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Title: The Simultaneous Assessment of Invasive Fractional Flow Reserve and SPECT Myocardial Ischemia Using Regadenoson in the Catheterization Laboratory.

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Background: Coronary revascularization guided by either invasive Fractional Flow Reserve (FFR) measurement or the presence and extent of myocardial ischemia on stress testing is associated with better outcome compared to coronary anatomy-based revascularization(1). The appropriate use criteria (AUC) increasingly emphasize the importance of establishing the functional significance of coronary lesions prior to percutaneous coronary interventions (PCI)(2). Myocardial ischemia is most often assessed by myocardial perfusion stress- single-photon emission computed tomography (MPS). However, FFR and MPS-derived ischemia measures do not always correlate, and disparities are known to exist in as many as 40% of cases (3). While the complex interplay between focal epicardial disease, diffuse epicardial disease and microvascular disease is the physiological basis for these disparities, technical factors including temporal and protocol differences between FFR estimation and ischemia estimation may also play a role. Initial validation studies found high correlation between stenosis with FFR <0.65 and myocardial ischemia in single vessel disease, while the contemporary practice is to attribute hemodynamic significance to FFR <0.80 (4,5). Furthermore these original studies were performed using dipyridamole or adenosine stress, which have different hyperemic flow profiles compared to regadenoson (6). This study aims to determine the correlation between simultaneous FFR and MPS obtained using regadenoson in the catheterization laboratory. The protocol is designed to eliminate temporal and stress protocol differences between FFR and MPS. Our group has previously validated the use of regadenoson for FFR estimation (7).

Aims:

1. To determine the correlation between FFR and ischemia (presence and extent) assessed simultaneously in the catheterization laboratory using regadenoson.
2. To determine the optimal cut off of FFR with regadenoson stress that predicts the presence of myocardial ischemia on MPS

Methodology:

Study Population:

Inclusion criteria:

Fifty patients aged ≥ 18 years, undergoing clinically-indicated FFR measurement (to determine the hemodynamic significance of intermediate degrees of stenosis) for single or two –vessel epicardial coronary disease during diagnostic coronary angiography for suspected coronary artery disease will be recruited. Patients with prior coronary stents will be included if they fulfill criteria. Patients with prior SPECT will be included if they provide informed consent to undergo another SPECT study as described in the protocol.

Exclusion criteria:

1. Patients with 3-vessel disease
2. Prior CABG
3. Patients with second or third- degree AV block, or sinus node dysfunction without a functioning pacemaker
4. Patients who have ingested caffeine-containing products within the past 12 hours.

Study Design:

Informed consent will be obtained prior to diagnostic coronary angiography. Based on current coronary angiography and FFR volumes and a conservative estimate, it is anticipated that we will need to screen (with consent) 500 patients in order to recruit 50 who will have FFR assessment.

Standard procedure will be followed for FFR testing using regadenoson. Regadenoson will be injected as a 10-15 sec bolus followed by a saline flush. Patients will have an injection of Tc-99m sestamibi 10-20 seconds after the saline flush (to mirror the standard stress testing protocol). A weight-based dosing scheme fir Tc-99m will be used (30mCi for patients weighing up to 200 lbs; additional 5 mCI for every 50 lbs over 200 lbs). Standard protocol for regadenoson-stress MPS will be performed. A minimum of 2 mins will be allowed to elapse between radiotracer administration and percutaneous coronary intervention (PCI), if indicated, to allow complete extraction of the radiotracer, and an accurate assessment of perfusion defect size. In patients with 2-vessel disease, who require FFR testing in both vessels, radiotracer injection will be performed during FFR testing of the more severe stenosis, as assessed by visual inspection of the coronary angiogram.

Patients will be brought to the nuclear cardiology laboratory 1-3 hours following the coronary angiogram (± coronary intervention) for a standard SPECT acquisition. Since the perfusion data will pertain to the time of tracer injection, patients could be vascularized as clinically indicated prior to the SPECT acquisition.

Patients will be monitored for 2-6 hours, or overnight, as clinically indicated following diagnostic coronary angiography and PCI, respectively.

A low dose resting MPS will be performed the next day, if the stress MPS is abnormal.

SPECT Analysis:

Perfusion image analysis will be performed using a standard 17 segment model and polar plots. Quantitative perfusion defect analysis using the QGS (Cedars-Sinal Medical Center, CA) will be used to determine the Total Perfusion Defect size, which will be the parameter used for analysis. Image interpretation will be performed physicians blinded to the results of FFR testing.

Statistical Analysis:

Standard statistical tests to correlate FFR with the presence and extent of MPS will be applied to patients groups with concordant and discordant FFR/SPECT studies. The percentage of patients with concordant FFR and SPECT results will be determined. The characteristics of patients with discordant FFR and SPECT results will be described (mean FFR and range of FFRs, single vs. two- vessel disease, lesion characteristics such as diffuse vs. discrete disease). An ROC curve analysis will be performed to define the cut-off of FFR that optimally predicts SPECT ischemia.

Adverse event monitoring:

All study procedures are clinically indicated except the Tc-99m injection and SPECT acquisition, which are clinically approved procedures. Any adverse events will be reported.

References

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