HEART HEALTH SCREENING OF CHILDREN FOR SUDDEN CARDIAC ARREST

Introduction

In children, sudden cardiac arrest (SCA) is associated with structural and electrical cardiac abnormalities including hypertrophic cardiomyopathy (HCM) and other cardiomyopathies, long QT syndrome (LQTS), Wolff-Parkinson-White (WPW) syndrome, coronary artery anomalies, congenital heart defects, and others resulting in 1,000-7,000 childhood deaths yearly in the United States (US). The deaths of nationally known professional athletes and high school athletes across the country have resulted in awareness of some of the conditions that cause SCA in the young. In children, sudden cardiac arrest (SCA) is associated with structural and electrical cardiac abnormalities including hypertrophic cardiomyopathy (HCM) and other cardiomyopathies, long QT syndrome (LQTS), Wolff-Parkinson-White (WPW) syndrome, coronary artery anomalies, congenital heart defects, and others.

Screening for Sudden Cardiac Arrest

Data from other countries with mandatory electrocardiographic (ECG) screening have demonstrated that ECG screening can identify children and adolescents with undiagnosed conditions predisposing to SCA, and is more sensitive in identifying those at risk for SCA than history or physical exam alone, the current standard in the United States. The effectiveness of the current methods of screening for SCA in the athletic arena has been discussed and debated. Although the current literature suggests screening for SCA with ECG may be more effective that the current system in place in the United States, a large-scale screening program has not been implemented or tested to date. Currently, most high school athletes in the US are screened through sports pre-participation history and physical exams, a process that has been shown to be inadequate in 20-40% of states and no data to indicate its efficacy.

Recommendations of European Society of Cardiology on Preparticipation Screening of Athletes: A common European screening program for young athletes based on the 12-lead ECG in addition to the focused history and physical exam was recommended in a 2005 consensus statement from the European Society of Cardiology on Cardiovascular Pre-Participation Screening of Young Competitive Athletes.

International Olympic Committee (IOC) Recommendations on Preparticipation Athletic Screening: The IOC Medical Commission issued a protocol for cardiovascular screening of athletes on December 10, 2004. This included a personal history and family history questionnaire, a physical exam and a 12-lead electrocardiogram.

Clinical experience suggests that SCA can occur not only in the setting of organized sports, but in children engaged in many levels of activity, or even in the absence of activity. Screening only athletes misses the nearly 25 million school children per year who do not participate in high school sports, but who may also have conditions that predispose them to SCA and warrant some type of screening process. Data from other countries with mandatory electrocardiographic (ECG) screening have demonstrated that ECG screening can identify children and adolescents with undiagnosed conditions that predispose to SCA and is more sensitive in identifying those at risk for SCA than history or physical exam alone-the current standard in the United States. No studies in the US have systematically screened large numbers of school children for conditions predisposing to SCA to identify those at risk and to prevent sudden cardiac death.

The primary aim of this study is to determine if early identification of those at risk for sudden cardiac death from arrhythmias can be accomplished by using an ECG based screening program in the population of school aged children 5-19 years of age not previously known to have any cardiac conditions. Up to 100,000 children and adolescents will answer a medical and family history questionnaire and have an ECG. The 8-10% with abnormalities will also have a cardiac exam and echocardiogram performed to obtain additional information and validate ECG findings. Additionally, the prevalence of these conditions commonly associated with SCA will be estimated in this population and the most sensitive and specific methodology to identify these conditions will be ascertained. To accomplish this second aim, 5000 of the total participants will have all studies and evaluations.
performed. Data obtained from all these ECGs will be used to develop a reference database to provide more specific and sensitive reference standards for ECG norms by age, gender, race and ethnicity.

Summary: The current method of screening the young for cardiac conditions associated with sudden cardiac arrest (SCA) has not been effective in identifying those children and adolescents who will experience SCA. This study will be the first to provide large scale information in the US on the prevalence of these conditions, to develop a methodology for effective cardiac screening in the young, and to determine normal ECG standards for different genders, races, and ethnicities to help provide the highest level of care to all groups in our very diverse country. Data from this study could become the basis for a public health mandate for screening to accomplish early identification of children at risk, which may lead to interventions and treatment strategies to prevent SCA and preserve young lives.

Pilot Study: Heart Health Screening Study for Sudden Cardiac Arrest in Healthy Children: Over the past year, we have conducted an IRB approved pilot research study at the Children's Hospital of Philadelphia (CHOP) to determine the feasibility of using ECGs in a heart health screening program in children and adolescents to identify structural and electrical cardiac abnormalities that predispose them to SCA including hypertrophic cardiomyopathy (HCM), long QT syndrome (LQTS), coronary artery anomalies, arrhythmogenic right ventricular dysplasia (ARVD) congenital heart defects, and Wolff-Parkinson-White syndrome (WPW). An additional goal was to use the pilot study to determine the methodology for a larger national multicenter study.

Methods: We screened 400 healthy 5-19 year olds with a personal medical and family history questionnaire, weight, height, blood pressure, heart rate, cardiac exam, ECG and echocardiogram. These examinations were performed in the clinical offices at CHOP main campus or one of two Ambulatory Care Centers in the surrounding area. All studies were obtained at the single study visit with subsequent clinical follow up for subjects with abnormalities identified that required further evaluation. Letters were sent to parents and personal physicians with the results of each subject’s evaluation.

Overall Results: Of the 400 children screened: 213 males, 187 females, 9.75% African American, 87% Caucasian, 2.25% Asian, 1% other races, 0.75% Hispanic. The mean age of the children screened was 11.75 ± 3.94 yrs. Ages were 5-9 yrs (153), 10-14 yrs (145), 15-19 yrs (102). 10.75% had previously undiagnosed cardiovascular (CV) abnormalities 5.75% were cardiac abnormalities (23), 5% (20) had hypertension (2 BP >95th percentile). Potentially threatening conditions are being treated with surgery, medications ± activity restrictions in 2.5%. Additional testing was performed in 6% and included exercise stress tests, Holters, MRI, and tilt table testing. Significant abnormalities included LQTS (2), WPW (1), nonsustained VT/complex ventricular ectopy (2), dilated aorta (2), anomalous coronary (1), ostium primum ASD (1), left ventricular dysfunction (1). Other undiagnosed heart disease (2.75%-11) identified included coronary cameral fistula (1), PDA (2), tricuspid regurgitation (2), aortic insufficiency plus MR (1), MR (1) vasodepressor syncope (2), frequent PVCs (2), 2° AV block (2). Eleven subjects were found to have PFOs. Two others were referred as possible connective tissue disease variants. One subject was suspected with possible ARVD and found to have a normal MRI. Twenty one subjects had blood pressures in the 90-94 percentile and were labeled as prehypertensive (22-5.5%).

RESEARCH DESIGN AND METHODS

Overview of Study Design: The center methodology will be described at CHOP and the other centers will be modeled after this methodology. Screenings can be done in medical facilities, schools, recreational centers, gymnasiums, and arenas with appropriate areas created for specific testing with privacy provided.

In the proposed study, healthy children and adolescents from 5-19 years of age will be screened to identify conditions leading to SCA. This study will use the ECG to screen school aged children for conditions associated with SCA including HCM and other cardiomyopathies including ARVD, and primary electrical diseases including LQTS, SQTS, and Brugada Syndrome. Specifically, this study aims to screen school aged children using ECGs and health questionnaires in a total of up to 100,000 children/adolescents 5 through 19 years of age. From our
pilot study, we estimate that 10-12% of children/adolescents will have abnormal ECGs or questionnaires and an echocardiogram (ECHO) will need to be performed to clarify or confirm the diagnosis.

The database from this study will be used to estimate the prevalence of ECG abnormalities that may place children at risk for SCA in the school aged population not previously screened.

**ECG Reference Database**: An additional aim of this study is to develop an ECG reference standard database with normal values for different ages, genders, races, and ethnicities. Data from both Cohort 1 and Cohort 2 will be entered into this database.

**Subject Flow**

```
Site PI selects Practices or Sites (schools, sports arenas, etc) and obtains approval from Study PI

Subjects identified and letters or flyers with study info sent to parents

Investigators visits practices or schools, talks with pediatricians, nurses, or administrators, teachers, etc

Location of Testing Identified

Recruitment list is complied and sent to study coordinator

Study coordinator contacts parents, screens patients for eligibility and sets up appointment for study visit.

Cohort 1: Questionnaire, Measurements, BP, ECG: ECHO, Cardiac Exam if Abnormal

Cohort 2: Questionnaire, Measurements, BP, ECG, ECHO, Cardiac Exam in all

Normal

Data Analyzed

Abnormal

Letter sent to parents, and doctor

Parents, doctor notified immediately. Follow-up testing, treatments
```
SUMMARY OF BUDGET NEEDS:

**Screenings:** Funds are needed to start local screenings. School districts or communities can be targeted according to the support provided. Thousands of children could be screened locally with an expected 5% with hypertension identified and 5% identified with cardiovascular abnormalities, with ~2% with serious abnormalities needing attention such as medication or surgery to prevent sudden cardiac arrest.

A **Cardiovascular Echo Core** and **ECG Core Laboratory** are being developed at CHOP and will be utilized for this study. Funds are needed to support ECG and Echocardiographic technicians’ time and the effort of the physician echocardiographers and Cardiologists who will be reading these echocardiograms and electrocardiograms.

**BUDGET REQUEST FOR 10,000 SUBJECTS**

All receive ECGs, ~10% receive ECHO  
Supplies: $5752 for supplies as itemized in budget.  
Other Expenses: Request: $6000 for miscellaneous costs as noted below.

- **ECG Technicians:** Request: $20,000 for labor cost.  
- **ECO Technicians:** Request: $7252 for labor cost.  
- **Nurses:** 2 @ $400/day = $800X 10 days (at 1000 subjects screened per day/session) = $8000  
  **Subtotal:** $47,004  
- **ECG Readers:** Request for $95,000.  
- **ECHO Readers:** Request for $50,000.  
  **Subtotal:** $145,000  
- **Administrative Costs:** $1/subject = $10,000

**TOTAL:** $202,004 = $ 20.20 per subject screened.

Budget Justification

**PERSONNEL**

The study personnel will consist of the Principal Investigator and Co-Investigators, a Research Nurse Program Coordinator, Research Nurse, an electrocardiogram (ECG) technician, an echocardiogram (ECHO) technician, an electrocardiographic (ECG) reader, and an echocardiographic reader. Salaries are based on per subject cost.

**Consultant or Equipment Costs:** No equipment or consultant requests. GE Healthcare Systems will provide ECG machines (Cardiosoft software and Acquisition models for PCs) for screening sites and portable echocardiographic machines (Vivid system). Potential for Mortara and Phillips Medical to be involved.

**Supplies:** $5752 for supplies as itemized in budget.

Supplies for ECGs will consist of ECG paper and electrodes. The ECHO supplies will be tapes, gel, and electrodes, and are written into per subject costs.

**Other Expenses:** Request: $6000 for miscellaneous costs as noted below.

A consent form will be signed at each study visit. A copy of the consent form will be given to each subject/parent after completing the visit. After the study visit each subject participating will receive a written letter of their results. A letter will be sent to their primary physician. The expected cost of mailings, paper, postage, and copying is $6000.
ECG Technician: Request: $20,000 for labor cost. The system we utilized for the pilot study was to have the Study Nurse perform most of the ECGs. With this larger study, we anticipate that we will need 2 additional ECG technical personnel and will need to pay for their time. The technician can perform approximately 9-10 ECG/hour. At $2/subject, the total ECG technical labor cost will be $20,000.

ECHO Technician: Request: $7252 for labor cost. The system we will utilize for the ECHOs will be to pay for the sonographers’ time. We have purchased a Research ECHO machine with CTSA and Cardiology Division funds and that machine will be available for our use as will other ECHO machines at CHOP, especially since many of the screenings will be done on weekends and evenings at CHOP. The technician can perform 4 ECHOs/hour. At $7.25/subject, the total ECG labor cost will be $7252. This is estimating that 10% of those receiving ECGs will get ECHOs.

ECG Reader: Request for $95,000. Dr. Vetter will read all of the ECGs with a second electrophysiologist from the ECG Core Lab verifying the reading. These readings will cost $9.50/subject.

ECHO Reader: Request for $50,000. An ECHO Core Lab will have at least 4 readers. One echocardiographer will read each study at $50/subject.

Administrative Costs: Scheduling, tracking, organization of screens, etc will cost $1/subject.

---------------------------------------------------------------------------------------------

**ECG Detailed Information:**

ECG tech salary = $18.20/hour
-@9-10 ECG/ hour = $2.00/subject

ECG paper = $0.12/sheet
Electrodes = 4,000 electrodes/case; 13 electrodes/subject; 307 subjects/case of electrodes
-Case of electrodes = $117.18/case; $0.38/subject ($117.18/307 subjects)

Cost of Supplies (ECG paper and electrodes) = $0.50/subject
ECG reader salary = $9.50/subject

Total cost of ECG = $12.00: labor {$2}, supplies {$0.50}, and reader {$9.50}

**ECHO Detailed Information:**

ECHO tech salary = $29.00/hour
-@4 ECHO/hour = $7.25/subject

ECHO tape = $2.32/tape; 4 ECHO studies/tape; $0.58/subject
Electrodes (3), gel, paper = $0.17/subject

Cost of Supplies (tape and electrodes) = $0.75/subject
ECHO reader salary = $50.00/subject

Total cost of ECHO = $58.00: labor {$7.25}, supplies {$0.75}, and reader {$50}
Reference List


