Cardiogoniometry for Detecting Coronary Artery Disease by CT Angiography

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1.   Abstract

Cardiogoniometry is a technique to process and evaluate vectorcardiography from regular ECG acquisitions. Vectorcardiography has a long tradition in cardiology for providing comprehensive information on myocardial function and integrity. Compared to standard electrocardiography, vectorcardiography has shown to be more sensitive to detect structural and ischemic heart disease. Unfortunately, the interpretation of vectorcardiography is complex which has hindered its widespread application. In recent years, computer assisted analysis has allowed automated interpretation of vectorcardiography with promising results in comparison to standard ECG for identifying patients with ischemic heart disease. However, the underlying mechanisms and threshold of altered cardiac vectors in the presence of coronary artery disease are not well understood. This research aims at exploring the relationship of computer assisted analysis of vectorcardiography with the presence, extent, severity, and location of coronary artery disease in comparison to standard ECG evaluation. Furthermore, we intent to follow up enrolled patients for the occurrence of adverse cardiovascular events for correlation with test findings. These data will provide comprehensive information on the diagnostic performance of noninvasive, inexpensive evaluation of cardiac vector loops for identifying patients at risk from coronary artery disease.

2.   Objectives

1)   Compare the diagnostic accuracy of cardiogoniometry with standard ECG for detecting coronary artery disease as assessed by CT angiography
2)   Investigate the relationship between abnormal cardiogoniometry findings and the extent/severity/location of coronary artery disease by CT angiography
3)   Compare the intermediate term prognosis of patients according to cardiogoniometry, standard ECG, and CT findings

3.   Background

Vectorcardiography has a long tradition in cardiology for the analysis of cardiac function and pathology.[1,2] Numerous reports documented the utility of vectorcardiography for assessing myocardial ischemia, infarction, reperfusion, ventricular hypertrophy, and conduction abnormalities. In many instances, the diagnostic accuracy of vectorcardiography surpasses that of standard 12-lead surface electrocardiogram (ECG). However, traditional vectorcardiography is demanding in terms of both acquisition and interpretation skills and despite its good performance in experienced hands was never accepted by main stream cardiology practice. Cardiogoniometry is a concept that utilizes only 4 leads to create a coordinate system allowing the analysis of cardiac vector loops including detailed description of its associated angles ("cardiogoniometry").[3,4] Clinical studies have demonstrated remarkable consistency of these loop angles within healthy individuals over time.[4] Deviations from established normal ranges indicate cardiac pathology. Several studies demonstrated good accuracy of cardiogoniometry to identify patients with chronic ischemic heart disease and acute coronary syndromes.[5-9] Test results in patients with ischemic heart disease do not seem to alter after revascularization procedures which may indicate that cardiogoniometry detects permanent structural changes in the myocardium rather than acute ischemia.[10] No adverse effects have been reported on the use of cardiogoniometry and such effects are not expected given its nature as a

variant application of electrocardiography. The purpose of this investigation is to gather information on the relationship of cardiogoniometry findings and presence and extent of coronary atherosclerotic disease as well as its prognosis in comparison to standard 12-lead ECG acquisition. Specifically, we are interested in identifying a 'threshold' of atherosclerotic disease which may be associated with alteration of vector loop angles. Previous studies only used obstructive coronary artery disease by cardiac catheterization as end point but it is conceivable that cardiogoniometry vector loops are altered earlier in the process of ischemic heart disease. This would represent an advantage in early detecting patients at risk of adverse events using noninvasive testing without X-ray radiation or contrast exposure. Furthermore, we are interested in investigating the rate of adverse cardiovascular events in patients associated with abnormal cardiogoniometry results. We believe cardiogoniometry has the potential to be an inexpensive alternative or addition to current noninvasive tools for identifying patients at risk from coronary heart disease.

4. **Study Procedures**
   a. The sole study procedure is an ECG acquisition prior to a **<u>clinical</u>** cardiac CT acquisition. An ECG is not routinely acquired before cardiac CT and thus it will be done for investigational purposes. The ECG will be acquired using an investigational cardiogoniometry device. In addition to standard lead placement for 12-lead ECG, 4 leads will be placed on the chest and back specifically to acquire vector loops. In deviation of routine ECG recording, the patient will be asked to hold his breath for the duration of recording, i.e., approximately 20 seconds. The entire procedure is expected to be completed within 5 minutes. Baseline demographics, patient medical history, study results, and risk factors for coronary artery disease will be recorded.
   b. The study duration will be 5 years. No additional patient visits will be required. The only physical encounter with patients will be at the time of their cardiac CT acquisition which is performed for **<u>clinical</u>** reasons. The patients will be contacted by phone or email every 12 months to inquire about adverse cardiovascular events for the duration of the study.
   c. Interpretation of the ECG and cardiogoniometry findings will be performed without knowledge of any patient or imaging details. No other blinding will be performed.
   d. The regular clinical care will not be affected except for the addition of the ECG acquisition prior to the clinically performed cardiac CT.
   e. The study does not contain any treatment or patient management actions.

5. **Inclusion/Exclusion Criteria**
   Patients age 18 or older who are referred for cardiac CT examination at the Johns Hopkins Hospital Division of Cardiology for evaluation of coronary artery disease will be asked to participate.
   Patients may be referred for an outpatient CT scan, when hospitalized, or via the emergency room.

   Exclusion criteria:
   Patients with hemodynamic instability in whom CT scanning is performed emergently will be excluded from this study.

6. **Devices**
   a. An investigational cardiogoniometry device 'Cardiologic Explorer' manufactured by ENVERDIS will be used for this study. It is the only device of this kind available worldwide.
   b. The device is not FDA approved for clinical use in the US at this time.
   c. The device was inspected by the Clinical Engineering Services of the Johns Hopkins Hospital and no safety concerns to patients were found. The cardiogoniometry device is powered from a laptop computer via the USB port and during ECG recording the laptop will operate on battery

power only. Under these conditions, there is no electrical safety risk to the patient in case of device malfunction.

7. Study Statistics
   a. Primary outcome variable is the diagnostic accuracy of cardiogoniometry to identify patients with coronary artery disease as defined by CT coronary angiography in comparison to standard 12-lead ECG.
   b. Secondary outcome variables include the hazard of adverse cardiovascular events determined by cardiogoniometry in comparison to standard 12-lead ECG and CT coronary angiography, the diagnostic accuracy of cardiogoniometry to identify patients with high risk coronary anatomy or baseline myocardial perfusion abnormalities by CT angiography.
   c. Assuming an area under the curve value of 0.60 for standard ECG to identify patients with coronary artery disease and an anticipated value of 0.70 for cardiogoniometry, the required sample size will be 356 for a significance level of 0.05 and 80% power.
   d. No early stopping rules will be applied to assure maximum power for the proposed analyses.

8. Risks
   a. No major medical risks are known to be associated with the study procedure. Minor risks include a skin reaction to ECG lead adhesives.
   b. To minimize risk of skin reactions to ECG leads, patients will be asked regarding prior reactions and a skin wash using warm water will be offered if positive.
   c. No plans exist for deviations from the study plan.
   d. Legal risks include breach of confidentiality and unauthorized dissemination of patient data. To minimize such risk, all patient data will be stored on a designated laptop computer which will remain on hospital premises under personal supervision of the principal investigator. Data backup will occur on designated hard discs which will be securely stored in the PI's office.
   e. No known financial risks to the participants will arise from this study.

9. Benefits
   a. There will be no benefits to study participants as result of this study. Potential benefits to society will arise on the availability of a noninvasive, inexpensive tool for the assessment of coronary artery disease.

10. Payment and Remuneration
   a. There will be no compensation to patients for their participation in this study.

11. Costs
   a. The cardiogoniometry device to be used for this study was provided by the manufacturer. Costs for laptop computer and data storage will be carried by the principal investigator. ECG acquisition will be performed by the principal investigator or volunteer research staff. Costs for patient follow up will be carried by the principal investigator. When preliminary study results become available, an application for research funding will be submitted to funding agencies.

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