A selection of recent original research papers

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Semiconductor Detectors Allow Low-Dose, Low-Dose 1-Day SPECT Myocardial Perfusion Imaging

Zurich, Switzerland

Nkoulou R, Pazhenkottil AP, Kuest SM, Ghadri JR, Wolfrum M, Husmann L, Fiechter M, Buechel RR, Herzog BA, Koepfli P, Buerger C, Gaemperli O, Kaufmann PA

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Context Cadmium zinc telluride (CZT) detectors with linear counting rate response enable count subtraction in sequential scanning. The objective of this study was to determine whether the use of CZT detectors coupled with background activity subtraction eliminated the need for high-dose injections in the second part of a 1-day stress-rest MPI protocol.

Methods and Results For 50 patients (mean age $\pm$ SD, 66 ± 12 years) with visually abnormal ($n = 42$) or equivocal ($n = 8$) adenosine-stress MPI (320 MBq of ^{99m}Tc -tetrofosmin) on a CZT camera, rest MPI was performed with a low-dose (320 MBq) and repeated after injection of an additional 640 MBq of ^{99m}Tc -tetrofosmin to achieve a standard 3-fold increased dose at rest (960 MBq), compared with stress (320 MBq). Low-dose rest myocardial perfusion images were reconstructed after subtracting the background activity of the preceding stress scan. Segmental percentage tracer uptake of the two rest myocardial perfusion images (320 vs 960 MBq) was compared using intraclass correlation and Bland-Altman limits of agreement. Patient- and coronary territory-based clinical agreement was assessed. The standard protocol revealed ischemia in 34 (68%) and a fixed defect in 8 (16%) patients, of whom 33 (97%) and 8 (100%) were correctly identified by low-dose MPI (clinical agreement, 98%). Segmental uptake correlated well between low- and standard-dose rest scans ($r = 0.94$, $P < .001$; Bland-Altman limits of agreement, -11% to $+11\%$).

Defect extent was 14.4% (low-dose) vs 13.1% (standard-dose) at rest ($P =$ not statistically significant) and 26.6% at stress ($P < .001$ vs rest scans). These promising results suggest that accurate assessment of ischemic myocardial disease is feasible with a low-dose to low-dose 1-day SPECT MPI protocol using a CZT device.

Significance These investigators tested a novel approach to radiation dose reduction for SPECT using a CZT camera. Since the protocol tested used a single-day stress-rest sequence, it has the potential for stress-only imaging, thus facilitating even further dose reduction.

Coronary Circulatory Function in Patients with the Metabolic Syndrome

Boston, Massachusetts and Los Angeles, California

Di Carli MF, Charytan D, McMahon GT, Ganz P, Dorbala S, Schelbert HR

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Context The metabolic syndrome affects 25% of the U.S. population and greatly increases the risk of diabetes and coronary artery disease (CAD). These investigators tested the hypothesis that the metabolic syndrome is associated with impaired coronary vasodilator function, a marker of atherosclerotic disease activity.

Methods and Results Four hundred sixty-two patients at risk for CAD, as defined by a low-density lipoprotein cholesterol ≥ 160 mg/dL with fewer than two coronary risk factors, a low-density lipoprotein cholesterol ≥ 130 mg/dL with two or more coronary risk factors, or with documented CAD were included. A subset of 234 individuals underwent repeated PET at 1 year. Myocardial blood flow (MBF) and vasodilator reserve were assessed by PET. Modified criteria of the National Cholesterol Education Program, Adult Treatment Panel III were used to characterize the metabolic syndrome. Adenosine- and cold-stimulated MBF were similar in patients with and without metabolic syndrome, whereas baseline MBF showed a stepwise increase with increasing features of the syndrome. Consequently, patients with metabolic syndrome showed a lower coronary flow reserve (CFR) (2.5 ± 1.0) than those without metabolic syndrome (3.0 ± 0.9 , $P = .004$). Differences in CFR were no longer present after correcting rest flows for the rate-pressure product. Change in MBF and CFR at 1 year was not different across groups of patients with increasing features of the

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metabolic syndrome. Thus, patients with metabolic syndrome demonstrate impaired CFR, which is related to the augmentation in resting coronary blood flow caused by hypertension. In high-risk individuals, peak adenosine- and cold-stimulated blood flows are impaired even in the absence of the metabolic syndrome.

Significance With the caveats of small sample size and limited follow-up, these provocative results suggest that progression to the metabolic syndrome is not associated with significant worsening of CFR already impaired by the presence of multiple coronary risk factors.

Comparative Effectiveness of Exercise Electrocardiography With or Without Myocardial Perfusion Single-Photon Emission Computed Tomography in Women with Suspected Coronary Artery Disease: Results from the What is the Optimal Method of Ischemia Evaluation in Women (WOMEN) Trial

Atlanta, Georgia; Manhasset, New York; Miami, Florida; Buffalo, New York; Columbus, Ohio; Cleveland, Ohio; Providence, Rhode Island; Los Angeles, California; Rochester, Minnesota; Hartford, Connecticut

Shaw LJ, Mieres JH, Hendel RH, Boden WE, Gulati M, Veledar E, Hachamovitch R, Arrighi JA, Bairey Merz CN, Gibbons RJ, Wenger NK, Heller GV for the WOMEN trial investigators

Circulation 2011;124:1239-1249

Context There are few randomized trials comparing an initial diagnostic strategy of exercise electrocardiography versus exercise myocardial perfusion imaging in symptomatic patients referred for stress testing. Initial diagnostic evaluation for suspected coronary artery disease (CAD) is particularly challenging in women.

Methods and Results The investigators randomized symptomatic women with suspected CAD, an interpretable ECG, and ≥ 5 metabolic equivalents on the Duke Activity Status Index to 1 of 2 diagnostic strategies: ETT or exercise MPI. The primary end point was 2-year incidence of major adverse cardiac events, defined as CAD death or hospitalization for an acute coronary syndrome or heart failure. A total of 824 women were randomized to ETT or exercise MPI. For women randomized to ETT, ECG results were normal in 64%, indeterminate in 16%, and abnormal in 20%. By comparison, the exercise MPI results were normal in 91%, mildly abnormal in 3%, and moderate to severely abnormal in 6%. At 2 years, there was no difference in major adverse cardiac events (98.0% for ETT and 97.7% for MPI; $P = .59$). Compared with ETT, index testing costs were higher for exercise MPI ($P < .001$), whereas downstream procedural costs were slightly lower ($P = .0008$). Overall, the cumulative diagnostic cost

savings was 48% for ETT compared with exercise MPI ($P < .001$). Thus, in low-risk, exercising women, a diagnostic strategy that uses ETT vs exercise MPI yields similar 2-year post-test outcomes while providing significant diagnostic cost savings. The ETT with selective follow-up testing should be considered as the initial diagnostic strategy in symptomatic women with suspected CAD.

Significance This trial provides important data pertaining to the highly relevant clinical issue of the initial diagnostic evaluation of symptomatic women with suspected CAD. However, the results should be interpreted in the context of a study population which consisted primarily of low risk women, and was statistically underpowered based on lower than anticipated event rate.

Myocardial Perfusion Imaging is a Strong Predictor of Death in Women

Curitiba and Sao Paulo, Brazil; Baltimore, Maryland; Nashville, Tennessee

Julio Cerci MS, Julio Cerci J, Julio Cerci R, Pereria Neto CC, Trindale E, Debelke D, Pereira da Cunha CL, Vitola JV

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Context Although the prognostic value of SPECT myocardial perfusion imaging is well established, much of the observational data to date pertain to cohorts consisting predominantly of men. These investigators sought to assess the prognostic value and risk classification improvement using contemporary single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) to predict all-cause mortality in women.

Methods and Results A total of 2,225 women referred for SPECT-MPI were followed for a mean period of 3.7 ± 1.4 years. SPECT-MPI results were classified as abnormal on the presence of any perfusion defect. Abnormal scans were further classified as with mild/moderate reversible, severe reversible, partial reversible, or fixed perfusion defects. Risk estimates for incident mortality were categorized as $<1\%$ /year, 1% to 2% /year, and $>2\%$ /year using Cox proportional hazard models. Risk-adjusted models incorporated clinical risk factors, left ventricular ejection fraction (LVEF), and perfusion variables. All-cause death occurred in 139 patients. SPECT-MPI significantly risk stratified the population; patients with abnormal scans had significantly higher death rates compared with patients with normal scans, 13.1% vs 4.0% , respectively ($P < 0.001$). Cox analysis demonstrated that after adjusting for clinical risk factors and LVEF, SPECT-MPI improved the

model discrimination (integrated discrimination index = 0.009; $P = .02$), added significant incremental prognostic information (global chi-square increased from 87.7 to 127.1; $P < .0001$), and improved risk prediction (net reclassification improvement = 0.12; $P = .005$). Thus, SPECT-MPI added significant incremental prognostic information to clinical and left ventricular functional variables while enhancing the ability to classify this Brazilian female population into low- and high-risk categories of all-cause mortality.

Significance This prospective study demonstrates the prognostic value of contemporary SPECT MPI in women. Importantly, it was a single-center study confined to Brazilian women aged 55–75 years.

Physiological Basis for Angina and ST-Segment Change: PET-Verified Thresholds Of Quantitative Stress Myocardial Perfusion and Coronary Flow Reserve

Houston, Texas

Johnson NP, Gould LK

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Context Vasodilator stress reveals differences in regional perfusion without ischemia in most patients. However, in patients with a perfusion defect, angina, and/or significant ST-segment depression during dipyridamole stress, quantitative absolute myocardial perfusion and coronary flow reserve (CFR) at the exact moment of definite ischemia have not been established. Defining these low-flow thresholds of angina or ST-segment changes may offer insight into physiological disease severity in patients with atherosclerosis. This study aimed to determine the quantitative low-flow threshold for stress-induced perfusion defects with severe angina and/or significant ST-segment depression during dipyridamole hyperemia.

Methods and Results Patients underwent rest-dipyridamole stress positron emission tomography (PET) with absolute flow quantification in mL/min/g. Definite ischemia was defined as a new or worse perfusion defect during dipyridamole stress with significant ST-segment depression and/or severe angina requiring pharmacological treatment. Indeterminate clinical features required only 1 of these 3 abnormalities. The comparison group included patients without prior myocardial infarction, or angina or electrocardiographic changes after dipyridamole. In 1,674 sequential PET studies, the investigators identified 194 (12%) with definite ischemia, 840 (50%) studies with no ischemia, and 301 (18%) that were clinically indeterminate. A vasodilator stress perfusion cutoff of 0.91 mL/min/g optimally separated definite from no ischemia with an

area under the receiver-operator characteristic curve (AUC) of 0.98 and a CFR cutoff of 1.74 with an AUC = 0.91, reflecting excellent discrimination at the exact moment of definite ischemia. Thus, thresholds of low myocardial vasodilator stress perfusion in mL/min/g and CFR sharply separate patients with angina or ST-segment change from those without these manifestations of ischemia during dipyridamole stress with excellent discrimination. Stress flow below 0.91 mL/min/g in dipyridamole-induced PET perfusion defects causes significant ST-segment depression and/or severe angina. However, when the worst vasodilator stress flow exceeds 1.12 mL/min/g, these manifestations of ischemia occur rarely.

Significance Prior studies have demonstrated the usefulness of absolute myocardial blood flow quantification over relative myocardial perfusion assessment for the diagnosis of multivessel disease and prognostication in patients with apparently normal perfusion. This study identifies the absolute myocardial blood flow correlate of stress-induced myocardial ischemia, and in a pilot sub study, demonstrates improvement of absolute flow after PCI.

A Prospective Pilot Study to Evaluate the Relationship Between Acute Change in LV Synchrony After Cardiac Resynchronization Therapy and Patient Outcome Using A Single-Injection Gated-SPECT Protocol

Pittsburgh, PA

Friehling M, Chen J, Saba S, Bazaz R, Schwartzman D, Adelstein EC, Garcia E, Follansbee W, Soman P
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Context There are ongoing efforts to optimize patient selection criteria for cardiac resynchronization therapy (CRT). In this regard, the relationship between acute change in left ventricular synchrony (LV) after CRT and patient outcome remains undefined.

Methods and Results A novel protocol was designed to evaluate acute change in left LV synchrony after CRT using phase analysis of standard gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging with a single injection of radiotracer, and prospectively applied to 44 patients undergoing CRT. Immediately after CRT, 18 (41%), 11 (25%), and 15 (34%) patients had an improvement, no change, or a worsening in LV synchrony. An algorithm incorporating the presence of baseline dyssynchrony, myocardial scar burden, and lead concordance predicted acute improvement or no change in LV synchrony with 72% sensitivity, 93% specificity, 96% positive predictive value, and 64% negative predictive value and had 96% negative predictive value for acute deterioration in

synchrony. Over a follow-up period of 9.6 ± 6.8 months, patients who had an acute deterioration in synchrony after CRT had a higher composite event rate of death, heart failure hospitalizations, appropriate defibrillator discharges, and CRT device deactivation for worsening heart failure symptoms, compared with patients who had an improvement or no change [hazard ratio, 4.6 (1.3 to 16.0); log rank test; $P = .003$]. Thus, in this single-

center pilot study, phase analysis of gated SPECT was successfully used to predict acute change in LV synchrony and patient outcome after CRT.

Significance Phase analysis of gated SPECT is an emerging, highly repeatable approach to LV dyssynchrony analysis. In this prospective study, the investigators demonstrate its utility for predicting outcome after CRT.