Magnetic Resonance Imaging Can Reliably Identify Heart Iron Overload in Patients With Thalassemia Major

Background: Patients with thalassemia major depend on continuous blood transfusions for survival. As a consequence, iron overload occurs in all organs including the heart. Heart biopsy is the only way to detect heart iron deposition, but it is invasive and not easily repeatable. We applied magnetic resonance imaging (MRI) for the assessment of myocardial iron deposition in patients with thalassemia and compared the results with cardiac biopsy data.

Methods: Twenty-five consecutive thalassemic patients, NYHA II-III, were studied using a 0.5 T system, ECG-gated, with TE=17-68 msec. T2 relaxation time of the interventricular septum was calculated assuming simple monoexponential decay in one square centimeter region of interest. Heart biopsy was performed within a week after the MR study.

Results: Seven of the 25 patients had heart biopsy indicative of low iron deposition (Group A) and the remaining 18 patients had heart biopsy indicative of high iron deposition (Group B). T2 relaxation time of the heart (T2H) was in agreement with heart biopsy in 86% of the patients in Group A vs. 78% of the patients in Group B (overall agreement 80%). Furthermore, in ferritin levels were in agreement with heart biopsy in 28% vs. 86%, respectively (overall agreement 72%). In Group A, MRI was in better agreement with biopsy compared to ferritin (86% vs. 28%, p=0.05).

Conclusions: Heart T2 relaxation time appears in agreement with cardiac biopsy, both in high and low iron deposition, and is a useful non-invasive index for serial evaluation in thalassemia.

Myocardial Infarct Age Determined by Contrast-Enhanced Cine Magnetic Resonance Imaging

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Background: In patients with acute chest pain and resting wall motion abnormalities, differentiating acute myocardial infarction (AMI) and chronic myocardial infarction (CMI) can have important therapeutic implications. Contrast-enhanced cine magnetic resonance imaging (CEC) has been shown to sensitively diagnose microvascular obstruction (MO), a signature of CMI that is rarely seen in CMI. The present study was designed to determine if CEC can distinguish between AMI and CMI.

Methods: In 43 patients with enzyme-detected AMI treated by reperfusion, we performed CEC within 9 hours of admission, and repeated this examination after 3 months. CEC imaging was performed approximately 1 minute after 0.20mmol/kg of I.V. gadolinium-DTPA contrast. Nine 8mm short-axis slices and two long-axis slices acquired, using an-EKG gated, segmented k-space true-FISP pulse sequence. At 10 minutes post-injection, after an inversion time scan for optimum myocardial nulling, an inversion-recovery turboFLASH delayed hyperenhancement (IR-DE) study was done in identical slices. MO was defined as discrete endocardially-based hyperenhancing regions that became all or partially enhanced on IR-DE. All studies were read by two blinded readers.

Results: Microvascular obstruction on CEC was seen in 35/43 (81%) of patients with AMI, and in only 4/43 (9%) after 3 months. The presence of MO on CEC 81% sensitive and 91% specific for AMI.

Conclusions: The presence of microvascular obstruction on contrast-enhanced cine MRI is a sensitive and specific predictor of acute MI. Its absence suggests chronic MI.

Systolic and Diastolic Strain Rates by Tagged Magnetic Resonance Imaging Distinguishes Regions With Different Degrees of Myocardial Injury After Acute Myocardial Infarction

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Background: Myocardial injury after acute myocardial infarction (AMI) is a regional and heterogeneous process that affects both systolic and diastolic function. Using tagged MRI, we evaluated regional systolic and diastolic function in areas with different degrees of myocardial injury after AMI and assessed whether both measures combined would allow us to better characterize and distinguish these regions.

Methods: Fourteen dogs underwent 90-min coronary artery occlusion followed by reperfusion. Five short-axis slices were acquired for each dog within the first 24h of reperfusion using 3 techniques: tagged MRI, first-pass perfusion and delayed-enhancement (DE). Regional blood flow (50% of the area) was calculated using coronary artery occlusion was used to define risk region. Each slice was divided in 6 segments that were classified in 4 categories: transmural AMI (DE=50% area, n=9), subendocardial AMI (DE=50% area, n=82), risk region (n=80) and remote area (n=163). For each segment, circumferential systolic strain ( Ecc), systolic strain rate (SSR) and early diastolic strain rate (DSR) were calculated.

Results: Transmural AMI segments displayed depressed systolic contractility compared to subendocardial AMI segments (P<0.01), and both showed reduced systolic and diastolic function compared to remote areas (Ecc = 2.1 ± 0.5 % versus -13.1 ± 0.5 %, SSR = -0.11 ± 0.10 s-1 versus -2.15 ± 0.08 s-1, DSR = 1.26 ± 0.09 s-1 and 1.50 ± 0.08 s-1), and both showed reduced systolic and diastolic function compared to remote areas. P<0.001 for all. In contrast, risk region segmentally exhibited diastolic impairment (DSR=1.62±0.09 s-1, P<0.001 for remote), but not systolic dysfunction (NS versus remote). Importantly, after controlling for segmental infarct extension, the presence of microvascular obstruction ("no flow") was related to further impairment of systolic and diastolic regional function (P<0.05 for both).

Conclusion: Regional systolic and diastolic functional assessment using strain rate analyses provides for superior characterization and distinction of regions with different degrees of myocardial injury after AMI.

Nuclear Blood Flow Studies

POSTER SESSION

Tuesday, March 09, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 4:00 p.m.-5:00 p.m.

Initial Results Regarding the Safety, Tolerability, and Hemodynamic Effects of CVT-3146, a Selective Adenosine A2A Agonist, in Patients Undergoing Pharmacologic Stress SPECT Myocardial Perfusion Imaging

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Background: CVT-3146 is a selective A2A adenosine receptor agonist shown to induce coronary hyperemia and potentially procure less adverse effects due to its limited stimulation of receptor subtypes not involved with coronary vasodilation. Thus, CVT-3146 may be an effective pharmacologic stress agent.

Methods: We studied 36 subjects (27 men, 9 women; 67±10 years) with two doses of CVT-3146 [400 mcg (n=18), 500 mcg (n=18)], administered by IV bolus, as part of a pharmacologic stress SPECT myocardial perfusion imaging protocol.

Results: Adverse effects (AE) occurred in 26 subjects (72%), including chest discomfort (33%), headache (25%), and abdominal pain (11%), with a similar incidence for both doses. Flushing, dyspnea, and dizziness were more frequent in the 500mcg group (44%, 44%, and 28%, respectively) than in the 400mcg group (17%, 17%, and 11%, respectively). Most AE’s were mild to moderate (96%) and resolved within 15 minutes without treatment (91%). One serious AE occurred, with exacerbation of a migraine headache, requiring hospitalization. ST and T wave abnormalities developed with CVT-3146 in 7 and 5 subjects, respectively. No 2nd or 3rd degree AV block was noted and there were no serious arrhythmias. Peak hemodynamic effects were noted at 4 minutes for systolic blood pressure (5.9±10.0 mmHg) and within 2 minutes for heart rate (<21.9±10.0 beats per minute). Systolic BP did not fall below 90 mmHg with either dose. The mean change in HR response was higher for the 500 mcg dose than for 400 mcg. Thirty minutes after CVT-3146, BP changes deviated <2% from baseline but HR remained above baseline by 8.6%.

Conclusion: CVT-3146 is well-tolerated and has acceptable hemodynamic effects. Minimal changes were noted in BP and HR responses between the 400 mcg and 500 mcg doses, but AE’s were more frequent at the higher dose. CVT-3146 appears safe and well-tolerated for bolus-mediated pharmacologic stress SPECT myocardial perfusion imaging.

Differential Vasodilatory Effects of CVT-3146, an A2A Adenosine Receptor Agonist in Various Vascular Beds in Anesthetized Dogs

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CVT-3146 is a novel selective A2A adenosine receptor agonist being developed as a pharmacologic stressor for radionuclide myocardial perfusion imaging. Previously it has been shown in awake dogs that CVT-3146 causes coronary vasodilation without significantly affecting either total peripheral resistance or renal blood flow. The goal of this study was to determine the differential effects of CVT-3146 on blood flow velocity in various vascular beds. The effect of CVT-3146 on the blood flow velocity in the canine left circumflex coronary artery (LCX), brain arterial vasculature (BA), forelimb artery (FA) and pulmonary artery (PA) of comparable diameters were quantified as the average peak blood flow velocity (APV) using intravascular Doppler transducer-tipped catheter. CVT-3146 (1.0 μg/kg) given as an intravenous bolus, transiently enhanced blood flow which was site specific: APV increased 3.1±0.2, 1.4±0.1, 1.2±0.1, and 1.1±0.1 fold in the LCX, BA, FA and PA, respectively, manifesting a site-potency rank order of LCX >BA>FA>PA (figure). The effect of CVT-3146 on blood flow velocity was short lasting; reaching a peak in less than 30 sec and dissipating in less than ten minutes. Increased blood flow velocity was associated with a small transient increase in heart rate (16 bpm).