Evaluating the Diagnostic Gap in Risk Stratification for Sudden Cardiac Death

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Abstract

Background: Prevention of sudden cardiac death (SCD) has, to date, focused on individuals with advanced heart disease due to the high risk of this population. Yet, the majority of SCD events occur in the general population, in particular those without known heart disease. As cardiovascular testing is generally not recommended in asymptomatic individuals. Our aim was to define the diagnostic gap in the subgroup of a primary care population deemed to be at moderate risk of SCD by a recently developed risk score. Methods: We conducted a cross-sectional study of primary care patients from two large academic institutions and excluded those with coronary artery disease, heart failure, and atrial fibrillation. We calculated the SCD risk score and classified them into low, intermediate and high-risk categories. We evaluated the period prevalence and odds ratio (OR) of echocardiography and stress testing by risk of SCD adjusted for age, gender, race, and ethnicity. Results: We identified 36,885 patients without heart disease from both institutions with a median SCD score of 9% (IQR 3.5-22). The period prevalence of having an echocardiogram was 18% for those in the lowest SCD risk and 36% for those in the highest SCD risk group. The percentage of patients who had a stress test was 18% for those in the lowest SCD risk and 23% for those in the highest SCD risk group. The OR of having any test was 1.09 (1.00-1.18) for those in the intermediate risk category and 1.22 (1.09-1.37) for those in the highest risk category compared to those with the lowest risk. Conclusions: In patients identified to be at moderate risk for SCD in a primary care population, cardiovascular testing occurs in only a third. It is possible that more extensive cardiovascular screening of these patients could detect subclinical disease associated with SCD risk.

Introduction

Out-of-hospital cardiac arrest is a leading cause of death among adults in the United States.[1] Even though the risk of sudden cardiac death (SCD) is higher in patients with heart failure (HF) and coronary artery disease (CAD), the majority of SCD cases occur in the general population who have cardiovascular (CV) risk factors and no known heart disease or no symptoms of heart disease.[23]Given the perennial low rate of successful resuscitation from out-of-hospital cardiac arrest, prevention of SCD must be the key approach. This requires good risk stratification to identify a high-risk group that might benefit from some prophylactic intervention. Yet, in the general population without symptoms or known heart disease, in which the majority of SCDs occur, the ACC/AHA/USPTF do not recommend CV testing.[4]

Population health can identify patients at risk of CV events. Recently, a race-based SCD score was derived from the Atherosclerosis Risk in Communities (ARIC) study [7] and uses commonly collected variables from the clinical encounter. Using the electronic health record (EHR) we can calculate risk scores to identify substantial subpopulations at risk of SCD – estimated to be 4-7% at 10 years in the highest decile. While this risk is substantial, further cardiac testing may be able to further refine this risk and identify potential

targets for treatment. The aim of this study was to evaluate the frequency of CV testing that occurs in patients at different risk profiles of the SCD score.

Methods

Study design and study population

We conducted a cross-sectional study of the research platforms of two large academic institutions with a common EHR. The University of Miami enterprise data environment and Vanderbilt University synthetic derivative. Both contain a de-identified image of the EHR from outpatient and inpatient encounters. The rationale for selecting both institutions is the common EHR and our ongoing U54 research collaboration that provided the framework to share de-identified data. The study was approved by both the University of Miami and Vanderbilt University IRB.

We identified from both institutions all primary care patients who had at least one primary care visit between 2012 and 2017, calculated the SCD score, and evaluated CV risk factors. To be included in the study, patients needed to have the elements necessary to calculate the score and have had no documented heart failure, coronary artery disease or atrial fibrillation.

Sudden death score

The SCD score is race based and includes commonly collected variables from primary care encounters. The accuracy of the score is high (c-statistic of 0.82;95% CI 0.79-0.86). [7]

The score formula is:

SCD score for Whites 1-0.99538 exp $^{([?]-8.19637)}$ and SCD score for Blacks 1-0.99135 exp $^{([?]-6.08333)}$

We used primary care encounter data to calculate the SCD score and divided the score by deciles. We classified patients as high risk if they were in deciles 9 or 10, all others were considered intermediate risk (deciles 5-8) and low risk (decile 1-4).[7] These cutoffs have been previously used and are based on the exponential SCD risk profile seen in ARIC and Framingham.[7, 8]

Cardiovascular diseases and risk factors

We used ICD 9 and 10 codes to identify patients with CAD, HF or atrial fibrillation. We selected hypertension and diabetes as the main risk factors and identified them using the same strategy. (see supplementary appendix table 1) Both CV risk factors and diseases were evaluated 3 months before or at the time of calculating the SCD score. The codes used have appropriate positive predictive value when compared to medical records.[9, 1011-13]

Outcome

Our primary outcome was the period prevalence of CV testing. We defined CV as having an echocardiogram or stress test 1 year before the SCD score and 2 years after the score. The rationale for including echocardiograms and stress tests is that they represent the most commonly initial tests used in cardiology. We did not include electrocardiograms as the rate was low and the possibility of undercoding. We defined having an echocardiogram or stress test done by the CPT code. (see table 1 supplementary appendix). The validity of these codes has been previously validated.[14]

Our secondary outcome was all cause mortality. The database captures mortality via the National Technical Information Service (NTIS) Limited Access Death Master File (LAMDF) as well as from an institutionally generated death flag within the EHR system.

Validity

We took a sample of 20 de-identified University of Miami records and asked the Health IT team to reidentify them. Our sample was randomly selected from the highest two deciles of SCD risk since this was the group in which we mostly wanted to determine the use of CV testing. We compared the data in our enterprise data

environment with the EHR to assess the validity of the components of the SCD score and if an echocardiogram or stress test was done. We defined accuracy if the same value of the CV risk factor or the CV testing was done on the same date when comparing the medical record and the data on the research environment.

Statistical analysis

We compared baseline characteristics by SCD group using chi square and t-test or ANOVA.

We calculated the period prevalence of CV testing by dividing the number of participants who had either an echocardiogram or stress test divided by the number of participants on each SCD risk category. We also calculated the odds ratio (OR) and corresponding 95% confidence interval (CI) stratified by age, gender, race and ethnicity.

Analyses were performed using STATA version 14 (College Station, Texas), and all significance tests were two-tailed.

Results

Baseline characteristics

Figure 1 of the supplementary appendix shows the flow chart of included patients. We included a total of 36,885 patients without known heart disease from both institutions with a median SCD score of 9% (IQR 3.5-22). Table 1 shows the baseline characteristics by SCD risk category. For both institutions those in the highest deciles of SCD risk were older, more likely to be male, and more likely to have cardiovascular risk factors ($p<0.01$). Our random sample had 100% accuracy of the CV risk factors, CV diseases and CV procedures when compared to the medical record. Those in the highest SCD risk had a 7% mortality rate compared to 6% in the intermediate risk and 5% in low SCD risk.

Cardiovascular testing

Figure 1 shows the percentage of patients who underwent cardiovascular testing by risk category and institution. The percentage of patients who had an echocardiogram for both institutions was 18% for those in the lowest SCD risk and 36% for those in the highest SCD risk. The percentage of patients who had a stress test for both institutions was 18% for those in the lowest SCD risk and 23% for those in the highest SCD risk. There were no significant differences between both institutions. Higher risk was associated with a trend to increasing any testing ($p<0.01$). Multivariate predictors of testing were SCD score (2.3;95% CI 1.8-2.7), belonging to a minority group (0.88;95% CI 0.82-0.95), and being a women (0.82;95% CI 0.76-0.88).

Discussion

Our study found that CV testing among patients with CV risk factors and without known heart disease occurs in about a third of patients at the highest level of SCD risk. Those in the highest SCD risk categories had a trend for more testing but this peaked at approximately one third of the patients. This higher rate of testing in those at highest SCD risk was associated with a 7% all cause mortality rate and a 45% chance of developing sudden death over 10 years. The strengths of these findings are supported by the use of data from two large academic centers, the diversity of the sample, the large cohort and the consistency of the findings.

Screening populations for SCD is a significant challenge.[1, 15] Out of hospital cardiac arrest is a leading cause of death among adults in the United States (approximately 300,000 events per year).[1] Even though the risk of SCD is higher in patients with heart failure and/or advanced cardiomyopathies, the majority of SCD cases occur in the general population with cardiovascular risk factors and no known heart disease.[23] Identifying people at risk of SCD without known heart disease is therefore challenging.[15] Left ventricular ejection fraction (LVEF) is a strong predictor of SCD, but it is neither sensitive nor specific.[17] Furthermore, population screening for ventricular function is not practical nor recommended for routine clinical practice.[4, 16] This inverse relationship between risk (or incidence) and actual cases of SCD was initially highlighted by Myerburg et al.[2] To date, there has been no systematic attempt to address SCD in the general population.

The first major breakthrough to enable risk stratification for SCD in the general population was the development of a simple clinically based risk score that could provide risk stratification for SCD in the general population. Bogle et al developed a risk model from ARIC and validated it in the Framingham study. Model covariates included age, sex, total cholesterol, lipid-lowering and hypertension medication use, blood pressure, smoking status, diabetes, and body mass index. The profile of risk score by decile yielded an exponential curve with the bulk of the SCD risk in the upper two deciles. While other risk scores have been proposed, they all include variables that may not be uniformly available in a primary care setting, such as an ECG. In our primary care cohorts, 90% of patients had all the variables required to calculate this risk score. One can argue that all of the variables in this risk score should be documented in the medical record.

In the report by Bogle et al, the predicted and observed 10-year rates of SCD in the upper two deciles were in the 2-6% range. While this is a substantial risk, it is not actionable as it is still fairly low and there are no identified targets for treatment. With this background, the current study was designed to identify how frequently these high risk patients are undergoing cardiac evaluation. These patients have a very high burden of cardiovascular risk factors. It is therefore possible that these patients have significant subclinical cardiovascular disease that can only be identified by cardiac testing. We demonstrate a very low rate of cardiac testing in this high risk population, and therefore identify a potentially practical opportunity to identify subclinical cardiac disease that could be targeted for treatment that may ultimately prevent SCD.

While this approach requires careful evaluation to establish its efficacy, this is a paradigm shifting approach. Currently, the three main bodies writing preventive cardiac guidelines do not support screening of asymptomatic individuals. Second, it is not cost-effective to screen for CV diseases in all patients seen. Third, insurance will not reimburse for asymptomatic testing and physicians do not order them because patients are not willing to pay out of pocket. However, echocardiograms in asymptomatic primary care patients have been able to identify incident cases of systolic and diastolic dysfunction which in turn lead to changes in treatment and this screening strategy has been proven to be cost-effective.[5, 6] As it would be cost-prohibitive to perform testing on all patients seeking care in the United States, testing in the highest risk deciles may be more practical. There is a clear need to act on the diagnostic gap identified in this study.

The nature of the further cardiac testing to recommend in these high risk deciles is certainly not established. Our group has found that testing seniors in a primary care practice using echocardiography can identify new HF patients and those with heart failure with preserved ejection fraction.[5, 6] We also have documented that by informing the clinicians of the echocardiogram findings there is medication intensification, improvement in CV risk factors and lower operative costs.[18] Also adding echocardiographic information to the SCD score improves the ability of the combined score to predict mortality.[19]

There are several limitations that deserve mention. First, we relied on ICD codes to identify comorbidities and used this as an exclusion criteria, this could have excluded patients with HF or CAD when the condition was not present. However, we conducted a chart review in a small sample and found that the accuracy of the codes was 100%. Second, we used a cross-sectional design to evaluate the outcome and this could have undercounted the number of procedures performed. However, we used period prevalence to calculate the procedures over time. Third, patients could have had their procedures done at other institutions and this could have led to undercounting of the procedures. Fourth, the generalizability of our findings is limited to the two medical centers included in the study.

In conclusion, this study provides evidence that the majority of patients from the general population at elevated risk for SCD based on a novel SCD risk score do not undergo any CV testing. We propose a new paradigm of further cardiac screening for these asymptomatic patients to identify subclinical cardiac disease that leads to SCD. Future studies should evaluate what the appropriate testing is and the therapeutic strategies to implement for those at risk.

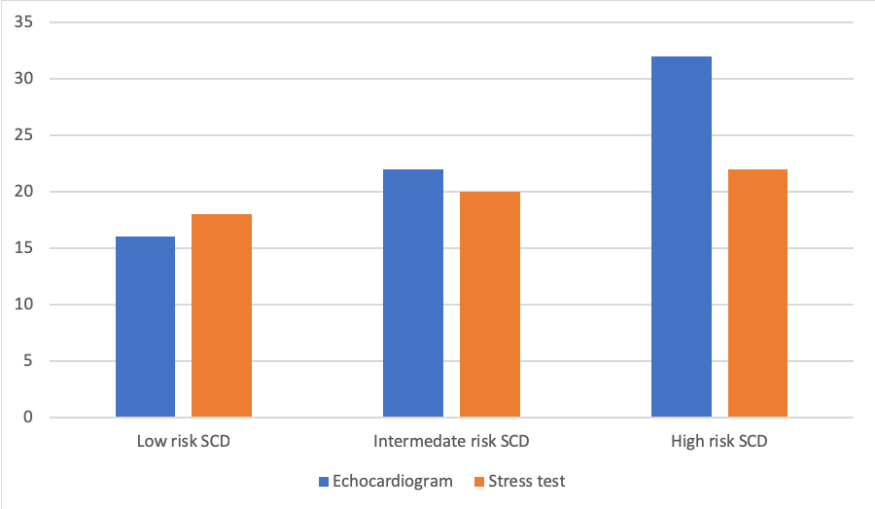
Table 1: Baseline characteristics by SCD risk: A) University of Miami B) Vanderbilt University

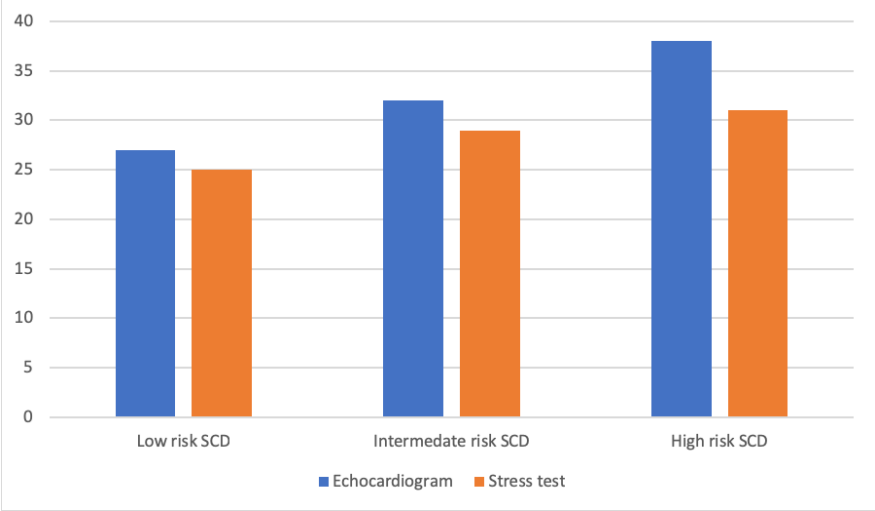
A)

Baseline characteristic	Low SCD score (decile 1-4)	Intermediate SCD score (decile 5-8)	High SCD score (Decile 9-10)	p-value
Number	8174	8174	4086	
Median SCD risk score (IQR)	2.8 (1.5-4.5)	9 (8-16)	40(28-62)	<0.01
Mean age	58.1±6.5	63.8±8.3	71.6±9.8	<0.01
Female gender, %	65	30	9	<0.01
Black, %	12	19	19	<0.01
Hispanic, %	35	33	32	0.02
Hypertension, %	60	75	88	<0.01
Diabetes, %	65	85	91	<0.01
Median systolic blood pressure (IQR)	124(116-132)	129.2 (121.3-137.6)	135(127.6-144.2)	<0.01
Median body mass index (IQR)	26.8(24-30)	28.3(25-32.4)	29.6(25.9-34.6)	<0.01

B)

Figure 2: A)University of Miami B)Vanderbilt University.





SCD risk	
Low	Ref
Intermediate	1.09 (1.00-1.18) 0.03
High	1.22 (1.09-1.37) <0.01

Adjusted for age, gender, race and ethnicity.

Appendix

Figure 1

Vanderbilt dataflow chart

43684 encounters

Excluded 27129 with heart failure, coronary artery disease or atrial fibrillation

16451 included

University of Miami data flowchart

38,927 encounters

Excluded 18493 with heart failure, coronary artery disease or atrial fibrillation

20,434 included

Table 1

ICD-9 and ICD-10 codes

CV risk factor or disease or procedure	ICD-9	ICD-10	CPT
Atrial fibrillation	427.31	40.0,48.1-4,48.9,48.91-92	
Heart failure	428.xx	50.xx	
Coronary artery disease	414.xx	25.1xx	
Hypertension	401.xx	10	
Stress testing			93015,93350,93351,78451,78452
Echocardiogram			93303,93304,93306,93307,93308

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