

A Paired-Comparison of the MultiFunction CardioGramSM (MCG) and Sestamibi SPECT Myocardial Perfusion Imaging to Quantitative Coronary Angiography for the Detection of Relevant Coronary Artery Stenosis (>70%) - A Single-Center Study of 116 Consecutive Patients Referred for Coronary Angiography.

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Background

Recent data from an expanded analysis of the National Cardiovascular Data Registry in the United States has revealed that only 38% of patients referred for coronary angiography actually have relevant coronary stenosis (>70%) of one or more coronary arteries. Accurate, pre-test, non-invasive diagnosis of relevant coronary artery disease (CAD) remains a challenge due to the documented low sensitivity/specificity of current accepted methods to detect myocardial ischemia caused by coronary obstruction and the limited short-term relevancy of risk factor analyses that identify patients with low, intermediate, or high pre-test risk of developing obstructive coronary disease and having a myocardial infarction or coronary death over a subsequent ten (10) year period.

Methods

To further assess the sensitivity and specificity of a new mathematical ECG signal analysis tool, MultiFunctionCardioGramTM(MCG), for the detection of relevant coronary stenosis ($\geq 70\%$) and compare its performance to stress SPECT myocardial perfusion imaging (MPI) with sestamibi, a single-center trial was undertaken in 165 consecutive symptomatic patients with known or suspected coronary disease and/or valvular heart disease who agreed to undergo cardiac catheterization and coronary angiography if stress myocardial perfusion imaging was abnormal, or if typical exertional coronary symptoms persisted despite optimum medical therapy with a negative SPECT MPI test, or if significant valvular heart disease was present. All patients underwent both resting MCG testing and stress myocardial perfusion imaging prior to their scheduled catheterization. A total of 49 patients with normal stress myocardial perfusion imaging and without persistent exertional symptoms or with insignificant valvular heart disease were not referred for catheterization and coronary angiography irrespective of their MCG results and were excluded from the study. A total of 116 patients were entered into the final analysis. Based on data from previously conducted trials⁶⁻¹⁰, an MCG severity score of ≥ 4.0 was considered abnormal and indicative of the presence of relevant coronary stenosis ($\geq 70\%$) in one or more coronary arteries. An MCG severity score of < 4.0 was considered normal or indicative of the absence of relevant coronary stenosis ($< 70\%$). All sestamibi myocardial perfusion studies were analyzed using Cedars Sinai Analysis software with inclusion of perfusion, wall motion, and wall thickening data. Standard nuclear stress test criteria were used to define the presence or absence of myocardial ischemia. Final reports and interpretation of MCG tests and nuclear stress tests were completed prior to catheterization in all cases. Patients enrolled in the trial may or may not have had prior angiography and/or coronary intervention.

Methods - Continued

Angiographic results in all patients were evaluated quantitatively and classified for hemodynamically relevant stenosis (> 70%) by consensus of two angiographers at the time of the catheterization. The second angiographer in all cases was an interventional cardiologist who was blinded to the MCG and SPECT MPI results. The personnel involved in obtaining the SPECT Nuclear data were blinded to the MCG and cardiac catheterization data, and the personnel involved in acquiring the MCG data were blinded to the SPECT Nuclear data and catheterization data.

Results

Hemodynamically relevant stenosis was diagnosed at cardiac catheterization in 53 of 116 patients (46%). The MCG device, after performing a computational analysis of two resting ECG leads (II and V5) in the frequency domain, calculated a “disease- severity” score from 0 to 20 for each patient. The severity score was significantly higher for patients with relevant coronary stenosis (5.4 ± 1.9 vs. 2.5 ± 1.9). The MCG (using a cut-off score for relevant stenosis of ≥ 4.0) correctly classified 103 of the 116 patients (89%) enrolled in the study as either having or not having relevant coronary stenosis (sensitivity- 91%; specificity- 87%; NPV- 92%; PPV- 86%). Subgroup analysis showed no significant influence of sex, age, history of hypertension, presence of LVH, history of diabetes, history of previous revascularization procedures (CABG or PCI), or resting ECG morphology, on the MCG device’s diagnostic performance. However, in 12 patients who were anemic at the time of their participation in the study, there was a trend toward a lower MCG specificity (71%) but this was not statistically significant due to the small number of anemic patients. SPECT nuclear myocardial perfusion imaging was abnormal in 99 of the 116 patients undergoing catheterization (85%), but only correctly classified 54 of the 116 patients (47%) entered in the study as either having or not having relevant coronary stenosis (sensitivity-85%; specificity-14%; NPV – 53%; PPV- 45%).

Conclusion

The new mathematical, resting ECG signal analysis tool (Multi-Function-CardioGramSM) has been shown in this paired-comparison trial between the MCG, SPECT nuclear myocardial perfusion imaging, and coronary angiography to safely, accurately, and objectively identify patients with relevant coronary stenosis (>70%) with high sensitivity and specificity and high negative predictive value. Its overall performance was equal to, if not better, than SPECT nuclear MPI. Its potential use in the early evaluation of symptomatic coronary patients should be considered.

References

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MCG vs. Nuclear Stress Imaging Overall Trial Results

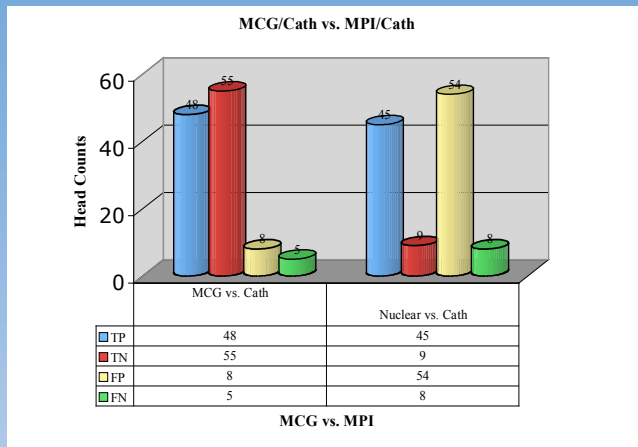


Figure 1.

MCG vs. Nuclear Stress Imaging Overall Trial Results

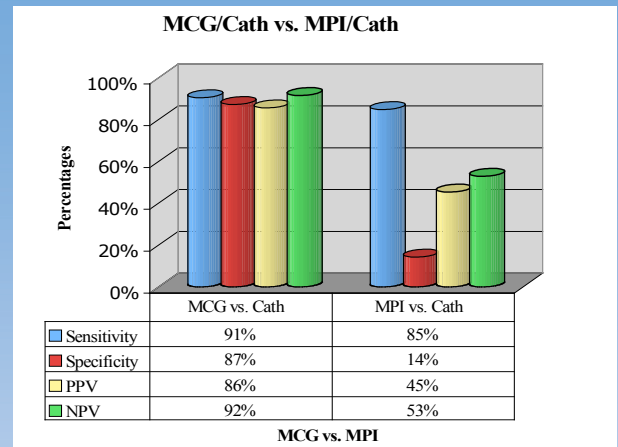


Figure 2.

Figures 1 MCG vs Nuclear Stress Imaging (all patients). Figure 1 illustrates the data from all 116 patients enrolled in the study showing the actual numbers of True Positive, True Negative, False Positive, and False Negative results for both MCG and Nuclear Stress Imaging. Note the significantly higher number of True Negative results when MCG is compared to Nuclear Stress testing. Figure 2. shows the calculated Sensitivity, Specificity, Negative Predictive, and Positive Predictive values from the raw data for both MCG and Nuclear Stress Imaging.

MCG vs. Nuclear Stress Imaging Females Cohort Results

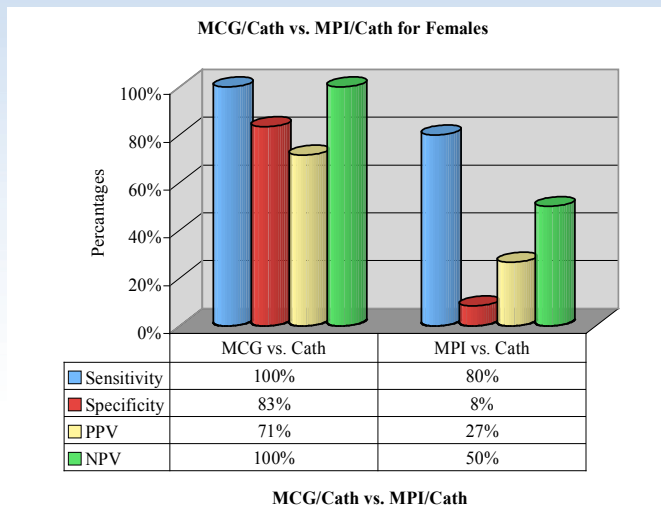


Figure 3.

MCG vs. Nuclear Stress Imaging Female Trial Results

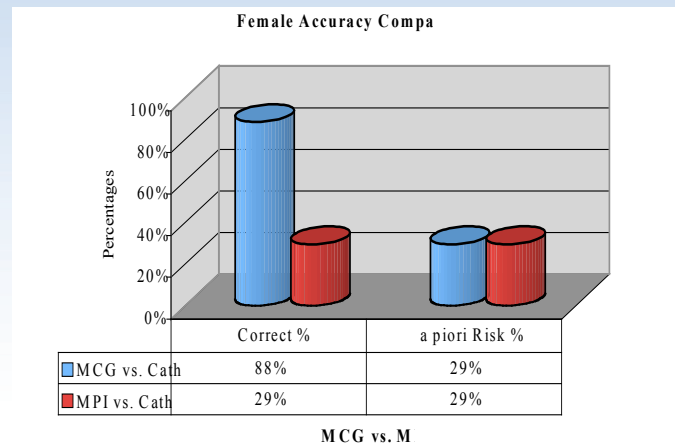


Figure 4.

Figure 3. MCG vs Nuclear Stress Imaging in the Female Cohort of the trial. Note the high sensitivity and high negative predictive value of MCG compared to Nuclear Stress Imaging. Figure 4. Overall accuracy of the MCG in the Female Cohort was 88% in the female cohort which is similar to all previously reported trials. The actual measured pre-test risk in the cohort of women was 29%. It is noteworthy that the MCG performed equally well in women as in men with such a low pre-test risk of relevant coronary disease.

MCG & Nuclear Stress

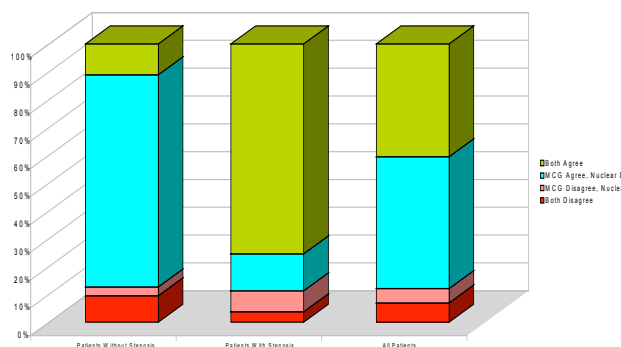


Figure 5.

MCG vs. Nuclear

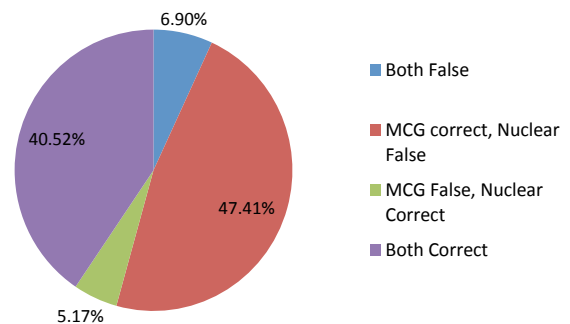


Figure 6.

Figures 5 - 6. Correct Detection of Relevant CAD Defined by Angiographic Results of MCG Compared to SPECT Nuclear Testing (absolute numbers of patients and percentages). Note that MCG correctly predicted the presence of relevant stenosis when SPECT Nuclear testing incorrectly predicted stenosis in 47.4% of patients.