) was assessed by high resolution ultrasound imaging. Results were compared to 13 age and sex-matched healthy controls. Cholesterol and HDL cholesterol were comparable in two groups but triglycerides were higher in patients receiving tamoxifen (187 ± 70 vs 138 ± 52 mg/dl, $p = 0.05$). Baseline diameter, baseline flow and degree of reactive hyperemia were similar in two groups. Flow-mediated dilatation was higher in patients receiving tamoxifen (12.5 ± 7 vs 8 ± 3.5%, $p = 0.05$) while nitroglycerin-induced dilatation was comparable in two groups (27 ± 12 vs 25 ± 10%, ns), indicating an improvement of endothelial function in tamoxifen group.

In Conclusion: this study provides evidence that tamoxifen leads to improvement of endothelial function in postmenopausal women that is independent of cholesterol reduction, which may contribute to a decrease in cardiovascular morbidity and mortality in these subjects.

1181-50 Long-term Estrogen Therapy Improves Endothelial Function in Women With Raynaud's Phenomenon

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Endothelial dysfunction is present in patients with Raynaud's phenomenon secondary to systemic sclerosis and acute estrogen administration can improve this dysfunction. It is not known whether long-term estrogen therapy improves endothelial function too. We therefore examined the impact of long-term estrogen therapy on endothelial function in 9 women with Raynaud's phenomenon secondary to systemic sclerosis (age 58 ± 8 years, range 47–71). We used high resolution ultrasound to image the brachial artery; the diameter was measured at baseline, during reactive hyperemia to assess flow-mediated endothelium-dependent dilatation (FMD) and following sublingual nitroglycerin to assess endothelium-independent vasodilation. FMD in patients (pts) was significantly lower compared to 10 female controls of similar age (2.1 ± 1.6% vs 8.2 ± 3.2%, $p = 0.000$); also endothelium-independent dilatation was reduced in pts (17.6 ± 4.8% vs 26 ± 8%, $p = 0.01$). Patients were entered into a randomized, double-blind, placebo controlled, crossover trial (4 weeks washout phase) of conjugated estrogens (Premarin 1.25 mg per day for 4 weeks). No significant changes were seen in vessel size, rest blood flow, degree of reactive hyperemia, cholesterol, triglycerides, HDL, LDL. Estrogen did not affect endothelium-independent dilatation compared to placebo (22.6 ± 9.1% vs 19.1 ± 6.9%, ns). FMD was greater with estrogen (6.6 ± 3.5%) as compared with placebo (1.5 ± 2%, $p < 0.05$). In conclusion long term estrogen therapy markedly improves abnormal endothelial function in pts with Raynaud's phenomenon. This beneficial effect is not related to changes of lipid profile.

1181-51 Use of Synchrotron Radiation Microangiography to Assess Endothelium-dependent Relaxation of Microvessels in a Rat Model of Hindlimb Ischemia

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Background: Current methods of angiography cannot provide images of arteries measuring less than 200 μm in diameter. We have recently developed a new angiography system which employs monochromatic synchrotron radiation (SR) and high-definition video system with a spatial resolution of 30 μm. In the present study, using this microangiography system, we sought to document endothelium-dependent relaxation of microvessels in the normal and the ischemic rat limbs.

Methods: Ischemia was induced in one limb of rats by excision of a femoral artery. Thirty days later, SR microangiography was performed to assess endothelium-dependent vasomotor responses of microvessels (n = 26).

Results: SR microangiography clearly visualized the fine network of microvessels (<100 μm in diameter) in both the normal and the ischemic limbs.