Frequency Cardio Graph™ Non-invasive Investigative Device for Coronary Arterial Disease Detection: A Controlled Prospective Clinical Trial

Frequency Cardio Graph™ Non-invasive Investigative Device for Coronary Arterial Disease Detection: A Controlled Prospective Clinical Trial

Dr. Clarizio, Dino, M.D.; Attending Medical Doctor and Owner, Arcadia Clinic; Arcadia, California

Ms Yu, Cecilia, ___; Position, Adams MediTech; Position, Law Offices of Cecilia Yu and Associates; City Of Industry, California

Dr. Koladia, Nirman, M.D., M.S.; Director, Logic Truth Medicine Corporation; Burbank, California

Corresponding author:
Nirman Koladia, M.D., M.S., Logic Truth Medicine Corporation, 1200 W Victory Blvd, Ste A, Burbank, CA, 91506; NirmanKoladia@NirmanKoladia.com

Background:

Coronary artery disease (CAD) is the foremost cause of death in United States. It is the leading cause of death for both men and women. CAD affects almost 1.3 million Americans and is most common form of heart disease. CAD and its complications, like arrhythmia, angina pectoris, and heart attack (myocardial infarction), are the leading causes of death in the United States. [1]

CAD disease is diagnosed when arteries that supply blood to the cardiac muscle become hardened and narrowed due to buildup of plaque on their inner walls. This buildup of plaque is termed atherosclerosis. Atherosclerosis may eventually increase in size leading to jeopardized blood flow (ischemia). [2]

An electrocardiogram (EKG) is a sensitive voltmeter based test that records the electrical activity of the heart. EKG is a very standard tool used almost on every patient presenting with ischemic or arrythmatic heart disease in the differential. [3] EKG taken in conjunction with exercise, also known as stress EKG is a valuable diagnostic tool for early detection of CAD. However, stress EKG comes with its known disadvantage of actually inducing an attack or cardiac damage, especially if appropriate precautions are not taken.

FCG™ employs the data obtained from standardized EKG and computing this data with complex mathematical algorithms including Fast Fourier Transform

(FFT), provides diagnostic value better than Stress EKG and comparable to Echocardiography (anecdotal evidence). The advantage of FCG™ is that it doesn't pose any more safety or intervention based risks to the patients since it simply takes the EKG data. Table 1.1 (below) shows the various indices obtained using FCG™. The FCG™ indices show better values in terms of ischemia (CAD, MI) and arrhythmias.

Anecdotal evidences and clinical trials in China [4] suggest FCG™ to be better than stress EKG reaching sensitivity and specificity values comparable to Echocardiography and Nuclear Studies. The aim of this pilot study was to find the exact sensitivity and specificity of the FCG™ device and obtain objective comparison to other cardiovascular investigative modalities, meanwhile verifying the claims in the aforementioned anecdotal evidences and studies.

Methods and Design:

The patient selection for this study was done using convenience sampling. The convenience sampling allows for better ethical conduct of the study with almost no loss of randomization in the data for this case. The convenience sampling effects little to no disturbance in the patient care. The randomization is dictated by the fact that patients coming to this clinic are a random sample of 'events occurring independently'. The sample in this study is close to the general population as the patients in this study are routine and special care patients in a 'given' clinic in a standardized setup which fairly represents the general population in this pilot study setting.

The inclusion criteria for this study were clinical determination of Coronary Artery Disease (CAD) investigation, age 18-99, male and female of all ethnicities were included. All patients chosen were clearly able to understand the study and patient consent. The patients were able to understand the study requirements and were able to provide informed consent.

The exclusion criteria for this study were any diseases that would affect investigative outcomes, such as infections or neurological deficits. Patients with uncontrolled mood disorders or patients with drug abuse were excluded from the study. Patient with cardiac pathology that would need surgical intervention were excluded from this study. As well as patients with workers compensation and active litigation, or pregnant patients were excluded from this study.

Each patient participating in this study was to provide written informed consent, as well, the patient was orally explained the study design and outcomes including clinical procedures and protocols. They were also explained that the study will not affect their investigative or treatment options. The data will be utilized for clinical research purposes. Also, there were explained that 'NOT' participating in the study will not affect their routine patient care.

The investigative protocol for this study was based on the FCG™ technique. The FCG™ involves the same procedure as for EKG. However, the initial EKG must be taken using the FCG™ device. The FCG™ device is a computer based (explained below) device that performs the routine EKG. The EKG data is further mathematically computed to obtain the FCG™ diagnostic profile. The FCG™ device, being based on EKG technique, does not pose any further safety risk for the patients. The FCG™ is a mathematical way of interpreting EKG™ data. [5]

This clinical study was primarily conducted in the private practice of Dr. Clarizio in his clinical located in Arcadia (Los Angeles), California. Also, two other private practice based clinics in Los Angeles County, California were involved in the research phase.

The study for a given patient was to stop immediately if the patient developed discomfort or changed medication that would affect the results. These patients would be removed from the study and routine Standard of Care (SOC) would be provided to these patients. Similarly, patients that developed different condition requiring attention or who would violate the study principles would be removed from this study. The patient was also free to quit the study anytime at will, with no questions.

Results:

The total number of patients in this study was 60. The numbers of females was 35 and that of males was 25. The mean age of the patient population in this study was 63.77 with a standard deviation of 20.56. The age range of patients in this study was 27 years – 94 years.

In the analysis grouping FCG™, routine EKG, and stress EKG, the sensitivity of H-index (FCG™) was 100. The sensitivities of A (FCG™) and F (FCG™) indices were 100. The sensitivity of routine EKG was 27. The sensitivities were obtained by assuming stress EKG as ideal. Specificities of 10 CAD locations were 100, of the remaining two the specificities were 87. The specificity of A-index was 87. The specificity of routine EKG was 75. Similar to sensitivity calculations, the specificity calculation was done assuming stress EKG as ideal. The Pearson's correlations were 0.90 for A-index and 0.61 for H and F indices. The Pearson's correlation for EKG was 0.03. The correlation was obtained with stress EKG patients. (Table 1.2)

For the analysis group FCG™, routine EKG, and Echocardiography using Echocardiography as the ideal for sensitivity and specificity calculations; and correlating FCG™ and EKG to Echocardiography; the sensitivity of H-index (FCG™) was 100. The sensitivities of A and F indices were 84 and 100, respectively. The sensitivity of routine EKG was 46. Specificities of all the 12

CAD locations were 100. The specificity of H-index and A -index were 75. The specificity of routine EKG was 75. The Pearson's correlations were 0.86 for H-index and 0.61 and 0.72 for A and F indices. The Pearson's correlation for EKG was 0.24. (Table 1.3)

In one of the patients (patient ID, HIPAA 002), the nuclear scan showed a coronary artery plaque with minimal evidence of ischemic compromise. The EKG in this case showed non specific ST changes and bradycardia. The H-index along with indices A, F and CAD location lead II were positive. The N-index was positive.

Discussion:

The sensitivity and specificity indices of FCG™ are very high in the stress EKG group. This establishes FCG™ as an investigation parallel to stress EKG. The routine EKG sensitivity and specificity are not very high in this study, the very reason for the need of a stress EKG. The stress EKG, however, comes at a health expense to the patient since there are risks involved in the stress EKG. FCG™ analysis (as explained above, in the background) does not pose any significant 'extra' risk to the patient then the routine EKG, and therefore would be of benefit to the patients. The Pearson's correlation of FCG™ to stress EKG reestablishes the same fact.

The sensitivity and specificity of FCG™ were exceptional in comparison group of Echocardiography. Similarly the Pearson's correlation between FCG™ and Echocardiography is very good. This allows for a conclusion that FCG™ analysis could be comparable to Echocardiography. Echocardiography besides being expensive also is not a very routine procedure since the hassle involved. FCG™ being practicable and easy enough could save the need of Echocardiography in some patients, as well as could determine the need of Echocardiography or Nuclear studies in another group of patients. In some cases FCG™ could also facilitate to confirm the Echocardiography results.

The Pearson's correlation of FCG™ with stress EKG is approximately in the range of 0.6 – 0.9; that for FCG™ with Echocardiography is in the range of 0.6 – 0.85. Since, Echocardiography is more objective than stress EKG; one possible conclusion is FCG™ fairs better than Stress EKG and is comparable to Echocardiography.

For the case HIPAA002, the patient had a coronary plaque with minimal evidence of ischemic compromise (confirmed by nuclear scan). A coronary artery plaque as we know would in future lead to further blockage and eventual ischemia – myocardial infarction. The EKG in this case showed non specific ST changes, which has occurred frequently in patients in this study and hence is not

interpretative. The H-index in FCG™ along with indices A, F, and CAD location lead II showed a positive sign. More importantly, index N, showed an injury!

Given the fact that FCG™ follows a mathematical, (Fourier transform / frequency based) analysis of the normal EKG data; and the fact that it equals Echocardiography and Nuclear studies establishes a high recommendation of the FCG™. Advantages being it equals echocardiography; equals some nuclear studies, prevents costs of Echocardiography and nuclear studies, time effective – results out at the time of routine EKG, practicable, reduces the 'non specific' results of EKG like 'non specific ST changes', no extra invasive effects! – done with the routine EKG. Disadvantages of the FCG™ would be initial setup, lack of clinical data and long term device history.

Further trials using a combination of the various indices of the FCG™ would probably have a greater overall diagnostic value and would be highly recommended. Larger multi-center trials would also be similarly useful to establish the results of this pilot study. Also, patient duration-effect analysis would be of high value.

Acknowledgements:

Dr. Dino Clarizio was the clinical investigator for this study. He performed the EKGs for each patient in this study. Dr. Clarizio also performed the SOC (Standard of Care) for each patient involved in this study as per the routine clinical protocols used in his clinic located at 1505 S Baldwin Ave, Arcadia CA 91007

Ms. Cary _____, R.N., assisted this research study. She trained to and performed the technical handling of the FCG™ device. She collected the data for each patient in this study including EKG and FCG™ graphs and routine history records of the patients at Dr. Clarizio's clinic located at 1505 S Baldwin Ave, Arcadia.

Dr. Koladia made the study design and analyzed the data, including medical writing for this study. Dr. Koladia also coordinated this study. Dr. Koladia is located at 1200 W Victory Blvd, Ste A, Burbank, CA 91506 and is available to answer any questions regarding this study as per contact information provided.

Ms. Cecilia Yu, _____, was responsible for study management and was thankfully, the sponsor of this study. Ms Cecilia Yu is a lawyer and located in the City of Industry, California.

Mr. Ken Yu, _____, helped with technological areas and study management and was thankfully, the sponsor of this study. Mr. Ken Yu is the CEO of Adams MediTech, located in the City of Industry, California.

Research Disclosure:

Dr. Dino Clarizio is not affected by device sales and participated in the trial voluntarily.

Dr. Nirman Koladia, was a third party consultant for this study, he was paid a service fee to conduct the study. Dr. Koladia is not affected by device sales.

Ms. Cecilia Yu was the sponsor of this study and is related directly to device sales. However, Ms Yu's participation in this study was limited to study management. Ms Yu did not affect the data collection, data analysis or results and conclusions of this study.

Reference:

[1] Texas Heart Institute, "Coronary Artery Disease", Texas Heart Institute publication, August 2005.

[2] National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), "Disease and Condition Index: Coronary Artery Disease", March 2006, http://www.nhlbi.nih.gov/health/dci/Diseases/Cad/CAD_WhatIs.html

[3] American Heart Association, "Diagnosing Heart Disease – Non Invasive Investigations", May 2006, http://www.americanheart.org/presenter.jhtml?identifier=330

[4] REFERENCE --- Anecdotal evidence, China Trials.

[5] Adams MediTech, "FCG™ Diagnostic Manual", Adams MediTech Medical Department Staff, September, 2005

Table and Graphs:

Table 1.1: FCG™ indices summary

Index	Diagnostic Value
I	**12 Lead Amplitude Spectrum**
H	Insufficient myocardial power caused by lack of blood supply (Early Ischemia)
N	Myocardial Injuries
B	Cardiomyopathy (Ischemia)
A	Myocardial Ischemia
A5	Ischemic Cardiomyopathy (auto-compensation set in for two years or more)
II	**CAD Location**
1	When there are three (3) consecutive columns over the diagnostic line, the lead with the highest column points out the area of CAD
2	I, aVL, V5, and V6 – Lateral (possibly caused by the obstruction of the Left Circumflex Artery)
3	V1 and V2 – Interventricular Septum
4	II, III, and aVF – Inferior
III	**Two Perpendicular Leads (II and V5)**
	PHASE ANGLE SHIFT
1	Over one unit zone - Poor blood flow to the heart (early stages of ischemia)
2	Greater deviations and fluctuations (axis deviation) – Poor or defective conduction function, poor blood circulation and change of blood dynamics
3	Severe deviation –(LBBB)
4	Sharp oscillation – Time delay caused by CAD, poor blood circulation, or MI
	IMPULSE RESPOSE
f	Conduction block (with H, A, A5 suggests MI)
M	Poor conductance, increased compliance, LV malfunction
RSR	Unstable cardiac conduction prior to formation of MI, increased localized ischemia – Early detection of MI
CSR	Unstable latent cardiac electrical activities at the beginning of contraction – detection of latent arrhythmia

MI – Myocardial Infarction
CAD – Coronary Artery Disease
LBBB – Left Bundle Branch Block

Table 1.2: FCG™, routine EKG, and stress EKG: Sensitivity, Specificity and Pearson's Correlation.

	FCG™: 12 Lead Amp Spectrum				FCG™: CAD Location												FCG™: Phase Angle	Routine EKG
Pearson's	0.61	0.45	0.90	0.61	0.20	0.20	0.37	0.29	-0.05	0.08	0.20	NA	NA	0.20	0.29	0.20	-0.29	0.03
Sensitivity	100	81	100	100	9	9	27	18	9	18	9	0	0	9	18	9	81	27
Specificity	50	62	87	50	100	100	100	100	87	87	100	100	100	100	100	100	0	75

Table 1.3: FCG™, routine EKG, And Echocardiography: Sensitivity, Specificity and Pearson's Correlation.

	FCG™: 12 Lead Amp Spectrum				FCG™: CAD Location												FCG™: Phase Angle	Routine EKG
Pearson's	0.86	0.27	0.61	0.72	0.22	0.28	0.38	0.22	0.15	0.15	0.22	NA	NA	0.22	0.28	0.22	-0.15	0.24
Sensitivity	100	69	84	100	15	23	38	15	7	7	15	0	0	15	23	15	92	46
Specificity	75	75	75	50	100	100	100	100	100	100	100	100	100	100	100	100	0	75