Effect of Tadalafil, a Phosphodiesterase 5 Inhibitor, on Myocardial Blood Flow in Patients With Coronary Artery Disease

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Background: Erectile dysfunction (ED) and coronary artery disease (CAD) share similar risk factors. Tadalafil is a phosphodiesterase 5 (PDE5) inhibitor used to treat ED. Although PDE5 inhibitors do not adversely affect hemodynamic parameters or exercise tolerance in patients with CAD, their direct effects on myocardial blood flow (MBF) are unknown.

Methods: In a randomized, double blind, crossover study we examined the effects of tadalafil 20 mg and placebo on MBF in subjects with stable CAD (N=7; 52-73 years old). MBF was measured (PET imaging with ¹⁸F-fluorodeoxyglucose (FDG)) at rest, during adenosine (maximal vasodilation: 0.14 mg/kg/min, IV over 6 minutes), and during dobutamine (increased myocardial workload). Dobutamine was titrated to achieve 75% of predicted maximal heart rate or 10 ug/kg/min, IV. PET images were interpreted based on a 9-segment model with segments defined as normal or abnormal (<75% maximum perfusion during adenosine).

Results: Tadalafil had no significant effect on resting MBF or on adenosine-induced increases in MBF (Table). However, tadalafil increased MBF during adrenergic stimulation with dobutamine in normal segments (p<0.01), and there was a trend for a tadalafil-induced increase in MBF during dobutamine infusion in abnormal segments.

Conclusion: This study demonstrates that tadalafil has no adverse effects on MBF in subjects with stable CAD and that tadalafil may actually improve MBF during periods of increased workload (dobutamine) in normal and poorly perfused myocardium.

Comparison of the Diagnostic Performance of Totally Automated Software for the Quantification of Myocardial Perfusion SPECT

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This study was done to compare the diagnostic performance of ECTb (Emory), QPS (Cedars), and 4DMSPECT (Michigan) quantitative programs in the assessment of CAD.

Methods: We selected 126 patients who had rest thallium and maximal exercise ECG-gated Tc99m-sestamibi myocardial perfusion SPECT, 32 with <5% likelihood of CAD (LLK) and 94 with coronary angiography (CA). Sixty-five of the 94 patients had coronary stenoses >50% (LAD: 51, LCX: 36, RCA: 31). All images were totally automatically processed by each program using the e.soft workstation. Automatic parameter selection failed in 4 patients using ECTb, 2 using QPS and 8 using 4DMSPECT, and was manually corrected. Normalcy, sensitivity (SEN), specificity (SPC), and accuracy (ACC) were calculated using LLK or CA as gold standard. No functional parameters were used in this analysis.

Results: ECTb and 4DMSPECT demonstrated higher normalcy, higher sensitivity and lower specificity in comparison with QPS. Nevertheless, the accuracies of the programs were not statistically different. The normalcy of QPS improved to 90% when manually correcting the automatic base selection. Specificity was artificially lowered due to patient referral bias, particularly ECTb specificity.

Conclusion: The accuracy of ECTb, QPS and 4DMSPECT are similar in the diagnosis of CAD. Nevertheless, diagnosticians should be aware of differences in sensitivity, specificity and normalcy when comparing results from serial studies in the same patient processed with different programs.

A Novel Approach in Risk Stratification: Combined Assessment of Regional Perfusion and Function From Rest/Stress Tc-99m Sestamibi Gated SPECT

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Background: Global assessment of ejection fraction (EF) from gated SPECT adds incremental prognostic value to stress myocardial perfusion imaging. The value of assessment of regional wall motion is unknown.

Methods: A prospectively gathered database of 9,460 patients (1996-2002) who underwent rest/stress Tc-99m sestamibi gated SPECT was analyzed. Patients revascularized within 60 days after gated SPECT (n=432) were censored. Perfusion and wall motion were assessed using an 8 and 5-region model, respectively. Summed stress score (SSS) and summed wall motion score (SWMS) were calculated. EF was generated using QGS software. Patients were followed (91% complete) for myocardial infarction and cardiac death over 29 +/- 17 months. Level of risk was categorized by using SSS in combination with either SWMS or EF: low risk: SSS=1 and either SWMS=1 or EF >50%; moderate risk: SSS=2-4 and either SWMS=2-5 or EF 35-49%; high risk: SSS=4 and both SWMS=2-5 or EF 35-49%, or SSS=4 and either SWMS=5 or EF <35%; very high risk: SSS>4 and either SWMS=5 or EF <35% (Table).

Results: The annualized event rates increased significantly as risk increased using either SWMS or EF in combination with SSS (figure). There were no differences in risk stratification between techniques.

Conclusion: This novel approach of combining perfusion and function from rest/stress Tc-99m sestamibi gated SPECT in risk stratification is highly effective in the prediction of future cardiac events.

Evaluation of the Roll-off of Radiotracer Uptake Under Adenosine, Dobutamine and Nitroglycerin Stress: Demonstration of Flow Dependence

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Background: Pharmacological stressors (ST) are thought to have different effects on radiotracer uptake. To evaluate ST effects we have studied permeability surface area product (PS), a unique index of radiotracer ‘roll-off’ emerging from uptake theory.

Methods: PS was evaluated from uptake (U) vs flow (Q) data for two radiotracers: Thallium-201 (TL) and Tc99m-sestamibi (MBI) and three STs: Adenosine (AD), Dobutamine (DB), and Nitroglycerin (NG). Anesthetized dogs (n = 16) were injected with radiolabeled microspheres at rest. Another set of microspheres and TL & MBI were injected under ST. Dogs were euthanized 5 min. later and the left ventricle cut into ~ 1000 cubes of size 4 mm. 3-dimensional U and Q maps from well-counting were analyzed with the U = C*Q*[1-exp(-PS/Q)] theory using new analyses that eliminate normalization biases. Indi-

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1: p<0.05 vs. QPS, 2: p<0.01 vs. QPS, 3: p<0.002 vs. QPS, 4: p<0.05 vs. ECTb, 5: p<0.051 vs. QPS, 6: p<0.014 vs. QPS, 7: p<0.0001 vs. 4DMSPECT, 8: p<0.01 vs. ECTb, 9: p<0.04 vs. 4DMSPECT
Effects of Off-Pump Versus On-Pump Coronary Surgery

Methods: There is biochemical evidence that off pump coronary artery bypass grafting (OPCABG) reduces myocardial injury when compared to the use of cardiopulmonary bypass (ONCABG), but the functional significance of this is uncertain. We hypothesized that OPCABG surgery would result in improved early and late left ventricular function compared with ONCABG.

Results: In a single centre randomised trial, 30 patients undergoing multi- vessel total arterial revascularization were randomly assigned to OPCABG and 30 patients to ONCABG surgery. Patients underwent pre-operative, early (day 6) and late (6 months) post-operative cine MRI for global left ventricular function and regional wall motion assessment.

Conclusions: The two surgical groups were well matched in terms of pre-operative (age, cardiopulmonary risk factors, pre-operative medication use) and peri-operative (number of distal anastomoses, inotropic requirements) factors. The mean pre-operative cardiac index was significantly higher in the OPCABG group (2.9 +/- 0.7 ONCABG; 2.9 +/- 0.8 OPCABG; p = 0.9). Early post-operatively, the cardiac index was significantly higher in the OPCABG group (2.7 +/- 0.6 ONCABG; 3.2 +/- 0.8 OPCABG; p = 0.9). The mean pre-operative ejection fraction was significantly higher in the OPCABG group (2.7 +/- 0.6 ONCABG; 3.2 +/- 0.8 OPCABG; p = 0.9). Early post-operatively, the cardiac index was significantly higher in the OPCABG group (2.7 +/- 0.6 ONCABG; 3.2 +/- 0.8 OPCABG; p = 0.9).

Conclusion: OPCABG reduces myocardial injury when compared to the use of cardiopulmonary bypass (ONCABG), but the functional significance of this is uncertain. We hypothesized that OPCABG surgery would result in improved early and late left ventricular function compared with ONCABG surgery.

855-1

855-2

Transmural Difference of Diastolic Function in Physiological Hypertrophy Versus Pathological Hypertrophy Using Tagged Magnetic Resonance Imaging

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Background: Athletes tend to develop remodeling primarily in the form of eccentric hypertrophy while concentric hypertrophy is prevalent in aortic stenosis (AS). The transmural patterns of contraction and relaxation in athletes and in AS have not been studied thoroughly. Our goal was to study the transmural patterns of contraction and relaxation in these types of remodeling using tagged magnetic resonance imaging (MRI).

Methods: Eleven elite rowers, 13 patients with AS and 13 healthy adults underwent C-SPAMM myocardial tagging MRI. Left ventricular endocardial, midwall and epicardial circumferential shortening, relaxation rates, and time to peak relaxation were analyzed in anterior, lateral, posterior and septal segments using semiautomatic tracking of the grid intersection points.

Results: Time to peak relaxation rate was substantially shorter in athletes compared to healthy individuals and patients with AS. That time to peak relaxation differences were evident throughout all segments and in all the layers. Average time to peak myocardial relaxation (100% is defined as end-systole) was 128.9±17.6, 152.5±16.9 and 142.8±18.6 in athletes, volunteers and patients with AS, respectively (p<0.01 in athletes vs. other groups). Peak midwall and epicardial relaxation rates were reduced in AS compared with physiological hypertrophy and normal individuals (-1.1+/-0.4, -1.3+/-0.5 and -1.7+/-0.5/sec, respectively - p<0.01).

Conclusions: This study demonstrates distinctive patterns of relaxation in normal individuals, physiologic hypertrophy and pathological hypertrophy. A shortened time to peak relaxation rate is evident in athletes and this may be a measurable marker of enhanced diastolic relaxation to improve mechanical efficiency in this sub-group. Reduced myocardial relaxation rate and shortening are evident in pathological hypertrophy and can be used as quantitative markers of negative remodeling.

4:30 p.m.

855-3

Correlation Between Hyphenenhancement on Delayed Contrast Enhanced Magnetic Resonance Imaging (MRI) and Diastolic Function Assessed by Steady State Cine MRI in Hypertrophic Cardiomyopathy

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Backgrounds: Diastolic dysfunction is common in patients with overt hypertrophic cardiomyopathy (HCM). Steady state cine magnetic resonance imaging (MRI) can provide accurate measurement of diastolic function of the left ventricle (LV), and delayed contrast enhanced MRI can delineate the presence and extent of fibrosis in HCM. The purpose of this study was to determine if altered diastolic function in HCM is related to the extent of myocardial fibrosis demonstrated by contrast enhanced MRI.

Methods: Seventeen patients (13 men, 4 women, mean age 57.7±9.8 years) with hypertrophic cardiomyopathy were studied. The severity index of myocardial enhancement on delayed contrast enhanced MRI was determined by scoring the extent of hyperenhanced tissue in 30 myocardial segments. The peak filling rate (PFR), LV ejection fraction (EF) and LV mass were determined by steady state cine MRI.

Results: Del-contrast enhanced MRI demonstrated myocardial enhancement in 97 of the 510 segments (19%) and 13 of the 17 patients (77%). The severity index determined by delayed contrast enhanced MRI demonstrated a significant negative correlation with the PFR (r=-0.86, p<0.01) and with the LVEF (r=-0.59, p<0.05). No significant correlation was observed between the severity index of hyperenhancement and LV mass (r=0.23, p=0.30).

Conclusions: The current study using delayed contrast enhanced MRI and steady state cine MRI demonstrated that the severity of myocardial fibrosis revealed by delayed contrast enhanced MRI has a strong relation with diastolic dysfunction in patients with HCM.

4:45 p.m.

855-4

Cardiac Magnetic Resonance Imaging-Derived Parameters of Right Ventricular Function Correlate Significantly With Hemodynamic Data in Patients With Pulmonary Hypertension

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Background: In patients with pulmonary hypertension (PH), the association between quantitative right ventricular (RV) morphological and functional cardiac magnetic resonance imaging (cMRI) parameters and hemodynamic parameters obtained at right heart catheterization (RHC) has been studied on small populations and yielded contradictory results.

Aim of the Study: To evaluate the relationship between cMRI-derived RV functional parameters and hemodynamics in a large cohort of patients with PH.

Methods: We included in the analysis 116 PH patients (82 women, 34 men, mean age of 48 years) who had both RHC and cMRI examination. We included in the analysis 116 PH patients (82 women, 34 men, mean age of 48 years) who had both RHC and cMRI examination. Most patients had moderate-to-severe PH (mean pulmonary artery pressure (mPAP) was 47 +/- 14 mmHg). cMRI was performed with a 1.5 Tesla scanner using a phased array cardiac coil as receiver. Image acquisition was performed using electrocardiography-gated, breath-hold, cine TrueFISP sequences and post-processing was done with ARGUS software. RV end-diastolic and end-systolic volumes and ejection fraction were determined by the Simpson’s method. RHC was performed per standard protocol and cardiac output was determined by thermodilution. Quantitative RV morphologic and functional cMRI-derived parameters and hemodynamic parameters at RHC were analyzed for correlation and linear regression.

Results: RV end-diastolic and end-systolic volumes obtained at cMRI showed significant positive correlation (r=0.45-0.6, p<0.01) with right atrial pressure and mPAP, and significant negative correlation with pulmonary artery oxygen saturation (r=-0.45, p<0.01). There was a significant positive (r=0.48, p<0.01) correlation between cMRI-determined RV ejection fraction and the pulmonary artery saturation and a negative correlation between RV ejection fraction and the right atrial pressure (r=-0.44, p<0.01). Furthermore, a linear relationship was present between cMRI and RHC-derived parameters of RV function.

Conclusion: cMRI-derived RV functional parameters correlate well with hemodynamic parameters of prognostic significance and thus may be an important non-invasive tool for the initial and follow-up evaluation of PH.