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ECG predictors of cardiac arrhythmias in older adults with syncope

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BCS conceived the study, designed the trial, and obtained research funding. BCS and ANY supervised the conduct of the trial and data collection. All authors undertook recruitment of participating centers and patients and managed the data, including quality control. ALL, REW, DKN, and BCS provided statistical advice on study design and analyzed the data. DKN drafted the manuscript, and all authors contributed substantially to its revision. DKN takes responsibility for the paper as a whole.

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Abstract

Objective—Cardiac arrhythmia is a life-threatening condition in older adults who present to the emergency department (ED) with syncope. Prior work suggests the initial ED electrocardiogram (ECG) can predict arrhythmia risk; however, specific ECG predictors have been variably specified. Our objective was to identify specific ECG abnormalities predictive of 30-day serious cardiac arrhythmias in older adults presenting to the ED with syncope.

Methods—We conducted a prospective, observational study at 11 EDs in adults 60 years or older who presented with syncope or near syncope. We excluded patients with a serious cardiac arrhythmia diagnosed during the ED evaluation from the primary analysis. The outcome was occurrence of 30-day serous cardiac arrhythmia. The exposure variables were predefined ECG abnormalities. Independent predictors were identified through multivariate logistic regression. The sensitivities and specificities of any predefined ECG abnormality and any ECG abnormality identified on adjusted analysis to predict 30-day serious cardiac arrhythmia were also calculated.

Results—After excluding 197 (5.5%; 95% CI 4.7 to 6.2%) patients with serious cardiac arrhythmias in the ED, the study cohort included 3,416 patients. Of these, 104 (3.0%; 2.5 to 3.7%) patients had a serious cardiac arrhythmia within 30 days from the index ED visit (median time to diagnosis 2 days [IQR 1 to 5 days]). The presence of non-sinus rhythm, multiple premature ventricular conductions, short PR interval, first degree atrioventricular block, complete left bundle branch block, and Q/ST/T segment abnormalities consistent with acute or chronic ischemia on the initial ED ECG increased the risk for a 30-day serious cardiac arrhythmia. This combination of ECG abnormalities had a similar sensitivity in predicting 30-day serious cardiac arrhythmia compared to any ECG abnormality (76.9% [95% CI 67.6 to 84.6%] vs. 77.9% [95% CI 68.7 to 85.4%]) and was more specific (55.1% [95% CI 53.4 to 56.8%] vs. 46.6% [44.9 to 48.3%]).

Conclusions—In older ED adults with syncope, about 3% are diagnosed with a serious cardiac arrhythmia not recognized on initial ED evaluation. The presence of specific abnormalities on the initial ED ECG increased the risk for 30-day serious cardiac arrhythmias.

INTRODUCTION

Background

Syncope is the transient loss of consciousness followed by spontaneous and complete recovery.[1] Syncope accounts for 740,000 emergency department (ED) visits and 250,000 hospital admissions in the US annually.[2] Differentiation between life-threatening etiologies such as arrhythmias or structural heart disease (cardiac syncope) and benign etiologies such as vasovagal syncope (neurally mediated syncope) is often difficult during an ED evaluation. This clinical dilemma is particularly pertinent to older adults (60 years or older) who have more co-morbidities and a higher prevalence of cardiac syncope than younger patients.[1] Older adults with syncope also have a relatively high incidence of adverse outcomes; 6% of older adults with undifferentiated etiology of syncope in the ED experience death or serious cardiac outcome within 30 days.[3]

Importance

The differentiation of cardiac and non-cardiac causes of syncope in older adults presenting to the ED with syncope is important. Patients with cardiac causes of syncope have a two-fold increased risk of mortality compared to patients with neurally mediated causes of syncope.[4–6] The initial diagnostic test typically available to ED clinicians is the electrocardiogram (ECG).[7] The ECG is widely available, inexpensive, rapidly conducted, and can provide important information to help differentiate between cardiac (most specifically arrhythmias) and non-cardiac etiologies of syncope.

Goals of This Investigation

Arrhythmias are the most common causes of cardiac syncope.[1] If the initial ECG demonstrates an arrhythmia such as third degree (complete) atrioventricular block or ventricular tachycardia, the diagnosis of arrhythmia-related syncope is likely confirmed. Even in the absence of an incident arrhythmia, the initial ECG may have findings predictive of a future arrhythmic event.[8] However, prior studies have had varying definitions of ECG abnormalities, and most did not assess the predictive value of specific ECG findings.[9,10] To address this knowledge gap, we identified specific ECG abnormalities that were predictors of 30-day serious cardiac arrhythmias. Because the initial ECG may also predict other serious outcomes (e.g., pulmonary embolism or myocardial infarction) we also identified specific ECG abnormalities that were predictors of *any* 30-day serious outcome.

MATERIALS AND METHODS

Study Design

We conducted a multicenter prospective cohort study of older adults with syncope or near syncope in the emergency department (ED) (ClinicalTrials.gov Identifier: NCT01802398). The study was approved by the Institutional Review Boards at all sites and written, informed consent was obtained from all participating subjects or their legally authorized representative. The enrollment period was from April 28, 2013 to September 21, 2016.

Study Setting and Population

We conducted the study at 11 academic EDs. Patients 60 years or older who presented to the ED with syncope or near-syncope were eligible for enrollment. Syncope was defined as a transient loss of consciousness, associated with loss of postural tone, with immediate, spontaneous, and complete recovery. Near-syncope was defined as the sensation of imminent syncope without loss of consciousness. Patients with a presumptive loss of consciousness due to seizure, stroke or transient ischemic attack, or hypoglycemia, patients who did not have an initial ED ECG completed, or patients with an arrhythmia on initial ED ECG were excluded. Patients who were intoxicated from alcohol or other drugs, required medical or electrical intervention to restore consciousness, were non-English or Spanish speaking, or who were unable or unwilling to provide informed consent and follow-up information were also excluded.

We excluded patients with a serious arrhythmia (defined below) identified during the ED evaluation, as the clinical focus for such patients is treatment rather than prediction.[10] This

approach also eliminates potential test incorporation bias, where an ECG finding (such as third-degree heart block) defines the outcome.

Study Protocol

All patients underwent standardized history, physical examination, laboratory testing, and 12-lead ECG testing. Additional testing and patient disposition were directed by the treating clinical providers.

We conducted 30-day patient follow-ups using previously described methods to minimize attrition.[11] A review of the electronic medical records was conducted by local research personnel to evaluate for serious cardiac arrhythmias and serious outcomes within 30 days from the index ED evaluation. Additionally, we called enrolled patients at 30 days to identify out-of-hospital deaths, ED visits, and hospitalizations that occurred outside of the study sites. If a patient or their authorized representative reported an ED or hospital visit that occurred outside of the study site, then their medical charts associated with those visits were obtained and reviewed. All potential serious cardiac arrhythmias and serious outcomes identified by research staff were reviewed and adjudicated by a study physician. To ensure adequate abstraction of 30-day outcome measures, 55 charts at each site were independently reviewed by the enrollment and the coordinating site. We demonstrated 100% sensitivity in identifying serious cardiac arrhythmias and serious outcomes (coordinating center review as reference standard) and verified high inter-rater reliability for all other chart review items (kappa > 0.8).

Measurements

Data variables collected were consistent with reporting guidelines for ED based syncope research.[12] We collected data on comorbid factors such as a history of heart failure or a history of arrhythmia with responses marked as present or not present/unknown. Data on current medications were organized by class of drug and included beta-blockers, calcium channel blockers, and other antiarrhythmic agents (e.g., amiodarone). Heart murmur on examination was marked as present, absent, or not assessed. ECG interpretations were based on the first ECG obtained in the ED and were abstracted by one of five research study physicians who were blinded to all clinical data and the study hypothesis. Research study physicians demonstrated high interrater reliability (kappa > 0.80) in distinguishing normal from abnormal ECGs in a training set of 50 ECGs. We did not calculate kappa statistics for specific ECG findings due to the low prevalence of specific findings. We used prior syncope research reporting guidelines to define ECG abnormalities.[12] ECGs were categorized into three mutually exclusive categories: normal, isolated nonspecific ST segment/T wave abnormalities, or abnormal. Abnormal ECG interpretations included non-sinus rhythms (included paced rhythms), multiple premature ventricular complexes (≥2), sinus bradycardias (≤ 40 bpm), ventricular hypertrophies, short PR segment intervals (<100 milliseconds [ms]), axis deviations, first degree blocks (>200 ms), complete bundle branch blocks, Brugada patterns, Wolff-Parkinson-White patterns, abnormal QRS duration (>120 ms) or abnormal QTc prolongations (>450 ms), Q/ST/T segment abnormalities suggestive of acute or chronic ischemia, and bifascicular block (both complete right bundle branch block and left axis deviation).

Outcome

The primary outcome was a serious cardiac arrhythmia identified within 30 days of the index ED evaluation. A serious cardiac arrhythmia was derived from 2017 American Heart Association Guidelines and included: ventricular fibrillation, ventricular tachycardia 30 seconds or longer with or without symptoms, symptomatic ventricular tachycardia less than 30 seconds, sick sinus disease with alternative sinus bradycardia and tachycardia, sinus pause longer than 3 seconds, Mobitz II heart block, complete heart block, symptomatic supraventricular tachycardia, symptomatic bradycardia <40 beats per minute, or pacemaker or implantable cardioverter-defibrillator malfunction with cardiac pauses.[7]

The secondary outcome was *any* serious outcome identified within 30 days of the index ED evaluation. This included serious cardiac arrhythmias (as defined above), myocardial infarction, cardiac intervention, new diagnosis of structural heart disease, stroke, pulmonary embolism, aortic dissection, subarachnoid hemorrhage, cardiopulmonary resuscitation, internal hemorrhage/anemia requiring transfusion, recurrent syncope/fall resulting in major traumatic injury, recurrent syncope after index hospital visit, and death within 30 days. Individual serious outcomes are further defined in eTable 1.

Analysis

Data analyses were performed using SAS 9.4 (SAS Institute Inc. Cary, NC, USA). Patient characteristics were described as proportions and medians with interquartile ranges (IQRs). We compared the proportion of subjects with missing patient characteristics by the presence or absence of serious cardiac arrhythmia identified after ED evaluation. We calculated odds ratios with 95% CIs for the overall ECG status (normal, nonspecific ST segment abnormalities, and any abnormal ECG finding) and each of the specific, predefined ECG findings to predict serious cardiac arrhythmia identified after ED evaluation but within 30 days of the index ED visit using logistic regression. Specific, predefined ECG findings and clinical site were analyzed in a fixed-effect multivariate logistic regression to predict serious cardiac arrhythmia identified after ED evaluation but within 30 days of the index ED (primary outcome) and any serious outcome within 30 days (secondary outcome). Specific ECG findings that were rare (<5) were not included into the regression model. Significance was defined as a p value < 0.05, and the results of the multivariate logistic regression model were presented as adjusted odds ratios with 95% confidence intervals (CIs). Model fit was evaluated using the c-statistic.[13] Multicollinearity was assessed by examination of the variance inflation factors calculated from a linear regression model of the same variables. We calculated the sensitivity and specificity (planned a priori) of an a) abnormal ECG (any abnormal ECG finding except for nonspecific ST segment abnormalities) and b) the combination of the specific ECG findings identified on regression analysis to predict a serious cardiac arrhythmia after ED evaluation and within 30 days of the index ED visit. We followed guidelines for reporting observational studies.[14]

RESULTS

Characteristics of the Subjects

There were 6,080 subjects that met inclusion and exclusion criteria, of which 3,613 (59.4%) subjects consented and were enrolled into the study (Figure). Subjects had a median age of 71 years (IQR 65–79 years), 1869 (51.7%) were male, and 2810 (77.8%) were admitted to the hospital. Characteristics of the study population are described in Table 1. There were no differences in missing patient characteristics in subjects with and without a serious cardiac arrhythmia identified after ED evaluation (eTable 2).

Main Results

Of the 3,613 enrolled subjects, 197 (5.5%; 95% CI 4.7 to 6.2%) had a serious cardiac arrhythmia during initial ED evaluation. One hundred and four (3.0%; 95% CI 2.5 to 3.7%) of the remaining 3,416 subjects had a serious cardiac arrhythmia identified after the initial ED visit but within 30 days of the index ED visit. The median time to diagnosis was 2 days (IQR 1 to 5 days). The most common serious cardiac arrhythmia identified after the initial ED evaluation was symptomatic supraventricular tachycardia (42 subjects, 40%) (Table 2).

Of the 104 subjects who had a serious cardiac arrhythmia identified after the initial ED visit, 81 (78%) had an abnormal finding on the initial ED ECG, 4 (3.8%) had isolated, nonspecific ST segment abnormalities, and 19 (18%) had a normal initial ED ECG (Table 3).

Specific ECG findings that were predictive for a serious cardiac arrhythmia included non-sinus rhythms (OR 2.8, 95% CI 1.7 to 4.6), multiple premature ventricular conductions (OR 2.4, 95% CI 1.1 to 5.2), short PR interval (OR 2.7, 95% CI 1.0 to 7.5), first degree atrioventricular blocks (OR 1.9, 95% CI 1.1 to 3.0), complete left bundle branch blocks (OR 2.4, 95% CI 1.0 to 5.6), and Q/ST/T segment abnormalities consistent with acute or chronic ischemia (OR 1.8, 95% CI 1.1 to 2.8) (Table 4). Using the area under the curve c-statistic, the overall logistic regression model was a good fit (c-statistic 0.764, cutpoint 0.7).[13] None of the predictor variables demonstrated multicollinearity.

An abnormal ECG (any predefined ECG abnormality) had a sensitivity of 77.9% (95% CI 68.7 to 85.4%) and a specificity of 46.6% (95% CI 44.9 to 48.3%) in predicting a serious cardiac arrhythmia within 30 days of the index ED visit. The presence of any ECG abnormality identified on adjusted analysis (non-sinus rhythms, multiple premature ventricular conductions, short PR interval, first degree atrioventricular blocks, complete left bundle branch blocks, and Q/ST/T segment abnormalities consistent with acute or chronic ischemia) had a sensitivity of 76.9% (95% CI 67.6 to 84.6%) and a specificity of 55.1% (95% CI 53.4 to 56.8%) (Table 5).

Of the 3,613 enrolled subjects, 423 (12%) had a serious outcome (secondary outcome) identified in the ED. Two-hundred and ninety (9.1%; 95% CI 8.1 to 10.1%) of remaining 3,190 subjects had a serious outcome identified after the initial ED visit but within 30 days of the index ED visit (secondary outcome). The most common serious outcomes diagnosed after the index ED visit were serious cardiac arrhythmia (89 subjects, 31%), recurrent syncope (77 subjects, 27%), and cardiac intervention (73 subjects, 25%) (eTable 3). Specific

ECG findings that were predictive for serious outcomes included complete left bundle branch blocks (OR 2.1, 95% CI 1.1 to 3.9), Q/ST/T segment abnormalities consistent with acute or chronic ischemia (OR 1.8, 95% CI 1.4 to 2.4), and non-sinus rhythms (OR 1.5, 95% CI 1.1 to 2.2) (eTable 4). The area under the curve c-statistic was 0.643. An abnormal ECG (any predefined ECG abnormality) had a sensitivity of 72.1% (95% CI 66.5 to 77.2%) and a specificity of 59.0% (95% CI 57.2 to 60.8%) in predicting a serious outcome within 30 days of the index ED visit. The presence of any ECG abnormality identified on adjusted analysis (complete left bundle branch block, Q/ST/T segment abnormalities consistent with acute or chronic ischemia, and non-sinus rhythm) had a sensitivity of 53.5% (95% CI 47.5 to 59.3%) and a specificity of 68.7% (95% CI 66.9 to 70.3%) (eTable 5).

LIMITATIONS

Our results should be interpreted in the context of some limitations. First, it is possible patients discharged from the ED or hospital had a serious cardiac arrhythmia within 30 days that was undiscovered. However, the definition of serious cardiac arrhythmia included arrhythmias that were symptomatic (e.g., symptomatic supraventricular tachycardia or symptomatic bradycardia) or would likely have caused symptoms (e.g., complete heart block or ventricular tachycardia lasting longer than 30 seconds). Thus, the majority of these patients would likely have sought medical care if these serious cardiac arrhythmias had occurred. Second, all ECGs were centrally interpreted by study physicians who may have had different ECG interpretations than ED clinicians. We previously demonstrated overall poor agreement between the initial ECG interpretation and the central reader for specific ECG findings.[15] We felt the advantages of using central readers (blinding of clinical characteristics and outcomes and likely greater accuracy in ECG interpretations) outweighed the disadvantages of not reflecting clinical practice. In addition, we were unable to calculate kappa statistics for specific ECG findings due to the low prevalence of specific ECG findings in our training set of 50 ECGs. However, we did demonstrate high interrater reliability (kappa > 0.80) in distinguishing normal from abnormal ECGs. Third, our study was a convenience sample of patients and thus sampling bias may have occurred leading to an incidence of serious cardiac arrhythmia in our study that may be different than actual practice. Fourth, 53% of eligible patients consented to participate in the study. There may be differences between patients who did and did not consent (nonresponse bias).

DISCUSSION

In this large, multicenter prospective observation study, we found that in older adults with a syncopal episode in the ED, approximately 5% will have an initial ED ECG with a serious cardiac arrhythmia and 3% will have a serious cardiac arrhythmia identified within the first 30 days after the index ED visit. We also identified specific ECG abnormalities that were independently predictive of a serious cardiac arrhythmia within the first 30 days after the index ED visit. The presence of non-sinus rhythms, multiple premature ventricular conductions, short PR interval, first degree atrioventricular blocks, complete left bundle branch blocks, and Q/ST/T segment abnormalities consistent with acute or chronic ischemia on the initial ED ECG increased the risk for a serious cardiac arrhythmia identified within the first 30 days after the index ED visit by 2–3 fold. This combination of ECG

abnormalities was as sensitive but was more specific than any ECG abnormality in predicting 30-day serious cardiac arrhythmia. Non-sinus rhythms, complete left bundle branch blocks, and Q/ST/T segment abnormalities consistent with acute or chronic ischemia on the initial ED ECG were also predictive of a serious outcome identified within 30 days after the index ED visit. However, the combination of these ECG abnormalities was not sensitive (sensitivity 54%) in predicting a serious outcome identified within 30 days after the index ED visit.

Cardiac arrhythmias are the most frequent cause of cardiac syncope. Arrhythmias are particularly challenging to clinicians as the arrhythmia may be intermittent and not captured on the initial ED ECG.[16] Patients with syncope caused by an arrhythmia may not have other clinical symptoms, signs, and diagnostic findings often associated with other causes of cardiac syncope (e.g., shortness of breath, presence of heart murmur, elevated brain natriuretic peptide in patients with structural heart disease). Thus the ECG is the primary diagnostic tool clinicians have to identify cardiac syncope caused by an arrhythmia.

With a 3% incidence of 30-day serious cardiac arrhythmia, it is not clear if all older adults with syncope should be admitted to the hospital for continued observation and evaluation. Our study demonstrated that specific abnormalities on the initial ED ECG increased the risk for 30-day serious cardiac arrhythmias. However, our study also demonstrated that a normal initial ECG does not rule out 30-day serious cardiac arrhythmia. Twenty-three of 104 patients (22%) with a 30-day serious cardiac arrhythmia had a normal ECG or an ECG with non-specific ST abnormalities on initial presentation. This suggests that in addition to ECG findings, clinical symptoms and signs, socioeconomic factors, the availability of outpatient follow-up, and patient or caregiver preferences, should also factor into determining the risk for 30-day serious cardiac arrhythmia and the decision-making process regarding ED disposition.

Two prior studies evaluated ECG findings in predicting cardiac outcomes after syncope. In a study by Quinn et al, adult ED patients with syncope had a 6.1% (42 of 684 patients) incidence of cardiac outcomes within 7 days of the index ED visit (defined as sudden death, myocardial infarction, arrhythmia captured on monitoring and thought to have had a temporal relationship to the syncopal event, structural heart disease thought to have caused the syncopal event, or cardiac intervention).[16] A left bundle branch block and a non-sinus rhythm were specific ECG findings that were predictive of a cardiac outcome on adjusted analysis. In a retrospective study by Thiruganasambandamoorthy et al, adult ED patients with syncope had a 5.3% (27/505 patients) incidence of serious cardiac outcomes within 30 days of the index ED visit (defined as death due cardiac or unknown cause, myocardial infarction, arrhythmia, or cardiac procedural intervention). Using binary recursive partitioning, specific ECG findings predictive of a serious cardiac outcome included: second-degree Mobitz type 2 or third-degree atrioventricular block, bundle branch block plus first-degree atrioventricular block, right bundle branch with either left anterior or posterior fascicular block, new ischemic changes, non-sinus rhythm, left axis deviation, and ED cardiac monitor abnormalities.[17]

Our study differed from these two studies in two important ways. First, we differentiated between serious cardiac arrhythmias diagnosed *during* ED evaluation and arrhythmias diagnosed *after* ED evaluation. This differentiation is important because patients with serious cardiac arrhythmias diagnosed *during* ED evaluation do not represent a clinical dilemma as the diagnosis of cardiac syncope is likely confirmed and these patients are generally admitted to the hospital for further management and observation. It also eliminates potential test incorporation bias where the predictor variable and outcome measure are the same (e.g., third degree heart block predicts third degree heart block). Unlike the Quinn and Thiruganasambandamoorthy studies, we excluded these patients with a serious cardiac arrhythmia during ED evaluation from our primary analysis. Second, our primary outcome measure was limited to serious cardiac arrhythmia after ED evaluation but within 30 days of the index ED visit. Unlike the Quinn and Thiruganasambandamoorthy studies, we did not include myocardial infarction or death as outcomes for our primary outcome measure (we did include these as serious outcomes for our secondary outcome measure). These outcomes have more sensitive diagnostic tools (e.g., troponin for myocardial infarction) than the ECG or may be caused by non-cardiac etiologies (e.g., death due to sepsis or acute blood loss).

In conclusion, about 3% of older ED adults with syncope are diagnosed with a serious cardiac arrhythmia not recognized on initial ED evaluation. The presence of specific, predefined abnormalities on the initial ED ECG increased the risk for 30-day serious cardiac arrhythmias. However the presence or absence of specific ECG findings does not rule in or rule out 30-day serious cardiac arrhythmia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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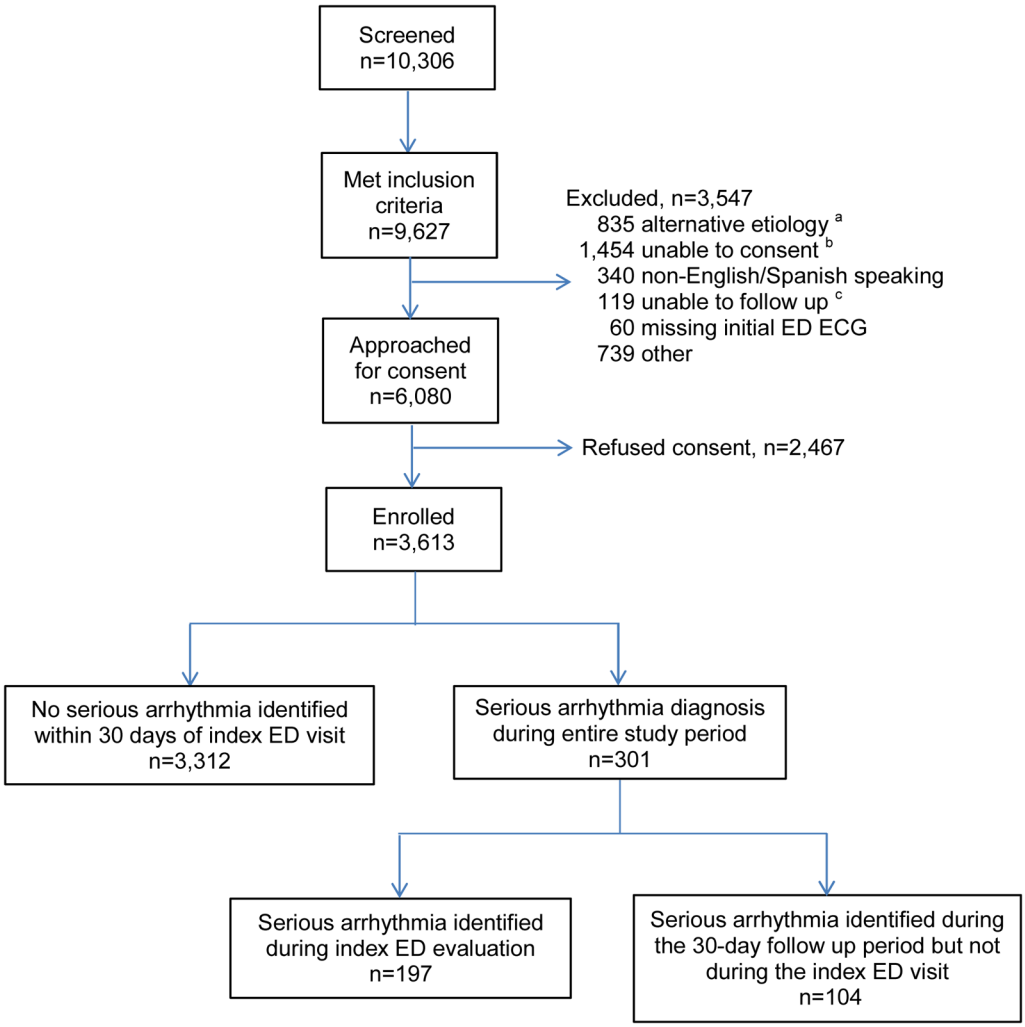

Figure.

Study flow chart

[a]- due to seizure, stroke or TIA, or hypoglycemia

[b]- unable to consent due to intoxication, altered level of consciousness requiring medical or electrical intervention, confusion from baseline, absence of legally authorized representative

[c]- subject lacking phone or address

Table 1

Patient characteristics by a) patients without a serious cardiac arrhythmia identified within 30 days of the index ED visit, b) patients with a serious cardiac arrhythmia identified during the index ED visit, c) patients with a serious cardiac arrhythmia identified after ED evaluation and within 30 days of the index ED visit, n=3,613 [a]

Characteristic	No serious cardiac arrhythmia identified, n=3,312 (91.7%)	Serious cardiac arrhythmia on initial ED evaluation n=197 (5.5%)	Serious cardiac arrhythmia identified after ED evaluation n=104 (2.9%)
	n (%)		
Age, median (IQR)	71(65–79)	72(66–79)	73(68–80)
Male	1696(51.2%)	117(59.4%)	56(53.8%)
Race			
White	2717(82.6%)	177(90.3%)	92(88.5%)
Black	471(14.3%)	14(7.1%)	8(7.7%)
Other	103(3.1%)	5(2.6%)	4(3.8%)
Hispanic/Latino	107(3.3%)	6(3.0%)	2(1.9%)
Initial ED systolic blood pressure, median (IQR)	130(114–149)	129.5(111–148)	130(113–145)
Initial ED diastolic blood pressure, median (IQR)	71(61–81)	73(61–85.5)	70(61–82)
Initial ED heart rate, median (IQR)	74(64–86)	79(65.5–98)	71(61–83)
Syncope occurred during exertion	617(18.7%)	40(20.4%)	13(12.6%)
Syncope associated with chest discomfort	291(9.0%)	23(11.8%)	8(7.8%)
Syncope associated with shortness of breath	674(20.8%)	57(29.8%)	26(25.2%)
Syncope associated with palpitations	397(12.5%)	58(30.7%)	19(18.8%)
History of congestive heart failure	392(11.8%)	39(19.8%)	27(26.0%)
History of ejection fracture <40%	102(3.1%)	17(8.6%)	4(3.8%)
History of structural heart disease [b]	394(11.9%)	40(20.3%)	17(16.3%)
History of permanent pacemaker	247(7.5%)	26(13.2%)	10(9.6%)
History of defibrillator	142(4.3%)	20(10.2%)	7(6.7%)
History of arrhythmia	626(18.9%)	130(66.0%)	49(47.1%)
History of coronary artery disease	905(27.3%)	57(28.9%)	33(31.7%)
Noted heart murmur on examination	321(9.8%)	19(9.9%)	11(10.7%)
Prior use of beta-blocker	1276(40.7%)	101(52.3%)	53(54.1%)

Characteristic	No serious cardiac arrhythmia identified, n=3,312 (91.7%)	Serious cardiac arrhythmia on initial ED evaluation n=197 (5.5%)	Serious cardiac arrhythmia identified after ED evaluation n=104 (2.9%)
	n (%)		
Prior use of calcium channel blocker	607(19.6%)	38(19.9%)	23(23.2%)
Prior use of other antiarrhythmic agent	189(6.1%)	30(15.8%)	19(19.6%)
Admitted to the hospital or observation unit	2530(76.4%)	185(93.9%)	95(91.3%)

[a] See appendix for information on missing data

[b] Includes aortic stenosis, pulmonary hypertension, cardiomyopathy, valvular heart disease, valve disease, and idiopathic hypertrophic subaortic stenosis

Abbreviations: IQR, interquartile range

Table 2

Description of serious cardiac arrhythmias in patients with a) serious cardiac arrhythmia identified during initial ED evaluation, b) serious cardiac arrhythmia identified after the initial ED evaluation and within 30 days of the index ED visit

Serious cardiac arrhythmia	Identified during initial ED evaluation, n=197	Identified after the initial ED evaluation and within 30 days of the index ED visit, n=104 [a]	Median time to diagnosis, days (IQR)
	n (%)		
Symptomatic supraventricular tachycardia	102(51.8%)	42(40.4%)	2(1–9)
Symptomatic bradycardia (pulse <40)	34(17.3%)	10(9.6%)	2(2–4)
Complete heart block	15(7.6%)	8(7.7%)	2(1.5–10)
Symptomatic ventricular tachycardia (<30 secs)	11(5.6%)	5(4.8%)	2(1–22)
Sick sinus disease with alternating sinus bradycardia and tachycardia	9(4.6%)	14(13.5%)	1(1–3)
Sinus pause >3 secs	9(4.6%)	5(4.8%)	0(0–1)
Mobitz type II AV heart block	7(3.6%)	5(4.8%)	5(2–7)
Ventricular tachycardia (>30 secs)	5(2.5%)	10(9.6%)	1.5(0–3)
Ventricular fibrillation	4(2.0%)	4(3.8%)	2.5(1.5–13)
Pacemaker or implantable cardioverter-defibrillator malfunction with cardiac pauses	1(0.5%)	1(1.0%)	0(0–0)

[a] Overall median time to diagnosis 2 days (IQR 1–5 days)

Abbreviations: IQR, interquartile range

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Table 3

Univariate analysis of specific ECG findings in predicting a serious cardiac arrhythmia identified after ED evaluation and within 30 days of the index ED visit

ECG Findings [a]	Overall, (n=3,416)	Serious cardiac arrhythmia identified after ED evaluation, (n=104)	No serious cardiac arrhythmia identified, (n=3,312)	OR for arrhythmia (95% CIs) [b, c]
Overall	n (%)			
Normal	1339(39.2%)	19(18.3%)	1320(39.9%)	Referent
Isolated, nonspecific ST segment abnormalities	228(6.7%)	4(3.8%)	224(6.8%)	1.2 (0.4–3.7)
Any abnormal ECG finding	1849(54.1%)	81(77.9%)	1768(53.4%)	**3.2 (1.9–5.3)**
Non-sinus rhythms (includes paced rhythm)	454(13.3%)	32(30.8%)	422(12.7%)	**3.0 (2.0–4.7)**
Multiple PVCs (>1)	115(3.4%)	8(7.7%)	107(3.2%)	**2.5 (1.2–5.3)**
Sinus bradycardia ≤ 40 per minute	1(0.0%)	0(0.0%)	1(0.0%)	-
Left ventricular hypertrophy	384(11.2%)	17(16.3%)	367(11.1%)	1.6 (0.9–2.7)
Right ventricular hypertrophy	12(0.4%)	0(0.0%)	12(0.4%)	1.9 (0.0–9.1)
Short PR interval (< 120ms)	62(1.8%)	5(4.8%)	57(1.7%)	**2.9 (1.1–7.4)**
Left axis deviation	394(11.5%)	18(17.3%)	376(11.4%)	**1.6 (1.0–2.7)**
Right axis deviation	40(1.2%)	2(1.9%)	38(1.1%)	1.7 (0.4–7.1)
First degree block (>200ms)	519(15.2%)	25(24.0%)	494(14.9%)	**1.8 (1.1–2.9)**
Complete left bundle branch block	128(3.7%)	11(10.6%)	117(3.5%)	**3.2 (1.7–6.2)**
Complete right bundle branch block	210(6.1%)	8(7.7%)	202(6.1%)	1.3 (0.6–2.7)
Brugada pattern	0(0.0%)	0(0.0%)	0(0.0%)	-
Delta waves (e.g. Wolff-Parkinson-White)	0(0.0%)	0(0.0%)	0(0.0%)	-
Prolonged QRS (>120 ms)	595(17.4%)	36(34.6%)	559(16.9%)	**2.6 (1.7–3.9)**
Prolonged QTc (>450 ms)	1508(44.1%)	60(57.7%)	1448(43.7%)	**1.8 (1.2–2.6)**
Q/ST/T changes consistent with acute or chronic ischemia	682(20.0%)	31(29.8%)	651(19.7%)	**1.7 (1.1–2.7)**
Bifascicular block [d]	71(2.1%)	4(3.8%)	67(2.0%)	1.9 (0.7–5.4)

[a] ECG may have more than one abnormality

[b] Odds ratios were not calculated when the ECG finding was found in less than 5 patients (sinus bradycardia ≤ 40 per minute, Brugada pattern and delta waves)

[c] Bold font highlight significant associations at alpha=.05

[d] Presence of both complete right bundle branch block and left axis deviation

Abbreviations: OR, odds ratio; PVC, premature ventricular conduction; CI, confidence interval

Table 4

Adjusted analysis for a serious cardiac arrhythmia identified after ED evaluation and within 30 days of the index ED visit

ECG Abnormality	OR (95% CIs) [b]
Non-sinus rhythms (includes paced rhythm)	**2.8(1.7–4.6)**
Multiple PVCs (>1)	**2.4(1.1–5.2)**
Sinus bradycardia ≤ 40 per minute	**
Left ventricular hypertrophy	1.6 (0.9–2.8)
Right ventricular hypertrophy	**
Short PR interval (< 120ms)	**2.7(1.0–7.5)**
Left axis deviation	0.9(0.5–1.6)
Right axis deviation	**
First degree block (>200ms)	**1.9(1.1–3.0)**
Complete left bundle branch block	**2.4(1.0–5.6)**
Complete right bundle branch block	0.8(0.3–2.1)
Brugada pattern	**
Delta waves (e.g. Wolff-Parkinson-White)	**
Prolonged QRS (>120 ms)	1.4(0.7–2.8)
Prolonged QTc (>450 ms)	1.1(0.7–1.7)
Q/ST/T segment abnormalities consistent with acute or chronic ischemia	**1.8(1.1–2.8)**
Bifascicular block [a]	0.7(0.2–2.4)

** Not included in the regression model due to sparse data (cell size <5). All other variables are included in the regression model.

[a] Presence of both complete right bundle branch block and left axis deviation

[b] Bold font highlight significant associations at alpha=.05

Abbreviations: OR, odds ratio; PVC, premature ventricular conduction; CI, confidence interval

Table 5

Sensitivity and specificity of an abnormal ECG and a combination of specific ECG abnormalities in predicting serious cardiac outcome after ED evaluation and within 30 days of the index ED visit

ECG criteria	Sensitivity		Specificity		LR+	LR−	PPV	NPV
	n	% (95% CIs)	n	% (95% CI)				
Abnormal ECG [a]	81/104	77.9 (68.7 to 85.4)	1544/3312	46.6 (44.9 to 48.3)	1.46 (1.31 to 1.62)	0.47 (0.33 to 0.68)	4.4 (4.0 to 4.9)	98.5 (97.9 to 99.0)
Combination of specific ECG abnormalities [b]	80/104	76.9 (67.6 to 84.6)	1826/3312	55.1 (53.4 to 56.8)	1.71 (1.53 to 1.92)	0.42 (0.29 to 0.60)	5.1 (4.6 to 5.7)	98.7 (98.2 to 99.1)

[a] Includes any abnormal ECG finding; c-statistic 0.764

[b] Includes specific ECG findings that were predictive of serious cardiac arrhythmia after ED evaluation and within 30 days of the index ED visit on adjusted analysis. These findings included: non-sinus rhythm, multiple PVCs, short PR interval, first degree atrioventricular block, complete left bundle branch block, and Q/ST/T segment abnormalities consistent with acute or chronic ischemia; c-statistic 0.756

Abbreviations: CI, confidence interval; LR, likelihood ratio; PPV, positive predictive value; NPV, negative predictive value